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Review

The role of specific early trauma in adult depression: A meta-analysis of published literature. Childhood trauma and adult depression

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ABSTRACT

Background: A large literature has long focused on the role of trauma in childhood and risk for psychological disorders in adulthood. Despite several studies performed, to date, it is not clear which weight have different childhood stressors specifically on the risk for depression in adult life. In the present study, we performed a meta-analysis of the literature in order to assess the effective role of childhood traumas as risk factor in the onset of depressive disorders in adults.
Methods: Previously published papers investigating the exposure to childhood trauma and their association with depression in adult subjects were retrieved in literature through common databases. Meta-analysis was conducted by the RevMan software. The quality of studies was evaluated by an adapted version of the New-Ottawa Quality Assessment Scale; bias publication was evaluated by the Egger's test. Meta-regression analysis was employed to detect potential confounders and/or moderating variables. Finally, a sensitivity analysis was post-hoc performed to control for potential confounders.
Results: Emotional abuse showed the strongest association with depression (OR = 2.78) followed by neglect (OR = 2.75) and sexual abuse (OR = 2.42). Significant associations were also found for domestic violence (OR = 2.06) and physical abuse (OR = 1.98). Nevertheless, in post-hoc analysis, emotional abuse and neglect showed the strongest associations with depression as compared to other kinds of child trauma.
Conclusions: These findings support the role of neglect and emotional abuse as significantly associated to depression. Sexual/physical abuse or violence in family may be unspecific risk factors for mental disturbance. Other kind of trauma may play a less relevant role in risk of adult depression, though they should be not underestimated.

1. Introduction

There is a growing awareness that childhood trauma is a relevant risk factor for developing depressive disorders in adulthood. Depression may occur after exposure to acute or chronic life stress, particularly in persons having experienced stressors in childhood: evidence has been reported that early traumatized individuals may be more sensitized to the adverse effects of subsequent stressors [63], thereby increasing the likelihood of developing stress-related disorders [54].

Clinically depressed individuals generally report more severe difficulties in childhood than those who do not suffer from depression [48,37,21,102]. These difficulties may include sexual, physical and emotional abuse, neglect, separation from a parent, or mental illness in a parent. Childhood trauma may exert deleterious effects on the development of children and adolescents, with long-term consequences that often persist in adulthood [55,75,56]. Some studies have also reported that a problematic childhood may increase the risk for the onset of depression in young age [41,42,18,67,36].

Though in the last decades the scientific research has been much focused on biological risk factors, driven by the development of new and advanced methods of molecular investigation and techniques of structural and functional analysis of brain structures and systems, such advance has lead to new insights which are renewed the interest in environmental risk factors, particularly related to the first years of life. The discovery of epigenetic mechanisms, i.e. mechanisms that alter the expression of genes depending on external environmental conditions, has lead to the

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exploration of biological and environmental interactions. This has resulted in an renewed interest in the role of the environment in etiology of depression, especially early environmental adversity [37,6,1].

The Adverse Childhood Experiences (ACE) Study (http://acestudy.org/) is one of the largest investigation aimed to assess the association between childhood maltreatment and health outcomes. It started in 1995 and it has involved more than 17,000 participants. This study has found that almost two-thirds of their study participants reported at least one child adversity, and more than one out of five patients reported three or more child adversities with long-term consequences, including major psychiatric disorders. The World report on violence and health (2002) (http://www.who.int/violence_injury_prevention/violence/world_report/en/) and the WHO Consultation on Child Abuse Prevention [95] identified four types of child maltreatment: sexual abuse, physical abuse, emotional and psychological abuse and neglect.

These different types of child stressors have been the focus of several studies. A large body of research has focused especially on the relationship between child sexual abuse and the onset of psychiatric disorders in adulthood [48,41,42,10,65,14,23,12]. Much evidence suggests that having been sexually abused in childhood may increase the likelihood to develop a broad range of symptomatology such as depression, anxiety, low self-esteem, guilt, fear, sexual difficulties, suicidality and self-harm behaviour. Prevalence studies confirm that there may be a strong association between child sexual abuse and development of adult depression [48,18,10,65,40,62]. Moreover a history of child sexual abuse increases significantly the risk of chronic depression in adults [97], suicidal behaviour and impulsivity levels [17]. The deleterious effect of child sexual abuse get worse when other negative experiences occur, such as parental indifference, psychological and/or physical abuse and poor parental care [57] and, frequently, child sexual abuse occurs within the context of a disturbed familial and domestic environment [74].

In light of this, early evidence has led to explore other adverse childhood experiences such as emotional abuse, physical maltreatment and emotional/physical neglect [37,6,26,5,32,76]. Several studies have found that, similarly to sexual abuse, physical abuse occurs more frequently in a context of other form of maltreatment and it is associated to the risk of psychological disturbances in adulthood [47,90,96].

The research demonstrates that psychological/emotional abuse is associated with increased risk for lifetime depressive disorders as well [21,12,5,47]. Moreover, psychological/emotional abuse seems enhancing the risk of comorbidity and chronicity in adult depression [59]. Psychological trauma may have tremendous negative impact on mental health as it can affect child's social, emotional, neurological, physical and sensory development, and more severely in children experiencing multiple and/or chronic episodes of emotional abuse [46]. This form of abuse is harder to identify because, differently from physical abuse, the marks are left on the inside instead of the outside [49].

Neglect, another type of maltreatment, have been associated with many negative effects on mental health functioning throughout the lifespan. As regard adult patients affected by major depression, they reported more child neglect than healthy individuals and child neglect has been reported increasing the likelihood to have a early onset of depression [11] and more depressive episodes [9].

According to such evidence, early environment may play a pivotal role in the etiology of depression, as well as other mental disorders, since traumatic experiences during developmental stages may alter the structure and functioning of brain systems, with enduring consequences in adulthood. A focused investigation on the role of childhood trauma and depression may therefore help to deepen the current knowledge in terms of its effect on psychological and emotional development, underlining biological mechanisms, specific environmental risk factors for depression and their interaction with other biological and individual risk factors (for example personality, life experiences later in life, social support, and so on). However, to date, evidence about the type of child adversity that confers a high risk for depressive disorders is relatively vague, because most studies focused on specific types of trauma or, at the opposite, to unspecified and mixed child adversity.

1.1. Objectives

The aim of this study is to clarify the role of different child traumatic experiences in the risk for depression. We specifically aimed to test the exclusive and separate contribution of sexual, physical and emotional abuse, neglect, significant loss and other family adversity to major depression.

2. Methods

2.1. Criteria for studies' selection and inclusion

2.1.1. Types of studies

In the present study, we included the studies that evaluated depression in adulthood taking into account childhood traumas such as sexual, physical, emotional abuse, neglect, early loss and parental separation. To be included in the meta-analysis, studies should assess both depression and childhood trauma by means of at least an evaluation tool or clinical interview.

2.1.2. Types of participants

Adult men and women of any race, ethnic or religious group, socio-economic status and aged at least 18 (adults).

2.1.3. Types of outcome measures

The presence of depression in adulthood assessed by means of clinical or structured interview or self-report questionnaires. The most frequently employed method to diagnose depression was on the basis of the Diagnostic and Statistical Manual criteria (DSM-III-R, DMS-IV, DSM-IV-TR) [2–4]. Most frequently employed diagnostic interviews were the Structured clinical interview for DMS (SCID-I) [88], the Composite International Diagnostic Interview (CIDI) [100], the Diagnostic Interview Schedule (DIS) [84], the MINI International Neuropsychiatric Interview (MINI) [87], the Present State examination (PSE) [98] or the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) [99]. In some studies diagnosis of depression was based on unstructured clinical interviews or self rated scales such as the Beck Depression Inventory (BDI) [8], the Center for Epidemiologic Studies Depression Scale (CES-D) [80], the Hamilton rating scale for Depression (HAMD) [52], the General Health Questionnaire (GHQ) [50], the Inventory of Depressive Symptomatology (IDS) [86], the instrument developed for Medical Outcomes Study [20], the Symptoms Checklist 90 Revised (SCL-90 R) [29] and the Patient Health Questionnaire (PHQ) [89] (for details see Depression Measures in Table 1).

2.1.4. Search methods for identification of studies

Studies investigating childhood events in depression were searched in common database such as PubMed, ENBASE, PsycINFO, ISI Web of Science through mesh keywords such as "childhood", "child", "sexual abuse", "physical abuse", "emotional abuse", "childhood maltreatment", "neglect", "trauma", "early adversity", "depression", "depressive disorder" "major depressive disorder"

Table 1
Childhood stressor and characteristics of included studies.

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
Sexual abuse	It consists of exposing or involvement of a child in sexual activities that may also include non-sexual contact, such as showing children pornography or using children to product pornographic material, exposing children to a sexual intercourse. The physical contact may include fondling children's genitals, oral-genital contact, using objects for vaginal or anal penetration, vaginal or anal intercourse. Child, dependent and develop - mentally immature, is not fully able to understand and to give informed consent or to refuse what it is exposed or involved	[10]	Retrospective population study (2 follow-up); London 286 working class-mothers, European or Afro-Caribbean, age 18–50 years	Semi-structured interview (before 17 year)	PSE	★★★	9% of women reported sexual abuse, of these 64% were depressed. Only 5% of sexual abuse was related to the cases of depression in the whole sample, if compared with 14% when accompanied by other negative early experience and 24% for these latter factors alone
		[40]	Longitudinal cohort study (10 years); Zurich 421 young adults, analysis on female only, age 30 (m)	Interview (before 16 year)	SCL-90 R; SPIKE (structured interview)	★★★★	11.5% of women reported sexual abuse, of these 52% had depression. Sexual abuse alone was not associated with depression but that family strain was related to adult depression
		[101]	Retrospective clinical population study; Michigan, 680 adults (mood and anxiety disorders), 67% female	Clinical interview	Clinical interview, SCID	★★★	12% of patients with major depression reported sexual abuse. Sexual abuse was less common than emotional and physical abuse. Sexual abuse appeared to influence the age of onset
		[23]	Retrospective case-control study; Dublin and a small town of Ireland, 237 women (depressed group and control group), age 18–87 years	Semi-structured interview; social problems questionnaire (Corney and Clare, 1985) (before 16 years)	GHQ; BDI; SADS (Endicott, 1978; Endicott and Spitzer, 1979)	★★★★	30.8% of women reported sexual abuse, of these 67% were depressed. There was a positive association between severe sexual abuse and depression (100% with penetration and 86% with attempted penetration)
		[5]	Retrospective Cohort study; San Diego 9346 adults, 54% female, age 56.6 ± 15.6 (m ± sd)	Questionnaire (before 18 years)	Screening instrument developed for Medical Outcomes Study (self-report)	★★	20% reported sexual abuse, of these 33.9% were depressed. Depressive disorders among adult with alcohol-abusing parents seem to be due to the greater likelihood of having had adverse childhood experiences (ACE)
		[45]	Retrospective clinical population study; 201 adults (anxiety disorders, major depression and chronic schizophrenia), 70% female; age 39 ± 13.0 (m ± sd).	LHQ (before 16 years)	SCID; BDI	★★	Among depressed patients, 43% reported sexual abuse.
		[102]	Retrospective case-control study; Porto Alegre, Brazil 140 adults, depressed group and control group, 93% female, age 46.5 ± 11.7 (m ± sd)	Family Experience Interview	M.I.N.I 5.0	★★★★	Patient with depression reported sexual abuse in 32.3% of the cases against 12.8% of controls, with significantly higher rates in manic patients. The association between sexual abuse and depression remained significant even considering potential confounding variables
		[25]	Retrospective cohort study; Philadelphia 1476 young pregnant women with low-income and low-education, African American, 75% single, age 24 ± 6 (m ± sd)	Structured interview (before 16 years)	CES-D 20-item scale	★★	13% of women reported sexual abuse, of these 35% was depressed. Sexual abuse was frequent among those lacking a positive maternal relationship and it was associated with depressive symptoms
		[73]	Retrospective case-control study; 66 adults depression group and control group, 57,6% female and age 38.9 ± 15.15 (m ± sd)	Semi-structured interview (before 15 years)	SCID; BDI; HAMD	★★★	Patients with major depression reported sexual abuse in 30.4% of the cases.
		[16]	Longitudinal cohort study (22 years); Quebec 1121 adults mean age 27.3	ACE Study Questionnaire (before 18 years)	DIS	★★★	20.5% of the subjects reported sexual abuse. Of these 19.1% were depressed

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
		[7]	Retrospective population study; German 2157 Caucasian adults, age 55.8 ± 13.8 (m ± sd), 52.7% female	CTQ	BDI-II; M-CIDI	★★★	3.6% adults reported sexual abuse; of these 33.3% were depressed.
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety and depressive disorders), age 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire (before 16 years)	CIDI; LCI (Lyketsos et al., 1994); IDS	★★★★	22.0% of the subjects reported sexual abuse; of these 43.2% were depressed.
		[43]	Longitudinal cohort study, 1265 New Zealand assessed at birth, 4 months, 1 year, annually to age 16,18, 21, 25, and 30. Analyses on sample of 950 adults, age 30 (m)	Self-report interview (before 16 years)	Structured interview using questionnaires based on CIDI	★★★	95.2% of those exposed to severe sexual abuse reported at least one mental health problem in adulthood.
		[44]	Retrospective case-control study; 455 adults depression group and control group, 66% female, age 46.3 ± 11.04 (m ± sd)	CTQ	SCAN; BDI	★★★	Depressed subjects reported 19% of moderate/severe sexual abuse as compared to 6.6% of unaffected controls.
Physical abuse	It is a physical harm that a child undergo from his/her caregiver; it is the most evident form of abuse and it may consist of hitting, pinching, kicking, biting, burning, poisoning, suffocating a child. The injury may result from inappropriate or excessive physical discipline	[101]	Retrospective clinical population study; Michigan, 680 adults (mood and anxiety disorders), 67% female	Clinical interview	Clinical interview, SCID	★★★	Patients with major depression reported 20% of physical abuse. Physical abuse was more common than sexual abuse, when physical abuse was associated with emotional abuse
		[5]	Retrospective Cohort study; San Diego 9346 adults, 54% female, 56.6 ± 15.6 (m ± sd)	Questionnaire (before 18 years)	Screening instrument developed for medical outcomes study (self-report)	★★	30.1%of the subjects reported physical abuse. Of these 32.5% were depressed.
		[45]	Retrospective clinical population study; 201 adults (anxiety disorders, major depression and chronic schizophrenia), 70% female; age 39 ± 13.0 (m ± sd)	LHQ (before 16 years)	SCID; BDI	★★	Among depressed patients, 40% reported physical abuse
		[102]	Retrospective case-control study; Porto Alegre, Brazil 140 adults, depressed and control group, 93% female, age 46.5 ± 11.7 (m ± sd)	Family Experience Interview	MINI 5.0	★★★★	Patient with depression reported physical abuse in 60.2% of the cases against 38.3% in the control group, with significantly higher rates in manic patients. The association between physical abuse and depression remained significant even considering potential confounding variables
		[25]	Retrospective Cohort study; Philadelphia 1476 young pregnant women, low-income and low-education, African/ American, 75% single, age 24 ± 6 (m ± sd)	Structured interview (before 16 years)	CES- D 20- item scale	★★	52% of the subjects reported physical abuse. Of these 25% were depressed. ACEs were related to depressive symptoms in a dose-response relationship
		[73]	Retrospective case-control study; 66 adults depression group and control group, 57.6% female, age 38.9 ± 15.15 (m ± sd)	Semi-structured interview (before 15 years)	SCID; BDI; HAMD	★★★	Patients with major depression reported physical abuse in 26.1% of the cases.
		[16]	Longitudinal cohort study (22 years); Quebec 1121 adults mean age 27.3	Revised Conflict Tactics Scales	DIS	★★★	28.2% of the subjects reported physical abuse; of these 15% were depressed.

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
		[7]	Retrospective population study; German 2157 Caucasian adults, age 55.8 ± 13.8 (m ± sd), 52.7% female	CTQ	BDI-II; M-CIDI	★★★	4.5% adults reported physical abuse; of these 27.8% were depressed.
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety disorder, depressive disorder), 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire (before 16 years)	CIDI; LCI; IDS	★★★★	18.4% of the subjects reported physical abuse. Of these 49.3% were depressed. Physical abuse was associated with persistent comorbid depressive and anxiety disorders at 2-year follow-up
		[44]	Retrospective case-control study; 455 adults depression group and control group, 66% female, age 46.3 ± 11.04 (m ± sd)	CTQ	SCAN; BDI	★★★	Depressed subjects reported 13.2% of moderate/severe physical abuse against 3.5% in unaffected controls.
Emotional abuse	It is a pattern of behavior or attitude by caregivers that may cause severe adverse effects on child's psychological growth and emotional development. It involves words, actions and indifference that they can include refusing to touch a child or not calling by name, convey to child feeling of worthless, being unloved or inadequate, belittling, criticizing, shaming, ridiculing, insulting or verbally threatening the child. In some case the child may be encouraged to take anti-social behavior or he/she can not be allowed to have normal social relationships with the peers or other adults	[101]	Retrospective clinical population study; Michigan, 680 adults (mood and anxiety disorders), 67% female	Clinical interview	Clinical interview, SCID	★★★	Patients with major depression reported emotional abuse in 34% of the cases. Emotional abuse was often associated with physical abuse. Disturbed family environment appeared to set up the conditions for emotional abuse
		[5]	Retrospective Cohort study; San Diego 9346 adults, 54% female, 56.6 ± 15.6 (m ± sd)	Questionnaire (before 18 years)	Screening instrument developed for Medical Outcomes Study (self-report)	★★	10.8% of the subjects reported emotional abuse; of these 46.1% were depressed
		[12]	Retrospective population study; London 204 women (adult vulnerability, childhood vulnerability and control group), mean age 35	CECA (before 17 years)	PSE; SCAN	★★★★	Psychological abuse was highly related to chronic/recurrent lifetime depression with rates from 83% at marked to 55% at mild levels. Psychological abuse was correlated with neglect and dislike from parent and also with sexual abuse.
		[25]	Retrospective Cohort study; Philadelphia 1476 young pregnant women with low-income and low-education, African American, 75% single, age 24 ± 6 (m ± sd)	Structured interview (before 16 years)	CES-D 20-item scale	★★	27% of the subjects reported verbal hostility. Of these 26.1% were depressed. ACEs were related to depressive symptoms in a dose-response relationship
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% of the subjects were depressed, of these 8.7% reported emotional abuse. The association between emotional abuse and late-life depression was significant
		[7]	Retrospective population study; German 2157 Caucasian adults, age 55.8 ± 13.8 (m ± sd), 52.7% female	CTQ	BDI-II; M-CIDI	★★★	3.6% adults reported emotional abuse; of these 47.4% were depressed
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety and depressive disorders), 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire	CIDI; LCI; IDS	★★★★	32% of the subjects reported psychological abuse; of these 48.8% were depressed. Psychological abuse was associated with persistent comorbid depressive and anxiety disorders at 2-year follow-up and also with more chronicity
		[44]	Retrospective case-control study; 455 adults depression group and control group, 66% female, age 46.3 ± 11.04 (m ± sd)	CTQ	SCAN; BDI	★★★	Depressed subjects reported 35.7% of moderate/severe emotional abuse against 6.6% of unaffected controls

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
NEGLECT	It is characterized by persistent failure of a parent or other significant person to provide to the child basic physical and/or psychological needs. It is an act of omission by a caregiver, which prevents the child's physical or mental health and do not promote an adequate development	[60]	Retrospective clinical population study; La Spezia, Italy 383 (general population, depressed, anxiety disorders)	Semi-structured interview (before 10 years)	MMPI (Dahlstrom et al. 1975)	★★★	36.8% of subjects were depressed; of these 61.1% reported lack of affectivity by the mother
		[19]	Retrospective population study; London 198 women age 20–50 years	CECA (before 17 years)	SCAN	★★★	50.5% of subjects reported mother's rejection and lack of affection. Of these 53% were depressed
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% of the subjects was depressed; of these 6.9% reported neglect. It was found a correlation between neglect and depressive episodes occurring before age 50
		[7]	Retrospective population study; German 2157 Caucasian adults, age 55.8 ± 13.8 (m ± sd), 52.7% female	CTQ	BDI-II; M-CIDI	★★★	16.2% adults reported physical neglect, of these 21.3% was depressed; 12.2% reported emotional neglect, of these 28.4% were depressed
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety disorder depressive disorder), 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire (before 16 years)	CIDI; LCI; IDS	★★★★	48.1% reported emotional neglect, of these 44.5% were depressed. Emotional neglect was associated with persistent comorbid depressive and anxiety disorders at 2-year follow-up and also with chronicity
		[44]	Retrospective case-control study; 455 adults depression group and control group, 66% female, age 46.3 ± 11.04 (m ± sd)	CTQ	SCAN; BDI	★★★	Depressed subjects reported 37% of moderate/severe emotional neglect than 8.3% of unaffected controls. There was no direct association between 5-HTTLPR and depression. Sexual abuse and less physical neglect showed significant interaction with additive and recessive 5-HTTLPR genetic models
Childhood maltreatment	It includes all forms of abuse such as sexual, physical, emotional/psychological abuse, neglect, exploitation that involve a harm or a threat of harm to child's well-being and impairs child's appropriate psychological, physical, emotional and social development	[10]	Retrospective cohort study (2 follow-up); 286 working class-mothers, European or Afro-Caribbean, age 18–50 years	Semi-structured (before 17 years)	PSE	★★★	24.8% of women reported maltreatment (sexual abuse, parental indifference, parental violence and institutional stay) of these 45% was depressed
		[101]	Retrospective clinical population study; Michigan, 680 adults with mood and anxiety disorders, 67% female	Clinical interview	Clinical interview, SCID	★★★	Patients with major depression reported 39% of childhood adversity (emotional, physical and sexual abuse). Childhood abuse was more common in women than men, it influenced the age of onset and the severity of depressive symptoms
		[12]	Retrospective population study; London 204 women (adult vulnerability, childhood vulnerability and control group) mean age 35	CECA (neglect, role reversal, physical, sexual, psychological abuse and antipathy) (before 17 years)	PSE; SCAN	★★★★	Neglect and antipathy from parent were correlated with psychological abuse. Abusive experiences were all individually related to depression and showed a dose-response relationship to chronic/recurrent depression
		[60]	Retrospective clinical population study; La Spezia, Italy 383 (general population, depressed, anxiety disorders)	Semi-structured interview (before 10 years)	MMPI	★★★	36.8% was depressed, of these 51.7% reported verbal or physical abuse by father
		[21]	Retrospective cohort study; San Diego 9460, 54% female, mean age 56.6	Questionnaire (before 18 years)	Screening instrument developed for Medical Outcomes Study (self-report)	★★	ACE showed to have a strong relationship with the risk of lifetime and current depressive disorders in adulthood. Emotional abuse exhibited the strongest relationship with depression among both men and women

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
		[19]	Retrospective population study; London 198 women age with sister 20–50 years	CECA-Q (before 17 years)	SCAN	★★★	57.1% reported childhood maltreatment (antipathy, indifference, supervision/ control, role reversal, companionship, rejection, intrusiveness, lack of affection, lack of concern, physical and sexual abuse) of these 53.1% was depressed
		[27]	Retrospective population study; 1887 elderly adults, age 71.9 ± 8.4 (m ± sd), 51% female	Interview	CES-D	★★★	14.4% reported childhood adversity; of these 37% was depressed
		[77]	Two prospective longitudinal cohort studies; (E-Risk Study) England, 1116 mothers with 5 years old twins, age 39.9±5.86 (m ± sd); (Dunedin Study) New Zealand 1037 children following up 32 years, 49% female	CTQ (E-Risk Study); not specified (Dunedin Study)	DIS	★★ (E-Risk Study); ★★★ (Dunedin Study)	22.4% (E-Risk Study), 30.9% (Dunedin Study) reported childhood maltreatment, of these 26.4% (E-Risk Study), 23.4% (Dunedin Study) was depressed. In the E-Risk Study, the TAT haplotype was associated with significant protection of women exposed to severe maltreatment against developing depression.
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% were depressed, of these 3.3% reported physical and/or sexual abuse
		[92]	Retrospective population study; 129 White not Hispanic adults, mean age 29.4, 60.5% female	CTQ	SCID	★★★	29.5% reported childhood maltreatment, of these 31.6% had depression Variation in the CRHR1 appeared to moderate the effect of childhood maltreatment on cortisol response to the Dex/CRH test
		[81]	Retrospective population study; 1392 African-American adult, low socioeconomic status, 62% female	CTQ	BDI; SCID	★★★★	When was analyzed the interaction of child abuse and 5-HTTLPR on lifetime depression among adults that reported child abuse 48.3% were depressed; when the interaction was analyzed with rs110402 A allele carriers the prevalence for depression was 48.5%
		[39]	Retrospective cohort study (NESDA Study); 1435 adult age 42.2±12.4 (m±sd), 69.3% female	Semi-structured interview (before 16 years)	CIDI	★★★★	57.3% reported childhood abuse of these 62.0% was depressed. In BDNF Met carries, exposure to childhood abuse was associated with reduced serum levels of BDNF, at least in adult with (lifetime) depression without comorbid anxiety
		[66]	Retrospective population study; 210 adults age 47.76 ± 12.13 (m ± sd), 66.2% female	Not specified	PHQ	★★	88% reported at least one category of ACE, the prevalence of depression ranged from 2.4% (1 category) to 50% (8 categories)
		[78]	Retrospective case-control study; 455 adults depression group and control group, 66% female, age 46.3 ± 11.04 (m ± sd)	CTQ	Clinical interview	★★★	Patients with depression reported 81% of child maltreatment, whilst control group reported 32% of child maltreatment. Early maltreatment and adult stressful life events interacted to produce increased risk for depression in adulthood. This association was not affected by 5-HTTLPR allele

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
PARENTAL DIVORCE/ SEPARATION	When parents of child decided to end their marriage or their existing relationship thereby causing the termination of the family as a unit. The time spent with one parent is limited and he/she can be tossed from one house to another	[101]	Retrospective clinical population study; Michigan, 680 adults (mood and anxiety disorders), 67% female	Clinical interview	Clinical interview, SCID	★★★	Patients with major depression reported 43% of parental divorce. Childhood adversity appeared to be linked to parental divorce and psychopathology in a parent set upping the conditions for emotional abuse
		[5]	Retrospective Cohort study; San Diego 9346 adults, 54% female, 56.6 ± 15.6 (m ± sd)	Questionnaire (before 18 years	Screening instrument developed for Medical Outcomes Study (self-report)	★★	21.9% reported parental divorce/separation, of these 30% were depressed. Depressive disorders among adult with alcohol-abusing parents seem to be due to the greater likelihood of having had ACE
		[45]	Retrospective clinical population study; 201 adults (anxiety disorders, major depression and chronic schizophrenia), 70% female; 39 ± 13.0 (m ± sd)	LHQ (before 16 years)	SCID; BDI	★★	Among depressed patients 61% reported parental divorce; there were few significant differences in the incidence of early childhood adverse events among four outpatients groups
		[60]	Retrospective clinical population study; La Spezia, Italy 383 (general population, depressed, anxiety disorders)	Semi-structured interview (before 10 years)	MMPI	★★★	36.8% was depressed of these 50.8% reported parent's marital problems
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% was depressed, of these 6.7% reported parental divorce/ separation
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety and depressive disorders) 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire (before 16 years)	CIDI; LCI; IDS	★★★★	13.6% reported divorce parents of these 40.6% were depressed. Divorce parents (childhood life event) was not associated with a poorer course outcome in adults with depressive disorders
DOMESTIC VIOLENCE	Direct and/or indirect exposure to some form of violence within the domestic environment	[5]	Retrospective Cohort study; San Diego 9346 adults, 54% female, 56.6 ± 15.6 (m ± sd)	Questionnaire (before 18 years)	Screening instrument developed for Medical Outcomes Study (self-report)	★★	12.2% reported violence domestic (battered mother), of these 37% was depressed. Depressive disorders among adult with alcohol-abusing parents seem to be due to the greater likelihood of having had ACE
		[25]	Retrospective cohort study; Philadelphia 1476 young pregnant women, low-income and low-education, African American, 75% single, age 24 ± 6 (m ± sd)	Structured interview (before 16 years)	CES-D 20-item scale	★★	14% reported domestic violence, of these 29% were depressed. ACEs were related to depressive symptoms in a dose-response relationship
LOSS/SEPARATION	Absence of a significant care-taker for a prolonged time. The loss entails the parental death, the departure of a parent because of a serious illness, a new job, incarceration or other reasons	[101]	Retrospective clinical population study; Michigan, 680 adults (mood and anxiety disorders), 67% female	Clinical interview	Clinical interview, SCID	★★★	Patients with major depression reported 24% of separation from a parent
		[45]	Retrospective clinical population study; 201 adults (anxiety disorders, major depression and chronic schizophrenia), 70% female; 39 ± 3.0 (m ± sd)	LHQ (before 16 years)	SCID; BDI	★★	Depressed patients reported 38% of maternal/paternal separation
		[60]	Retrospective clinical population study; La Spezia, Italy 383 (general population, depressed, anxiety disorders)	Semi-structured interview (before 10 years)	MMPI	★★★	36.8% was depressed of these 72.7% reported death of a parent

Table 1 (*Continued*)

Childhood stressor	Definition	Study	Sample	Stressor measure (s)	Depression measure (s)	Quality	Conclusions
		[102]	Retrospective Case-control study; Porto Alegre, Brazil 140 adults, depressed and control group, 93% female, age 46.5 ± 11.7 (m ± sd)	Family Experience Interview	MINI 5.0	★★★★	Patient with depression disorder reported 41.9% of loss events than 38.3% in the control group, the differences were not significant probably because of poor background of families in either groups
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% was depressed, of these 16.4% reported death of a parent
		[59]	Longitudinal cohort study (8 years, 2 follow-up); Netherlands 1209 (general population, anxiety and depressive disorders) 42.1 ± 12.3 (m ± sd); 66% female	Structured interview; The Childhood Trauma NEMESIS Questionnaire (before 16 years)	CIDI; LCI; IDS	★★★★	7.5% reported early parental loss, of these 39.6% was depressed. Early parental loss (childhood life event) was not associated with a poorer course outcome in adults with depressive disorders
Hospitalization	Condition wherein the child is sick and because of illness he/she can't go to the school or he/she is limited in daily activities, or medical condition requires hospitalization for a time that ranges from few days to some months	[45]	Retrospective clinical population study; 201 adults (anxiety disorders, major depression and chronic schizophrenia), 70% female; 39 ± 13.0 (m ± sd)	LHQ (before 16 years)	SCID; BDI	★★	Among depressed patients 40% reported childhood illness; there were few significant differences in the incidence of early childhood adverse events among four outpatients groups
		[83]	Retrospective cohort study (2 follow-up) Montpellier 942 elderly adults, mean age 72, 58% female	Self-report questionnaire	MINI; CES-D	★★★	41.3% was depressed, of these 13.8% reported serious childhood illness

Childhood stressor measures: CECA: childhood experience of care and abuse; CTQ: Child Trauma Questionnaire; LHQ: Life History Questionnaire.
Depression measures: BDI: Beck Depression Inventory; CES-D: Center for Epidemiologic Studies Depression Scale; CIDI: Composite International Diagnostic Interview; DIS: Diagnostic Interview Schedule for Adults; GHQ: 30 item general health questionnaire; HAMD: Hamilton Depression Rating Scale; IDS: 30-item Inventory of Depressive Symptomatology; LCI: Life Chart Interview; M-CIDI: Munich-Composite International Diagnostic Interview; MINI 5.0: Mini International Neuropsychiatric Interview 5.0: MMPI: Minnesota Multiphasic Personality Inventory; PHQ: Patient Health Questionnaire; PSE: Present State Examination; SADS: Schedule for affective disorders and schizophrenia; SCAN: Schedule for Clinical Assessment in Neuropsychiatry; SCID: Structured Clinical Interview; SCL-90-R Symptoms Checklist 90 Revised.

"psychopathology", "mood disorder", "mood depression" and combinations of these keywords. The reference list of the studies was also reviewed in order to detect further studies. Only studies published in English language were considered.

2.1.5. Data collection and analysis

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. Data were analyzed by RevMan [82], with Mantel-Haenszel as statistical method and random effect as analysis model. Odds ratio (OR) and 95% confidence intervals (CI) were calculated as well. These analyses were carried out for types of child stressors divided by category. Meta-regression was performed to control for potential confounders (such as number of females in the different studies, mean age of subjects, quality of the studies) and to estimate their effect on depression estimates (odd ratios).

2.1.6. Assessment of quality of studies

To assess the quality of studies we employed the Newcastle–Ottawa Scale (NOS) [94] for cohort studies. NOS allows assessing the quality of a study according to 3 perspectives: selection, comparability and outcome. "Selection" provides information about representativeness of the exposed cohort (in our case representativeness of the exposed subjects to child trauma or other child negative events), selection of the non exposed cohort, ascertainment of exposure (structured interview or written self-report) and demonstration that the outcome of interest was not present at start of study. "Comparability" is calculated on the basis of the design or analysis. Finally "outcome" ensures assessment of outcome, length of follow-up and its appropriateness. Studies could earn a maximum of one star for each item within the selection and outcome categories, while a maximum of two stars for comparability category. Since most of the included studies were not cohort studies, therefore lacking of a follow-up, the last two items within the outcomes category of the NOS were not considered, so assessment of the quality was based on six items instead of 8. We choose the "cohort" version instead of that for "case-control" studies since the section of "exposure" in the former did not add much information about the quality of the studies we considered, since studies with a good quality in "exposure" was a criterion of inclusion. Further, the "case-control studies" does not include the evaluation of "outcome" (1st item only as stated above), which allow to distinguish studies employing high/low quality assessment of depression.

2.1.7. Heterogeneity

We measured heterogeneity among studies by Chi^2 test for each forms of child adversity. A *P*-value lower than 0.05 indicates significant heterogeneity. The heterogeneity coefficient I^2 indicate that heterogeneity among studies is null or might not be important when ranging between 0–40%, moderate when between 30–60%, substantial when between 50–90% and considerable between 75%–100%.

2.1.8. Publication bias

Publication bias, i.e. a bias with regard to what is more likely to be published, occurs when the publication of research results

depends not just on the quality of the research but on its nature and direction [30]. The effect of this bias is that published studies may not be truly representative of all valid studies undertaken, leading to possible relevant distortions in meta-analyses. Publication bias is usually analyzed by the visualization of the funnel plot, a scatter-plot of treatment/group effect against a measure of the study size [38]. Other than visual examination of the funnel plot, we tested its asymmetry by the Egger's linear regression method [38]. Linear regression is employed to measure funnel plot asymmetry on the logarithm scale of the OR. The normalized standard deviation, defined as the OR divided by its standard error (SE), is regressed on the inverse of SE. Publication bias is considered positive when the intercept in the regression model significantly deviates from 0.

2.1.9. Sensitivity analysis

Post-hoc sensitivity analysis was used to explore the influence of following variables:

- quality of studies (measured with Newcastle – Ottawa Quality Assessment Scale);
- outlier studies, i.e. studies that are not representative of the general population but representative of a selected group of population, such as samples with females only, women with sisters or twins, elderly adults;
- sub-analysis on psychiatric samples only and community samples only.

3. Results

3.1. Studies included

We identified about 261 studies (1991 to May 2014), through electronic database and references list, investigating the association between depression in adulthood and specific child trauma or early life stress. Of these 21 were removed since duplicates studies. A total of 240 articles were selected but 170 were excluded soon after abstract review. Of the remaining 70, 44 were excluded since not meeting the criteria for inclusion (depression in adulthood and specification of childhood adversity exposure). Finally, 26 studies were included in this meta-analysis (Fig. 1). Studies involving general population samples with or without major depression diagnosis, case-only studies (i.e. on affected individuals only) and studies on patients with other psychiatric diagnosis were all considered for the present study. Studies on specific populations, for example women with children only, were considered as well. The characteristics of included studies with type of child stressor investigated are showed in the Table 1. We finally identified 14 studies on sexual abuse, 10 on physical abuse, eight on emotional abuse, six on neglect, 16 on unspecified maltreatment, 6 on parental divorce or separation, six on significant loss, two on domestic violence and two on child prolonged hospitalization. The large part of the included studies was composed by population-based studies, and some of these were longitudinal cohort studies, three were case-control studies and four were "case-only" studies (see Table 1).

3.2. Association between child adversity and adult depression

Overall, studies focused on maltreatment in general (unspecified) confirmed a significant impact on the risk to develop depression in adulthood (OR = 2.80, Z = 7.70, $P < 0.001$), though high heterogeneity among studies ($I^2 = 85\%$). When looking at specific childhood stressors, emotional abuse showed that the strongest association with depression (OR = 2.78), though again strong heterogeneity among studies ($I^2 = 91\%$;) (Fig. 2a). Neglect (OR = 2.75) (Fig. 2b), sexual abuse (OR = 2.42) (Fig. 2c), domestic violence (OR = 2.06) (Fig. 2d), physical abuse (OR = 1.98) (Fig. 2e), were associated to depression in adulthood as well, though with high heterogeneity, with the exception of physical abuse ($I^2 = 42\%$)

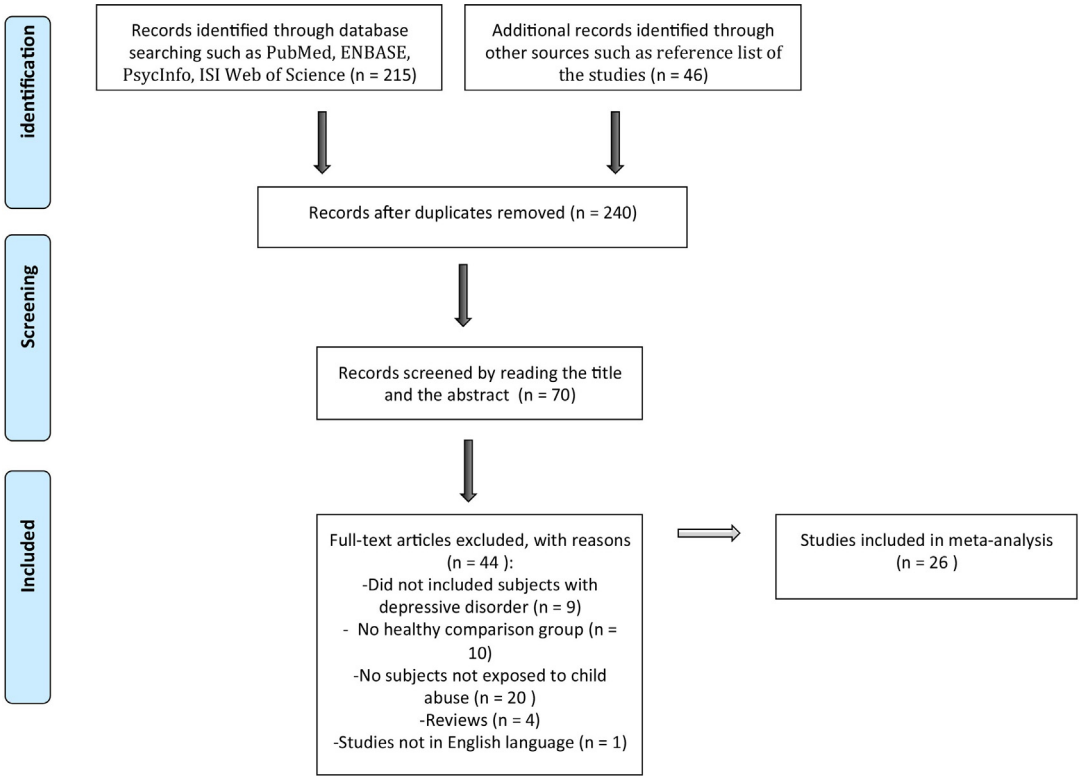
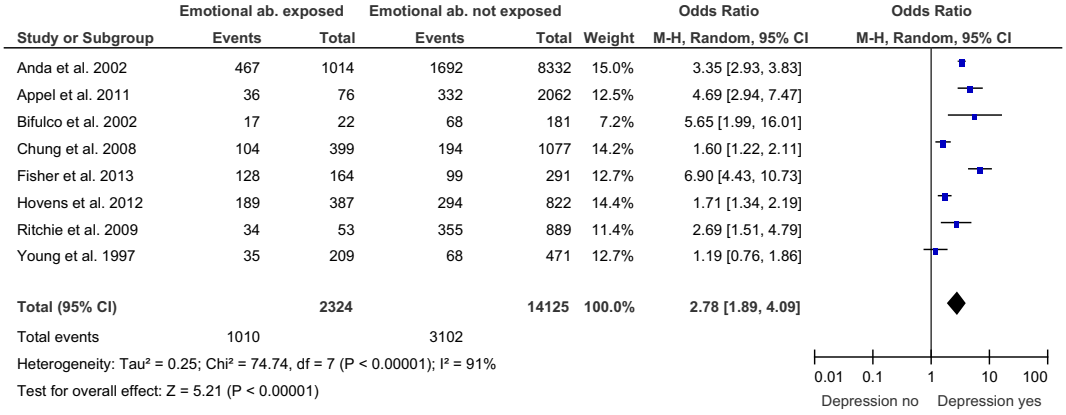


Fig. 1.

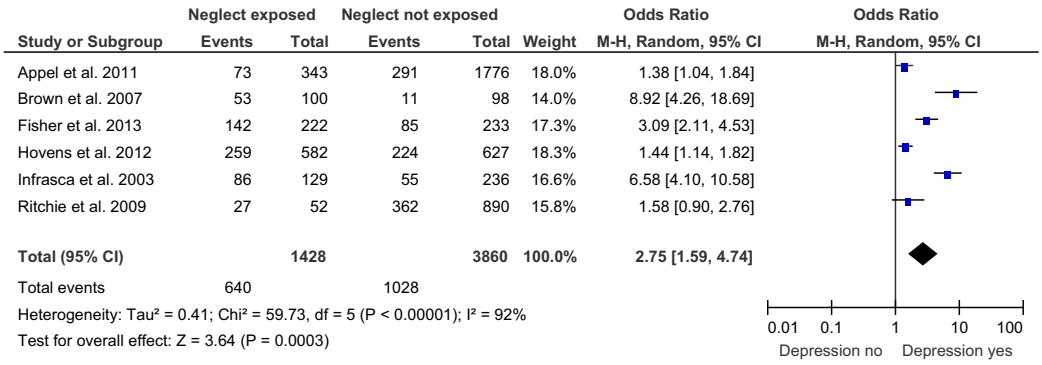
and domestic violence (I^2 = 37%). Parental divorce or separation (OR = 1.56 [1.09–2.22], Z = 2.46, P = 0.01, I^2 = 82%) and hospitalization in childhood (OR = 1.50 [1.04–2.17], Z = 2.15; P = 0.03; I^2 = 0%) were associated to depressive risk to a lower extent. Loss of a loved one was not associated to depressive risk (OR = 1.69 [0.71–4.02], Z = 1.20 P = 0.23, I^2 = 94%) in six studies retrieved (total number of subjects: 3537).

The significance of these associations remained when controlling for confounding variables by post-hoc regression analysis and none of these had an effect on depressive risk with the

a) Emotional abuse



b) Neglect



c) Sexual abuse

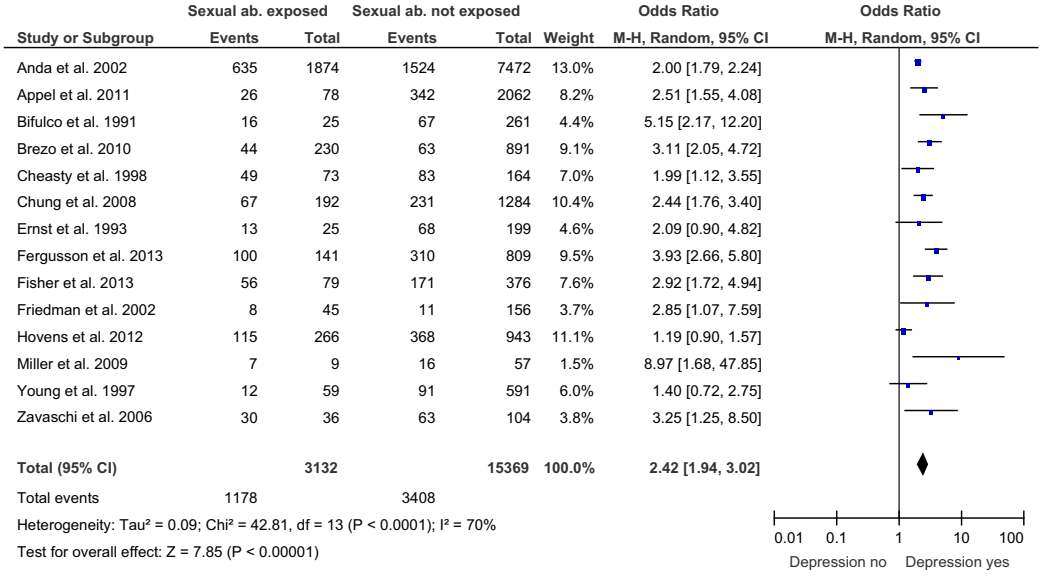
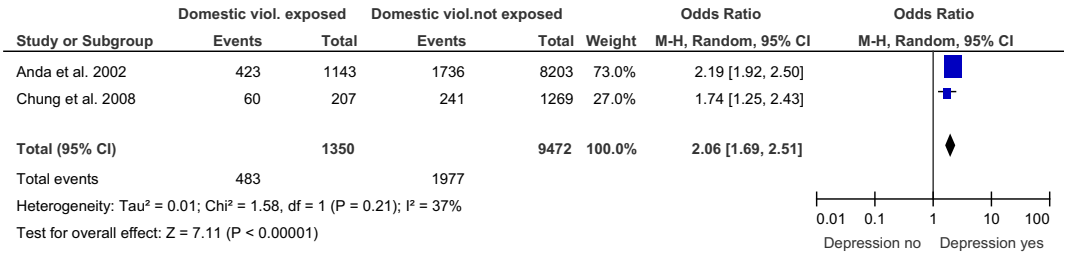


Fig. 2. Depression in adults exposed and not-exposed to traumas in childhood. (a) Depression in adults exposed and not-exposed to emotional abuse in Childhood. (b) Depression in adults exposed and not-exposed to neglect in Childhood. (c) Depression in adults exposed and not-exposed to sexual abuse in Childhood. (d) Depression in adults exposed and not-exposed to domestic violence in Childhood. (e) Depression in adults exposed and not-exposed to physical abuse in Childhood.

d) Domestic violence



e) Physical abuse

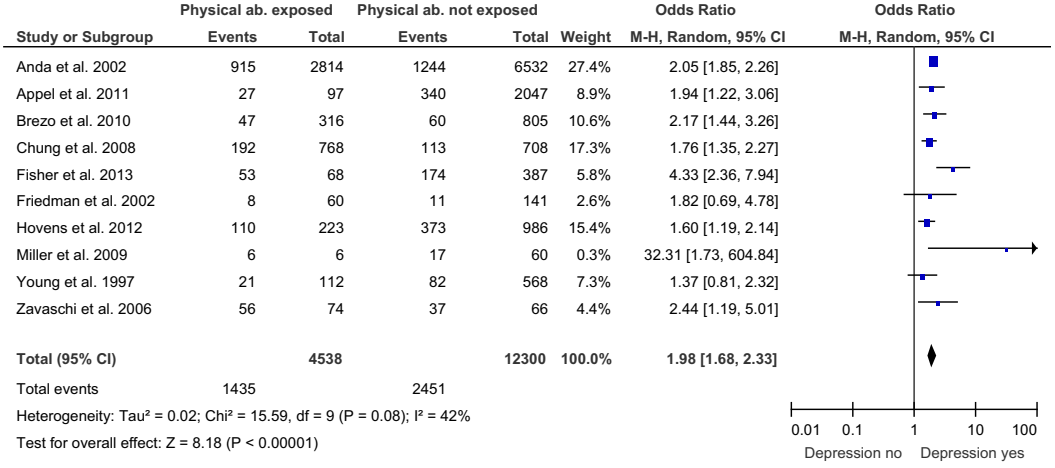


Fig. 2. (*Continued*).

exception of gender and quality of studies in the case of neglect. Neglected female child/adolescents had indeed a slightly higher depressive risk than neglected males (B = 0.03, $P = 0.003$). Quality of studies reduced the estimate of neglect effect (B = –1.78, $P = 0.046$).

3.3. Publication bias

Our results were not significantly affected by publication bias according to the Egger's test for almost all kinds of childhood trauma: neglect (B= 23.50; $P = 0.07$), childhood maltreatment (B = 7.14; $P = 0.11$), emotional abuse (B = 2.47; $P = 0.74$), physical abuse (B = 4.63; $P = 0.19$), early loss (B = –12.76; $P = 0.73$), parental divorce or separation (B = 1.33; $P = 0.69$). It was not possible to calculate the publication bias for domestic violence and hospitalization because of the few included studies. Only results on sexual abuse were significantly affected by publication bias (B = 3.86; $P = 0.04$).

3.4. Sensitivity analysis

We repeated the analysis by RevMan considering some factors that can affect the heterogeneity of studies. For each child adversity category we excluded studies which have divergent features such as low quality defined by a study with less than three stars, outlier studies such as those on women only, mothers only, women with sisters only, elderly adults, psychiatric samples. Whilst most of the outliers had poor impact on results, the inclusion/exclusion of studies on psychiatric samples showed remarkable effects on results (Table 2). Considering studies on psychiatric samples, neglect had the highest impact on depressive risk in adulthood (OR = 3.04 [0.69–13.44], $I^2 = 97\%$), though the

Table 2
Effect of childhood traumas in clinical and community samples.

Stressor	Clinical samples				Community samples			
	OR	I^2 (%)	*P* value	*n*[a]	OR	I^2 (%	*P* value	*n*[a]
Emotional abuse	1.50 [1.07-2.12]	49	0.02	1,889	3.53 [2.31-5.41]	88	<0.001	14,560
Neglect	3.04 [0.69-13.44]	97	0.14	1,574	2.64 [1.33-5.24]	89	0.005	3714
Sexual abuse	1.39 [0.94-2.05]	31	0.09	2,060	2.72 [2.20-3.36]	56	<0.001	16,441
Domestic violence	–	–	–	–	2.06 [1.69-2.51]	37	<0.001	10,822
Physical abuse	1.56 [1.22-2.00]	0	0.0004	2,090	2.15 [1.77-2.61]	45	<0.001	14,748
Loss/separation	2.18 [0.58-8.17]	96	0.25	2,455	.97 [0.71-1.32]	0	0.83	1082
Parental divorce/separation	1.78 [0.91-3.48]	87	0.09	2,455	1.43 [0.95-2.16]	62	0.09	10,261
Hospitalization[b]	–	–	–	–	–	–	–	–

[a] Total number of subjects.
[b] Not analyzed since only two studies, one clinical, one on a community sample.

effect lost of statistical significance ($P = .14$, total number of subjects: 1574). Considering studies on community samples only, the effect remained high (OR = 2.64 [1.33–5.24], $I^2 = 89\%$) and significant ($P = 0.005$, total number of subjects: 3714). Emotional abuse had the highest and significant impact in community samples studies (OR = 3.53 [2.31–5.41], $I^2 = 88\%$, $P < 0.001$, total number of subjects: 14,560), though a lower, but still significant effect in clinical samples studies could be observed (OR = 1.50 [1.07–2.12], $I^2 = 49\%$, $P = 0.02$, total number of subjects: 1889).

In psychiatric samples studies, separation/divorce of parents had a high impact on depressive risk (OR = 1.78 [0.91–3.48], $I^2 = 87\%$), though only as a trend ($P = 0.09$, total nr of subjects: 2455), whilst in community samples studies the impact was less relevant, though a trend was maintained (OR = 1.43 [0.95–2.16], $I^2 = 62\%$, $P = 0.09$, total number of subjects: 10,261).

Sexual abuse showed a relevant impact on depressive risk in both clinical and community samples studies, with a prominent effect in community samples studies (OR = 2.72 [2.20–3.36], $I^2 = 56\%$ $P < 0.001$, total number of subjects: 16,441), less strong and just as a trend in clinical samples studies (OR = 1.39 [0.94–2.05] $I^2 = 31\%$, $P = 0.09$, total number of subjects: 2060). Similarly, physical abuse had prominent effect in community samples studies (OR = 2.15 [1.77–2.61], $I^2 = 45\%$, $P < 0.001$, total nr of subjects: 14,748). However, the effect was significant in clinical samples as well (OR = 1.56 [1.22–2.00], $I^2 = 0\%$, $P = 0.0004$, total number of subjects: 2090).

In summary, according to post-hoc analyses, neglect in childhood had the highest impact on depressive risk in both clinical and community samples, though in community samples, emotional abuse impacted even more on this risk. Significant and homogeneous associations were observed for sexual abuse in community samples, and for physical abuse in both clinical and community samples. Other early stressors were less consistently associated to depressive risk, with the exception of domestic violence, though evaluated in community samples only.

4. Discussion

Results from this study confirm previous evidence that early adversity overall increase the risk to develop depressive symptoms with ORs ranging from about 2.00 to 3.00. Neglect was found to be the strongest risk factor for developing depression/depressive symptoms, particularly in females. However, emotional, sexual and physical abuse and domestic violence showed strong association with depressive risk as well. At the opposite, early loss, parental separation/divorce and prolonged hospitalization in childhood did not significantly increase the risk for depression in adulthood. Further, according to the results obtained by sensitivity analysis, neglect and emotional abuse showed a strong impact on depressive risk. In particular, considering studies on clinical samples only, neglect and parents' separation/divorce had a strong impact on depressive risk, higher than that of sexual/physical abuse. Emotional abuse had instead the highest impact in community samples, though being consistently associated to depressive risk in clinical samples as well.

The data obtained in this study are consistent with previous data reported in literature. For example, recently Hovens et al. [59] have found that a history of emotional neglect and psychological abuse can predict comorbidity and chronicity in adults with depression, whilst a relevant predictive effect was not found for sexual abuse. Accordingly, sexual abuse, though consistently associated to adult depression in our analysis, seems to confer a slightly lower risk than neglect, particularly when considering subjects with a clinical diagnosis of depression. However, it has to be taken into account that children sexually abused are often also emotionally/physically abused and/or emotionally/physically neglected [10,40,28]. The co-occurrence of multiple adverse child experiences is indeed common. Dong et al. [32] have found that individuals exposed to one form of child abuse have a high probability to be exposed to other forms of child maltreatment. Moreover the presence of multiple forms of child abuse seems to be associated to more complicated psychopathological conditions in adulthood [79]. Unfortunately, most of the studies here analyzed did not distinguish between children exposed to a single specific trauma and multiple-traumatized children, or they simply focus on a specific trauma (for example sexual abuse) with disregard of other kind of traumas. Therefore, as a limitation that we will discuss later, we are unable to exclude that individuals exposed or non-exposed to a certain trauma were actually exposed to another kind of trauma.

Neglect (broadly defined as including physical, emotional/psychological and educational child disregard) [51,35], is the most frequent form of early adversity with up to 78.5% of children exposed to this form of maltreatment, followed by 17.6% of children exposed to physical abuse and 9.1% to sexual abuse (http://www.acf.hhs.gov/programs/cb/research-data-technology/reporting-systems/ncands).

According to our analysis, neglect and emotional abuse seems to confer the highest risk for depressive states in adulthood. This finding may also supports a substantial overlap between these two forms of trauma. Indeed, there is uncertainty about an effective distinction between these two traumas. As discussed by McSherry [70] and emphasized by Dubowitz [34] there is a persistent ambiguity and inconsistency in neglect definitions. According to the U.S. Department of Health and Human Services, neglect is defined as "*the failure to provide for the child's basic needs. Neglect can be physical, educational, or emotional [. . .]. Psychological neglect includes the lack of any emotional support and love, chronic inattention to the child, exposure to spouse abuse, or drug and alcohol abuse*" [51]. Therefore, exposure to a kind of neglect, including emotional neglect (i.e. emotional abuse) may be an overall trauma that may impede a proper development of emotional processes in the child with an increased risk to develop depressive states in adulthood [56].

Nevertheless, sexual abuse, physical abuse and domestic violence maintained a significant and strong association with depressive risk. According to sensitivity analysis on sexual and physical abuse, on clinical and community samples separately, with equal number of studies, the effects of these traumas in community samples' studies were higher but less consistent (homogeneous) than those obtained analyzing clinical samples studies only. However, community studies are often less reliable from a diagnostic point of view, as often based on self-rated scales, as often focused on a condition with disregard of other organic/psychiatric disturbances that may lead, for example, to secondary depressive symptoms. At the opposite, studies on clinical samples usually evaluate psychiatric conditions according to DSM or ICD criteria and employ more strict selection criteria. Therefore, we may hypothesize that sexual/physical abuse, though important risk factors for mental disorders in general, are less specific for depression as compared to neglect broadly defined.

A systematic meta-analysis of the literature reported that sexual abuse is associated with an increased risk of a lifetime diagnosis of multiple psychiatric disorders, though major associations were found for anxiety and depressive disorders, eating and sleep disorders, and suicide [24]. However previous studies [10,72] sustained that, in women, a major long-term consequences of sexual abuse is avoidance of men. Other evidence suggests that sexual abuse in young age is associated to scarce use contraceptives, promiscuity, unwanted pregnancies and/or voluntary abortions in women [91,15]. We may therefore hypothesize that a main consequence of sexual abuse is the difficulty to have stable

and intimate relationship with others persons, which in turn may increase the likelyhood to develop depressive states..

Early physical abuse has been mostly associated with violent, criminal behavior, abusive or coercive behaviors in dating relationships, and an increased risk for victimization during adulthood (reviewed in [85]). Further, a recent study investigated three dimensions of depression and anxiety symptomatology (general distress, anhedonic depression and anxious arousal) and reported that only emotional neglect was associated with all the three symptom dimensions, whilst sexual abuse was associated with general distress and anxious arousal, and physical abuse with anxious arousal only [93].

As regards other traumatic events such as loss of a loved one or prolonged hospitalization, according to our data, they were no or less consistently associated to depressive risk. Wiersma et al. [97] found a significant association between emotional neglect, psychological, physical and sexual abuse with recurrent depression, while parental loss and prolonged separation from parents had no effect. However, analyzing clinical samples' studies, parents' divorce had an important effect on depressive risk. Nevertheless, one may hypothesize that this event may imply the exposure of the child to adverse familial environment (including verbal/physical domestic violence), along with and followed by a form of neglect/emotional abuse [32].

Nevertheless, two major issues should be considered. First, it is not possible to predict reliably the outcome of early traumatic experiences: new situations and relational contexts in the lifespan may counteract the negative effects of early traumatic experiences. Not all children exposed to traumas develop mental distress in adulthood, because of following psychosocial adjustment or development of evolved abilities to cope with stress and adversity, a concept defined as "resilience", i.e. the capacity to recover quickly from illness, change, or misfortune [58,13,22]. Second, it is well established that depression is partly explained by a genetic predisposition, which in turn interact with environmental–interpersonal factors in modulating the risk to develop depression, as well as other psychiatric diseases [64,68].

4.1. Limitations

The results obtained by the present meta-analysis may be affected by a number of important limitations. First, in all studies the assessment of childhood trauma was done retrospectively by means of structured interview or self-report questionnaire, possibly increasing the risk of recall bias [69], though several studies sustain a certain reliability in retrospective evaluation of adverse life events [12,53,33]. On the other hand, over-reporting of negative events in depressed patients has been observed [61,71]. A more accurate assessment of traumatic childhood experiences is obviously obtained by prospective, longitudinal study designs [96].

Second, as stated above, many studies focused on child sexual abuse consequences [10,40,28,31] sustained that such abuse occurs in a context of other negative experiences, such as physical and emotional abuse or neglect that could have a strong association with the development of psychopathology in adulthood. In the present study, we were unable to distinguish multiple from single forms of abuse, since most of studies investigated the exposure to several types of child maltreatment not specifying the specific effect of each form of abuse.

Third, though in our study neglect and emotional abuse showed the strongest impact on depressive risk in primary analysis and remained consistent after sensitivity analysis, the inclusion/exclusion of clinical samples' studies had notable effects on results from a statistical point of view. We can assume that, in many cases, decreased significance when considering studies on clinical samples only could be explained by the lower number of included studies and smaller sample sizes. Studies on community samples were indeed more in number, had usually larger samples sizes and, therefore, higher statistical power. On the other hand, as mentioned above, genuine depressed patients are less frequent in studies in community samples, simply because of the characteristic of the study design and less reliable diagnostic assessments.

Forth, in clinical samples studies, the results may be affected by several factors going along with a psychiatric condition as well as by genetic predisposition. On the other hand, in community samples, as already mentioned, subjects may have other undiagnosed and undetected mental disorders. Studies on community sample are usually focused on a specific pathological condition and do not take into account other potential confounding variables simply because not evaluated.

Finally, in some studies there was often an overlap between definition of emotional or psychological abuse and neglect; we tried to cluster neglect and emotional abuse on the basis of some characteristics: for neglect we considered indifference, coldness and lack of interest for child's emotional and physical needs; for emotional abuse we considered verbal humiliation, severe rejection, terrorizing. Nevertheless, a degree of overlap between emotional abuse and neglect seems to exist and it may have had implications for analyzing their association with adult depression, not allowing to explain clearly the weight on psychopathology since both showed a strong impact on depression in adulthood. On the other hand, as stated above, emotional abuse and neglect display a high degree of overlap [70,34].

4.2. Conclusions

Taking into account the abovementioned limitations of the study, data obtained support neglect and emotional abuse as having a relevant impact in adult depression, while sexual and physical abuse, which have been traditionally considered as major risk factors for depression and though maintaining a strong association with this condition, may be less specific for this disorder. Other early stressors, with the exception of violence within the family, seem to be less consistently associated with adult depression.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Aguilera M, Arias B, Wichers M, Barrantes-Vidal N, Moya J, Villa H, et al. Early adversity and 5-HTT/BDNF genes: new evidence of gene-environment interactions on depressive symptoms in a general population. Psychol Med 2009;39:1425–32.
[2] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition revised, Washington DC: American Psychiatric Association; 1987.
[3] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition., Washington, DC: American Psychiatric Association; 1994.
[4] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: American Psychiatric Association; 2000.
[5] Anda RF, Whitfield CL, Felitti VJ, Chapman D, Edwards VJ, Dube SR, et al. Adverse childhood experiences, alcoholic parents, and later risk of alcoholism and depression. Psychiatr Serv 2002;53:1001–9.
[6] Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, et al. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. Eur Arch Psychiatry Clin Neurosci 2006;256:174–86.
[7] Appel K, Schwahn C, Mahler J, Schulz A, Spitzer C, Fenske K, et al. Moderation of adult depression by a polymorphism in the FKBP5 gene and childhood physical abuse in the general population. Neuropsychopharmacology 2011;36:1982–91.

[8] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–71.
[9] Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. Depress Anxiety 1999;9:169–74.
[10] Bifulco A, Brown GW, Adler Z. Early sexual abuse and clinical depression in adult life. Br J Psychiatry 1991;159:115–22.
[11] Bifulco A, Brown GW, Moran P. Predicting depression in women: the role of past and present vulnerability. Psychol Med 1998;28:39–50.
[12] Bifulco A, Moran PM, Baines R, Bunn A, Stanford K. Exploring psychological abuse in childhood: II. Association with other abuse and adult clinical depression. Bull Menninger Clin 2002;66:241–58.
[13] Bonanno GA. Loss, trauma, and human resilience: have we underestimated the human capacity to thrive after extremely aversive events? Am Psychol 2004;59:20–8.
[14] Boudewyn AC, Liem JH. Childhood sexual abuse as a precursor to depression and self-destructive behavior in adulthood. J Trauma Stress 1995;8:445–59.
[15] Boyer D, Fine D. Sexual abuse as a factor in adolescent pregnancy and child maltreatment. Fam Plann Perspect 1992;24. 4–11, 9.
[16] Brezo J, Bureau A, Merette C, Jomphe V, Barker ED, Vitaro F, et al. Differences and similarities in the serotonergic diathesis for suicide attempts and mood disorders: a 22-year longitudinal gene-environment study. Mol Psychiatry 2010;15:831–43.
[17] Brodsky BS, Oquendo M, Ellis SP, Haas GL, Malone KM, Mann JJ. The relationship of childhood abuse to impulsivity and suicidal behavior in adults with major depression. Am J Psychiatry 2001;158:1871–7.
[18] Brown J, Cohen P, Johnson JG, Smailes EM. Childhood abuse and neglect: specificity of effects on adolescent and young adult depression and suicidality. J Am Acad Child Adolesc Psychiatry 1999;38:1490–6.
[19] Brown GW, Craig TK, Harris TO, Handley RV, Harvey AL. Development of a retrospective interview measure of parental maltreatment using the childhood experience of care and abuse (CECA) instrument – a life-course study of adult chronic depression – 1. J Affect Disord 2007;103:205–15.
[20] Burnam MA, Wells KB, Leake B, Landsverk J. Development of a brief screening instrument for detecting depressive disorders. Med Care 1988;26:775–89.
[21] Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse childhood experiences and the risk of depressive disorders in adulthood. J Affect Disord 2004;82:217–25.
[22] Charney DS. Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. Am J Psychiatry 2004;161:195–216.
[23] Cheasty M, Clare AW, Collins C. Relation between sexual abuse in childhood and adult depression: case-control study. BMJ 1998;316:198–201.
[24] Chen LP, Murad MH, Paras ML, Colbenson KM, Sattler AL, Goranson EN, et al. Sexual abuse and lifetime diagnosis of psychiatric disorders: systematic review and meta-analysis. Mayo Clin Proc 2010;85:618–29.
[25] Chung EK, Mathew L, Elo IT, Coyne JC, Culhane JF. Depressive symptoms in disadvantaged women receiving prenatal care: the influence of adverse and positive childhood experiences. Ambul Pediatr 2008;8:109–16.
[26] Cohen H, Loewenthal U, Matar M, Kotler M. Association of autonomic dysfunction and clozapine. Heart rate variability and risk for sudden death in patients with schizophrenia on long-term psychotropic medication. Br J Psychiatry 2001;179:167–71.
[27] Comijs HC, Beekman AT, Smit F, Bremmer M, van Tilburg T, Deeg DJ. Childhood adversity, recent life events and depression in late life. J Affect Disord 2007;103:243–6.
[28] Cotter PA. Sexual abuse is not the only childhood adversity that may lead to later depression. BMJ 1998;316:1244.
[29] Derogatis L. SCL-90. Administration, scoring and procedures Manual-I for the R (revised) version and other instruments of the Psychopathology Rating Scale Series. Chicago: Johns Hopkins University School of Medicine; 1977.
[30] Dickersin K. The existence of publication bias and risk factors for its occurrence. JAMA 1990;263:1385–9.
[31] Dong M, Anda RF, Dube SR, Giles WH, Felitti VJ. The relationship of exposure to childhood sexual abuse to other forms of abuse, neglect, and household dysfunction during childhood. Child Abuse Negl 2003;27:625–39.
[32] Dong M, Anda RF, Felitti VJ, Dube SR, Williamson DF, Thompson TJ, et al. The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. Child Abuse Negl 2004;28:771–84.
[33] Dube SR, Williamson DF, Thompson T, Felitti VJ, Anda RF. Assessing the reliability of retrospective reports of adverse childhood experiences among adult HMO members attending a primary care clinic. Child Abuse Negl 2004;28:729–37.
[34] Dubowitz H. Understanding and addressing the "neglect of neglect:" digging into the molehill. Child Abuse Negl 2007;31:603–6.
[35] Dubowitz H, Pitts SC, Black MM. Measurement of three major subtypes of child neglect. Child Maltreat 2004;9:344–56.
[36] Dunn EC, McLaughlin KA, Slopen N, Rosand J, Smoller JW. Developmental timing of child maltreatment and symptoms of depression and suicidal ideation in young adulthood: results from the national longitudinal study of adolescent health. Depress Anxiety 2013;30:955–64.
[37] Edwards VJ, Holden GW, Felitti VJ, Anda RF. Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: results from the adverse childhood experiences study. Am J Psychiatry 2003;160:1453–60.
[38] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[39] Elzinga BM, Molendijk ML, Oude Voshaar RC, Bus BA, Prickaerts J, Spinhoven P, et al. The impact of childhood abuse and recent stress on serum brain-derived neurotrophic factor and the moderating role of BDNF Val66Met. Psychopharmacology (Berl) 2011;214:319–28.
[40] Ernst C, Angst J, Foldenyi M. The Zurich Study. XVII. Sexual abuse in childhood. Frequency and relevance for adult morbidity data of a longitudinal epidemiological study. Eur Arch Psychiatry Clin Neurosci 1993;242:293–300.
[41] Fergusson DM, Horwood LJ, Lynskey MT. Childhood sexual abuse and psychiatric disorder in young adulthood: II. Psychiatric outcomes of childhood sexual abuse. J Am Acad Child Adolesc Psychiatry 1996;35:1365–74.
[42] Fergusson DM, Lynskey MT, Horwood LJ. Childhood sexual abuse and psychiatric disorder in young adulthood: I. Prevalence of sexual abuse and factors associated with sexual abuse. J Am Acad Child Adolesc Psychiatry 1996;35:1355–64.
[43] Fergusson DM, McLeod GF, Horwood LJ. Childhood sexual abuse and adult developmental outcomes: findings from a 30-year longitudinal study in New Zealand. Child Abuse Negl 2013;37:664–74.
[44] Fisher HL, Cohen-Woods S, Hosang GM, Korszun A, Owen M, Craddock N, et al. Interaction between specific forms of childhood maltreatment and the serotonin transporter gene (5-HTT) in recurrent depressive disorder. J Affect Disord 2013;145:136–41.
[45] Friedman S, Smith L, Fogel D, Paradis C, Viswanathan R, Ackerman R, et al. The incidence and influence of early traumatic life events in patients with panic disorder: a comparison with other psychiatric outpatients. J Anxiety Disord 2002;16:259–72.
[46] Garbarino J, Garbarino A. Emotional maltreatment of children, 2nd Ed., Chicago: National Committee to Prevent Child Abuse; 1994.
[47] Gibb BE, Chelminski I, Zimmerman M. Childhood emotional, physical, and sexual abuse, and diagnoses of depressive and anxiety disorders in adult psychiatric outpatients. Depress Anxiety 2007;24:256–63.
[48] Gladstone G, Parker G, Wilhelm K, Mitchell P, Austin MP. Characteristics of depressed patients who report childhood sexual abuse. Am J Psychiatry 1999;156:431–7.
[49] Glaser D. Emotional abuse and neglect (psychological maltreatment): a conceptual framework. Child Abuse Negl 2002;26:697–714.
[50] Goldberg D. Manual of the general health questionnaire. Windsor: NFER-Nelson; 1987.
[51] Goldman J, Salus MK, Wolcott D, Kennedy KY. A coordinated response to child abuse and neglect: the Foundation for Practice. U.S. Department of Health and Human Services; 2003.
[52] Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62.
[53] Hardt J, Rutter M. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. J Child Psychol Psychiatry 2004;45:260–73.
[54] Heim C, Binder EB. Current research trends in early life stress and depression: review of human studies on sensitive periods, gene-environment interactions, and epigenetics. Exp Neurol 2012;233:102–11.
[55] Heim C, Nemeroff CB. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol Psychiatry 2001;49:1023–39.
[56] Heim C, Shugart M, Craighead WE, Nemeroff CB. Neurobiological and psychiatric consequences of child abuse and neglect. Dev Psychobiol 2010;52:671–90.
[57] Hill J, Pickles A, Burnside E, Byatt M, Rollinson L, Davis R, et al. Child sexual abuse, poor parental care and adult depression: evidence for different mechanisms. Br J Psychiatry 2001;179:104–9.
[58] Holahan CJ, Moos RH. Life stressors, personal and social resources, and depression: a 4-year structural model. J Abnorm Psychol 1991;100:31–8.
[59] Hovens JG, Giltay EJ, Wiersma JE, Spinhoven P, Penninx BW, Zitman FG. Impact of childhood life events and trauma on the course of depressive and anxiety disorders. Acta Psychiatr Scand 2012;126:198–207.
[60] Infrasca R. Childhood adversities and adult depression: an experimental study on childhood depressogenic markers. J Affect Disord 2003;76:103–11.
[61] Jorm AF, Henderson AS. Memory bias in depression: implications for risk factor studies relying on self-reports of exposure. Int J Methods Psychiatr Res 1992;2:312–38.
[62] Kendler KS, Bulik CM, Silberg J, Hettema JM, Myers J, Prescott CA. Childhood sexual abuse and adult psychiatric and substance use disorders in women: an epidemiological and cotwin control analysis. Arch Gen Psychiatry 2000;57:953–9.
[63] Kendler KS, Kuhn JW, Prescott CA. Childhood sexual abuse, stressful life events and risk for major depression in women. Psychol Med 2004;34:1475–82.
[64] Klengel T, Binder EB. Gene-environment interactions in major depressive disorder. Can J Psychiatry 2013;58:76–83.
[65] Koverola C, Pound J, Heger A, Lytle C. Relationship of child sexual abuse to depression. Child Abuse Negl 1993;17:393–400.
[66] LaNoue M, Graeber D, de Hernandez BU, Warner TD, Helitzer DL. Direct and indirect effects of childhood adversity on adult depression. Community Ment Health J 2012;48:187–92.
[67] Lenze SN, Xiong C, Sheline YI. Childhood adversity predicts earlier onset of major depression but not reduced hippocampal volume. Psychiatry Res 2008;162:39–49.
[68] Mandelli L, Serretti A. Gene environment interaction studies in depression and suicidal behavior: an update. Neurosci Biobehav Rev 2013.

[69] Maughan B, Rutter M. Retrospective reporting of childhood adversity: issues in assessing long-term recall. J Pers Disord 1997;11:19–33.
[70] McSherry D. Understanding and addressing the "neglect of neglect": why are we making a mole-hill out of a mountain? Child Abuse Negl 2007;31: 607–14.
[71] Mechanic MB, Resick PA, Griffin MG. A comparison of normal forgetting, psychopathology, and information-processing models of reported amnesia for recent sexual trauma. J Consult Clin Psychol 1998;66:948–57.
[72] Meiselman K. Incest: a psychological study outs causes and effects with treatment recomedations. San Francisco: Jossey-Bass; 1978.
[73] Miller JM, Kinnally EL, Ogden RT, Oquendo MA, Mann JJ, Parsey RV. Reported childhood abuse is associated with low serotonin transporter binding in vivo in major depressive disorder. Synapse 2009;63:565–73.
[74] Peleikis DE, Mykletun A, Dahl AA. The relative influence of childhood sexual abuse and other family background risk factors on adult adversities in female outpatients treated for anxiety disorders and depression. Child Abuse Negl 2004;28:61–76.
[75] Penza KM, Heim C, Nemeroff CB. Neurobiological effects of childhood abuse: implications for the pathophysiology of depression and anxiety. Arch Womens Ment Health 2003;6:15–22.
[76] Pirkola SP, Isometsa E, Suvisaari J, Aro H, Joukamaa M, Poikolainen K, et al. DSM-IV mood-, anxiety- and alcohol use disorders and their comorbidity in the Finnish general population – results from the Health 2000 Study. Soc Psychiatry Psychiatr Epidemiol 2005;40:1–10.
[77] Polanczyk G, Caspi A, Williams B, Price TS, Danese A, Sugden K, et al. Protective effect of CRHR1 gene variants on the development of adult depression following childhood maltreatment: replication and extension. Arch Gen Psychiatry 2009;66:978–85.
[78] Power RA, Lecky-Thompson L, Fisher HL, Cohen-Woods S, Hosang GM, Uher R, et al. The interaction between child maltreatment, adult stressful life events and the 5-HTTLPR in major depression. J Psychiatr Res 2013;47:1032–5.
[79] Putnam KT, Harris WW, Putnam FW. Synergistic childhood adversities and complex adult psychopathology. J Trauma Stress 2013;26:435–42.
[80] Radloff LS. The CES-D scale: a self report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
[81] Ressler KJ, Bradley B, Mercer KB, Deveau TC, Smith AK, Gillespie CF, et al. Polymorphisms in CRHR1 and the serotonin transporter loci: gene x gene x environment interactions on depressive symptoms. Am J Med Genet B Neuropsychiatr Genet 2010;153B:812–24.
[82] RevMan. Review Manager. Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration; 2012.
[83] Ritchie K, Jaussent I, Stewart R, Dupuy AM, Courtet P, Ancelin ML, et al. Association of adverse childhood environment with late-life depression. J Clin Psychiatry 2009;70:1281–8.
[84] Robins LN, Cottler L, Bucholtz K, Compton W. Diagnostic Interview Schedule for DSM-IV. St Louis, MO: Washington University; 1995.
[85] Runyon MK, Deblinger E, Ryan EE, Thakkar-Kolar R. An overview of child physical abuse: developing an integrated parent-child cognitive-behavioral treatment approach. Trauma Violence Abuse 2004;5:65–85.
[86] Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. Psychol Med 1996;26:477–86.
[87] Sheehan DV, Lecrubier Y, Sheehan KH, Janavs J, Weiller E, Keskiner A, et al. The validity of the mini international neuropsychiatric interview (MINI) according to the SCID-P and its reliability. Eur Psychiatry 1997;12:232–41.
[88] Spitzer RL, Williams JBW, Gibbon M, First MB. Structured clinical interview for DSM-III-R (SCID). Inc: American Psychiatric Press; 1990.
[89] Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary care evaluation of mental disorders. Patient Health Questionnaire. JAMA 1999;282:1737–44.
[90] Springer KW, Sheridan J, Kuo D, Carnes M. Long-term physical and mental health consequences of childhood physical abuse: results from a large population-based sample of men and women. Child Abuse Negl 2007;31:517–30.
[91] Stock JL, Bell MA, Boyer DK, Connell FA. Adolescent pregnancy and sexual risk-taking among sexually abused girls. Fam Plann Perspect 1997;29. 200–3, 27.
[92] Tyrka AR, Price LH, Gelernter J, Schepker C, Anderson GM, Carpenter LL. Interaction of childhood maltreatment with the corticotropin-releasing hormone receptor gene: effects on hypothalamic-pituitary-adrenal axis reactivity. Biol Psychiatry 2009;66:681–5.
[93] van Veen T, Wardenaar KJ, Carlier IV, Spinhoven P, Penninx BW, Zitman FG. Are childhood and adult life adversities differentially associated with specific symptom dimensions of depression and anxiety? Testing the tripartite model. J Affect Disord 2013;146:238–45.
[94] Wells G, Shea B, O'connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis; 2010.
[95] WHO global consultation on violence and health. Violence: a public health priority (WHO/EHA/SPI.POA.2). Génève: World Health Organisation; 1999.
[96] Widom CS, DuMont K, Czaja SJ. A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. Arch Gen Psychiatry 2007;64:49–56.
[97] Wiersma JE, Hovens JG, van Oppen P, Giltay EJ, van Schaik DJ, Beekman AT, et al. The importance of childhood trauma and childhood life events for chronicity of depression in adults. J Clin Psychiatry 2009;70:983–9.
[98] Wing JK, Cooper JE, Sartorius N. The measurement and classification of psychiatric symptoms. London: Cambridge University Press; 1974.
[99] Wing JK, Babor T, Brugha T, Burke J, Cooper JE, Giel R, et al. SCAN. Schedules for Clinical Assessment in Neuropsychiatry. Arch Gen Psychiatry 1990;47:589–93.
[100] Wittchen HU, Robins LN, Cottler LB, Sartorius N, Burke JD, Regier D. Cross-cultural feasibility, reliability and sources of variance of the Composite International Diagnostic Interview (CIDI). The Multicentre WHO/ADAMHA Field Trials. Br J Psychiatry 1991;159. 645–53, 58.
[101] Young EA, Abelson JL, Curtis GC, Nesse RM. Childhood adversity and vulnerability to mood and anxiety disorders. Depress Anxiety 1997;5:66–72.
[102] Zavaschi ML, Graeff ME, Menegassi MT, Mardini V, Pires DW, Carvalho RH, et al. Adult mood disorders and childhood psychological trauma. Rev Bras Psiquiatr 2006;28:184–90.