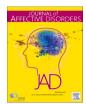
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Review article



What are the predictive variables that increase the risk of developing a complex trauma? A meta-analysis

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ABSTRACT

In 2018, Complex Post Traumatic Stress Disorder (CPTSD) was officially recognized as a distinct syndrome in the International Classification of Diseases, 11th Revision (ICD-11). This recognition aimed to differentiate between neurotic disorders secondary to stressful situations and somatoform disorders, and disorders specifically associated with stress. The inclusion of CPTSD in the ICD-11 marked the culmination of two decades of research focused on understanding its symptoms, treatments, and risk factors. However, despite the progress made, a comprehensive meta-analysis to elucidate the specific risk factors and impact on the development of CPTSD is still lacking. The objective of this article is to conduct such a meta-analysis. A total of 24 studies were selected for analysis, and the findings revealed several key risk factors associated with the development of CPTSD. The main risk factor identified is having experienced sexual abuse in childhood (k = 12; OR = 2.880). In addition, childhood physical abuse (k = 11; OR = 2.841), experiencing emotional neglect during childhood (k = 5; OR = 2.510), physical abuse throughout life (k = 8; OR = 2.149) and being a woman (k = 13; OR = 1.726) were also significant risk factors.

1. Introduction

In 2018, the 11th edition of the International Classification of Diseases (ICD-11) introduced a new category of psychopathology called "Disorders Specifically Associated with Stress" (World Health Organization, 2018). This modification provides a distinction between the group of Neurotic Disorders secondary to stressful situations and somatoform disorders, and disorders specifically related to stress (World Health Organization, 2016, 2018). The revised edition also includes a description of the main disorders related to traumatic events, which are Posttraumatic Stress Disorder (PTSD) and Complex Posttraumatic Stress Disorder (CPTSD). Although both conditions are related to traumatic events, there are notable differences in their underlying symptoms and dimensions (Brewin et al., 2017; Karatzias et al., 2017a). While PTSD encompasses dimensions such as re-experiencing the event, memory avoidance, and hypervigilance, CPTSD includes these dimensions as well as three additional ones: severe problems with emotional and behavioural regulation, persistent beliefs about oneself as diminished,

defeated, or worthless, and persistent difficulties in maintaining relationships and bonds with others (Karatzias et al., 2017b; World Health Organization, 2018).

Consistent evidence supporting the construct validity of the ICD-11 for PTSD and CPTSD has accumulated in recent years (Brewin, 2020; Brewin et al., 2017). Mainly using the International Trauma Questionnaire (ITQ; Cloitre et al., 2015; Cloitre et al., 2018) self-report instrument for the evaluation of the diagnoses of PTSD and CPTSD according to the ICD-11 (World Health Organization, 2018) (ITQ versions; https://www.traumameasuresglobal.com/itq). In clinical populations (Böttche et al., 2018; Choi et al., 2021; Dhingra et al., 2015; Dorahy et al., 2009; Folke et al., 2021; Kazlauskas et al., 2018) and general (nonclinical) population exposed to trauma (Frost et al., 2019a; Cloitre et al., 2013; Camden et al., 2023; Frewen et al., 2023) studies that confirm the six dimensions of CPTSD, findings consistent with the ICD-11 definition (World Health Organization, 2018). Furthermore, evidence from clinical samples, as well as general population samples, suggests that CPTSD is a more common condition than PTSD (Karatzias

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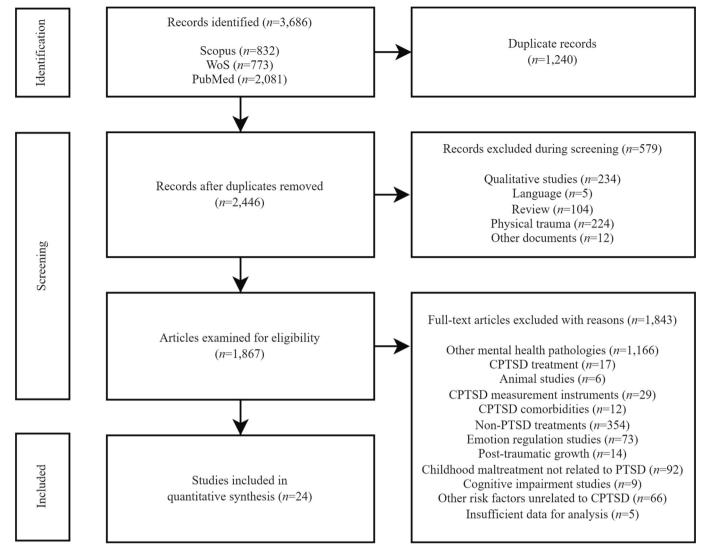


Fig. 1. Flow diagram.

et al., 2019). In addition, evidence from clinical samples also suggests that CPTSD is a highly comorbid condition and is more likely to be associated with depression, borderline personality disorder (BPD), dissociative disorder (Hyland et al., 2017a; Borroni et al., 2021), generalized anxiety disorder (Facer-Irwin et al., 2021; Karatzias et al., 2019), somatization (Astill Wright et al., 2021) and suicide (Jannini et al., 2023).

Furthermore, recent results provide the first evidence for distinct neural profiles of CPTSD and PTSD during threat processing. Agreeing with the proposal that CPTSD is distinguished from PTSD by disturbances in emotion regulation (Bryant et al., 2019).

Regarding its prevalence, studies developed in Denmark, the United States, Israel, and Germany have explored its epidemiology. In 2008 and 2009, the National Center for Social Research in Denmark (Center for Security Studies, 2017) evaluated CPTSD in 2980 individuals indicating that about 1 % of the population could present this condition, being three times more likely to occur in women (Hyland et al., 2017b). In 2017, a representative sample of U.S. households indicated a CPTSD prevalence of about 3.3 %, a probability that increases to twice as high if female (Karatzias et al., 2017b) while in Israel PTSD (9.0 %) was more common than CPTSD (2.6 %). A similar study conducted in 2018 in Germany indicated that, in a sample of 2524 individuals tested, 1 % had symptoms of CPTSD, being more common in women (0.7 %) than in men (0.3 %) (Ben-Ezra et al., 2018; Maercker et al., 2018), which is in line

with the Danish study.

Despite advances in the definition and epidemiology of CPTSD, there is still controversy regarding the identification and relevance of its risk factors.

CPTSD would be associated with multiple or sustained exposure to potentially traumatic events (Dorahy et al., 2009; Cloitre et al., 2009) for example: torture, slavery, prolonged domestic violence (World Health Organization, 2018). This characteristic has been present since Judith Herman in 1992 described CPTSD as a syndrome originating in situations of chronic and prolonged victimization, experienced in a particularly intense way by the affected individual, giving rise to symptoms markedly different from classic stress (PTSD) (Herman, 1992). In this regard, Maercker et al. point out that this type of disorder typically develops because of severe stressors of a prolonged nature or multiple or repeated adverse events from which separation is not possible" (Maercker et al., 2013).

In this regard, recent findings in adult samples have indicated that cumulative childhood trauma, particularly childhood sexual or physical abuse, is more strongly related to CPTSD than to PTSD (Hyland et al., 2017b; Zerach et al., 2019). Furthermore, repeated, or chronic trauma is a risk factor, especially if it is related to situations in which escape is difficult or impossible, as in childhood sexual or physical abuse within the family (Brewin et al., 2017; Cloitre, 2020). This is relevant, as prolonged exposure to potentially traumatic events is associated with more

severe and complex symptomatology than a single event (Brewin et al., 2017; Cloitre et al., 2011).

In this regard, the study of exposure to traumatic events during childhood is particularly important. In fact, being a victim of sexual abuse during childhood (Ben-Ezra et al., 2018; Frost et al., 2019a; Karatzias et al., 2017a), experiencing emotional neglect in childhood (Dorahy et al., 2009; Frost et al., 2019b; Karatzias et al., 2020) and physical abuse in childhood (Hyland et al., 2017b; Karatzias et al., 2017b; Karatzias et al., 2018) are events that impact psychobiological development (Dannlowski et al., 2012; Kirke-Smith et al., 2014), even altering the trajectory of brain development, affecting sensory systems, network architecture, and circuits involved in threat detection and emotional regulation (Teicher et al., 2016), increase the probability of developing mental health problems (Ford and Courtois, 2020; Van Der Kolk et al., 2016) associated with higher levels of emotional and behavioural dysregulation (Villalta et al., 2020), and symptoms more severe and intense than those contemplated by the classical dimensions of post-traumatic stress disorder (Herman, 1992; Roth et al., 1997; Villalta et al., 2020).

In addition to the developmental period in which maltreatment events occur as a relevant variable of study, it is generally accepted that psychological trauma resulting from a single traumatic event ("simple" post-traumatic stress) should be differentiated from complex psychological trauma, which is often a consequence of persistent maltreatment (Herman, 1992; World Health Organization, 2018).

This perspective on the impact of maltreatment events according to their frequency has been reported since the early 1990s with the first studies on trauma with complex characteristics, in which more severe symptoms than those reported for PTSD are present in people who have experienced multiple maltreatment events (Herman, 1992; Roth et al., 1997; Terr, 1991), which has been validated by subsequent studies that have identified that the number of traumatic experiences experienced (cumulative childhood trauma) has been reported to be an especially strong predictor of symptom severity and complexity in relation to trauma and multiple mental health problems (Cloitre et al., 2019; Facer-Irwin et al., 2021).

However, this distinction between the frequency of maltreatment (single or repetitive event), stage of development at which it occurs, and its relationship to the type of symptomatology developed (simple or complex trauma) requires further study (Briere and Scott, 2015). In 2018 the World Health Organization indicates that this symptomatology can develop on exposure to an event or a series of events extremely severe in nature (World Health Organization, 2018). In this sense, the evidence of the last three decades indicates the need to include distinctions for the origin, development and particularities of traumatic symptomatology (Gershuny and Thayer, 1999; Herman, 1992; Huszonek, 1991; Roth et al., 1997).

It is in this sense that Brewin et al. (2017) highlight a crucial aspect in the study of CPTSD: the need to specify whether the type of traumatic event, as well as the period of development in which it occurs (whether in childhood or in adulthood), entails a differentiated risk level for the development of this condition. That is, there are specific risk factors that are mostly related to the appearance of CPTSD.

However, the effect that such risk factors would have on the development of CPTSD, and the hierarchy of relevance of such risk factors, has yet to be determined. To resolve these questions, a meta-analysis is desirable. Therefore, the aim of this study is to conduct such a meta-analysis to contribute to the debate on risk factors for CPTSD.

2. Method

2.1. Search strategy

Reporting methods and procedures were in accordance with the PRISMA checklist (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). A flowchart is provided in Fig. 1 (Checklist PRISMA) (Hutton et al., 2015; Tricco et al., 2018; Page et al., 2021).

English-language articles published in peer-reviewed journals (indexes) up to February 2023 were processed for inclusion. The search was performed in three scientific literature databases: Web of Science, Scopus, and PubMed. The search terms entered in the bibliographic databases included the following combinations: TITLE-ABS-KEY ("complex PTSD" OR "symptom of complex post-traumatic stress" OR "complex posttraumatic stress disorder" OR "CPTSD" OR "complex trauma") AND ("risk factors" OR "predictors"). Due to the quantitative focus of this study, we excluded documents such as book chapters, theoretical reviews, systematic reviews, editorial comments, letters or notes, case studies, and other articles that provided non-quantitative information

Table 1Quality assessment tool for observational cohort and cross-sectional studies.

ID	Authors	Crite	ria													Score	Quality rating
		Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14				
1	Ben-Ezra et al. (2018)	1	1	0	0.5	1	0	0	0	1	0	1	0	0	1	6.5	Fair
2	Brewin (2020)	1	1	1	1	0	0	0	1	1	0	1	0	0	1	8	Good
3	Cloitre et al. (2019)	1	1	0	1	0	0	0	1	1	0	1	0	0	1	7	Good
4	Dorahy et al. (2009)	1	1	1	0.5	0	0	0	1	1	0	1	0	0	1	7.5	Good
5	Eidhof et al. (2019)	1	1	1	0.5	0	0	0	1	1	0	1	0	0	1	7.5	Good
6	Facer-Irwin et al. (2021)	1	1	0	1	1	0	0	1	1	0	1	0	0	1	8	Good
7	Frost et al. (2019a)	1	1	1	0.5	0.5	0	0	1	1	0	1	0	0	1	8	Good
8	Frost et al. (2019b)	1	1	0	0.5	1	0	0	1	1	0	1	0	0	1	7.5	Good
9	Hyland et al. (2017a, 2017b)	1	1	1	0.5	1	0	0	0	1	0	1	0	0	1	7.5	Good
10	Hyland et al. (2018)	1	1	1	0.5	0	0	0	0	1	0	1	0	0	1	6.5	Fair
11	Hyland et al. (2020)	1	1	0	0.5	0.5	0	0	1	1	0	1	0	0	1	7	Good
12	Kairyte et al. (2022)	1	1	1	1	0	0	0	1	1	0	1	0	0	1	8	Good
13	Karatzias et al. (2017a, 2017b)	1	1	1	0.5	0	0	0	0	1	0	1	0	0	1	6.5	Fair
14	Karatzias et al. (2018)	1	1	1	0.5	0	0	0	0	1	0	1	0	0	1	6.5	Fair
15	Kazlauskas et al. (2018)	1	1	1	1	0	0	0	1	1	0	1	1	0	1	9	Good
16	Kvedaraite et al. (2022)	1	1	1	1	0	0	0	1	1	0	1	1	0	1	9	Good
17	Lewis et al. (2022)	1	1	0	1	0	0	0	0	1	0	1	0	0	1	6	Fair
18	Liddell et al. (2019)	1	1	1	0.5	0	0	0	0	1	0	1	1	0	1	7.5	Good
19	Maercker et al. (2018)	1	1	1	1	0	0	0	0	1	0	1	0	0	1	7	Good
20	Murphy et al. (2021)	1	1	1	0.5	0	0	0	1	1	0	1	0	0	1	7.5	Good
21	Sachser et al. (2017)	1	1	1	1	0	0	0	0	1	0	1	1	0	1	8	Good
22	Simon et al. (2019)	1	1	1	1	0	0	0	0	1	0	1	1	0	1	8	Good
23	Spitzer et al. (2006)	1	1	1	0	0	0	0	0	1	0	1	0	0	1	6	Fair
24	Vang et al. (2019)	1	1	1	0.5	0	0	0	1	1	0	1	0	0	1	7.5	Good

Note: Ratings were conducted in accordance with the NIH quality assessment tool.

on risk factors for CPTSD. This study was not pre-registered.

2.2. Inclusion and exclusion criteria

Studies included in the meta-analysis met the following criteria: a) examined at least one potential risk factor (predictor) for the development of CPTSD; b) reported at least one of the following data: 1) Odds Ratio (OR) and corresponding 95 % confidence intervals (CI); 2) Frequency of occurrence of at least one risk factor in the population with CPTSD and in the population without CPTSD, information with which data conversion is performed for further analysis.

In addition, studies were excluded for: (a) addressing physical trauma (i.e., especially musculoskeletal pathologies) and not CPTSD; (b) absence of meta-analyzable data (OR and Frequency); (c) the study contained insufficient data to calculate univariate effect sizes, and such data could not be obtained from the study author; or (d) absence of risk factors for CPTSD; (e) the article was a review or qualitative study that did not present new data or only presented qualitative analyses; (g) the study used a single-case design.

Finally, if more than one article presented data from the same sample, the most recent and complete article was included in our metaanalysis.

2.3. Assessment of quality

The assessment of methodological rigor and potential presence of bias in each of the incorporated studies were determined using the quality assessment tool of the National Institute of Health (NIH) version "Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies" (National Institute Health, 2021). This tool comprises 14 areas of analysis, covering crucial aspects such as: formulation of the research question, composition of the studied population, recruitment procedures, study power, methods for measuring exposures and results, dropout rate, and statistical approaches used.

Each original assessment question is categorized as "yes", "no", "cannot determine", "not applicable", or "not reported". In the present study, we have adopted a scoring system that assigns a score of 1 for "yes" responses, 0.5 for partial statements, and 0 for "no" or unclear responses. This scoring system has been recommended by similar research (Gaythorpe et al., 2021) and aims to quantify the results coherently.

The description of each criterion is detailed in Supplementary Table S1. As a criterion for final classification, studies obtaining 7 or more points were categorized as high quality (good), while those scoring between 5 and 6 points were considered acceptable (fair). On the other hand, studies obtaining less than 5 points were classified as poor quality. The quality assessment process was independently carried out by two independent researchers, and the results were thoroughly discussed. Any disagreements that arose were resolved through constructive discussion. The findings of the quality assessment are summarized in Table 1.

2.4. Data extraction

The initial search was performed by one of the authors, to identify the articles according to the search terms. This was followed by manual inspection to select those that met the selection criteria. Screening was performed by three of the authors independently, reviewing titles, abstracts, or the full article if relevant. Differences in interpretation were resolved by discussion with an additional reviewer to develop a final consensus and coding. According to the inclusion criteria, the selected articles were read in their entirety. To classify them, a color code was used: included in green, excluded in red, doubts in yellow and orange not found, according to Cochrane recommendations (Higgins, 2012).

Excel software was used for data extraction and collection, Mendeley for article management (selection, eligibility, and inclusion), and Review Manager for analysis and writing. The following information was extracted for each eligible study: first author's last name, year of publication, study location, sample size, percentages of women, age and standard deviations of the sample, prevalence of CPTSD, number of people exposed to potentially traumatic factors, the estimated effect size (OR), corresponding 95 % CI and adjusted covariates in the statistical analysis, as well as frequency of exposure to the risk factor event). In addition, the variance of the logarithm of each factor was calculated for analysis.

If a study reported multiple multivariate estimates of the adjusted effect, the estimate that adjusted for the largest number of potential variables was selected.

2.5. Statistical analysis

Our analysis was based on ORs as the main effect size measure. OR values were obtained directly from each study when reported by the authors. Alternatively, OR were manually calculated based on frequency of exposure reported by the authors. In addition, other effect size measures such as correlations (between risk factors and CPTSD) or mean differences (between non-exposed vs exposed in terms of CPTSD, or between no-CPTSD vs CPTSD in terms of exposure to the risk factor) were transformed into OR using rESCMA, an open-source web-based calculator and effect size converter (rescma.com; Villacura-Herrera and Kenner, 2020).

A random-effects model was used, which assumes that the actual potential effect varies among the included studies (Riley et al., 2011). Heterogeneity among effects was assessed using Cochran's Q test and the heterogeneity index (I²), where a significant *p*-value in the Q test would indicate heterogeneity among effects, while the I² index indicates the percentage of existing heterogeneity (Botella and Sánchez-Meca, 2015). Each analysis was conducted following the current recommendations for OR-based meta-analysis (Higgins et al., 2008; Chang and Hoaglin, 2017), transforming the raw OR values into its natural logarithmic expression (logOR) for a more robust approach towards the precision of the pooled estimates, and then back-transforming them into OR for interpretation.

Publication bias was assessed using the Rosenthal failsafe number N (FSN), which determines how many zero-effect studies would be necessary to invalidate the results of the analysis. An FSN higher than that established by the "Rosenthal rule" (k * 5 + 10; where k is the number of studies included in the analysis) (k * 5 + 10; where k is the number of studies included in the analysis) (Fragkos et al., 2017), the results would be free of publication bias. Moreover, we examined the funnel plots and Egger's Z regression to check for evidence of potential publication bias and asymmetry on the effects' distribution.

All analyses were conducted in RStudio version 2023.06.0 with R version 4.3.1, using the *metafor* package (Viechtbauer, 2010).

3. Results

This literature search yields a preliminary database of 3686 published articles, which are subsequently reviewed for inclusion in the meta-analysis using various inclusion and exclusion criteria, ending with a total of 24 studies for analysis. Fig. 1 presents the flow diagram for the study selection process.

3.1. Assessment of quality

The methodological quality within the included studies varied. Table 1 provides an overview of the 14 quality assessment areas and the overall quality rating indicating risk of bias. Using the guidance provided by the National Institute Health (2021) tool, (18) studies were rated 'good' quality rating, indicating low risk of bias, and (6) studies were rated 'fair' quality rating, indicating some risk of bias.

The main shortcoming in the quality of the included studies is due to

Table 2
Characteristics of studies included with risk factors for CPTSD.

D	Authors	Sample type	Designs	Country	N	% female	Age (M \pm SD)	Sample CPTSD	Sample Exposed	Risk factor	OR	VarLo OR
	Ben-Ezra et al. (2018)	General Population	Cross- sectional	Israel	1003	51.7 %	40.6 ± 14.5	26	66	Childhood physical abuse	3.30	0.014
		•							128	Childhood sexual abuse	1.89	0.013
									365	Adulthood physical abuse	2.44	0.013
	Brewin (2020)	Police officers	Cross-	United	16857	_	18-70	1310	819	Sex (female)	0.78	0.016
			sectional	Kingdom					8224	Adulthood physical abuse	0.85	0.016
	Cloitre et al. (2019)	General Population	Cross- sectional	United States	1839	52 %	18–70	70	-	Childhood physical abuse	4.40	0.008
		au					40.7		-	Childhood sexual abuse	3.88	0.008
	Dorahy et al. (2009)	Clinical population	Cross- sectional	Ireland	81	25.9	40.5 ±	20	64	Childhood emotional neglect	1.24	0.165
	Eidhof et al. (2019)	Clinical population	Cross- sectional	Netherlands	218	50 %	53.2 ± 7.4	52	114	Sex (female)	0.88	0.164
	Facer-Irwin et al. (2021)	Prisoners	Cross- sectional	United Kingdom	221	0 %	31.3 ± 9.0	37	28	Childhood physical abuse	3.5	0.066
									23	Childhood	3.4	0.066
									32	emotional neglect Childhood sexual abuse	2.5	0.063
	Frost et al. (2019a)	Refugee	Cross- sectional	United States.	308	56 %	37.42	15	30	Childhood sexual abuse	7.60	0.056
									172	Sex (female)	10.49	0.060
									35	Adulthood physical abuse	7.42	0.055
	Frost et al. (2019b)	General population	Cross- sectional	United Kingdom	1051	68.4 %	$\begin{array}{c} 47.18 \\ \pm \ 15 \end{array}$	204	114	Childhood emotional neglect	3.22	0.013
									99	Childhood physical abuse	1.18	0.012
									49	Childhood sexual abuse	1.84	0.012
									165	Sex (female)	1.54	0.012
	Hyland et al. (2017a, 2017b)	General population	Cross- sectional	Denmark	2591	54.6 %	24	26	66 436	Childhood sexual abuse Adulthood	9.43 6.80	0.007
									160	physical abuse Unemployment	6.99	0.000
									1263	Childhood physical abuse	3.62	0.00
									1245	Sex (female)	2.02	0.005
	Hyland et al.	Refugees	Cross-	Lebanon	110	51 %	43.10	79	88	Unemployment	2.21	0.126
	(2018)		sectional				\pm 15.12		80	Sex (female)	2.83	0.130
	Hyland et al. (2020)	General population	Cross- sectional	Republic of Ireland	1020	51 %	-	78	520 -	Sex (female) Unemployment	1.30 2.21	0.013
	Kairyte et al. (2022)	General population	Cross- sectional	Lithuania	158	85.4 %	$\begin{array}{c} 33.6 \pm \\ 9.7 \end{array}$	59	99	Childhood physical abuse	2.71	0.090
									95	Adulthood physical abuse	1.93	0.086
									48	Childhood sexual abuse	3.05	0.091
	Karatzias et al. (2017a, 2017b)	Clinical population	Cross- sectional	Scotland	193	65.1 %	$\begin{array}{c} 41 \pm \\ 12.4 \end{array}$	146	130	Childhood emotional neglect	3.81	0.077
									109	Childhood physical abuse	3.64	0.077
	**	0 1			501	70.0/	00.0	40	93	Childhood sexual abuse	3.40	0.076
	Karatzias et al. (2018)	General population	Cross- sectional	Israel	521	78 %	33.3 ± 11.9	49	49	Childhood sexual abuse	2.65	0.027
									16 83	Childhood physical abuse	6.66	0.032
	Kazlauskas	Clinical	Cross-	Lithuania	280	15.4 %	39.4 ±	77	83 55	Adulthood physical abuse Sex (female)	2.74 0.63	0.027
	et al. (2018)	population	sectional	EIGHAILIA	200	13.4 %	39.4 ± 13.3	//	45	Childhood physical abuse	2.98	0.047
	Kvedaraite et al. (2022)	General population	Cross- sectional	Lithuania	885	63.4 %	37.96 ± 14.67	16	205	Childhood physical abuse	2.69	0.019
		r - r							354	Adulthood	0.62	0.018

(continued on next page)

Table 2 (continued)

ID	Authors	Sample type	Designs	Country	N	% female	Age (M \pm SD)	Sample CPTSD	Sample Exposed	Risk factor	OR	VarLog OR
									21	Childhood sexual abuse	2.35	0.0193
17	Lewis et al. (2022)	Clinical population	Cross- sectional	United Kingdom	1305	75.33 %	-	166	983	Sex (female)	1.12	0.0101
18	Liddell et al. (2019)	Traumatized Refugees	Cross- sectional	Australia	112	33.9 %	-	33	38	Sex (female)	14.18	0.1819
19	Maercker et al. (2018)	General population	Cross- sectional	Germany	530	55 %	-	13	27	Childhood sexual abuse	1.72	0.0254
									72	Adulthood physical abuse	1.33	0.0250
20	Murphy et al. (2016)	Veterans	Cross- sectional	United Kingdom	177	4.9 %	-	96	21	Unemployment	0.50	0.0774
21	Sachser et al. (2017)	Clinical population	Cross- sectional	Germany	155	72.3 %	$13.01 \\ \pm 2.8$	62	112	Sex (female)	2.19	0.0894
22	Simon et al. (2019)	Clinical population	Cross- sectional	Netherlands	187	50 %	-	94	123	Sex (female) Unemployment	0.84 1.88	0.0709 0.0728
23	Spitzer et al. (2006)	Clinical population	Cross- sectional	Germany	82	7.5 %	36.9 ± 11.8	14	33	Childhood physical abuse	0.78	0.1632
									31	Childhood sexual abuse	1.15	0.1637
									59	Childhood emotional neglect	0.72	0.8705
24	Vang et al. (2019)	General population	Cross- sectional	Israel	834	49.9 %	$\begin{array}{c} 40.9 \pm \\ 14.3 \end{array}$	38	416	Sex (female)	0.85	0.0159

Abbreviations: CPTSD = Complex Post-Traumatic Stress Disorder; OR = Odds Ratio; VarLogOR = Odds Ratio's Logarithmic Variance.

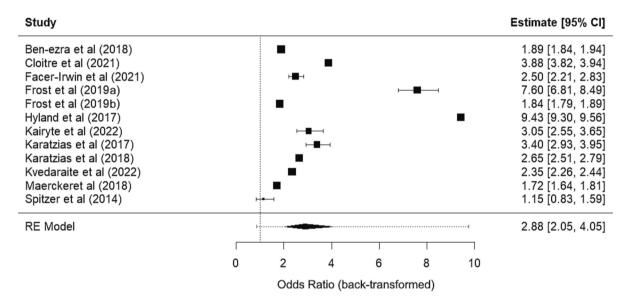


Fig. 2. Forest plots for childhood sexual abuse as a risk factor for CPTSD based on back-transformed effect sizes.

the type of "cross-sectional" study design, which for questions "6, 7 & 13" obtained the minimum score since they evaluate characteristics of longitudinal studies.

3.2. Meta-analysis

Six main risk factors are identified that show a significant effect on CPTSD (Table 2). Having suffered childhood sexual abuse is the risk factor that most increases the odds of developing CPTSD (n=9217; k=12; OR = 2.880; CI = 2.050–4.048; p=.000; FSN = 33,002; RR = 70; p=.000; Fig. 2), followed by childhood physical abuse (n=8659; k=11; OR = 2.841; CI = 2.013–4.008; p=.000; FSN = 11,003; RR = 65; p=.000; Fig. 3), and childhood emotional neglect (n=1628; k=5; OR = 2.510; CI = 1.540–4.100; p=.000; FSN = 21,438; RR = 35; p=.000; Fig. 4). In addition, adverse experiences during adulthood, such as physical abuse, double the likelihood of developing CPTSD compared to individuals who have not suffered these types of abuse (n=22,688; k=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=22,688; k=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=22,688; k=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1000; CPTSD compared to individuals who have not suffered these types of abuse (n=1

8; OR = 2.149; CI = 1.157–3.992; p = .016; FSN = 14,758; RR = 50; p = .000; Fig. 5), further reinforcing its relevance as risk factors associated with CPTSD. (See Table 3.)

Regarding sex (female), several studies present it as a risk factor for belonging to the CPTSD group. For this factor, two types of analysis are performed. First, a meta-analysis with all studies that report female sex as a risk factor ($n=25,028;\,k=13;\,\mathrm{OR}=1.726;\,\mathrm{CI}=1.020-2.920;\,p=.042;\,\mathrm{FSN}=5658;\,\mathrm{RR}=75;\,p=.000;\,\mathrm{Fig.}$ 6). Subsequently, a sensitivity analysis is performed that excludes two studies a) Frost et al. (2019a) and b) Liddell et al. (2019) due to its effect sizes raising the mean results significantly ($n=24,608;\,k=11;\,\mathrm{OR}=1.214;\,\mathrm{CI}=0.184-0.912;\,p=.184;\,\mathrm{FSN}=5354;\,\mathrm{RR}=65;\,p<.000;\,\mathrm{Fig.}$ 7). The first results align with previous epidemiological studies, in which being female is a significant risk factor for the probability of developing CPTSD, compared to being male. However, after excluding two studies that acted as potential outliers, this effect was not significant (p=.184). Interpretation of these results and its discrepancies require more robust evidence.

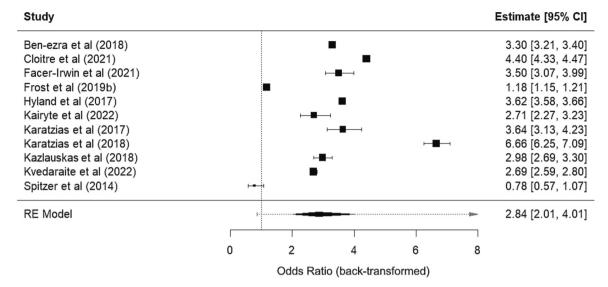


Fig. 3. Forest plots for childhood physical abuse as a risk factor for CPTSD based on back-transformed effect sizes.

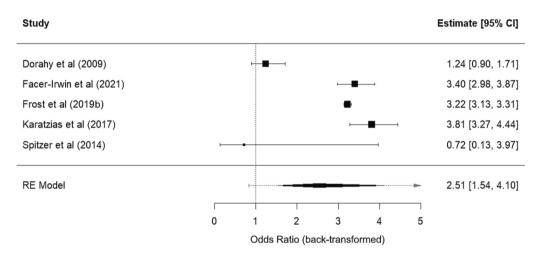


Fig. 4. Forest plots for childhood emotional neglect as a risk factor for CPTSD based on back-transformed effect sizes.

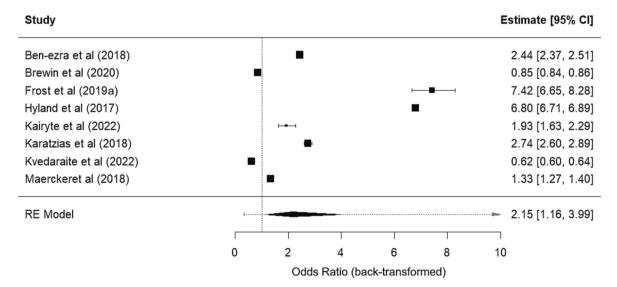


Fig. 5. Forest plots for adulthood physical abuse as a risk factor for CPTSD based on back-transformed effect sizes.

Table 3

Meta-analysis results for risk factors for CPTSD

Factor	k	и	REM							Heterogeneity tests	ity tests		Publica	Publication bias			
			logOR	OR	d	95 % CI		14 % 56									
						Lower	Upper	Lower	Upper	I^2	ð	d	RR	Fail-safe	d	ZEgger	d
Childhood sexual abuse	12	9217	1.058	2.880	0.000	2.050	4.048	0.850	9.762	99.92 %	23519.893	0.000	70	33002	0.000	-1.078	0.281
Childhood physical abuse	11	8659	1.044	2.841	0.000	2.013	4.008	0.868	9.298	99.93 %	8821.275	0.000	65	11003	0.000	-1.799	0.072
Childhood emotional neglect	2	1628	0.920	2.510	0.000	1.540	4.100	0.827	7.618	98.12 %	41.714	0.000	35	21438	0.000	-1.668	0.059
Adulthood physical abuse	∞	22688	0.765	2.149	0.016	1.157	3.992	0.336	13.757	% 86.66	71148.323	0.000	20	14758	0.000	0.519	0.604
Female sex (a)	13	25028	0.546	1.726	0.042	1.020	2.920	0.243	12.252	% 66.66	25643.784	0.000	80	5685	0.000	1.747	0.081
Female sex (b)	11	20608	0.194	1.214	0.184	0.912	1.614	0.456	3.228	100.00 %	24042.479	0.000	70	5354	0.000	0.573	0.567
Unemployment	2	4085	0.695	2.004	0.098	0.880	4.566	0.268	14.978	99.95 %	7109.796	0.000	35	1240	0.000	-0.961	0.034

Abbreviations: k = number of included studies; n = Sample size of included studies; (a) CPTSD=Complex Post-Traumatic Stress Disorder; logOR = Natural log of Odds Ratio; OR = Odds Ratio (back-transformed); = Heterogeneity index; Q = Cochran's test; FSN=Failsafe N test; RR = Rosenthal's Rule (k*5 + 10); Z_{Egger} = Egger's regression. (a) = Including all studies; (b) CI=Confidence intervals; PI=Prediction intervals; I² Excluding two studies based on sensitivity analysis. Finally, we examined the effect of unemployment, which is generally regarded as one of the risk factors most strongly related to CPTSD. However our results show a non-significant pooled effect (n=4085; k=5; OR = 2.004; CI = 0.880–4.566; p=.098; FSN = 1240; RR = 35; p=.000; Fig. 8). These opposing results may indicate that the association between unemployment and CPTSD may be linked to other factors, or that it comes as a consequence of CPTSD more than a risk factor. No publication bias was detected for any of these factors.

4. Discussion

The primary finding of this study is that being a victim of childhood sexual abuse serves as the risk factor with the most significant impact on the development of Complex Post-Traumatic Stress Disorder (CPTSD). Individuals within this group display a prevalence of CPTSD that is almost three times higher compared to groups who have not undergone such experiences. This is consistent with what has been found in the main studies regarding CPTSD (Karatzias et al., 2017b; Spitzer et al., 2006). The effect of suffering sexual abuse, particularly in childhood, is greater than the effect of physical and emotional abuse separately, as experiences of childhood sexual abuse often include other types of implicit abuse, such as physical and emotional (Vachon et al., 2015). This means that the presentation of sexual abuse does not occur in a vacuum but is accompanied by other adverse experiences. In fact, children who have been sexually abused have experienced other types of abuse more frequently than those who have not been sexually abused (Vaillancourt-Morel et al., 2016).

In addition, the literature concerning trauma and psychopathology suggests that early interpersonal abuse, particularly that of a sexual nature, generates a broad spectrum of psychological difficulties. The Janoff-Bulman Cognitive Impact Model describes that the victimization experience disturbs different areas of the self, shaping behaviors, values, beliefs, and attitudes in the affected individual. The cognitive impact generates an increased perception of vulnerability and threat. Simultaneously, new beliefs regarding social injustice are created, originating from the abusive experience, along with an imbalance of self-perception and self-image (Janoff-Bulman, 2013) and distortions similar to those described for CPTSD symptoms. This leads to harmful coping mechanisms for those who have experienced it (Gray and Rarick, 2018; Terr, 1991; Wurtele, 2009). In addition, childhood sexual abuse experiences generally lead to the presentation of episodes of emotion dysregulation (Maercker et al., 2013; Mallett and Schall, 2019) increase the likelihood of developing dissociative episodes, hallucinations (Gómez and Freyd, 2017) and eating disorders (Wohab and Akhter, 2010) along with an increased likelihood of having suicide attempts in adulthood, (Daray et al., 2016; Maniglio, 2009). Therefore, it is a relevant risk factor for mental health and the development of psychopathology, including CPTSD.

A risk factor with as profound an impact as sexual abuse is the effect of physical abuse. The literature indicates that childhood abuse experiences are more significant in relation to this disorder (CPTSD), and our results confirm this by indicating that physical abuse suffered in both childhood and adulthood are linked to an increased probability of developing CPTSD, with childhood physical abuse being as relevant as sexual abuse. Regarding adulthood physical abuse, a possible explanation for this finding is that individuals who report having suffered this kind of abuse in adulthood have probably also experienced either physical or sexual abuse in childhood and are describing a type of adverse experience that is cumulative over time, probably due to the measurement methods used to measure adverse experiences (Papalia et al., 2021; Messman-Moore and Long, 2000; Rivera-Rivera et al., 2006).

In addition, previous studies, including systematic reviews and metaanalyses, have highlighted sexual abuse as a significant risk factor for the development of Posttraumatic Stress Disorder (PTSD) in the general population (OR = 2.34; 95 % CI, 1.59-3.43; Chen et al., 2010). This risk

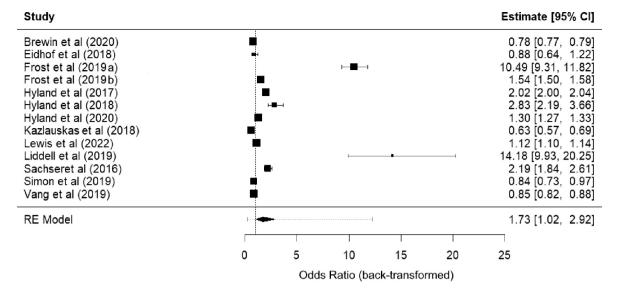


Fig. 6. Forest plots for female sex (a) as a risk factor for CPTSD based on back-transformed effect sizes.

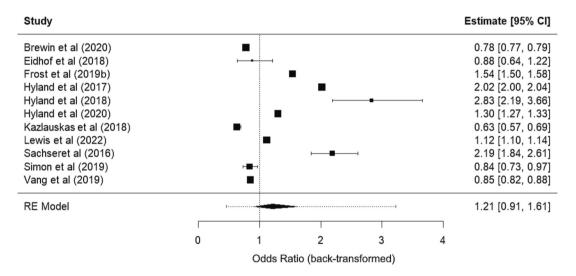


Fig. 7. Forest plots for female sex (b) as a risk factor for CPTSD based on back-transformed effect sizes.

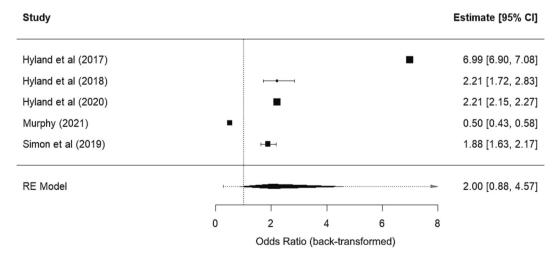


Fig. 8. Forest plots for unemployment as a risk factor for CPTSD based on back-transformed effect sizes.

is accentuated in child populations, with a higher incidence of PTSD in boys (OR = 2.86; 95 % CI, 2.09–3.91) and girls (OR = 2.38; 95 % CI, 1.76–3.23) (Boumpa et al., 2022). However, our research findings indicate that the experience of childhood sexual abuse is more closely associated with the development of Complex Posttraumatic Stress Disorder (CPTSD) than with the onset of PTSD. This finding aligns with the current trauma literature, which posits that early interpersonal abuse, particularly sexual abuse, leads to a broad spectrum of severe psychological difficulties. These difficulties are best identified by the symptoms of CPTSD.

An interesting fact to note is that early analyses indicate that women would be almost two times more likely to develop CPTSD compared to men, which is consistent with epidemiological findings (Karatzias et al., 2017b; Maercker et al., 2018). This could be attributed to the fact that, culturally and socially, women are more exposed to potentially traumatic events, particularly sexual and physical abuse both in childhood and adulthood (NCADV, 2019; United Nations, 2018). However, it is important to mention that two of the included studies; a) Frost et al. (2019a) and b) Liddell et al. (2019), present above average effects (a, OR = 10.49; b, OR = 14.18). The significant increase as a risk factor (being female) for CPTSD in these studies, is mainly attributed to the type of adverse experiences experienced by the samples in these studies (refugees fleeing their countries due to a real life threat). However, when calculating the results excluding these studies, it was found that CPTSD symptoms are not particularly more frequent among women.

Literature suggests that unemployment has a significant effect on CPTSD, where authors propose that it may be more of a consequence than a risk factor in itself (Serrano et al., 2021). It has been indicated in systematic reviews that unemployment status constitutes a risk factor for mental health. The mean percentage of unemployed people with psychological problems was 34 %, compared with 16 % among employed people (Paul and Moser, 2009). Although unemployment may differentially affect groups of people depending on their age, sex, or educational level, a significant relationship is established between being unemployed and impaired mental health (Norström et al., 2014). Our results align with this perspective, as unemployment had not a significant effect on CPTSD. The relationship between this disorder and unemployment observer through the literature may also suggest that there might be other variables mediating or confounding this effect. Future research should aim to elucidate the true nature of the association between this factor and the development of CPTSD in different populations.

From an economic perspective, Frey and Stutzer have explored the association between unemployment and mental health in relation to human well-being. They concluded that unemployment is a risk factor for depressive and anxiety disorders, highlighting the importance of psychosocial factors in relation to psychopathology (Frey and Stutzer, 2010). Regardless of the relationship between CPTSD and unemployment, these findings are especially relevant when designing public policies on occupational and mental health.

It is essential to highlight that the present study exhibits significant levels of heterogeneity in its results, which we hypothesize can be mainly caused by two factors. First, the results may reflect a statistical heterogeneity, which is observed due to disparities in sample sizes present in the included articles. Second, the characteristics of the samples of the incorporated studies, which includes differences in the levels of exposure to risk factors in terms of frequency, severity, and duration of exposure, may cause heterogeneity based on clinical features (Borenstein et al., 2009; Higgins, 2012). As this study represented the first meta-analytic approach towards understanding the risk factors for CPTSD, these findings also provide useful information regarding the current state of research on this disorder, where these risk factors have been studied in fairly different contexts. In this sense, high heterogeneity levels are to be expected. This highlights a growing need for evidence on the effects of each of these risk factors across populations in order to obtain more precise estimates of their true effect for the development of CPTSD.

Although these results enrich our understanding of how risk factors specifically affect CPTSD, the present meta-analysis has certain limitations. First, this study has focused solely on CPTSD as a single variable, without considering the specific dimensions of CPTSD. That is, the particular risk factors for the groups described by the ICD-11: 1) reexperiencing, 2) avoidance, 3) sense of threat and, in addition, disorganization of self-organization: 1) affective dysregulation, 2) negative self-concept, 3) interpersonal problems (Cloitre et al., 2013). Second, a methodological limitation, at some degree, is that this review was not previously registered. We also did not examine the impact of the frequency of potentially traumatic events as a risk factor for CPTSD. This omission points to a relevant line of research, not only on the content of the traumatic event, but also on its frequency over time. Finally, through quality assessment we detected an absence of longitudinal studies on risk factors for the development of CPTSD. This can be considered a relevant limitation of the existing literature, as evaluations with multiple measurements makes it possible to more accurately attribute the causal effect to an exposure variable, allowing researchers to observe changes over time.

Hence, this study provides important insights on the study of CPTSD and the role of childhood adverse experiences as a highly relevant risk factor for the development of this disorder. Our findings highlight the significant impact of abuse experiences in general on mental health and psychological wellbeing. While further studies will always be required to determine how closely related are these risk factors to the development of CPTSD, this review contributes with the current need for synthesizing and examining the existing evidence on this disorder and the factors associated with its development in later stages of life. Future research should then aim to further examine the role of both existing and emerging risk factors, while also providing resources and recommendations for clinical practice.

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Credit authorship contribution statement

 ${\it Marcelo\ Leiva-Bianchi}^1, Conceptualization$ - Data curation - Formal analysis - Fund Acquisition.

Marcelo Nvo-Fernandez¹, Conceptualization - Data curation - Formal analysis - proofreading and editing - Preparation.

César Villacura-Herrera 1,2 , Writing - Proofreading and editing - Preparation - Formal analysis.

Valentina Miño-Reyes², Data curation - Formal analysis. Nicol Parra¹, Research - Methodology.

Declaration of competing interest

The authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2023.10.002.

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