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Evidence-Based Report

Childhood Sexual Abuse and Depressive Disorders

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Important Note:

- The purpose of this brief report is to summarise the evidence for the association between childhood sexual abuse and the development of depressive disorders.
- It is not intended to replace clinical judgement, or be used as a clinical protocol.
- A reasonable attempt has been made to find and review papers relevant to the focus of this report; however, it does not claim to be exhaustive.
- This report is based upon information supplied up to October 2015.

1. Executive Summary

- Childhood sexual abuse can have significant short- and long-term effects, including the subsequent development of depressive disorders.
- The purpose of this report is to provide an evidence-based guide on the association between childhood sexual abuse and depressive disorders (i.e., major depressive disorder, dysthymia) as a teenager/adult. These findings will be used to assist in the decision making process regarding cover and entitlements of those who have experienced childhood sexual abuse and later developed a depressive disorder.
- A literature search was conducted in October 2015 using Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Cochrane Database of Systematic Reviews, PsycINFO, and the Worldwide Web. Further literature was also located through reading the reference list of review articles.
- Findings from the four systematic reviews and three meta-analyses identified in this report showed that:
    - Victims of childhood sexual abuse are more likely to develop depressive disorders than are non-victims.
    - There is fair quality evidence that childhood sexual abuse is a likely risk factor for the development of depression, with an odds ratio of between 1.55 and 6.5.
    - There is some evidence that severity of childhood sexual abuse (i.e., rape, abuse with penetration) strengthens the association with depression in later life.
    - There is some evidence that experience of childhood sexual abuse is associated with a higher odds ratio of developing depression than childhood physical abuse, domestic violence, community violence, and complex trauma. There are mixed findings regarding whether childhood sexual abuse is associated with a higher risk of developing depression compared to childhood neglect.
    - In one meta-analysis which examined the effects of sexual, physical, emotional abuse, neglect, early loss and parental separation on psychological disorders in adulthood, emotional abuse had the strongest association with depression, followed by neglect and sexual abuse.
    - Limitations of the current research examining the association between childhood sexual abuse and depressive disorders include the number of poor quality of studies conducted, childhood sexual abuse and outcomes being assessed using a variety of different methods, abuse being reported retrospectively, and the range of confounding variables present within and across studies.

- There is some evidence for the association between childhood/lifetime history of sexual abuse and depression during prenatal, antepartum, and postpartum; however, results for postpartum are mixed
- Mediators of the link between childhood sexual abuse and the development of depressive disorders may include an individual's cognitive attribution style, shame or self-blame, interpersonal difficulties, and avoidant coping strategies. Additional mediators include the functioning and regulation of the hypothalamic–pituitary–adrenal (HPA) axis, dysfunctional parenting/chaotic home environment, and disadvantaged life circumstances post-childhood sexual abuse. Research regarding the role of childhood sexual abuse on the development of depressive disorders is not yet fully understood, and the current research presents with a number of methodological issues.
- Given the identified limitations of the current literature and that there are likely to be many causes of and risk factors for depressive disorders, it is difficult to conclude whether childhood sexual abuse is a direct and sufficient cause of depressive disorders. However, there is some good quality evidence that childhood sexual abuse is likely to be a risk factor for developing depressive disorders later in life.

2. Introduction

Depressive disorders are the leading cause of disability worldwide (as measured by Years Lived with Disability; Mathers, Fat, & Boerma, 2008), and are a major contributor to the overall global burden of disease, ranking second for the leading cause of disability in 2010 (Ferrari et al., 2013). Global lifetime prevalence estimates for any mood disorder are around 12%, and 12-month prevalence estimates are approximately 6% (Kessler et al., 2009). Prevalence of depressive disorders are generally higher in developed Western countries than in developing countries (Kessler et al., 2009), with the lifetime prevalence of depressive disorders in the United States estimated at 20.8% (Kessler et al., 2005).

The estimated prevalence of childhood sexual abuse for females is between 8 to 31%, and between 3 to 17% for males; the wide estimate ranges reflecting the heterogeneity of studies (Barth, Bermetz, Heim, Trelle, & Tonia, 2013). Despite the methodological challenges inherent in conducting international systematic reviews and meta-analyses, most studies have consistently shown that worldwide more than 1 out of 5 women, and 1 out of 10 men experience childhood sexual abuse (Pereda, Guilera, Forns, & Gómez-Benito, 2009). However, underreporting of childhood sexual abuse is a well-documented phenomena and likely impacts these prevalence rates (Leclerc & Wortley, 2015).

For victims of childhood sexual abuse, the effects can be devastating both in the short- and long-term. Frequently reported short-term effects include fear, anxiety, depression, aggression, anger and hostility, and sexually inappropriate behaviour. Long-term effects include ongoing depression and anxiety, poor self-esteem, difficulty in trusting others, self-harm and suicide, a tendency toward revictimisation, feelings of isolation and stigma, substance abuse, and a host other mental health problems (Browne & Finkelhor, 1986; Fergusson, McLeod, & Horwood, 2013; Paolucci, Genuis, & Violato, 2001). One such group of mental health disorders which has been linked to childhood sexual abuse is depressive disorders, which is the focus of this report.

3. Background

ACC Research subcontracted Associated Professor Ian Lambie to conduct an evidence-based review to investigate the association between childhood sexual abuse and the subsequent development of depressive disorders (i.e., major depressive disorder, dysthymia) as a teenager/adult.

This evidence-based report will be used to provide ACC clinical advisors, claims management staff and service providers with an evidence-based guide on the relationship between childhood sexual abuse and the development of depressive disorders. In addition, this report will be used to assist in the development of an approach to deciding cover and entitlements for people who have experienced childhood sexual abuse and develop a depressive disorder at an older age.

4. Investigation

A search was conducted in October 2015 of the following databases: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Cochrane Database of Systematic Reviews, and PsycINFO. Further literature was also located through searching the Worldwide Web and reading the reference list of review articles. Only articles in English and published between 2005 and 2015 were included.

Search terms used included: major depressive disorder, major depression, dysthymia, depression, childhood sexual abuse, child sexual abuse, sexual abuse.

Inclusion criteria: systematic reviews and meta-analyses looking at the relationship between childhood sexual abuse and depressive disorders.

Exclusion criteria: non-English studies, animal or laboratory studies, narrative reviews, letters or editorials; study designs other than systematic review or meta-analysis.

This resulted in identifying 67 articles, of which four systematic reviews and three meta-analyses were used in this report.

Evidence tables were created for each systematic review and meta-analysis, and they can be found in Appendix 1. A table of the excluded studies can be found in Appendix 2.

Any relevant papers were assessed for their methodological quality using the following SIGN[1] criteria:

Levels of evidence (LOE)	
1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort or studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

[1] Scottish Intercollegiate Guidelines Network http://www.sign.ac.uk/

5. Findings

Systematic Reviews

Four systematic reviews are included in this report: Lindert et al. (2014)[1], Carr et al. (2013)[2], Maniglio (2010)[3], and Chen et al. (2010)[4].

The most recent systematic review and meta-analysis by Lindert et al. (2014)[1] looked at epidemiological studies that described the association between childhood physical or sexual abuse and depression or anxiety. The authors included 19 studies; 18 studies were cross-sectional and 1 was longitudinal (a New Zealand birth cohort study; Moffitt et al. 2007). Fourteen studies assessed depression, thirteen studies assessed anxiety, and eight studies assessed distress (i.e., depression or anxiety). The cross-sectional studies included some form of random sampling of a general population, in which prior child abuse was assessed retrospectively and psychological outcomes were assessed at the time of recruitment. In the longitudinal study, the participants self-reported child abuse at age 32 years. All studies contrasted abuse exposure versus no abuse exposure before age 16 years to depression and/or anxiety after age 16 years.

The odds of people with childhood sexual abuse (CSA) having depression in adulthood were significantly greater than in people with no CSA (OR[†] = 2.04; 95% CI[±]: 1.65 to 2.53). This pooled estimate was based on fourteen studies. The data exhibited substantial heterogeneity (I^2 = 81%[§], p <.0001; see forest plots in evidence table for more details). Childhood physical abuse was also found to be associated with an increased risk of developing depression in adulthood (OR =1.49; 95% CI: 1.29 to 1.72).

The odds of people with CSA having distress (i.e., depression or anxiety) in adulthood were significantly greater than in people with no CSA (OR = 3.01; 95% CI: 2.41 to 3.76). There was modest heterogeneity among the studies (I^2 = 45%, p = 0.119). The results were essentially unchanged when the longitudinal study was excluded. Childhood physical abuse was also found to be associated with an increased risk of having distress in adulthood (OR =2.16; 95% CI: 1.38 to 3.40).

Age group- or gender-specific results were not reported in most studies; therefore a random effects meta-regression was used to assess the influence of these factors. There was no evidence of a relationship between age or gender of subjects and the OR for either physical

[†] odds ratio

[±] 95% confidence interval

[§] a measure of heterogeneity (i.e., variation in treatment effects above that expected by chance); see Appendix 3 for more details about heterogeneity and the I^2 statistic

or sexual abuse and depression or anxiety. Publication bias was assessed using a funnel plot, which found no obvious bias. The results of this systematic review and meta-analysis support the hypothesis that sexual abuse in childhood is associated with depression in adulthood.

This systematic review and meta-analysis was of fair methodological quality (1+). Limitations of the systematic review and meta-analysis include abuse among subjects being reported retrospectively in all studies; studies included were restricted to only original research studies reporting adjusted ORs; abuse was assessed with a variety of different methods; there was no detailed data on the important aspects of abuse (e.g. frequency, duration and severity); the variety of outcome definitions used; and only one study included in the review reported gender-specific outcomes.

The second systematic review by Carr et al. (2013)[2] was of fair methodological quality (1-), and examined studies investigating early life stresses (i.e., sexual abuse, physical abuse, emotional abuse, physical neglect, and emotional neglect) and their association with psychiatric disorders in adulthood. The authors included 44 articles, of which 43 evaluated sexual abuse as an early life stress. Nineteen studies used a control group. The comparator groups included subjects without mental disorders (n = 14), and subjects without early life stressors (n = 5).

Sexual abuse and its association with mood disorders was examined in 20 studies. Nineteen studies found support for the association between sexual abuse and mood disorders, particularly with major depression and bipolar illnesses. Only one study (Rubino et al. 2009) found sexual abuse not significantly associated with depression. The authors noted that sexual abuse can be seen as an independent determinant of chronicity of depression, contributing to the severity of psychopathology and an earlier onset of first depressive episode. Physical abuse and unspecified neglect were also found to be associated with depression. However, due to lack of any statistical analyses and methodological assessment of study quality, this review is hypothesis-generating.

The systematic review by Maniglio (2010)[3] examined published reviews investigating the role of child sexual abuse (CSA) in the aetiology of depression. This fair quality (1+) systematic review included four reviews: Jumper (1995; 3 meta-analyses examining the relationship between CSA and depression, self-esteem and other psychological problems), Neumann et al. (1996; 15 meta-analyses investigating the relationship between CSA and a variety of psychological, behavioural and sexual problems), Rind et al. (1998; 18 meta-analyses examining the relationship between CSA and a variety of psychological, behavioural and sexual problems), and Paolucci et al. (2001; 6 meta-analyses examining the relationship between CSA and a variety of psychological, behavioural and sexual problems). Paolucci et

al. (2001) reviewed a range of samples (i.e., young and adult, male and female, clinical and nonclinical samples), Jumper (1995) included male and female adult patients and non-patient samples, Neumann et al. (1996) focused on adult female (both clinical and nonclinical) samples, and Rind et al. (1998) used college (both male and female) samples.

All four reviews found a significant association between CSA and depression (Jumper 1995 (r [ŦŦ] = .22; 95% CI: .21 to .35); Neumann et al. 1996 (d[¢] =.37; 95% CI: .33 to .41); Paolucci et al. 2001 (d = .44; 95% CI: .41 to .47); Rind et al. 1996 (r= .12; 95% CI: .10 to .14; χ^2 [φ] = 25.71)). [*]

Moderator variables [ϕ] included sample source (samples from non-clinical populations yielded smaller effect sizes than clinical samples) and definition of abuse (contact and consensual abuse generated larger effect sizes than did non-contact abuse). Moderators concerning aspects of the abuse experience (i.e., age when abused, incestuous forms of abuse, contact, use of force, frequency, duration of abuse) generated conflicting or non-significant results.

The authors concluded that there is evidence across methodologies, samples and measures that those who have experienced CSA are significantly at risk for depression. However, the presence of confounding variables and the poor quality of studies included in each review do not allow for causal inferences to be made; therefore, results should be interpreted with caution. The authors also noted that child sexual abuse was significantly related to a variety of other forms of psychopathology; thus, child sexual abuse is not a specific risk factor for depression. Instead, this early traumatic experience may contribute to the development of several other symptoms or disorders.

The final systematic review by Chen et al. (2010)[4] was of good methodological quality (1++) and investigated sexual abuse and a lifetime diagnosis of psychiatric disorders by looking at any longitudinal observational studies in the clinical literature. The authors included 37 studies, 17 of which were case control studies and 20 cohort studies, with a total of 3,162,318 participants. Sixteen studies examined the association between a history of sexual abuse and lifetime diagnosis of depression.

[ŦŦ] correlation coefficient; measure of effect size
[¢] Cohen's d; measure of effect size
[φ] Chi-squared test
[*] converted effect size to OR for depression: Jumper (1995): 2.27; Neumann et al. (1996): 1.96; Paolucci et al. 2001: 2.22; Rind et al. (1998): 1.55.
[ϕ] variables that account for significant heterogeneity in effect size estimates; variable that affects the strength of relationship

The authors found that sexual abuse was significantly associated with a lifetime diagnosis of depression (OR=2.66; 95% CI: 2.14 to 3.30). No significant subgroup-effect interactions were found for victim's sex or age at the time of the abuse.

A history of rape was found to strengthen the association with lifetime diagnosis of depression (OR= 6.27; 95% CI: 1.96 to 20.06). Publication bias was assessed using a funnel plot and found no obvious bias.

Meta-Analyses

Three meta-analyses are included in this report: Amado et al. (2015)[5], Mandelli et al. (2015)[6], and Martinez et al. (2014)[7].

The meta-analysis by Amado et al. (2015)[5] was of fair methodological quality (1-) and investigated the effects of child/adolescent sexual abuse on victims' likelihood of developing symptoms of internalising injury, specifically depression and anxiety. The authors included 78 studies with 19,360 participants.

They found that sexual abuse was significantly associated with general sequelae (i.e., internalising injury), depression, and anxiety. Victims of child/adolescent sexual abuse had a 66% higher probability of depression than non-victims. Victims of child/adolescent sexual abuse had a greater probability of developing major depressive disorder (OR = 3.25; r = .26; 95% CI: .25 to .27) and dysthymia (OR = 6.59; r = .38; 95% CI: .37 to .39), with injury (i.e., psychological injury) quantified as 31% and 46%, respectively.

With regards to moderators, the authors found female and male child/adolescent sexual abuse victims were more likely to develop depression than non-victims (ORs =5.40 and 1.44, respectively). The effect size found in females was significantly higher than for males (q_s^{Ψ}=0.388, p <.05), with results generalizable for females but not for males (the effects of the moderators could not be assessed for males due to the very small k). Injury in depression for female and male victims was 2.26 and 1.60 times greater than for non-victims, respectively. Depression derived from abuse with penetration was significantly higher than abuse with no contact for depression (q_s= 0.093, p <.05).

Limitations of the meta-analysis include the use of self-reports of a retrospective nature for classification of abuse; primary studies assume that injury to mental health is sequelae to abuse without appraising other possible causes; the effect of the variable under analysis in primary studies was not completely isolated (as in many studies victims of sexual abuse,

$^{\Psi}$ Cohen's q; measure of effect size with correlational differences

physical abuse, neglect and other categories appear under the same umbrella); and some studies had no control group, the normative population was taken as contrast group, or it was not equivalent to the experimental one with the subsequent potential for distortion in the calculated effect sizes.

Mandelli et al. (2015)[6] was of fair methodological quality (1-) and looked at the role of trauma in childhood (i.e., sexual, physical, emotional abuse, neglect, early loss and parental separation) and risk for depression in adulthood. The authors included 26 studies, 14 of which examined sexual abuse.

Sexual abuse was associated with an increased risk of developing depression in adulthood (OR = 2.42; I^2 =70%), as was neglect (OR = 2.75; I^2 =92%), domestic violence (OR = 2.06; I^2 =37%) and physical abuse (OR = 1.98; I^2 =42%). Emotional abuse showed the strongest association with depression (OR = 2.78; I^2 =91%).

Results were not significantly affected by publication bias for neglect, childhood maltreatment, emotional abuse, physical abuse, early loss, parental divorce or separation. However, results on sexual abuse were significantly affected by publication bias [Ŷ] (B = 3.86; p = 0.04).

Limitations of the study include publication bias of studies examining sexual abuse; retrospective assessment of childhood trauma; inability to distinguish multiple from single forms of abuse (as most studies investigated the exposure to several types of maltreatment not specifying the specific effect of each form of abuse); limited number of included studies with clinical samples; smaller sample sizes in clinical samples; results may be affected by several factors that go with a psychiatric condition and genetic predisposition; and overlap in some of the studies between definitions of emotional or psychological abuse and neglect.

The third meta-analysis by Martinez et al. (2014)[7] was of fair quality (1+) and looked at determinants of differential responses to trauma exposure. The authors included 74 studies with samples of youth exposed to traumatic events and who completed the Trauma Symptom Checklist for Children (TSCC).

The authors found that sexual abuse was associated with higher depressive symptoms than child abuse/neglect ($t^{ч}$ (23) = 2.95, p = .007), community violence (t(26) = 4.95, p < .001), and complex trauma (t(23) = 3.63, p=.001). Among sexual abuse samples, female representation was associated with higher posttraumatic stress, anger and dissociation but not anxiety or depression. Among sexual abuse samples, older age was associated with higher depression

[Ŷ] Egger's test
[ч] t-test

(β [Ø] =.51, *Q* [*](1,16)=6.00, p=.014), as well as posttraumatic stress, anxiety and dissociation. Furthermore, there was a higher sample representation of ethnic minorities associated with lower depression (*Q* (1, 33) = 6.27, p = .012).

Limitations of the meta-analysis include only including published studies which may have resulted in a bias in the study sample, and the decision to focus only on the Trauma Symptom Checklist for Children disregarding other measures of symptomology (e.g. structured interviews or other symptom checklists).

6. Additional Information

Postpartum and Perinatal Depression

Although not the focus of this report, childhood sexual abuse has also been linked with the development of postpartum and perinatal depression. This can provide further understanding to the effects of childhood sexual abuse and specific depression types. Two sources were used (with no formal methodological appraisal): a systematic review by Alvarez-Segura et al. (2014) and an epidemiologic review by Wosu et al. (2015).

Alvarez-Segura et al. (2014)

This systematic review investigated the association between maternal lifetime abuse and perinatal depressive symptoms. The authors included 43 studies: 29 cross-sectional and 14 longitudinal. Twenty-two articles focused on the postpartum period, 17 on the pregnancy period, two on the pregnancy and postpartum periods, and two included separate samples for antenatal and postpartum periods.

They found that all studies reported a significant elevation in depression scores during antepartum and/or postpartum period among women who had lifetime abuse histories (specifically sexual or physical abuse). However, three studies found an association between depression scores and emotional abuse, but not with physical or sexual abuse, and one study found no significant relationship between childhood abuse (i.e., physical, sexual or emotional abuse) and postpartum depression. Among studies that adjusted the association for confounding factors (i.e., 25 of 43 studies), the association between lifetime abuse histories and depression during antepartum and/or postpartum period remained significant for the majority of cases (20 studies; 80%).

[Ø] standardised regression coefficient

[*] *Q* statistic; used to assess the magnitude of variability in the weighted mean t-scores

Limitations of the systematic review include inconsistent definitions of abuse; self-reported retrospective exposure; important risk factors for antenatal or postnatal depression (e.g. history of psychiatric illness) not adequately considered in some studies; use of screening tests for the assessment of depression (only one study included a validated diagnostic assessment tool); and most of the studies examined Caucasian women.

Wosu et al. (2015)

This epidemiologic review looked at the relationship between childhood sexual abuse and depression or depressive symptoms among pregnant and postpartum women. The authors included 14 studies: 7 studies on the prenatal period (all cross-sectional) and 7 studies on the postpartum period (5 prospective, 2 cross-sectional). A narrative review was provided of all 14 studies.

Only three prenatal studies provided information that was suitable and sufficient for meta-analysis; however, due to the small number of studies, a quantitative summary was not able to be provided. Six postpartum depression studies had information that was suitable and sufficient for meta-analysis, and were therefore meta-analysed.

With regards to prenatal depression, findings from all but one study observed statistically significant associations between maternal history of childhood sexual abuse and prenatal depression or depressive symptoms. In relation to postpartum depression, associations with maternal history of childhood sexual abuse were mixed, with pooled unadjusted and adjusted odds ratios of 1.82 (95% CI: 0.9 to 3.60) and 1.20 (95% CI: 0.81 to 1.76), respectively.

Limitations of this review include instruments used to assess childhood sexual abuse and depressive characteristics varied across studies and could have accounted for heterogeneity in research findings; for the majority of studies it was not the primary objective to examine the association between childhood sexual abuse and depression; most studies lacked information on maternal pre-pregnancy depression status and so the authors were unable to establish the incidence of depression or depressive symptoms during the prenatal and postpartum periods; and all studies were conducted in high-income countries which limits generalizability of findings.

Other Risk Factors of Depressive Disorders

Similarly, although not the focus of this report, other risk factors for the development of depressive disorders will help provide context to the evidence about childhood sexual abuse. One source was used (with no formal methodological appraisal): *DynaMed*™[***].

DynaMed™

Likely risk factors:

- Family or personal history of major depression and/or substance abuse
- Chronic medical illness
- Stressful life events including loss (including bereavement or divorce)
- Trauma
- Major life changes such as job change or financial difficulty
- Domestic abuse or violence
- Female sex
- Middle age
- Never or previous marriage
- Low income and unemployment
- Disability
- History of depressive symptoms or episodes:
    - adolescent self-harm with or without suicidal intent associated with increased risk of depression and anxiety disorder diagnosis in young adulthood
        - based on prospective cohort study of 4,799 adults
    - symptoms of depression in adolescence strongly predict major depression in adulthood
        - based on cohort study of 776 adolescents
    - previous depressive episodes and partner conflicts associated with major depression in pregnancy
        - based on prospective cohort study of 154 women seeking prenatal care at single facility in Italy
    - subthreshold depression may progress to major depression in about 8%-10% older and elderly adults

[***] a clinical reference resource tool created by physicians for physicians and other health care professionals with conclusions based on the best available clinical evidence which has been consistently and systematically identified, evaluated and selected

        - based on systematic review of 181 studies evaluating effects of late-life subthreshold depression
- Genetic factors:
    - serotonin transporter promoter polymorphism (5-HTTLPR) plus stress associated with increased risk of depression
        - based on systematic review of observational studies with clinical heterogeneity
    - genetic variant impairing folate metabolism associated with major depression
        - based on systematic review of observational studies
    - specific single-nucleotide polymorphisms associated with increased risk of neuropsychiatric disorders
        - based on case-control study of 33,332 patients with autism spectrum disorders, attention deficit hyperactivity disorder, bipolar disorder, major depressive disorder, or schizophrenia
- Alcohol dependence or excessive use:
    - past alcohol dependence associated with increased risk for major depression
        - based on cross-sectional survey of 6,050 United States adults who reported past drinking of at least 12 drinks yearly but had not used alcohol, tobacco or other drugs within the past 12 months were analysed for presence of diagnosis for major depression
    - alcohol abuse and dependence associated with major depression
        - based on cohort study of 1,055 children in New Zealand
    - excessive alcohol use associated with increased risk of depressed mood after 6 years
        - based on prospective study of 1,169 adults in the Netherlands
- Physical illness or injury:
    - major depression common and persistent after acute myocardial infarction
        - based on systematic review
    - clinically significant depression reported in 21.5% of heart failure patients
        - based on systematic review
    - heart failure associated with major depression among persons > 70 years old
        - based on cross-sectional study of 6,125 persons > 70 years old
    - major depression common in heart failure and associated with worsening health status at 6 weeks
        - based on prospective cohort study of 460 outpatients with heart failure and left ventricular ejection fraction
    - history of cancer associated with increased risk of hospitalization due to major depression

        - based on cohort of 608,591 adults from Danish Cancer Registry
    - history of stroke and diabetes mellitus may be associated with depressive symptoms, and stroke may be associated with clinically significant depressive symptoms at 2 years after index stroke
        - based on prospective cohort study with cross-sectional analysis of 1,134 patients aged ≥ 65 year
    - incidence of depression about 22% after spinal cord injury
        - based on systematic review of cohort studies
- Chronic medical conditions:
    - diabetes mellitus type 2 associated with increased risk for depression
        - based on multiple systematic reviews
- Sleep disorders:
    - insomnia symptoms associated with increased risk of depression
        - based on systematic review of cohort studies
    - increasing severity of sleep-related breathing disorder may be associated with increased risk for depression
        - based on prospective cohort study
- Other factors:
    - low folate levels associated with depression
        - based on systematic review of observational studies and cross-sectional survey
    - lower-than-normal levels of testosterone may be associated with increased prevalence and risk for depression in older men, but insufficient evidence for association with freely circulating testosterone levels
        - based on 2 cohort studies
    - perimenopause may be associated with increased risk for depressive symptoms and major depression
        - based on systematic review of observational studies
    - estradiol withdrawal may be associated with major depression in postmenopausal women with history of perimenopausal depression
        - based on subgroup analysis of small randomized trial
    - social anxiety disorder associated with increased risk for major depression
        - based on prospective cohort study of 3,021 persons aged 14-24 in Munich, Germany; followed for up to 10 years

Possible risk factors:

- Cannabis use:

    - major depression associated with increased incidence of cannabis use, but daily cannabis use may not be associated with increased incidence of either major depression or bipolar disorder
        - based on prospective cohort study of 28,630 adults from wave 1 and 2 of National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)
- Head injury:
    - traumatic brain injury associated with increased risk for depression
        - based on systematic review
    - head injury associated with increased lifetime risk for major depression;
        - based on case-control study
- Psychosocial stressor associations:
    - experiencing intimate partner violence associated with increased major depression and suicide attempts in women and increased major depression in men
        - based on systematic review of observational studies
    - exposure to country level conflict associated with posttraumatic stress disorder (PTSD) in 12.4% and severe major depression in 19.8% in Libya
        - based on retrospective population-based cohort study of 1,236,600 residents of Libya exposed to high level of political terror and traumatic events during 2011 conflict
    - childhood abuse associated with increased overall risk of major depression, and neglect associated with major depression in young adulthood
        - based on case-control study of 676 children aged ≤ 11 years with substantiated physical or sexual abuse were matched with 520 non-abused children and followed into young adulthood (mean age 28 years)
    - war-related internal displacement (seeking refuge in secure areas of own country) associated with increased risk of major depression
        - based on cross-sectional study of 1,517 Jaffna District households in Sri Lanka
    - being primary caregiver for grandchildren associated with higher levels of depressive symptoms
        - based on subgroup of cross-sectional study
- Other factors:
    - low birth weight (LBW) may be associated with depression
        - based on systematic review
    - major depression common in persons with Dhat syndrome

Mediators of the Association between Childhood Sexual Abuse and Depressive Disorders

Understanding of possible mediators can help provide further understanding into the association between childhood sexual abuse and depressive disorders. Here, one source is reviewed (with no formal methodological appraisal): a narrative review by Whiffen and MacIntosh (2005). This is followed by a brief overview of several theories that have been proposed to help explain the relationship between childhood sexual abuse and subsequent development of depressive disorders.

Whiffen and MacIntosh (2005)

This critical review looked at empirical literature on mediators of the link between childhood sexual abuse and emotional distress (including symptoms of depression, anxiety, dissociation, and trauma). The authors reviewed 19 studies assessing shame or self-blame, interpersonal difficulties, family environment, and coping as mediators of the link between childhood sexual abuse or maltreatment and adult emotional distress.

The authors found support for the roles of shame or self-blame, interpersonal difficulties and avoidant coping strategies as mediators. The authors also found that emotional distress appeared to mediate links between childhood sexual abuse and other adverse outcomes such as alcohol abuse and revictimisation.

The authors noted limitations in the literature including methodological and conceptual problems, specifically that researchers do not always use standardized procedures for determining mediation and confusion between mediators and proxy variables.

Theories

A number of theories have been proposed to help explain the association between childhood sexual abuse and the development of depressive disorders in later life.

One such theory postulates that the individual's cognitive attributional style plays a critical role in their response to the environment, and how they are subsequently affected by stressful events such as childhood sexual abuse (Gold, 1986). Empirical work supports this claim, where women who had been sexually abused as children and scored higher on depressive scales tended to have attributional styles that were internal, stable, and global (i.e., a pessimistic attribution style); however conclusions regarding causality are tentative given the correlational nature of the studies (Feiring, Taska, & Lewis, 2002; Gold, 1986).

Neurobiological explanations have also been developed to explain the link between childhood sexual abuse and the development of depressive disorders. A number of studies have demonstrated that early life stressors, such as childhood sexual abuse, can result in both acute and chronic changes in the functioning and regulation of the HPA axis, primarily in the form of hypersecretion of corticotropin-releasing hormone (CRH) – an effect well documented among depressive individuals (see Weiss, Longhurst, and Mazure (1999) for a more detailed neurobiological explanation).

Additional potential mediators between childhood sexual abuse and depression include a dysfunctional parenting/chaotic home environment (Brown, Cohen, Johnson, & Smailes, 1999) and disadvantaged life circumstances that may occur post-abuse (Maniglio, 2010).As stated previously, Waffen and MacIntosh (2005) identified shame or self-blame, interpersonal difficulties and avoidant coping strategies as mediators of the relationship between childhood sexual abuse and emotional distress.

Although well established, literature in this area presents with a number of methodological challenges, limiting any conclusions to be made regarding causality of childhood sexual abuse in the development of depressive disorders. The most recent review on the subject states that the role of childhood sexual abuse in developing depression in later life needs further careful consideration (Maniglio, 2010). It is also important to note that no single theory is sufficient to explain the development of depression among those who have experienced childhood sexual abuse, and that the mechanisms are likely to be influenced by individual factors.

7. Conclusions

The four systematic reviews and three meta-analyses in this report found:

- Fair quality evidence (i.e., the review was of fair methodological quality (1+/1-)) from one systematic review that people with childhood sexual abuse have significantly greater odds (OR = 2.04) of having depression in adulthood compared to those with no childhood sexual abuse. Experience of childhood sexual abuse was also associated with higher odds of developing depression than childhood physical abuse (ORs = 2.04 versus 1.49, respectively)[1]
- Fair quality evidence from one systematic review of an association between sexual abuse and depression[2]
- Fair quality evidence from one systematic review of an association between childhood sexual abuse and depression (OR range =1.55 to 2.27)[3]
- Quality evidence (i.e., the review was of good methodological quality (1++)) from one systematic review that childhood sexual abuse significantly increases the risk of lifetime diagnosis of depression (OR = 2.66)[4]
- Fair quality evidence from one meta-analysis that victims of childhood/adolescent sexual abuse were more likely to develop depression than were non-victims (major depressive disorder: OR = 3.25; dysthymia: OR = 6.59)[5]
- Fair quality evidence from one meta-analysis that sexual abuse was associated with increased risk of developing depression in adulthood (OR = 2.42). Emotional abuse had the strongest association with depression (OR = 2.78), followed by neglect (OR = 2.75), sexual abuse, domestic violence (OR = 2.06), and physical abuse (OR = 1.98) [6]
- Fair quality evidence from one meta-analysis that sexual abuse was associated with higher depressive symptoms than child abuse/neglect, community violence, and complex trauma[7]

This report also found some evidence for the association between childhood/lifetime history of sexual abuse and depression during prenatal, antepartum, and postpartum; however, results for postpartum were mixed.

Using Bradford Hill's guide to causation (Appendix 4), the strength of association between childhood sexual abuse and the development of a depressive disorder is in the order of 1.55 to 6.5 increased odds, and appears to be relatively consistent. Temporality (i.e., abuse occurs before the development of a depressive disorder) cannot be certain due to the retrospective design of studies.

The biological gradient (i.e., greater exposure leads to greater incidence of the effect) was investigated by several authors[3,4,5]. In one systematic review, aspects of the abuse experience (force, frequency, duration of abuse, age of victim when abused, level of contact) were not found to be statistically significant moderator variables; however, the absence of a dose-response relationship does not rule out causality. One systematic review found that a history of rape strengthened the association with depression[4], and one meta-analysis found depression resulting from abuse with penetration was significantly higher than abuse with no contact[5].

In relation to plausibility, there may be evidence for the roles of shame or self-blame, interpersonal difficulties, and avoidant coping strategies as mediators of the link between childhood sexual abuse and adult emotional distress (including depressive symptoms). Additional mediators identified include cognitive attribution style, the functioning and regulation of the HPA axis, dysfunctional parenting/chaotic home environment, and disadvantaged life circumstances post-abuse. Research regarding the role of childhood sexual abuse on the development of depressive disorders is not yet fully understood, and the current research presents with a number of methodological issues.

Limitations of the current research examining the association between childhood sexual abuse and depressive disorders include the number of poor quality studies conducted, childhood sexual abuse and outcomes being assessed using a variety of different methods, abuse being reported retrospectively, and the range of confounding variables present across studies.

Given the identified limitations of the current literature and that there are likely to be many causes of and risk factors for depressive disorders, it is difficult to provide a strong conclusion as to whether childhood sexual abuse is a direct and sufficient cause of depressive disorders. However, there is some good quality evidence that childhood sexual abuse is likely to be a risk factor for developing a depressive disorder later in life.

8. Limitations of this report

As only English language articles were included, the presence of publication bias in this report is a possibility. In addition, only focussing on systematic reviews and meta-analyses may have missed more recent research.

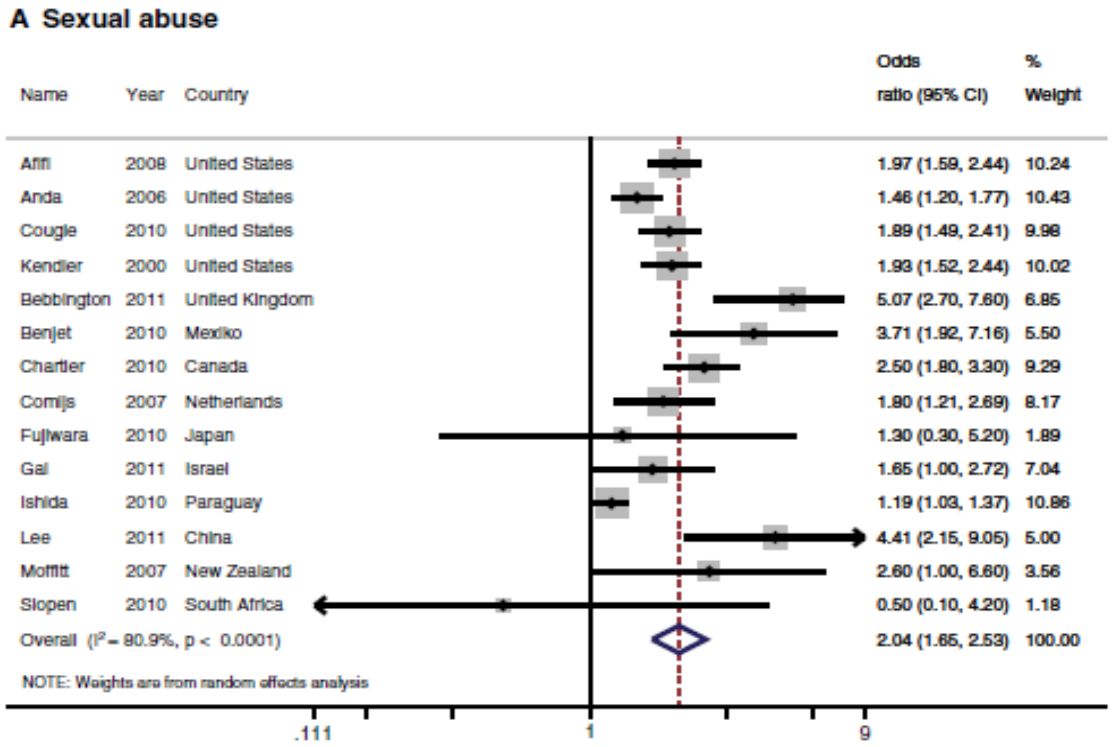
9. Appendix 1: Evidence Tables

Reference and study design	Studies	Exposure	Outcome Measure	Results	Conclusions
Lindert et al. (2014). "Sexual and physical abuse in childhood is associated with depression and anxiety over the life course: Systematic review and meta-analysis." International Journal of Public Health **59**:359-372 Germany Included studies: *Total:* Afifi et al. 2009, Anda et al. 2006, Bebbington et al. 2011, Benjet et al. 2010, Chartier et al. 2010, Comijs et al. 2007, Cougle et al. 2010, Draper et al. 2008, Fujiwara & Kawakami 2011, Gal et al. 2011, Ishida et al. 2010, Jirapramukpitak et al. 2011, Kendler et al. 2000, Lee et al. 2011, Luo et al. 2008, Moffit et al. 2007, Ramiro et al. 2010, Slopen et al. 2010, Thompson et al. 2004	Number of studies: Total = 19; child sexual abuse and depression = 14 Total number of participants in the studies: 115,579 Child sexual abuse and depression: N =72,107 Inclusion criteria: Assessed exposure to physical or sexual abuse in childhood or adolescence before the age of 16 years and depression or anxiety in subjects at least 16 years old; presented original data from an epidemiologic cross-sectional or longitudinal study in peer-reviewed literature; included at least 100 participants who were from the general community; used quantitative categorical assessment of child abuse before age 16 years; assessed depression and anxiety with validated scales or clinical diagnoses after age 16 years; and reported effect estimates with confidence intervals.	Child sexual abuse, child physical abuse	Odds ratio (OR) of depression, anxiety, or distress (i.e., depression or anxiety) in adulthood.	**Child sexual abuse and depression (N = 14 studies)** OR = 2.04 (95% CI: 1.65 to 2.53) I^2 = 81%, p < 0.0001 **Child sexual abuse and distress (i.e., depression or anxiety; N not reported)** OR = 3.01 (95% CI: 2.41 to 3.76) I^2, 45%, p = 0.119 **Child sexual abuse and anxiety (N =13 studies)** OR = 2.52 (95% CI: 2.12 to 2.98) I^2 = 58.7%, p = 0.004 **Child physical abuse and depression (N = 7 studies)** OR = 1.49 (95% CI: 1.29 to 1.72) I^2 = 36%, p = 0.16 **Child physical abuse and distress (N not reported)**	Author's conclusions: High levels of depression, anxiety and distress are reported in adults exposed to childhood sexual and physical abuse. Reviewer's conclusions: This systematic review and meta-analysis indicates that the odds of people with childhood sexual abuse having depression in adulthood is significantly greater than in people with no childhood sexual abuse.

Child sexual abuse and depression: Afifi et al. 2009; Chartier et al. 2010; Cougle et al. 2010; Fujiwara and Kawakami 2011; Kendler et al. 2000; Lee et al. 2011; Bebbington et al. 2011; Comijs et al. 2007; Gal et al. 2011; Ishida et al. 2010; Slopen et al. 2010; Moffitt et al. 2007; Anda et al. 2006; Benjet et al. 2010)	Exclusion criteria: Not explicitly reported; however, studies excluded included those on special populations, not original studies, no confidence intervals reported, only reporting data on psychosis. Other reviews were also excluded. Databases used: PubMed/MEDLINE (National Library of Medicine), EMBASE (Elsevier), PsycINFO (EBSCO), MeSH (NLM), EMTREE (Elsevier), Thesaurus of Psychological Index Terms (APA) (Jan 2000 – March 2012) Description of the methodological assessment of studies: not conducted Fixed or variable effects: random effects; fixed effect methods with Mantel-Haenszel weighting for one study. Heterogeneity: Cochrane Q test, quantified using I^2 statistic			OR = 2.16 (95% CI: 1.38 to 3.40) I^2, 96.6%, $p < 0.0001$ **Child physical abuse and anxiety (N = 7 studies)** OR = 1.70 (95% CI: 1.33 to 2.18) I^2, 95%, $p < 0.001$ No evidence of a linear relationship between mean age of the study samples and the OR for either type of abuse and anxiety or depression (all $p \geq 0.53$). No linear relationship between gender and the OR for either type of abuse and anxiety or depression (all $p \geq 0.60$).	

Forest plots for meta-analyses

Fig. 1 meta-analysis of child sexual abuse on depression.
The side of the shaded box around the individual study ORs represents the weight for that study for the pooled analysis.



Note: there was no forest plot conducted for child sexual abuse on distress.

Study type: Systematic review with meta-analysis

Quality: 1+

Comments: Adequately conducted systematic review with meta-analysis. Systematic search of three databases. No language restriction. Methodological assessment not reported. Publication bias assessed by funnel plot – no obvious pub bias present. Heterogeneity considered. Subgroup analysis undertaken. Meta-analysis appears appropriate.

<table>
<tr><th>Reference and study design</th><th>Studies</th><th>Results</th></tr>
<tr>
<td>Carr et al. 2013

“The role of early life stress in adult psychiatric disorders: A systematic review according to childhood trauma subtypes.”

<u>The Journal of Nervous and Mental Disease</u> 201(12): 1007-1018.

Brazil

<u>Included studies:</u>
Total:
Becker & Grilo, 2011; Heins et al. 2011, Laporte et al. 2011, Wingenfeld et al. 2011, Jonas et al. 2011, Khoury et al. 2010, McLaughlin et al. 2010b, Kessler et al. 2010, Green et al. 2010, McLaughlin et al. 2010a, Steiger et al. 2010, Hovens et al. 2010, Wiersma et al. 2009, Rubino et al. 2009, Steel et al. 2009, Afifi et al. 2009, Tyrka et al. 2009,</td>
<td><u>Number of studies:</u> 44

<u>Total number of participants in the studies:</u> 145,507

<u>Inclusion criteria:</u> Study included at least one of the defined forms of early life stress: emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect; publications from 2001-2011; in English or Portuguese; in humans; and adults ranging in age from 18 to 64 years.

<u>Exclusion criteria:</u> Did not mention early life stress, genetic or neurobiological perspective, psychiatric disorders not mentioned, child or teenager sample, a review article, therapeutic or instruments, other idiom, abusers profile, cognitive or behavioural aspects, politic or legal aspects, specific groups, other clinical conditions.</td>
<td><u>Overview of results from articles (N = 20) examining the association between sexual abuse and mood disorder in adulthood</u>
<table>
<tr><th>Author/year</th><th>ELS[H] Instrument</th><th>Diagnosis</th><th>Main Results</th></tr>
<tr><td>Afifi et al. 2006</td><td>CTS, PBI</td><td>MD, AD, SAD, DBD</td><td>The prevalence of psychiatric disorders progressively increased as the severity SA increased</td></tr>
<tr><td>Afifi et al. 2008</td><td>Open questions</td><td>MD, AD, SAD</td><td>SA was associated with all psychiatric disorders and suicide ideation. When associated with physical abuse, increased odds of suicidal attempts</td></tr>
<tr><td>Afifi et al. 2009</td><td>CTS, FHRDC</td><td>MD, AD, SAD, DBD, PD</td><td>SA was associated with psychiatric disorders and suicidal ideation and attempts</td></tr>
<tr><td>Bulik et al. 2001</td><td>Structured questions</td><td>MD, AD, ED, SAD</td><td>Positive link between SA and increased risk for psychopathology, but not a predictive one</td></tr>
<tr><td>Green et al. 2010</td><td>FHRDC, CTS</td><td>MD, AD, SAD, DBD</td><td>SA has powerful and often subadditive associations with the onset of many types of largely primary mental disorders throughout the life course</td></tr>
<tr><td>Hovens et al. 2010</td><td>CTI</td><td>MD, AD</td><td>SA was associated with pure anxiety, pure depression, and anxiety and depression comorbid group. Contributing to the severity of psychopathology</td></tr>
<tr><td>Jonas et al. 2011</td><td>TSQ</td><td>MD, AD, SAD, ED</td><td>In all cases, the overall association of SA with each disorder was highly significant. The highest scores were associated with non-consensual sexual intercourse, particularly with phobia and symptoms of PTSD, except panic</td></tr>
</table>
</td>
</tr>
</table>

Caspi et al. 2008, Sfoggia et al. 2008, Afifi et al. 2008, Wonderlich et al. 2007, Grover et al. 2007, Uçok and Bikmaz 2007, Gibb et al. 2007, Afifi et al. 2006, Zavaschi et al. 2006, Sar et al. 2006, Sareen et al. 2005, Bradley et al. 2005, Katerndahl et al. 2005, Bandelow et al. 2005, Bebbington et al. 2004, Lang et al. 2004, Rayworth et al 2004, Holowka et al. 2003, Zanarini et al. 2002, Roy 2002, Lewis-Fernández et al. 2002, Leverich et al. 2008, Wonderlich et al. 2001, Bulik et al. 2001, Molnar et al. 2001a, Johnson et al. 2001, Molnar et al. 2001b.	<u>Databases used:</u> PubMed, SciELO, LILACS, PsycINFO (2001-2011), + manual search <u>Description of the methodological assessment of studies:</u> not reported <u>Fixed or variable effects:</u> not applicable <u>Heterogeneity:</u> not discussed	Katerndahl et al. 2005	CSAAS, FOQ, PBI	MD, AD, SAD, PD, ED	SA was associated with borderline personality disorder, substance abuse, major depressive episode, suicidality, bulimia, agoraphobia, and panic disorder. Multiple perpetrators increase the probability of developing mental disorders
		Kessler et al. 2010	FHRDC, CTS	MD, AD, DBD, SAD	SA has strong associations with all classes of disorders at all life-course stages in all groups of World Mental Health countries
		Leverich et al. 2002	Open questions	MD, SAD	SA was associated with mood disorders and a more severe course of illness. SA was associated with earlier onset of bipolar illness and an increased number of axis I, II, and III comorbid disorders, including drug and alcohol abuse, faster cycling frequencies, and a higher rate of suicides attempts
		McLaughlin et al. 2010a	FHRDC, CTS	MD, AD, SAD, DBD	SA was significantly but modestly related to persistence of mood, substance, and anxiety disorders. Exposure to multiple other childhood adversities increased the persistence of mood and anxiety disorders throughout the life course
		McLaughlin et al. 2010b	FHRDC, CTS	MD, AD, DBD	SA particularly associated with anxiety disorders but also with mood and disruptive behaviour disorders. Predictive effects persisted throughout the life course
		Molnar et al. 2001a	CTS	MD, AD, SAD	SA is associated with substantial increased risk for subsequent psychopathology

[ǂ] Early Life Stress (i.e., emotional abuse, physical abuse, sexual abuse, emotional neglect or physical neglect)

		Molnar et al. 2001b	CTS, FHRDC, DIS	MD, AD, SAD	Association between SA and suicidal behaviour, mediated by psychopathology. SA increased the risk for suicide attempts
		Rubino et al. 2009	TAQ	S, MD	SA was not associated with schizophrenia or depression even though when it was restricted to intercourse
		Sareen et al. 2005	CMHSR, FHRDC	MD, AD, SAD, ED	SA was independently and significantly associated with mental disorders
		Wiersma et al. 2009	CTI	MD	SA is an independent determinant of chronicity of depression. SA was associated to prevalence of comorbid anxiety, severe depression, and an earlier onset of depression. Greater number of trauma subtypes may lead to lifetime chronic depression
		Wingenfeld et al. 2011	ETI, ETI	MD, PD, AD, DD	SA was a significant predictor of all aspects of measured psychopathology
		Wonderlich et al. 2007	CTI	PD, AD, MD, SAD	SA was associated with mood disorders, anxiety disorders, daily purging frequency, and self-destructive behaviour
		Zavaschi et al. 2006	FEI, SSCECV	MD	Association between SA and adult mood disorders, especially for manic patients
		AD = Anxiety Disorder; DBD = Disruptive Behaviour Disorder; ED = Eating Disorder; MD = Mood Disorder; PD = Personality Disorder; S = Schizophrenia; SAD = Substance Abuse Disorder. CMHSR = Childhood Maltreatment History Self-Report; CSAAS = Child Sexual Abuse and Assault Survey; CTI = Childhood Trauma Interview; CTS = Conflict Tactics Scale; CTQ = Childhood Trauma Questionnaire; DIS = Diagnostic Interview Schedule; ETI = Early Trauma Inventory; FEI = Familial Experiences Interview; FHRDC = Family History Research Diagnostic Criteria; FOQ = Family-of-Origin Questionnaire; PBI = Parental Bonding Index; SSCECV = Screening Survey of Children's Exposure to Community Violence; TAQ = Traumatic			

		Antecedents Questionnaire; TEI = Traumatic Events Inventory; TSQ = Trauma Screening Questionnaire.

Conclusions

Author's conclusions: Sexual abuse was associated with mood disorders in 19 studies, and particularly with major depression and bipolar illnesses. Sexual abuse can be seen as an independent determinant of chronicity of depression, contributing to the severity of psychopathology and an earlier onset of first depressive episode. Only one study (Rubino et al. 2009) found sexual abuse not significantly associated with depression.

Reviewer's conclusions: This systematic review presents evidence suggestive of an association between childhood sexual abuse and mood disorders, but is not definitive.

Study type: Systematic review

Quality: 1-

Comments: Wide ranging systematic review with no meta-analysis. Adequate search of multiple databases. No formal methodological assessment.

Reference and study design	Studies	Results				
Maniglio (2010) "Child sexual abuse in the etiology of depression: A systematic review of reviews." <u>Depression and Anxiety</u> **27**: 631-642. Italy <u>Included studies</u>: Jumper, 1995; Neumann et al. 1996, Paolucci et al. 2001, Rind et al. 1998	<u>Number of studies:</u> 4 <u>Total number of participants in the studies:</u> ~ 59,164 <u>Inclusion criteria:</u> appeared in peer-reviewed journals; were published in full; were critical reviews of the literature; were not dissertation papers, editorials, letters, conference proceedings, books, and book chapters; reviewed studies sampling human subjects; investigated medical, neurobiological, psychological, behavioural, sexual, or other health problems following childhood sexual abuse; and had primary and sufficient data derived from longitudinal, cross-sectional, case-control, or cohort studies. For the purpose of this systematic review, only reviews that investigated depressive symptoms or disorders following childhood sexual abuse were included. <u>Exclusion criteria:</u> Not explicitly stated, but must	**Source**	**Subjects**	**Outcome variables**	**Significant outcomes (effect sizes or odds ratios [95%CI]; homogeneity**	**Significant moderators (between-group homogeneity)**
		Jumper (1995)	Male and female adult patients and non-patients (26 studies, ~7,000 subjects)	Depression, self-esteem, other psychological problems (i.e. suicidal ideation or behaviour, anxiety, personality, psychotic, somatoform, and dissociative disorders)	Depression: (r =.22 [.21–.35], p <.001; Q_T = 84.11, p <.001), self-esteem: (r = .17 [.14–.34], p <.001; Q_T =85.95, p <.001), other (r =.27 [.20–.32], P <.001; Q_T = 147.77, p <.001)	Depression: sample source (Q_B = 49.64, p <.001), contact/consent (Q_B = 33.09, p <.001); self-esteem: sample source (Q_B 5 64.59, p <.001), contact/consent (Q_B 5 65.43, p <.001), publication date (Q_B 5 15.30, p <.01), gender (Q_B = 29.61, p <.001); other: sample source (Q_B = 65.75, p<.001), contact/consent (Q_B = 15.28, p <.001), publication date (Q_B = 20.25, p <.001)
		Neumann et al., 1996	Female adult patients & nonpatients (38 studies, 11,162 subjects)	Overall psychopathology, anger, anxiety, depression, revictimization, self-mutilation, sex problems, substance abuse, suicide, self-concept,	Overall psychopathology (d = .37 [.33, .41]; Q= 62.36, p<.01), Depression (d= .41 [.36, .46]),Anxiety (d =.40 [.34,.47]), obsessions/ compulsions (d= .34 [.22, .46]), posttraumatic stress (d =.52 [.44, .59]), anger (d =.39 [.25, .51]), revictimization (d= .67 [.50,	Overall impairment: sample source (Q_B =9.40, p < .01)

	meet inclusion criteria above. <u>Databases used:</u> AMED, Cochrane Reviews, EBSCO, ERIC, MEDLINE, PsycINFO, ScienceDirect (Jan 1996 – December 2008)+ manual search of reference lists <u>Description of the methodological assessment of studies:</u> Each study assessed on the basis of evidence identification, study selection, data extraction, quality assessment, and data synthesis and analysis. <u>Fixed or variable effects:</u> not applicable <u>Heterogeneity:</u> Jumper (1995) used the homogeneity statistic (Q_B); Neumann et al. (1996) used Hedges' between-group heterogeneity statistic (Q_{BET}); Rind et al. (1998) used normal deviate z (equivalent to Q_{BET}). Paolucci et al. (2001) did not use statistics to quantify heterogeneity of effect sizes.			interpersonal problems, dissociation, obsessions or compulsions, somatization, posttraumatic stress, and general symptoms	.84]), self-mutilation (d= .42 [.19, .64]), sex problems (d =.36 [.30, .42]), substance abuse (d= .41 [.31, .51]), suicide (d = .34 [.24, .44]), self-concept (d = .32 [.32, .47]), interpersonal problems (d =.39 [.22, .46]), dissociation (d= .39 [.32, .47]), somatization (d= .34 [.24, .45]), general symptoms (d =.46 [.40, .52]).	
		Paolucci et al., 2001	Male & female young & adult patients & nonpatients (37 studies, 88 samples, 25,367 subjects)	Posttraumatic stress, depression, suicide or self-injury, early sex or prostitution, sex perpetration, intelligence or learning	Depression (d = .44 [.41, .47]), posttraumatic stress (d = .40 [.37, .43]), suicide/ self-injury (d = .44 [.40, .48]), early sex/ prostitution (d = .29 [.25-.32]), sex perpetration (d = .16 [.11, .21]), intelligence/ learning (d = .19 [.12, .26])	
		Rind et al., 1998	Male & female adult nonpatients (59 studies, 51 samples, 15,635 subjects)	Overall psychopathology, anxiety, depression, obsessions or compulsions, phobia, alcohol, dissociation, eating disorders, hostility, interpersonal sensitivity, locus of control, paranoia, psychosis, self-	Overall psychopathology (r = .09 [.08, .11]; χ^2 =49.19, p > .50), depression (r = .12 [.10, .14]; χ^2 = 25.71), anxiety (r = .13 [.10, .15]; χ^2 = 4.62), obsessions / compulsions (r= .10 [.06, .15]; χ^2 = 5.01), phobia (r =.12 [.07, .17]; χ^2 = 8.08), alcohol (r =.07 [.02, .12]; χ^2 = 2.97), dissociation (r = .09 [.04, .15]; χ^2 = 1.86), eating disorders (r = .06 [.02, .10]; χ^2 = 9.92),	Overall impairment: published study (r = .25, p= .08), incest (r = .09 [.01- .17]; χ^2 = 15.20), consent/gender interaction (z = 2.51, p>.02; females, r=.11 [.09-.13]; χ^2 = 14.50)

			esteem, sex problems, social impairment, somatization, suicide, general symptoms.	hostility (r = .11 [.06, .16]; χ^2 = 11.22, p < .05), interpersonal sensitivity (r = .10 [.06, .15]; χ^2 =11.78), paranoia (r = .11 [.07, .16]; χ^2 = 10.34), psychosis (r = .11 [.06, .15]; χ^2 =10.13), self-esteem (r = .04 [.01, .07]; χ^2 = 51.31, p < .05), sex problems (r =.09 [.07, .11]; χ^2 = 39.49, p < .05), social impairment (r = .07 [.04, .10]; χ^2 = 20.37), somatization (r = .09 [.06, .12]; χ^2 = 15.20), suicide (r = .09 [.06, .12]; χ^2 = 10.94), general symptoms (r = .12 [.08, .15]; χ^2 =18.77).

Conclusions

Author's conclusions: There is evidence that across methodologies, samples and measures, survivors of child sexual abuse are significantly at risk of depression. However, it should be noted that child sexual abuse was significantly related also to a variety of other forms of psychopathology; thus, child sexual abuse is not a specific risk factor for depression. Instead, this early traumatic experience may contribute to the development of several other symptoms or disorders.

Reviewer's conclusions: This systematic review presents evidence suggestive of an association between childhood sexual abuse and depression, but is not definitive due to the limitations of the studies and confounding variables.

Study type: Systematic review

Quality: 1+

Comments: Adequately conducted systematic review with no meta-analysis. Multiple databases searched. Heterogeneity considered.

Reference and study design	Studies	Exposure	Outcome Measure	Results	Conclusions
Chen et al. (2010). "Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis." Mayo Clinic Proceedings **85**(7): 618-29. USA Included studies: *Case-control studies*: Brown 1997, Cachelin 2005, Cheasty 1998, De Bellis 1994, Deep 1999, Figueroa 1997, Garnefski 1992, Pettigrew 1997, Price 2002, Roelofs 2002, Spitzer 2008, Steiger 2000, Striegel-Moore 2002, Stuart 1990, Tanskanen 2004, Welch 1996, Wise 2001 *Cohort studies*: Aglan 2008, Brezo 2008, Brown 1999, Buist 2001, Chowdhary 2008, Dinwiddie 2000, Ernst 1993, Fergusson 2000,	Number of studies: N=37 (17 case-control, 20 cohort) Total number of patients in the studies: n=3,162,318 Inclusion criteria: cohort and case-control studies comparing individuals with a history of sexual abuse to another control group; outcomes included anxiety disorders, bipolar disorder, depression, eating disorders, obsessive-compulsive disorder, PTSD, schizophrenia, sleep disorders, somatoform disorders, and suicide attempts. Exclusion criteria: none reported Databases used: PsycINFO, Medline, EMBASE, CINAHL, Current Contents, ACP Journal Club, CCTR, CDSR & DARE (Jan 1980 to Dec 2008) Description of the methodological assessment	Sexual abuse[¥¥]	Odds ratio (OR) of lifetime diagnosis of a psychiatric disorder	Depression (N=16 studies) OR=2.66 (2.14 to 3.30) I^2=57% Anxiety disorder (N=8 studies) OR=3.09 (95% CI: 2.43 to 3.94) I^2=40% Eating disorders (N=11 studies) OR=2.72 (2.04 to 3.63) I^2=20% Post-traumatic stress disorder (N=3) OR=2.34 (1.59 to 3.43) I^2=0% Sleep disorders (N=1) OR=16.17 (2.06 to 126.76) I^2 not applicable Suicide attempts (N=19) OR=4.14 (2.98 to 5.76) I^2=60% Schizophrenia (N=3) OR=1.36 (0.81 to 2.03) I^2=0% Somatoform disorders (N=3) OR=1.90 (0.81 to 4.47)	Authors' conclusion: A history of sexual abuse is associated with an increased risk of a lifetime diagnosis of multiple psychiatric disorders. There was no statistically significant association between sexual abuse and a diagnosis of schizophrenia or somatoform disorders. Reviewer's conclusion: Well conducted systematic review and meta-analysis that found a statistically significant association between sexual abuse and a lifetime diagnosis of depression. This is based on a meta-analysis of 16 studies.

[¥¥] see full text paper for definition

Fergusson 2002, Fergusson 2008, Fiorentine 1999, Frank 1987, Gutner 2006, Harvey 1994, Kolko 2003, Pearce 2008, Plunkett 2001, Rimsza 1988, Spataro 2004, Widom 1999	of studies: Newcastle-Ottawa assessment scale Fixed or variable effects: random effects Heterogeneity: I^2 statistic			I^2=4%	
Study type: Systematic review with meta-analysis **Quality: 1++** **Comments:** Well conducted SR with meta-analysis. Comprehensive search of multiple databases. No language restriction. Unpublished research included. Publication bias assessed by funnel plot and statistical tests – no obvious pub bias present. Methodological assessment good. Sensitivity analysis undertaken. Heterogeneity considered. Subgroup analysis undertaken. Meta-analysis appears appropriate.					

Reference and study design	Studies	Exposure	Outcome Measure	Results	Conclusions
Amado et al. (2015) "Psychological injury in victims of child sexual abuse: A meta-analytic review." Psychosocial Intervention **24**: 49-62 Spain Included studies: Balsam et al. 2010, Bonomi et al. 20008, Briere & Elliot 2003, Brown et al. 1999, Canton-Cortes et al. 2012, Canton-Cortes & Justicia 2008, Carey et al. 2008, Cheasty et al. 1998, Chen et al. 2004a, Chen et al. 2004b, Chen et al. 2006, Chen et al. 2014a, Chen et al. 2014b, Chen et al. 2014c, Comijs et al. 2013, Cortes-Arboleda et al. 2011a, Cortes-Arboleda et al. 2011b, Cutajar et al 2010a, Cutajar et al. 2010b, Doerfler et al. 2009, Dube et al. 2005, Feeney et al. 2013, Feerick & Snow, 2005, Fergusson et al. 2008a, Fergusson et al. 2008b,	Number of studies: 78 Total number of participants in the studies: 19,360 Inclusion criteria: Studies assessed the sequelae of child/adolescent sexual abuse in terms of depression and anxiety internalising variables; studies reporting the effect sizes of child/adolescent sexual abuse, sequelae (in which variables and/or statistics enabled group size, mean and standard deviation of sequelae measurement variables for each group, prevalence, specificity, and sensitivity to be calculated); studies defining the ground truth for classifying participants as victims of child/adolescent sexual abuse or the measure of abuse; and studies providing descriptive data on the sample employed. Exclusion criteria: After contacting the authors, the data required was not facilitated for the computation of the effect sizes, studies with data errors (e.g., lack of consistency in group size	Child sexual abuse	Weighted effect size (Cohen's d; r), Odds Ratio of general sequelae (i.e., internalising injury), depression and anxiety	**Child sexual abuse and general sequelae (i.e., internalising injury)** k=91; r = .28, 95% CI: .27 to .29 Victims of child/adolescent sexual abuse 70% higher probability of internalising injury than non-victims Injury = 34% **Child sexual abuse and Depression** k=87; r = .24, 95% CI: .23 to .25 66% higher probability of internalising injury among victims versus non-victims Injury = 28% **Child sexual abuse and Anxiety** k=62; r = .26, 95% CI: .25 to .27 68% higher probability of internalising injury among victims versus non-victims Injury = 31% **Child sexual abuse and major depressive disorder:** OR = 3.25; r = .26; 95% CI: .25 to .27	Author's conclusions: The results of the study support a significant and positive effect of child/adolescent sexual abuse on mental health (of a small to large size and generalizable). Reviewer's conclusions: This meta-analysis presents evidence that suggests child/adolescent sexual abuse is significantly associated with depression, including major depressive disorder and dysthymia.

Fergusson et al. 2008c, Fergusson & Dacey 1997, Fergusson et al. 2013, Fondacaro et al. 1999, Frias et al. 2014, Godbout et al. 2013, Gudjonsson et al. 2011, Haj-Yahia & Tamish 2001, Henderson et al. 2002, Hobfoll et al. 2002, Jonas et al. 2011, Kendler et al. 2000, Kent & Walker 1998, Kugler et al. 2012, Kuo et al. 2011, Lamoreux et al. 2012, Leck et al. 2006, Li et al. 2012, Linskey & Fergusson 1997, López et al. 1995, Lumley & Harkness 2007, Lutrek et al. 2004, MacMillan et al. 2001a, MacMillan et al. 2001b, Manion et al. 1998a, Mannion et al. 1998b, Mapp 2006, Mchichi Alami & Kadri 2004, McLean et al. 2014, McLeer et al. 1998, Merril 2001, Messman-Moore et al. 2000, Meston et al. 2006, Meyerson et al. 2002, Miller 2006, Molnar et al. 2001a, Molnar et al. 2001b, Mullen et al. 1996, Musliner & Singer 2014, Nelson et al. 2002a, Nelson et al. 2002b, Newcomb et al. 2009a,	throughout the study not attributable to missing data), studies failing to guarantee the mutual exclusion of the victim of sexual abuse condition from other forms of maltreatment (e.g., studies undertaking a single comprehensive analysis of victims of sexual and physical abuse or neglect). Databases used: Web of Science, Core Collection, Current Contents, Medline, Scielo, KCI-Korean + meta-search engines: Google, Yahoo, Google Scholar (1995-2015) Description of the methodological assessment of studies: not reported Fixed or variable effects: not reported Heterogeneity: not discussed			Injury = 31% **Child sexual abuse and dysthymia:** OR = 6.59; r = .38; 95% CI: .37 to .39 Injury = 46% **Child sexual abuse and generalised anxiety:** OR = 5.12l; r = .34, 95% CI: .33 to .35 Injury = 41% **Child sexual abuse and specific phobia:** OR = 7.62; r = .41; 95% CI: .40 to .42 Injury = 49% **Child sexual abuse and social phobia:** OR = 4.85; r = .34; 95% CI: .33 to .35 Injury = 40% **Child sexual abuse panic disorder:** OR = 5.60; r = .36; 95% CI: .35 to .37 Injury = 43%	

Newcomb et al. 2009b, Offen et al. 2003, Peleikis et al. 2004, Peleikis et al. 2005, Pérez-Fuentes et al. 2013, Portegijs et al. 1996, Rich et al. 2005a, Rich et al. 2005b, Schaaf & McCanne, 1998, Silverman et al. 1996, Spertus et al. 2003, Steel et al. 2004, Subica 2013, Sun et al. 2008, Swanston et al. 2003, Thomas et al. 2011, Thompson et al. 2003, Trowell et al. 1999, van Vugt et al. 2013, Villarroel et al. 2012, Widom et al. 2007, Young et al. 2007a, Young 2007b.				**Gender** Female and male child/adolescent sexual abuse victims more likely to develop depression (ORs=5.40 and 1.44, respectively) and anxiety disorders (ORs =2.43 and 1.66, respectively) than non-victims. For depression and anxiety, the effect size found in females was significantly higher than for males (q_s=0.388, p <.05 and q_s=0.104, p <.05, respectively), with results generalizable for females but not for males (effects of the moderators could not be assessed for males due to the very small k). Injury in anxiety for female and male victims was 2.26 and 1.73 times greater than for non-victims, respectively. For depression: 2.26 and 1.60, respectively. **Type of abuse** Injury derived from abuse with penetration was significantly higher than injury in the no-contact abuse condition for depression (q_s=0.093, p <.05) and anxiety (q_s=0.092, p <.05).	

Study type: Meta-Analysis

Quality: 1-

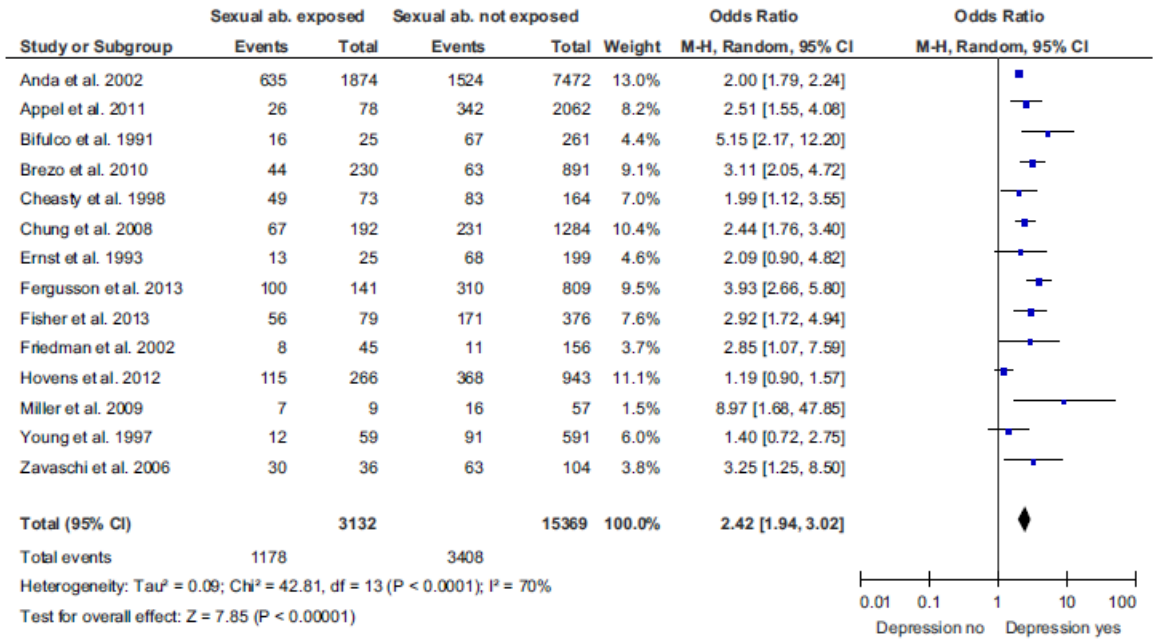
Comments: Adequately conducted meta-analysis. Multiple databases searched. Subgroup analysis undertaken.

Reference and study design	Studies	Exposure	Outcome Measure	Results	Conclusions
Mandelli et al. 2015 "The role of specific early trauma in adult depression: A meta-analysis of published literature. Childhood Trauma and Adult Depression". European Psychiatry **30**: 665-680. Italy Included Studies: Anda et al. 2002, Appel et al. 2011, Bifulco et al. 1991, Bifulco et al. 2002, Brezo et al. 2010, Brown et al. 2007, Chapman et al. 2004, Cheasty et al. 1998, Chung et al. 2008, Comijs et al. 2007, Elzinga et al. 2011, Ernst et al. 1993, Fergusson et al. 2013, Fisher et al. 2013, Friedman et al. 2002, Hovens et al. 2012, Infrasca 2003, LaNoue et al. 2012, Miller et al. 2009, Polanczyk et al. 2009, Ritchie et al. 2009, Tyrka et al. 2009, Young et al.	Number of studies: 26 Total number of participants in the studies: not reported Inclusion criteria: Studies had to assess both depression and childhood trauma (such as sexual, physical, emotional abuse, neglect, early loss and parental separation) by means of at least an evaluation tool or clinical interview; Studies published in English. Participants aged at least 18 years, Only studies reporting the number of exposed and non-exposed to stressful child events and number of subjects with depression were considered for the analysis Exclusion criteria: Not stated Databases used: PubMed, ENBASE, PsycINFO, ISI Web of Science + manual reference list searches Description of the methodological assessment of studies: adapted version of Newcastle-Ottawa Scale Fixed or variable effects: not conducted	Childhood trauma (Including sexual, physical, emotional abuse, neglect, early loss and parental separation)	Odds Ratio (OR) of depressive disorders in adulthood.	Sexual abuse and depression: OR = 2.42 Heterogeneity: I^2 = 70% Emotional abuse and depression: OR = 2.78 Heterogeneity: I^2 = 91% Neglect and depression: OR = 2.75 Heterogeneity: I^2 = 92% Domestic violence and depression: OR = 2.06 Heterogeneity: I^2 = 37% Physical abuse and depression: (OR = 1.98) Heterogeneity: I^2 = 42% Parental divorce or separation (OR = 1.56 [1.09–2.22], Z = 2.46, P = 0.01, I^2 = 82%) and hospitalization in childhood (OR = 1.50 [1.04–2.17], Z = 2.15; P = 0.03; I^2 = 0%) were associated to depressive risk to a lower extent. Loss of a loved one was not associated to depressive risk (OR = 1.69 [0.71–4.02], Z = 1.20 P = 0.23, I^2 = 94%)	Author's conclusions: Early adversity increases the risk of development of depressive symptom with ORs ranging from 2.00-3.00. Emotional, sexual and physical abuse and domestic violence risk are associated with depressive risk. Neglect is the strongest risk factor for developing depression/depressive symptoms. Reviewer's conclusions: This meta-analysis indicates that the odds of people with childhood sexual abuse having depression in adulthood is significantly greater than people with no childhood sexual abuse. Results on sexual abuse were significantly affected by publication bias.

1997, Zavaschi et al. 2006	Heterogeneity: χ^2 test; I^2 statistic			**Community vs. clinical samples** Sexual abuse showed a relevant impact on depressive risk in both clinical and community samples studies.	

Fig. 1 Depression in adults exposed and not-exposed to sexual abuse in childhood

c) Sexual abuse



Study type: Meta-analysis

Quality: 1-

Comments: Well conducted meta-analysis. Comprehensive search of multiple databases. Unpublished research included. Publication bias assessed by Egger's test – results on sexual abuse were significantly affected by publication bias (B =3.86; p=0.04). Methodological assessment good. Sensitivity analysis undertaken. Heterogeneity considered.

Reference and study design	Studies	Exposure	Outcome Measure	Results	Conclusions
Martinez et al. (2014). "Symptom variation on the trauma symptom checklist for children: A within-scale meta-analytic review". Journal of Traumatic Stress **27**(6): 655-663. United States Included Studies: not explicitly stated.	Number of studies: 74 Total number of participants in the studies: 14,867 Inclusion criteria: Studies that provided raw (US or international) or T scores (US only) for at least one TSCC subscale; Included participants exposed to a traumatic event; Included youth ages 8-16 years; Published in a peer-reviewed journal in English; Had a sample size of 15 or greater. Exclusion criteria: Not stated Databases used: Social Sciences Citations Index, PsycINFO, PubMed, Published International Literature on Traumatic Stress Description of the methodological assessment of studies: not reported Fixed or variable effects: random effects Heterogeneity: Q statistic and I^2 statistic	Trauma (sexual abuse, child abuse/neglect, community violence, complex trauma)	Trauma Symptom Checklist for Children (TSCC; Briere, 1996): Posttraumatic stress, anxiety, depression, anger, dissociation (t-scores)	**U.S versus international samples** International samples of youth reported greater posttraumatic stress ($Q(1, 63) = 6.90$, $p = .009$), anxiety ($Q(1, 57) = 8.43$, $p = .004$), and depressive symptoms ($Q(1, 53) = 6.36$, $p = .012$) than youth in U.S. samples. No differences found for anger or dissociation **Sexual abuse vs. other trauma types** Sexual abuse associated with higher depressive symptoms than child abuse/neglect ($t(23) = 2.95$, $p = .007$), community violence ($t(26) = 4.95$, $p < .001$), or complex trauma ($t(23) = 3.63$, $p = .001$). Sexual abuse associated with higher anxiety than child abuse/neglect ($t(20) = 3.53$, $p = .002$), community violence ($t(25) = 5.76$, $p < .001$), and complex trauma ($t(21) = 3.69$, $p = .001$). Sexual abuse associated with higher symptoms of posttraumatic stress than child abuse/neglect ($t(19) = 3.19$, $p = .005$), community violence ($t(24) = 5.47$, $p < .001$), and complex trauma ($t(20) = 3.66$, $p = .002$).	Author's conclusions: A substantial percentage of youth exposed to a traumatic event do not develop clinically significant levels of posttraumatic symptomology. Youth who experienced sexual abuse displayed the greatest symptoms of depression, posttraumatic stress, anxiety, and dissociation compared to exposure to community violence. Older age was associated with higher anxiety, posttraumatic stress, depression and dissociation in sexual abuse samples. Reviewer's conclusions: This meta-analysis presents evidence suggesting that sexual abuse is associated with higher depression than child abuse/neglect, community violence, and complex trauma. In addition, older age is associated with higher depression, and a higher sample representation of ethnic minorities is associated with lower depression.

				No significant differences across trauma types for dissociative or anger symptoms. **Gender** Significant positive relationships between the percentage of females in a sample and posttraumatic stress (β = .51, Q(1, 68) = 24.62, p < .001), anxiety (β = .50, Q(1, 60) = 22.53, p < .001), depression (β = .52, Q(1, 56) = 18.36, p < .001), and dissociation (β = .35, Q(1, 59) = 8.48, p = .004). No significant relationship was found between gender and anger symptoms. Among sexual abuse samples, female representation was associated with higher posttraumatic stress (β = .62, Q(1, 17) = 10.88, p = .001), anger (β = .47, Q(1, 18) = 4.69, p = .030), and dissociation (β = .53, Q(1, 18) = 8.03, p = .005), but not anxiety or depression. **Age**	

				Age not significantly associated with any TSCC subscale. Among sexual abuse samples, older age associated with higher posttraumatic stress (β = .60, Q(1, 15) = 8.30, p = 004), anxiety (β = .57, Q(1, 17) = 8.96, p < .003), depression (β = .51, Q(1, 16) = 6.00, p = .014), and dissociation (β = .50, Q(1, 16) = 5.78, p = .016). No significant interaction found between age and sexual abuse for anger symptoms. **Ethnicity** Higher sample representation of ethnic minorities (β = −.40) associated with lower depression (Q(1, 33) = 6.27, p = .012). No significant relationships between ethnic minority representation and other subscales found. No significant interactions found between ethnic minority representation and trauma type for any TSCC subscale.	

Study type: Meta-Analysis

Quality: 1+

Comments: Adequately conducted meta-analysis. Multiple databases searched. Heterogeneity considered. Subgroup analysis undertaken. No formal methodological assessment.

10. Appendix 2: Excluded Study Table

The 57 studies excluded from this report are presented in the table below. These studies had the term “review”, “systematic review”, and/or “meta-analysis” stated in its abstract.

An additional 1000+ articles were identified by the literature searches conducted. However, these articles were not included in this report based on the exclusion criteria (i.e., non-English studies, animal or laboratory studies, narrative reviews, letters or editorials; study designs other than systematic review or meta-analysis).

Reference	Reason for exclusion
Alexander 2007	Review, not systematic review or meta-analysis
Al-Modallal et al. 2008	Focus not on childhood sexual abuse
Beghi et al. 2013	Literature review; Focus not on depression and childhood sexual abuse
Bolen & Gergely 2015	Meta-analysis; Focus not on depression and childhood sexual abuse
Campbell et al. 2009	Focus not on childhood sexual abuse
Capaldi et al. 2012	Systematic review; Focus not on depression
Colson et al. 2013	Meta-analysis; Focus on perpetrators of sexual abuse not victims
de Abreu et al. 2009	Focus not on depression and childhood sexual abuse
Desrochers et al. 2008	Critical review; Focus not on depression and childhood sexual abuse
Dillon et al. 2013	Review; Focus not on childhood sexual abuse
Douglas et al. 2011	Review and case study
Dvir et al. 2014	Review, not systematic review or meta-analysis
Draper et al. 2008	Not a review, systematic review, or meta-analysis
Essaba et al. 2015	Review of cases; Focus not on depression
Fang et al. 2015	Systematic review; Focus not on depression or childhood sexual abuse
Fliege et al. 2009	Systematic review; Focus not on depression
Foy et al. 2012	Focus not on depression and childhood sexual abuse
Franko et al. 2006	Focus not on depression and childhood sexual abuse
Gillies et al. 2013	Review; Focus not on depression
Garcia 2010	Focus not on depression and childhood sexual abuse
Gray 2008	Dissertation
Halfon et al. 2013	Review; Focus not on depression and childhood sexual abuse
Harms 2013	Focus not on causation. Dissertation
Hassan & Ali 2011	Literature review; Focus not on childhood sexual abuse

Hauser et al. 2013	Systematic Review: Focus not on depression and childhood sexual abuse
Hillberg et al. 2011	Systematic review; Focus is on methodology quality – not about causation
Hulme 2007	Integrative review
Hyde 2007	Not a review, systematic review, or meta-analysis
Jacobson & Gould 2007	Critical review; Focus not on depression and childhood sexual abuse
Kirkcaldy 2006	Review; Focus not on depression
Lalor & McElvaney 2010	Focus not on depression
Latthe et al. 2006	Systematic review; Focus not on depression
Leeners et al. 2006	Systematic review; Focus not on depression
Macdonald et al. 2012	Focus is on intervention - not about causation
Maguire et al. 2015	Systematic review; Focus not on childhood sexual abuse
Martsolf & Draucker 2005	Focus is on intervention - not about causation.
Matheson et al. 2013	Systematic meta-analysis; Focus not on depression
McCall & Lauridsen-Hoegh 2014	Review; Focus not on depression and childhood sexual abuse
Meewisse et al. 2007	Systematic review and meta-analysis; Focus not on depression
Mikton et al. 2014	Systematic review; Focus not on depression and childhood sexual abuse
Miller et al. 2013	Focus not on depression
Ono et al. 2015	Focus not on depression and childhood sexual abuse
Overton 2006	Dissertation.
Panagakis 2012	Dissertation
Pattison & Harris 2006	Review; Focus is on intervention - not about causation
Regehr et al. 2013	Systematic review; Focus is on intervention - not about causation; also adult rape not childhood sexual abuse
Rhodes 2015	Focus not on depression and childhood sexual abuse. Dissertation
Richa et al. 2014	Focus not on depression and childhood sexual abuse
Sanchez-Meca et al. 2011	Meta-analysis; Focus is on intervention not about causation
Stokes et al. 2015	Review; Focus not on depression
Trask 2009	Focus is on intervention - not about causation. Dissertation
Walsh et al. 2012	Review; Theoretical
Wasserman et al. 2010	Focus not on depression and childhood sexual abuse
Wigham et al. 2011	Systematic review; Focus not on depression and childhood sexual abuse
Wilen 2015	Systematic review and meta-analysis; Focus is on psychosocial intervention – not about causation

Wilson 2010	Literature review
Yuodelis-Flores & Ries 2015	Review; Focus not on depression and childhood sexual abuse

11. Appendix 3: Heterogeneity and the I^2 statistic

Heterogeneity is the variation between the results of a set of studies. It can be clinical, methodological and/or statistical. Clinical heterogeneity can be caused by differences between the studies with respect to participants, interventions, and/or outcome.

Methodological heterogeneity can be caused by differences between studies regarding design and/or conduct e.g. blinding, allocation concealment etc.

Statistical heterogeneity is the excessive variation in the results of studies above that expected by chance. Statistical heterogeneity is identified graphically and by using a statistical test e.g. the "I^2" statistic.

The degree of heterogeneity measured by the I^2 statistic assists determination of whether a meta-analysis is appropriate and, if so, what model to use in pooling the results.

I^2 statistic	**Suggested interpretation from Matheson (2013)**
0-40%	Might not be important
50-75%	May be important
>75%	Should be regarded as considerable

12. Appendix 4: Bradford Hill's Criteria of Causation

A suggested guide to assessing the likelihood of causation

- **Strength of the association**: A small association does not mean that there is not a causal effect, though the larger the association, the more likely that it is causal.
- **Consistency of the association**: Consistent findings observed by different persons in different places with different samples strengthen the likelihood of an effect.
- **Specificity**: Causation is likely if a very specific population at a specific site and disease with no other likely explanation. The more specific an association between a factor and an effect is, the bigger the probability of a causal relationship.
- **Temporality**: The effect has to occur after the cause (and if there is an expected delay between the cause and expected effect, then the effect must occur after that delay).
- **Biological gradient**: Greater exposure should generally lead to greater incidence of the effect. However, in some cases, the mere presence of the factor can trigger the effect. In other cases, an inverse proportion is observed: greater exposure leads to lower incidence.
- **Plausibility:** A plausible mechanism between cause and effect is helpful (but Hill noted that knowledge of the mechanism is limited by current knowledge).
- **Coherence**: Coherence between epidemiological and laboratory findings increases the likelihood of an effect. However, Hill noted that "... lack of such [laboratory] evidence cannot nullify the epidemiological effect on associations".
- **Experiment**: "Occasionally it is possible to appeal to experimental evidence".
- **Analogy**: The effect of similar factors may be considered.

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