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Review Article

The prevalence, clinical impact, and therapeutic considerations of trauma in adults with bipolar disorder: A systematic review

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ABSTRACT

Background: Exposure to severe stressful life events (e.g., physical, sexual, emotional abuse and/or physical or emotional neglect) is common among adults with bipolar disorder (BD) and is associated with poor prognosis and clinical outcomes. This systematic review aims to evaluate the prevalence, clinical impact, and therapeutic considerations of trauma in adults with BD.

Methods: A systematic review of primary research was conducted using Embase, PsycInfo, MEDLINE, and PubMed databases from inception to January 2025, following PRISMA criteria. Sixteen human studies evaluating the prevalence, clinical impact, and therapeutic considerations of trauma in adults with BD were included.

Results: Prevalence rates of trauma in adults with BD have been variably estimated at approximately 40–60%. Childhood physical maltreatment is highly associated with comorbidities (e.g., metabolic disorders) and symptom severity in adults with BD. Childhood emotional maltreatment is associated with an earlier age of onset, greater illness severity, comorbidity and suicidality in BD. The moderating effects of trauma on treatment response across disparate modalities of treatment are not adequately characterized in persons with BD.

Conclusions: Trauma, especially childhood trauma, is prevalent and has a severe negative clinical impact on the presentation, progression, treatment, and outcomes of adults with BD. The research strategic priority is to characterize the biosignature of trauma in BD, the impact of trauma on treatment outcomes, and to empirically evaluate integrated models of care in persons with BD with a history of trauma.

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1. Introduction

Bipolar disorder (BD) is a spectrum of common, severe, debilitating, lifelong, heterogeneous, and costly mood disorders. It is characterized by recurring and alternating episodes of depression and mania/hypomania, and affects approximately 2–4 % of the adult population worldwide (McIntyre et al., 2020). Several genetic and environmental factors may contribute to the development of BD, with a prominent psychosocial factor being a history of trauma (Johnson et al., 2016; Guillen-Burgos et al., 2023; McIntyre, 2022). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) currently recognizes bipolar disorder type 1 (BDI) and type 2 (BDII), as well as cyclothymic disorder as subtypes of bipolar disorders (American Psychiatric Association, 2022). BDI is characterized by mania, associated with symptoms such as hyperactivity, euphoria, and delusions. BDII is characterized by hypomania, associated with symptoms such as elevated mood, activity, and energy levels. Cyclothymic disorder is characterized by hypomanic and depressive episodes which cycle rapidly, but do not meet the full criteria for BDII or major depressive disorder (MDD).

Trauma has been broadly defined as exposure to adverse experiences that result in diverse and heterogeneous emotional and/or physiological responses in affected individuals, such as adverse childhood experiences, natural disaster, terrorism and violence, and traumatic grief (Williams et al., 2016; Teicher et al., 2022). Experiencing traumatic events is associated with an increased risk of developing mental disorders such as BD, MDD, posttraumatic stress disorder (PTSD), personality disorders, and dissociative disorders (Bremner and Wittbrodt, 2020). It is important to note that exposure to trauma is dissociable from a diagnosis of PTSD, as trauma does not eventuate in PTSD in most cases. Consequently, there is a need to synthesize extant evidence on the prevalence and clinical impact of trauma exposure in persons with BD.

Trauma is often not a singular event, wherein multiple traumatic exposures and different types of trauma exposures are often reported. Herein, we evaluate studies reporting on adults with PTSD comorbid with BD, as well as adults living with BD who report a history of adverse childhood experiences (McCraw and Parker, 2017).

Trauma is reported as a frequent occurence in the general population. For example, a 2015 survey conducted by Benjet et al., reported that >70% of respondents comprising of 68,894 adults from 24 countries reported having experienced a traumatic event (Benjet et al., 2016). However, the majority of those who have experienced a traumatic event often do not develop symptoms which meet the criteria for a formal diagnosis of PTSD (McCraw and Parker, 2017). Notwithstanding the high prevalence of trauma in the aforementioned survey, it is separately reported by the World Health Organization that 3.9 % of individuals, receive a diagnosis of PTSD (Koenen et al., 2017). A separate study in adults with BDI (n = 116) reported a history of childhood trauma in 61.2 % of respondants (Erten et al., 2014). Replicated evidence indicates that a history of trauma in persons with BD is associated with a less favourable outcome across several facets including symptom severity, higher rate of psychiatric and medical comorbidity, suicidality, relapse rate, diminished response to treatment, overall quality of life and function (Johnson et al., 2016).

Herein, via systematic review, we aim to summarize current literature on the prevalence, impact, and therapeutic considerations of 1) childhood physical maltreatment; 2) childhood emotional maltreatment; 3) childhood sexual abuse; and, 4) comorbid PTSD in adults with BD. Furthermore, we aim to identify current gaps in the literature which may provide potential directions for future research vistas exploring this topic.

2. Methods

2.1. Search string and strategy

The systematic review adhered to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). A comprehensive literature search of online databases: Pubmed and OVID (MEDLINE, Embase, PsychINFO) was conducted from inception to December 23, 2024. The initial search query for all databases included: (trauma* OR advers* OR ptsd OR abuse OR posttraumatic stress disorder OR neglect OR maltreatment OR assault OR physical trauma OR emotional trauma OR mental trauma OR sexual trauma) AND bipolar. These terms were selected based on existing literature exploring a range of trauma-related exposures such as abuse, neglect, and various forms of psychological and physical trauma, which correlate to adults with BD. To expand the scope of the study, complex posttraumatic stress disorder (CPTSD) was incorporated to reflect its emerging recognition in literature potentially overlapping with BD, and a revised search query was applied across all databases: (trauma* OR advers* OR ptsd OR abuse OR posttraumatic stress disorder OR neglect OR maltreatment OR assault OR physical trauma OR emotional trauma OR mental trauma OR sexual trauma OR cptsd OR complex ptsd OR complex posttraumatic stress disorder) AND bipolar. The updated search was conducted on January 5, 2025.

2.2. Eligibility criteria

All retrieved studies were screened in accordance with the following eligibility criteria. The population included adults with BD who have a comorbid diagnosis of PTSD or experience symptoms, as well as animal models of BD and PTSD. The intervention included any form of treatment for BD. Comparators consisted of healthy adults with BD who do not have a comorbid diagnosis of PTSD or do not experience PTSD symptoms. Outcomes of interest included differences in the efficacy of various treatment methods or prognoses for adults with BD and comorbid PTSD, as well as outcomes observed in animal models. Both animal and clinical studies were eligible for inclusion. Animal models were included for their critical role in shaping preclinical testing of pharmacological and non-pharmacological interventions that may help inform clinical research. Studies were excluded if they involved pediatric individuals, were in vitro studies, were not available in full text, were not published in English, or were abstracts, protocols, or editorials. Pediatric individuals were excluded because the onset and course of BD and PTSD can differ greatly in children compared to adults. This focus on adults allows for greater consistency in diagnostic criteria across the included studies.

2.3. Study selection

Studies were identified and screened based on the predefined eligibility criteria to ensure they were in line with the review's objectives. Five reviewers (K.X., H.S., J.X., X.Z., and J.A.) utilized Covidence to screen the retrieved studies independently (Covidence, 2024). The studies were first screened based on their titles and abstracts. The papers deemed relevant by any reviewer were then subject to full-text screening against our eligibility criteria.

2.4. Data extraction

Key information was systematically collected from each of the included studies to synthesize results. Data extraction was completed by five reviewers (K.X., H.S., J.X., X.Z., and J.A.) using a standardized data extraction table, and any discrepancies were resolved through discussion. The data table included the following: 1) sample size, 2) sex distribution, 3) sample age, 4) diagnoses, 5) type of trauma, 6) dosage, 7) method of administration, 8) measurement tool, 9) outcome of interest, 10) mean, 11) standard deviation, and 12) *p*-value of results. (Table 1).

2.5. Risk of Bias assessment

Each included study's methodological quality was evaluated to

identify potential sources of bias that may affect the validity of the findings. The risk of bias assessment criteria included proper randomization and concealment of allocation, blinding of participants, providers, and outcome assessors, baseline group similarity, acceptable dropout and adherence rates, control of co-interventions, use of valid outcome measures, adequate sample size for statistical power, pre-specification of outcomes, and intention-to-treat analysis. Risk of bias was assessed by five reviewers (K.X., H.S., J.X., X.Z., and J.A.) using the NHLBI's Quality Assessment of Controlled Intervention Studies or Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (Hooijmans et al., 2014) (Table 2). Childhood trauma was assessed using the Childhood Trauma Questionnaire (CTQ), which has demonstrated high internal consistency (Cronbach's $\alpha = 0.79–0.94$) and solid convergent validity with clinical interviews (Bernstein et al., 2003).

Depressive symptoms were measured using the Montgomery–Åsberg Depression Rating Scale (MADRS), which shows strong inter-rater reliability (intraclass correlation coefficient [ICC] = 0.93) and sensitivity to change (Montgomery and Åsberg, 1979). General psychopathology was assessed using The Brief Psychiatric Rating Scale (BPRS), with established inter-rater reliability (ICC > 0.80) and solid construct validity (Overall and Gorham, 1962). Eye Movement Desensitization and Reprocessing (EMDR) therapy has been empirically validated in PTSD populations and is supported by randomized controlled trials (Shapiro, 2014). Attachment style was measured using the Experiences in Close Relationships Inventory-Revised (ECR-R), which demonstrated great internal consistency ($\alpha = 0.90–0.94$) and test-retest reliability (Sibley and Liu, 2004). PTSD symptoms were assessed using the PTSD Checklist for DSM-5 (PCL-5), which shows strong internal consistency ($\alpha = 0.94$) and valid test-retest reliability (ICC = 0.82) (Blevins et al., 2015). Manic symptoms were evaluated using the Young Mania Rating Scale (YMRS), which has solid inter-rater reliability ($r = 0.93$) and high internal consistency ($\alpha = 0.79$) (Young et al., 1978).

3. Results

3.1. Search results and study characteristics

Our systematic search of online databases identified 126,963 studies. An additional 20 studies were identified by manual citation searching. Of these, 111,914 duplicates were automatically removed through Covidence. As a result, 15,069 studies were screened by title and abstract. From the identified articles, 182 studies underwent full-text review, and 36 studies were deemed eligible for inclusion in the review herein. The complete details of our systematic search and article screening process are shown in Fig. 1.

All 36 studies investigated adults with a primary diagnosis of BD, with a total sample size of 2658 adults. Generally, the studies included adults aged 18–65, with 1120 male participants and 1538 female participants in total. Six studies investigated the effect of childhood trauma or maltreatment in adults with BD. These included: Rowe et al. (2024), Wrobel et al. (2022), Ehrlich et al. (2023), Oymak Yenilmez et al. (2019), McCraw and Parker (2017), and Palagini et al. (2021). Four other studies focused on emotional or physical neglect or abuse in adults with BD: Schwarz et al. (2024), Hogg et al. (2024), Novo et al. (2014), and Daglas et al. (2014). An additional four studies examined the impact of diagnosed PTSD in this population: Guillen-Burgos et al. (2025), Katz et al. (2024), Frost et al. (2020), and Chessen et al. (2011).

3.2. Results from risk of Bias assessment

The risk of bias assessment for the studies showed an average assessment of "Fair/Good." The most common concern for the studies was the lack of mention of the treatment group's adherence to the intervention protocols and the sample size not being large enough to detect a difference in the main outcome with 80 % power. The studies performed by Rosenberg et al. (2004), Nishith et al. (2024), and Schneeberger et al. (2014) all received an overall risk of bias assessment of "Poor" and were therefore removed from inclusion. This rating was due to insufficient details regarding the randomization and blinding of treatment groups and providers. Similarly, Leverich and Post (2006) was removed from inclusion due to a lack of details regarding blinding of people assessing the outcomes and control of important baseline characteristics in groups. On the other hand, the study by Ihme et al. (2022) was removed due to the priority of the study on suicide ideation rather than BD.

3.3. Prevalence of trauma in adults with bipolar disorder

From the included studies, three studies investigated the prevalence of trauma, rather than a diagnosis of PTSD, in adults with BD: McCraw and Parker (2017), Cho et al. (2021), and Xie et al. (2018).

McCraw and Parker (2017) evaluated 747 participants with BD (n = 334) or MDD (n = 413) with an overarching aim to estimate the percentage reporting stressful life events and associated outcomes. Within the sample of persons with BD, 44 (13 %) had BD-I while 290 (87 %) had BD-II.

Compared to the unipolar group, the BD group reported a significantly higher prevalence of trauma despite being—on average—$M = 7.3$ years younger, ($p < 0.001$). Among individuals with BD, 40.7 % ($p < 0.001$) reported a traumatic childhood, and 69.6 % of them noted a significant life impact. Additionally, the BD group reported higher rates of physical or sexual assault or abuse as an adult [an 8.6 % increase ($p < 0.01$)], serious disputes with a relative, employer, close friend, or neighbour [an 11.1 % increase ($p < 0.01$)], major difficulties in close relationships [an 12.4 % increase ($p < 0.01$)], break-ups of close relationships [an 9.2 % increase ($p < 0.05$)], legal problems (an 7.5 % increase, $p < 0.05$), major financial crises [an 9.6 % increase ($p < 0.01$)], serious drug or alcohol issues [an 9.7 % increase ($p < 0.01$)]. The majority (56.7 %–72.9 %) of participants with BD who have experienced these events reported that it has significantly impacted their lives. Furthermore, the authors note that almost twice as many BD participants met the criteria for PTSD compared to MDD participants, highlighting that adults living with BD may be more vulnerable to developing PTSD after a traumatic event compared to those with MDD.

When examining the effects of gender on the prevalence of traumatic events in participants, both male and female participants with BD were similarly likely to experience potentially traumatic events, 53.3 % and 62.6 %, respectively. However, it may be relevant to note that Hyun et al. (2000) concluded that, in addition to the aforementioned prevalence of trauma among persons with BD, women are generally more likely to have experienced childhood sexual abuse. Moreover, 24.3 % of males with BD and 27.8 % of females with BD met the criteria for a diagnosis of PTSD. As a result of these observations, McCraw and Parker (2017) concluded that there was no significant gender/sex difference in PTSD rates among participants with BD who were exposed to traumatic events.

In comparison, Cho et al. (2021) examined the prevalence of childhood trauma in a sample of adults with BD compared to adults with schizophrenia. The aforementioned study by Cho et al. (2021) did not find any significant differences in the prevalence of childhood trauma in adults with BD when compared to schizophrenia.

In contrast, Xie et al. (2018) observed that in a sample of adults in Southern China, there were higher prevalence rates and greater severity of childhood trauma in adults with BD compared to healthy controls. Moreover, Xie et al. (2018) reported that childhood trauma is associated with poor social support and suicidal ideation. Specifically, in their sample, 32.4 % of BD adults experienced childhood trauma, defined by a total score of ≥50 on the Childhood Trauma Questionnaire (CTQ). In comparison, only 2.3 % of controls experienced childhood trauma, highlighting the significant gap in prevalence between adults with BD and healthy adults.

Table 1
Characteristics of included studies.

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
Guillen-Burgos et al. (2024)	49 patients met inclusion criteria and were administered lithium, 34 in maintenance phase	Acute phase (before maintenance phase): 19 males 30 females Maintenance phase: 6 males 28 females	Acute phase mean: 31.77 Maintenance phase mean: 33.02	BD and comorbid PTSDBD with PTSD	PTSD	Lithium (600 mg)was initially given once daily for 7 days, and doses were adjusted based on the clinician criteria (where doses can go up to 1800 mg in order to obtain a therapeutic range (0.80–1.50 mEq/L) in the serum concentration. Quetiapine was initially 50 mg, and was divided into two doses per day. Qyetiapin was also adjusted up to 800 mg depending on clinician's judgment.	Not reported	BD and PTSD YMRS MADRS CGI-BP-Severity	1. Difference in treating patients with comorbid PTSD and BD with monotherapy vs combination therapy. 2. Risk of recurring mood events.	1. Lithium paired with quetiapine resulted in a 85 % reduction risk of mood episodes recurring compared to using only MS. 2. Monotherapy results in a higher rise in mean scores of YMRS, MADRS, and CGI-BP-S.	Overall score change from baseline: Day 14: -1.05 ± 0.34 Day 28: -2.17 ± 0.46 Day 56: -2.67 ± 0.47 Day 84: -3.20 ± 0.88	Not reported	All are $p < 0.001$ for mean values in table
Katz et al. (2024)	32 patients (75 % completing all treatments)	22 females 10 males	Mean age: 34.8	Patients with comorbid BD and PTSD	PTSD	Prolonged exposure therapy (10 sessions)	PE following the PE manual	For baseline PTSD and BD diagnosis: the Mini-International Neuropsychiatric Interview PCL-5 CHRT C-SSRS SIAT QIDS-SR STAI ASRM	1. Explore feasibility, as well as preliminary efficacy of prolonged exposure therapy in patients with comorbid PTSD and BD. 2. PTSD symptoms and suicide risk. 3. Depression, mania symptoms, state and trait anxiety.	1.PSTD symptoms and suicidality decreased when comparing session 10 to baseline. 2. Suicidal thinking and depressive symptoms decreased originally from baseline to session 10, rebounded but remained below baseline levels. 3. State and trait anxiety increased in the	Session 10: PCL-5: -26.79 CHRT: -4.46 6 months: PCL-5: -30.62 CHRT: -2.62	N/A	A < 0.001, except for CHRT at 6 months ($p = 0.082$)

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
										beginning and decreased. After session 5, stayed relatively stable. Mania was stable.			
Rowe et al. (2024)	114 patients	97 females 17 males	all are over 18	Patients with BD I (41.2 %) or II (52.8 %)	childhood cumulative trauma	N/A	N/A	MADRS subscale DASS subscale MADRS item 10 (for suicidal ideation) YMRS and ASRM (for mania severity) SCID-5-RV (for number of mood episodes) DASS anxiety subscale QoL-BD	Determining childhood cumulative trauma, perceived social support, and perceived stress can possibly predict BD illness as well as quality of life outcomes.	Childhood cumulative trauma, perceived social support, and perceived stress account for a significant portion of the variance in measures of quality of life.	Regression coefficients: Clinical interview: Depression (MADRS): 0.21 Mania (YMRS): 0.02 Suicidal ideation (MADRS): 0.17 Predicting self-reported outcomes: Depression (MADRS): 0.50 Mania (YMRS): 0.03 Anxiety (DASS): 0.35 Quality of life (QoL-BD): 0.62	N/A	All are <0.05, some are <0.01
Wrobel et al. (2022)	692 patients were screened, 482 were randomized	282 females 200 males	18–62	Patients with BD	Childhood trauma	Only reported maximum dose: No childhood trauma Lithium = 995 mg Quetiapine = 340 mg Childhood trauma:	Oral	Baseline: Mini-International Neuropsychiatric Interview (MINI) Baseline and follow-up: Bipolar Inventory of Symptoms Scale (BISS) CGI-BP Longitudinal Interval Follow-up Evaluation-Range of	Association of childhood trauma and the outcome of different treatments in patients with BD.	Participants with history of childhood trauma had more symptom severity and functional impairment, but showed similar rates of improvement in symptom severity and	Patients: With childhood trauma = 8.90 Without childhood trauma = 9.44	Patients: With childhood trauma = 6.12 Without childhood trauma = 6.30	$p = 0.34$

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
						Lithium = 1040 mg Quetiapine = 349 mg		Impaired Functioning Tool (LIFE-RIFT) Necessary Clinical Adjustments (NCAs)		functional improvement over 24 weeks of treatment.			
Ehrlich et al. (2023)	405 adults with BD, 136 controls	BP High = BP with high level of childhood trauma BP Low = BP with low level of childhood trauma 173F/71M in BP High 103F/58M in BP Low	BP High: 41.27 BP Low: 36.30	BD1, BD2, or BD-NOS	Childhood trauma	N/A	N/A	CTQ Neuropsychological battery	Effects of childhood trauma on memory in adult BD patients.	Adults with BP, along with higher childhood trauma, are determined to have worse memory performance when compared to the group with lower childhood trauma.	Across all 8 factors of cognition, BP high < BP low < controls, including visual and auditory memory Visual memory: High (−0.119) Low (0.194) Control (0.415) Auditory memory: High (−0.089) Low (0.265) Control (0.297)	Visual memory: High (0.921) Low (0.873) Control (0.790) Auditory memory: High (0.911) Low (0.799) Control (0.737)	$p < 0.05$
Schwarz et al. (2024)	71 bipolar patients	43F/28M	39.61	BD diagnosis using ICD-10	Emotional, physical, sexual abuse emotional, physical neglect	N/A	N/A	Mini International Neuropsychiatric Interview CTQ Functioning Assessment Short Test (FAST)	Effects of childhood trauma on functioning in BD.	Childhood trauma and emotional coping have largest impact on FAST scores.	CTQ: 54.77	CTQ: 14.09	$p < 0.05$
Oymak Yenilmez et al. (2019)	252 subjects total 85 patients with BD, 81 MDD in remission, 86 healthy participants	BD 46F/39M MDD-RE 53F/28M Healthy 51F/35M	18–65 years of age	BD and Recurrent MDD	Childhood maltreatment and emotion dysregulation	N/A	N/A	Structured Clinical Interview for DSM-IV Axis I (SCID-I) The Metacognitions Questionnaire −30 (MCQ-30) Automatic Thoughts Questionnaire (ATQ) Difficulties in Emotion Regulation Scale (DERS) CTQ YMRS Beck Depression	If childhood maltreatment and emotion dysregulation impairs automatic thoughts and meta-cognitions in those with BD and recurrent MDD.	Childhood emotional dysregulation and adversities are associated with MCs and ATs in MDD-RE and BD.	CTQ BD mean: 56.94 CTQ MDD-RE mean: 62.43 CTQ control mean: 51.35 DERS BD mean: 102.78 DERS MDD-RE mean: 95.21 DERS control mean: 77.86	CTQ BD: 15.41 CTQ MDD-RE: 16.07 CTQ control: 22.35 DERS BD: 25.31 DERS MDD-RE: 18.40 DERS control: 20.24	$p < 0.01$

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
								Inventory (BDI) Hypomania Checklist - 32 (HCL-32) State-Trait Anxiety Inventory (STAI)					
Hogg et al. (2024)	77 patients with BD and current trauma-related symptoms 39 in eye movement desensitization and reprocessing (EMDR) group 38 in supportive therapy (ST) group	EMDR 8 M/ 31F ST 10 M/28F Total: 18 M/ 59F	Age 18–65	Patients diagnosed with BD with at least 1 traumatic event according to clinician-administered PTSD scale (CAPS)	Episodes of hypomanic, manic, or depressive episodes from trauma	N/A	20 × 1 h weekly therapy sessions (EMDR or ST) in medical facility or assigned therapist's office	Case Report Forms (CRF) at baseline, 6-months post-treatment, and 12 and 24 month follow-ups Bipolar Depression Rating Scale (BDRS) YMRS Clinician-administered PTSD scale (CAPS) Dissociative Experiences Scale (DES) Impact of Events Scale-Revised (IES-R) Functioning Assessment Short Test (FAST) Screen for Cognitive Impairment in Psychiatry (SCIP-S)	Primary: Relapse of mood episode. Secondary: affective and trauma-related symptoms, functioning and cognitive impairment.	1. No significant difference in relapse rates when relating back to difference in treatment conditions 2. EDMR was more superior to SD in reducing depressive and manic symptoms at 12-month follow-up, as well as functional improvement.	X	X	For affective symptoms and manic symptoms, EMDR was more effective ($p = 0.0006$, $p = 0.027$) Significant reduction of trauma symptoms by both interventions ($p < 0.01$)
Novo et al. (2014)	20 participants Eye Movement Desensitization and Reprocessing therapy (EMDR) ($n = 10$) or TAU (n = 10)	EMDR: 43.90 ± 6.87 TAU: 44.80 ± 6.86	Male: 8 Female: 12	Participants with a diagnosis of BD I or II according to DSM-IV criteria showing subsyndromal affective symptoms	At least 3 documentable traumatic experiences	N/A	N/A	All participants were assessed by a single assessor Affective symptoms assessed using the HDRS, the YMRS and the CGI-BP Symptoms of PTSD was assessed using the IES-R and CAPS Premorbid IQ was assessed using the	Determining if traumatic events are frequent in bipolar patients, and if its presence can worsen the course of the disease in the patients.	EMDR had a mood stabilising effect of depressive and hypomanic symptoms in unstable bipolar patients. Bipolar patients with subsyndromal symptoms that	1)YMRS EMDR 24 weeks difference: −4.00 2)HDRS EMDR 24 weeks difference: −4.60 3)YMRS TAU 24 weeks difference: −1.60	1)SD = 3.97 2)SD = 2.79 3)SD = 4.19 4)SD = 5.01	$p \leq 0.05$

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
								Word Accentuation Test The effects of treatment was assessed using the repeated-measures analysis of variance (RMANOVA)		underwent treatment with EMDR improved in trauma-related symptoms.	3)HDR TAU 24 weeks difference: −2.60		
Frost et al. (2020)	81 participants PTSD (27) and no PTSD (54)	PTSD: 44.78 ± 9.10 No PTSD: 44.28 ± 13.13	Male: 26 Female: 55	Participants with a DSM-IV diagnosis of BD I or II	PTSD	N/A	N/A	Psychiatric diagnosis was screened using the Structured Clinical Interview for Axis I (SCID-I) Depression severity was assessed using Beck Depression Inventory-II (BDI-II) Depression was measured using the HDRS Depressive and manic symptoms was assessed using the ISS Manic symptoms was assessed using the Bech–Rafaelsen Mania Rating Scale (BMRS) The severity of generalized anxiety was measured using the Generalized Anxiety Disorder-7 (GAD-7) Extreme positive and negative appraisals of activated states was measured using the Hypomanic Attitudes and Positive Predictions Inventory (HAPPI)	Determining if PTSD is related to the patient's current depressive and manic bipolar symptoms.	Participants with comorbid diagnosis of BD and PTSD had higher depressive symptoms and more conflicting appraisals compared to those with no PTSD PTSD was associated with depressive symptoms but not manic symptoms.	NR	NR	$P = 0.05$
McCraw and	747 participants	55.6 % female	39.7 ± 13.1	Patients with a primary	Stressful life events	N/A	N/A	Mini International Neuropsychiatric	Determining if mood states can	The BP group reported a	1)MAP DSM-IV criteria for BP	1)SD = 1.8	1)p ≤0.001

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
Parker (2017)	Unipolar (n = 412) and bipolar (n = 334)			diagnosis of a mood disorder	Childhood and adulthood abuse			structured Interview (MINI) Mood disorders assessed according to the formal DSM-IV criteria Trauma exposure was screened using the Mood Assessment Program (MAP) Data analyzed using the Statistical Package for Social Sciences (SPSS)	have a mediating effect on prevalence of anxiety symptoms.	higher prevalence of trauma (stressful life events) than the UP group. The BP group reported higher lifetime rates of different types of anxiety compared to the UP group Nearly twice as many participants from the BP group affirmed criteria which measures a lifetime diagnosis of PTSD compared to the UP group.	group: 2.4 2)MAP DSM-IV criteria for UP group: 1.3 3) BP with a traumatic childhood: 40.7 % 4)BP with exposure to an extremely stressful or upsetting event across lifetime: 44.9 % 5)BP with evidence of lifetime PTSD: 58.7 %	2)SD = 1.5 3)NR 4)NR 5)NR	2)$p \leq 0.001$ 3)$p \leq 0.001$ 4)$p \leq 0.5$ 5)$p \leq 0.01$
Chessen et al. (2011)	260 clients recruited (3 excluded) 74 clients completed the assessment and were interviewed	62 % male (46) 38 % female (28)	44.7 ± 7.8	Clients with severe and persistent axis 1 psychiatric disorders and a past or current psychoactive substance use disorder	Violence in the military, accidents, natural disasters, physical or sexual assaults, loss of a family member or friend to violence, other incidents involving death or injury to oneself or one's friends or family PTSD	N/A	N/A	Trauma was measured using the Trauma Assessment for Adults (TAA) PTSD was measured using a Posttraumatic Stress Diagnostic Scale (PDS) Treatment experiences were measured using a Treatment Experiences Questionnaire Statistical analysis completed using SPSS data system	Determining the degree trauma was addressed in patients being treated for severe mental illness, as well as substance abuse.	Treatment in community mental health clinics was more likely to focus on trauma for patients with a diagnosis of depression than patients with a diagnosis of schizophrenia or schizoaffective disorders. Clinicians report having little to no training in discussing, bringing up, or treating trauma within psychotic populations.	1)Global Assessment of Functioning for schizophrenia and schizoaffective disorders was 37.7 2)Number of categories of trauma experienced was 3.3 3)PDS score was 22.2 4)Desire to talk about trauma: 2.5 5)Focus of trauma in treatment: 1.7 6)Upsetting to	1) ± 12.7 2) ± 1.5 3) ± 16.3 4)SD = 1.2 5)SD = 0.8 6)SD = 1.1	Bipolar model 1b: $p = 0.32$ Bipolar model 2c: $p = 0.25$ Bipolar model 3d: $p = 0.47$

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
											talk about trauma in treatment: 2.4		
Daglas et al. (2014)	65 participants	44 M/21F	15–29 years 21.60 average	Patients experiencing first episode psychotic mania according to the DSM-IV-TR	History of sexual abuse/assault, physical abuse/assault, and emotional abuse/neglect	N/A	N/A	Trauma defined by DSM-IV-TR Brief Psychiatric Rating Scale, MADRS, YMRS	Determining if prior traumatic events were related to patients having worse outcomes after the first mania episode.	Nearly half of patients experiencing fist episode psychotic mania reported past trauma. Patients with a history of trauma experience worse outcomes in symptoms and depression. mania, and is associated with worse functioning 12 months after the episode.	YMRS = 35.67 MADRS = 13.19 BPRS = 61.9	YMRS = 7.77 MADRS = 4.94 BPRS = 13.88	YMRS = 0.82 MADRS = 0.02 BPRS = 0.33
Palagini et al. (2021)	162 adult participants	64 M/98F	18–65 years 47 ± 12.5	Diagnosis of BD I/II and experiencing a major depressive episode with and without mixed features according to DSM-5	Early life general stress, physical stress, emotional stress, and sexual abuse	N/A	N/A	Structured Clinical Interview for DSM-5, Early Trauma Inventory Self-Report-Short Form, Beck Hopelessness Scale, Insomnia Severity Index, Scale for Suicide Ideation, Beck Depression Inventory-II, YMRS	Determining the potential role insomnia symptoms plays in mood symptoms, suicide idealation, and hopelessness and mediating it during early exposure of stressful events.	Symptoms of insomnia may contribute to the relationship between early life stressors clinical features in adult BD and hopelessness.	In general, individuals with clinically significant insomnia experienced more early life stress in all 4 categories and hopelessness when compared to individuals with non clinically significant insomnia	For categories under early life stress and hopelessness, the SD typically ranged from 1–3, except for the BHS total score, for which both groups had an SD of 5.7	For early life stress, general, physical, and emotional stress had $p <$ 0.05. For early life sexual abuse, $p = 0.567$ For hopelessness, all categories except future expectations had $p > 0.05$. For future expectations, $p = 0.05$
Savitz et al. (2008)	230 largely euthymic participants from 47 families (49 BDI, 19 BDII, 44 MDE-R, 33 MDE—S, 20 DSM-IV)	NR	47.75 - BDI 36.66 BDII 47.47 MED-R 51.91 MED-S	BDI, BDII, MDE—S, MDE-R	Childhood trauma	N/A	N/A	WAIS general knowledge Beck Depression Inventory Altman Self-Rating Mania Scale	Explore whether neurocognitive deficits in BD I extend to relatives with BD II and UPD. Assess if these	Sexual/ emotional abuse and emotional neglect are correlated with poor cognitive performance when	In ORDER: BDI, BDII, MDE—S, MDE-R WAIS: (11.26, 11.11, 11.03, 11.33) Beck: (10.23,	In ORDER: BDI, BDII, MDE—S, MDE-R WAIS: (1.47, 1.84, 1.67, 1.76) Beck: (9.93, 9.93, 7.86, 4.97)	RAVLT total learning – Sexual Abuse (No Med Model): 0.0804 RAVLT total learning –

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
								Child Trauma Questionnaire (Emotional Abuse, Physical Abuse, Sexual Abuse, Emotional Neglect, Physical Neglect, Denial) Controlled Oral Word Association Test Rey Complex Figure Rey Auditory Verbal Learning Test Wisconsin Card Sorting Test	deficits stem from childhood abuse. Consider the impact of medication and alcohol abuse.	compared with healthy relatives. Adults with BDI with a history of childhood trauma perform significantly poorer in verbal recall memory when compared to relatives.	17.53, 9.30, 6.55) Altman: (3.33, 3.27, 2.70, 2.38) CTQ EA: (10.87, 14.31, 11.60, 9.00) CTQ PA: (8.09,11.25, 8.88, 6.86) CTQ SA: (9.11, 9.63, 7.55, 5.79) CTQ EN: (11.02, 13.38, 11.83, 9.17) CTQ PN: (7.45, 9.31,6.90,6.93) CTQ Denial: (0.64, 0.63, 0.76, 0.83)	Altman: (3.55, 3.43, 2.48, 2.90) CTQ EA: (5.48, 6.14, 5.36, 4.04) CTQ PA: (4.74, 6.85, 5.08, 3.84) CTQ SA: (5.96, 6.97, 4.45, 2.51) CTQ EN: (5.17, 5.90, 4.82, 3.53) CTQ PN: (3.75,3.84,2.22, 2.14) CTQ Denial: (0.92, 1.09, 1.14, 1.00)	Emotional Abuse (No Med Model): 0.4042 RAVLT total learning – Emotional Neglect (No Med Model): 0.1381
Jansen et al. (2016)	228 young adults	Female (%) Community Controls (n = 94): 58 % MDD (n = 82): 77 % BD (n = 52): 74 %	18–24 years	BD, MDD	Childhood trauma	N/A	N/A	CTQ Portuguese (Emotional Neglect, Physical Neglect, Emotional Abuse, Physical Abuse)	Assess prevalence of childhood trauma in young adults with mood disorders vs. those without mood disorders. Identify types of trauma based on mood disorder diagnosis. Investigate how family history of mood disorders and childhood trauma interact and affect mood disorder diagnosis.	All types of childhood trauma are associated with MDD and BD sexcept sexual abuse, which is only associated with BD.	Emotional Neglect: Prevalence: 21.2 % in BD participants Physical Neglect: Prevalence: 28.8 % in BD participants Emotional Abuse: Prevalence: 44.2 % in BD participants Physical Abuse: Prevalence: 25.0 % in BD participants Sexual Abuse: Prevalence: 21.2 % in BD participants	NR	$P < 0.001$

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
											Any trauma Prevalence: 53.9 % in BD participants		
Janiri et al. (2015)	104 outpatients from Sant'Andrea Hospital and Santa Lucia Foundation in Rome	Males: (39 BDI, 23 BDII) Females: (19 BDI, 23 BDII)	BDI: 43.93 (13.55 SD) BDII: 46.32 (13.69 SD)	BD (58 BDI, 46 BDII)	Childhood trauma	N/A	N/A	CTQ YMRS HDRS HAMA	Investigate how different types of childhood trauma are linked to BD I and BD II subtypes. Assess the influence of childhood trauma on suicidality.	In the sample, all adults with BD had more severe childhood trauma than controls. When compared to controls, BDI is strongly associated with sexual abuse, and BD II is strongly associated with emotional neglect.	IN ORDER: BDI, BDI, CONTROL Trauma Summary Score: 39.13, 40.89, 33.09 Emotional Abuse: 7.67, 8.87, 6.19 Physical Abuse: 6.22, 6.43, 5.56 Sexual Abuse: 6.37, 5.91, 5.19 Emotional Neglect: 11.29, 12.76, 9.48 Physical Neglect: 7.56, 6.91, 6.66	IN ORDER: BDI, BDI, CONTROL Trauma Summary Score: 12.12, 10.75, 7.34 Emotional Abuse: 3.67, 4.40, 2.10 Physical Abuse: 2.59, 3.06, 1.43 Sexual Abuse: 2.91, 1.76, 0.81 Emotional Neglect: 5.44, 4.95, 4.49 Physical Neglect: 2.76, 1.96, 3.64	IN ORDER: trauma, EA, PA, SA, EN, PN HC vs BDI: 0.0009, 0.02, 0.19, 0.0006, 0.08, 0.20 HC vs BDII: <0.0001, <0.0001, 0.09, 0.91, 0.001, 0.89 BDI vs BDII: 0.65,0.16, 0.89, 0.44, 0.31, 0.56
Upthegrove et al. (2015)	2019 participants	1415 female, 604 male	47 years	DSM-IV diagnosis of BDI History of Psychosis	Childhood trauma	N/A	N/A	Schedules for Clinical Assesment in Neuropsychiatry Semi-structured Interview Childhood Life Events Questionnaire: CLEQ	Explore the link between adverse childhood events and psychotic symptoms in a large, well-characterized sample of BD patients.	In adults with BD, childhood trauma is not associated with psychosis and delusions. Sexual abuse is strongly associated with auditory hallucinations.	NR	NR	
Pavlova et al. (2018)	174 adults	98 female, 76 male	41.79 (SD = 12.71)	BD I (81, 46.6 %) One lifetime anxiety disorder (50, 28.7 %) 2+ Lifetime Anxiety Disorder (34, 19.5 %)	Childhood trauma	N/A	N/A	CTQ Severity Index Sensitivity Index	Clarify if both factors contribute equally to poor outcomes in BD. Determine if assessing both factors improves outcome prediction and	In adults with BD, childhood trauma is associated with the number of lifetime anxiety disorders, though it is more associated with suicide attempts.	Effect of childhood maltreatment on suicide attempts: OR = 1.7	NR	$P = 0.008$

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
									intervention targeting.				
McIntyre et al. (2008)	381 outpatients who utilized clinical serveis at Mmood Disocrds Pharmacology Unit of UHN	212 female 169 males	18–65	DSM-IV-TR diagnosis of BD (BDI, BDII, Cyclothymic Disorder, and BD NOS)	Childhood sexual and physical abuse	N/A	N/A	DSM-IV-TR for diagnosis Case report to capture data from medical charts Interview with MDPU consultant	Determine whether there is an association between childhood abuse and sucidality in BD.	1. A history of childhood abuse was a significant predictor of lifetime suicidality 2. Subtyping abuse was not statistically significant for either physical or sexual abuse	63 % BP patients with CA history reported lifetime suicidality versus 45.7 % without CA (6.89) Higher attempted suicides for patients with CA vs no CA (11.79)	NR	Lifetime suicidality CA vs no CA 0.009 Attempted suicide CA vs no CA 0.003
Fowke et al. (2012)	70 total, 35 adults with BD and 35 control w/ no history	44 female 26 male	BD group: 45.57 (SD = 9.89) Control group: 46.20 (SD = 12.70)	BD diagnosis and part of National Health Service outpatients and/or local members of national BD support group	Childhood trauma and internalized shame	N/A	N/A	ISS Hospital Anxiety and Depression Scale CTQ Internalized Shame Scale	Examine the effects of childhood trauma and its effects on internalized shame in adults with BD.	BD group reported significantly greater frequency of high levels of childhood trauma compared to control; childhood emotional abuse and neglect were particularly high. Significant correlations observed between current internalized shame and childhood emotional abuse/neglect.	CTQ BD 50.06 control 33.57 CTQ BD emotional abuse 12.63 Control 7.34	CTQ BD 21.61 control 10.51 CTQ BD emotional abuse 6.19 control 3.33	CTQ 0.001 CTQ emotional abuse <0.001
Conus et al. (2010)	118 patients admitted for first espidoe of psychotic mania and received final diagnosis of BDI	71 male 47 female	15–29	Admitted into Early Psychosis Prevention anad Intervention Centre (EPPIC) for first episode of psychotic mania who	Childhood and adolescent sexual/ physical abuse	N/A	N/A	DSM-IV for diagnosis EPFQ Global Assessment of Functioning Scale Clinical Global Impressions-	Examine the prevalence and clinical correlates of childhood sexual/physical abuse in BD.	1. SPA is highly prevalent in BDI patients presenting with first episode of psychotic mania. 2. Exposed patients have lower	80 % BDI patients present for first episode psychotic mania had been exposed to at least one type of stressful event during childhood	NR	NR

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
				also received a final diagnosis of BDI				Severity of Illness Scale		premorbid functional levels and worse response to treatment.			
Watson et al. (2014)	60 outpatients with BD, 55 controls	62 males 53 females	18–65	BDI or BDII	Childhood trauma	N/A	N/A	National Adult Reading Test 17-item version of HDRS CTQ with 28-items DSM-IV for diagnosis	Examine the clinical impact of different subtypes of childhood trauma on adults with BD.	1. Significantly higher rates of childhood trauma seen in BDI and BD II patients compared to controls. 2. Emotional neglect is only significant CTQ subscale associated with BD diagnosis. 3. Childhood sexual abuse not significant predictor of BD diagnosis later in life.	BD CTQ 44.4 control 31.2 Emotional neglect BD CTQ 12.4 control 8.2	BD CTQ 19.1 control 8.0 Emotional neglect BD 6.0 control 3.5	BD vs control CTQ 0.003 Emotional neglect 0.008
Cho et al. (2021)	80 eligible, 71 participated	26 men, 45 women	Mean age of 36.7 years	Current BD or schizophrenia	Childhood trauma	N/A	N/A	CTQ–Short version Trauma antecedents questionnaire Impact of events scale – Revised (IES-R) Dissociative experiences scale-Taxon Compliance rating scale	Compare the prevalence of childhood trauma in BD vs. schizophrenia.	When compared to individuals with schizophrenia, those with BD do not experience significantly more childhood trauma.	CTQ: Bipolar = 49.97, Schizophrenia = 49.73 IES-R: Bipolar = 24.23, Schizophrenia = 27.37	CTQ: Bipolar = 13.29, Schizophrenia = 13.92 IES-R: Bipolar = 19.72, Schizophrenia = 18.99	CTQ: p = 0.833 IES-R: p = 0.267
Cakir et al. (2016)	166 eligible, 135 participated	82 female, 53 male	Mean age: 40.6 (±12.8) years	Type 1 BD	Childhood trauma	N/A	N/A	Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) CTQ	Examine the effects of different subtypes of childhood trauma on treatment outcomes in BD.	1. BD group reported significantly greater frequency of high levels of childhood trauma compared to control; childhood emotional	Mean CTQ: 40.55	CTQ: 12.32	p = 0.05

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
										abuse and neglect particularly high. 2.Significant correlations observed between current internalized shame and childhood emotional abuse/neglect.			
Cascino et al. (2021)	97 patients (74 BD type 1, 23 BD type 2) 37 treated with lithium 60 treated with anticonvulsants 38 CM- 59 CM+	CM-: 23 male, 15 female CM+: 25 male, 34 female	CM-: 51.3 ± 10.8 years CM+: 48.2 ± 14.0 years	BD type 1 or type 2	Childhood maltreatment (CM)	N/A	N/A	Alda scale CTQ	In patients with BD, there was no significant difference in response to anticonvulsant MS treatments between patients with or without CM. There was a poorer response to lithium treatment in patients with CM and higher physical abuse.	1. SPA is highly prevalent in BDI patients presenting with first episode of psychotic mania. 2. Exposed patients have lower premorbid functional levels and worse response to treatment.	Total Alda: CM- = 4.0, CM+ = 3.4 Lithium Alda: CM- = 5.0, CM+ = 3.3 Anticonvulsants Alda: CM- = 3.4, CM+ = 3.7	Total Alda: CM- = 2.6, CM+ = 2.5 Lithium Alda: CM- = 2.5, CM+ = 2.3 Anticonvulsants Alda: CM- = 2.6, CM+ = 2.6	Lithium: p = 0.04
Hyun et al. (2000)	Total: 333 (142 bipolar, 191 depression)	Men: Bipolar = 38.9 ± 14.3 years, Depression = 44.4 ± 13.4 years Women: Bipolar = 40.6 ± 11.8 years, Depression = 41.3 ± 12.8 years	Men: Bipolar = 52, depression = 80 Women: Bipolar = 90, depression = 111	BD or unipolar disorder	Childhood physical and sexual abuse	N/A	N/A	Semi-structured clinical interview assessing symptoms for major mental disorders (97 % concordance with the structured clinical interview for DSM-III-R) DSM-IV criteria	There were significantly higher incidences of childhood sexual abuse in the bipolar group compared to the unipolar group. There were higher rates of sexual abuse in female subjects compared to male subjects. There was no difference in	Significantly higher rates of childhood trauma seen in BDI and BDII patients compared to controls. Emotional neglect is only significant CTQ subscale associated with BD diagnosis. Childhood sexual abuse not significant predictor of BD	Men (Bipolar): SA = 4 %, PA = 1 %, SA and PA = 7 % Men (Depression): SA = 3 %, PA = 8 %, SA and PA = 1 % Women (Bipolar): SA = 18 %, PA = 4 %, SA and PA = 12 % Women (Depression): SA = 16 %, PA	N/A	N/A

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
									physical abuse by diagnosis or gender.	diagnosis later in life.	= 6 %, SA and PA = 14 %		
Aas et al. (2017)	342 (300 France, 42 Norway)	136 male, 206 female	41.4 ± 13.1	BD (types I, II or NOS)	Childhood trauma	N/A	N/A	ALS CTQ	A higher score on ALS was associated with more severe clinical symptoms of BD. Emotional abuse was a risk factor for BD severity and increased affective liability. Affective liability links childhood trauma with an increased risk of suicide attempts, mixed episodes, and anxiety disorders.	There was no specific type of childhood trauma which differentiated patients with BD vs. patients with schizophrenia. The most common type of childhood trauma was physical neglect.	ALS-SF Total mean score: 1.15 Childhood trauma severity all trauma mean score: 42.42	ALS-SF: ± 0.71 Childhood trauma severity all trauma: ± 13.39	N/A
Hosang et al. (2018)	674 participants, 72 BD	Within BD, 56 female, 16 male	48.36 ± 9.43	BD vs. unipolar vs. control	Physical abuse/neglect, emotional abuse/neglect, sexual abuse	N/A	N/A	SCAN interview CTQ	Childhood maltreatment is associated with adult medical physical comorbidities in BD.	Patients with psychotic symptoms had higher CTQ and physical neglect scores. There was no difference in CTQ scores between patients who had good and poor responses to lithium treatment. Emotional abuse and physical abuse scores were higher in the group with a poor response	In BD group, there exists a dose-response relationship between number of maltreatment histories and number of physical comorbidities.	N/A	$p < 0.001$ for all maltreatment types $p = 0.016$ for correlation between 1 type of maltreatment and dose-response relationship to comorbidities $p = 0.012$ for 2+ types

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
										to anticonvulsant treatment.			
Li et al. (2014)	152 eligible, 132 agreed to participate	41 male 91 female	16–65; mean 31.51 (SD 10.70)	DSM-IV diagnosis of BD	Childhood abuse/trauma	N/A	N/A	CTQ-Short Form Childhood Experience of Care and Abuse Questionnaire (CECA.Q) Impact of Events Scale-Revised (IES-R) State-Trait Anxiety Inventory (STAI)	Significant number of patients with BD experienced childhood abuse and neglect. Exposure to childhood trauma associated with comorbid PTSD and anxiety symptoms.	Childhood trauma in adults with BD is associated with earlier age of onset, comorbid PTSD, ans anxiety symptoms.	NR	NR	$p < 0.05$
Etain et al. (2010)	206 bipolar patients	84 male, 122 women (BD group) 58 male, 36 women (control)	41.7 in BD group 41.2 in control	155 BDI 51 BDII	childhood emotional abuse	N/A	N/A	Diagnostic Interview for Genetic Studies (French) CTQ MADRS Mania Rating Scale	Assess how common and severe different types of childhood trauma are in bipolar patients. Examine whether certain types of trauma are more strongly linked to BD. Analyze whether the severity of trauma affects outcomes in a dose-dependent way.	Emotional abuse has a dose-effect on BP symptom severity.	In ORDER: None %, Low %, Moderate %, Severe % Emotional Neglect (Bipolar): 15.53, 45.63, 22.82,16.02 Emotional Abuse (Bipolar): 50.97, 24.27, 9.71,15.05 Physical Neglect (Bipolar): 72.81, 17.48, 5.34, 4.37 Physical Abuse (Bipolar): 77.67, 12.14, 5.34, 4.85 Sexual Abuse (Bipolar): 68.93, 11.17, 9.71, 10.19	NR (all data is in percentages)	Emotional Neglect: 0.03 Emotional Abuse: 0.00 Physical Neglect: 0.01 Physical Abuse: 0.04 Sexual Abuse: 0.10
Etain et al. (2017)	148 patients	89 females 59 males	45.84	BDI, BDII	Childhood trauma	N/A	N/A	CTQ Alda scale	Determining if childhood trauma can possibly impact patients with BD and result in a poorer	A higher level of physical abuse is significantly correlated to a lower level of response to lithium.	CTQ: 41.12	CTQ: 11.66	CTQ: 0.07 Physical abuse: 0.009

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
									response to lithium.				
Garno et al. (2005)	100 patients	50 female 50 male	No history of abuse: 41.1 History of abuse: 41.6	BD	Childhood abuse	N/A	N/A	CTQ 28-item self-report measure 17-item HDRS	1. Determine possible relationship between childhood trauma subtypes in these patients and their clinical outcome.	Patients with a history of severe abuse was significantly younger at illness onset and had a higher severity level of the manic symptoms they currently have.	Age at first episode with no severe abuse: 21.6 Age at first episode with severe abuse: 15.8 Lifetime manic episodes with no severe abuse: 7.0 Lifetime manic episodes with severe abuse: 17.7 Lifetime depressive episodes with no severe abuse: 12.0 Lifetime depressive episodes with severe abuse: 30.4	N/A	Lifetime manic episodes: 0.058 Age at first episode: 0.001 Lifetime depressive episodes: 0.026
Xie et al. (2018)	553 patients 132 controls	336 females 343 male	Depreesion: 27.78 ± 8.126 Bipolar: 25.50 ± 9.358 Schizophrenia:27.86 ± 4.831 Control: 27.86 ± 4.831	229 patients with depression 102 patients with BD 216 patients with schizophrenia 132 healthy patients (control)	Childhood trauma	N/A	N/A	1. Demographic questionnaire 2. CTQ–Short Form 3. Social Support Rating Scale (SSRS) 4. Self-rating Idea of Suicide Scale (SIOSS) 5. ICD-10	Determining childhood trauma's impact on patients with mental disorders, including BD.	1. 61.8 % of patients with BD reported at least one type of trauma. 2. Physical neglect and emotional neglect were the most reported, while sexual abuse and physical abuse were the least reported.	Only for bipolar group: CTQ-SF total: 44.00 SSRS total: 33.56	Only for bipolar group: CTQ-SF total: 12.994 SSRS total: 7.180	P is <0.001 for both
Erten et al. (2014)	116 patients	71 female, 43 male	38.34 + − 8.46	bipolar I disorder	childhood trauma	N/A	N/A	1. YMRS 2. HDRS 3. CANQ 4. 36-item medical outcome study	1. Determining how childhood trauma can impact clinical expression of BD.	Childhood traumatic events are associated with illness in more serious forms,	Absence of child abuse: Physical functioning: 85.55	Absence of child abuse: Physical functioning: 18.22	Physical functioning: 0.028 Physical role problem:

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Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
								short form health survey (SF-36)	2. Childhood trauma impacting the quality of life in patients with BDI.	more prone to depressive episodes, more suicide attempts and a higher total number of episodes.	Physical role problem: 74.44 Pain: 82.31 General health: 68.26 Vitality: 63.77 Social function: 80.83 Emotional role problem: 71.11 Mental health: 69.33 Presence of childhood abuse: Physical functioning: 79.08 Physical role problem: 64.43 Pain: 69.76 General health: 58.30 Vitality: 55.63 Social function: 71.83 Emotional role problem: 54.92 Mental health: 62.47	Physical role problem: 35.14 Pain: 20.47 General health: 20.74 Vitality: 15.63 Social function: 17.39 Emotional role problem: 32.25 Mental health: 14.89 Presence of childhood abuse: Physical functioning: 18.36 Physical role problem: 35.52 Pain: 23.14 General health: 22.39 Vitality: 21.11 Social function: 23.11 Emotional role problem: 41.05 Mental health: 17.88	0.094 Pain: 0.005 General health: 0.018 Vitality: 0.019 Social function: 0.019 Emotional role problem: 0.042 Mental health: 0.034

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Table 1 (*continued*)

Study	Sample Size	Sex distribution	Sample age	Diagnoses	Type of trauma	Dosage	Method of administration	Measurement tool	Outcome of interest	Results	Mean	SD	P-value
Etain et al. (2013)	587 patients (418 from France and 169 from Norway)	NR	NR	DSM-IV-defined BD	Childhood adverse events	N/A	N/A	CTQ	To determine any possible associations between clinical presentations of BD and childhood trauma subtypes.	1.Difference between the two sample sizes in alcohol dependence was significant. 2.Two samples were similar in CTQ total score. 3.All frequencies of traumas subtypes were also very similar between the groups, except for physical neglect which is more frequent in norway.	N/A	N/A	1.p = 0 3.p = 0.001

Abbreviations: BD - Bipolar Disorder; PTSD - Posttraumatic Stress Disorder; MDD - Major Depressive Disorder; CTQ - childhood trauma questionnaire; YMRS - Young mania rating scale; HDRS- Hamilton depression rating scale; HAMA - Hamilton rating scale for anxiety; ISS - interal states scale; MADRS - Montgomery-Asberg depression rating scale; CANQ - childhood abuse and neglect questionnaire; CGI-BP - clinical global impression-Bipolar Disorder; MS - mood stabilizer; EMDR - Eye Movement Desensitization and Reprocessing; MDD-RE - Recurrent Major Depressive Disorder.

3.4. Clinical impact of childhood physical abuse and neglect in adults with bipolar disorder

A total of 16 included studies have investigated the clinical impact of childhood physical abuse and neglect in adults with BD, as well as therapeutic considerations for treatment (McCraw and Parker, 2017; Oymak Yenilmez et al., 2019; Schwarz et al., 2024; Wrobel et al., 2022; Savitz et al., 2008; Jansen et al., 2016; Janiri et al., 2015; Upthegrove et al., 2015; Pavlova et al., 2018; McIntyre et al., 2008; Conus et al., 2010; Cascino et al., 2021; Hosang et al., 2018; Li et al., 2014; Etain et al., 2017; Garno et al., 2005). McCraw and Parker (2017) reported that 40.7 % ($p < 0.001$) of BD adults had experienced childhood trauma, including physical or sexual abuse, with 69.5 % of those adults stating that these experiences had a major impact on their lives.

Similarly, Oymak Yenilmez et al. (2019) reported that adults with recurrent MDD (MDD-RE) had significantly higher CTQ scores for physical abuse and neglect compared to a control group, suggesting ongoing effects of childhood maltreatment even in remission. Schwarz et al. (2024) observed higher mean scores for physical abuse and neglect in BD compared with MDD, indicating that trauma may be a shared risk factor across mood disorders. Jansen et al. (2016) reported that childhood physical abuse and neglect mediated the association between a family history of mood disorders and developing any mood disorder (prevalence ratio = 5.21).

Multiple studies have reported on the effect of childhood physical maltreatment on clinical outcomes in persons with BD: Wrobel et al. (2022), Upthegrove et al. (2015), McIntyre et al. (2008), Etain et al. (2017), Cascino et al. (2021), Li et al. (2014), Garno et al. (2005), Conus et al. (2010), Janiri et al. (2015), Savitz et al. (2008), Pavlova et al. (2018), and Hosang et al. (2018). These include an increased likelihood of experiencing psychotic symptoms, such as auditory hallucinations ($p = 0.09$; $OR = 1.45$) and visual hallucinations ($p = 0.02$; $OR = 1.81$). Suicidality is also more common, with higher rates of lifetime suicidal ideation ($p = 0.010$; $OR = 2.05$) and suicide attempts ($p = 0.003$). Treatment response tends to be poorer, particularly regarding the effectiveness of mood stabilizers ($OR = 0.78$; $p = 0.005$). Additionally, individuals with a history of childhood physical abuse show greater vulnerability to various comorbidities, including substance misuse ($OR = 2.01–3.53$), past-year rapid cycling ($OR = 4.04$), and elevated risks of anxiety-related disorders and PTSD. The aforementioned associations are further supported by significant findings related to medical comorbidities ($\chi^2 = 19.42–25.57$; $p < 0.001$).

3.5. Clinical impact of childhood emotional abuse and neglect in adults with bipolar disorder

Of the included studies, 23 studies investigated the clinical impact of childhood emotional abuse and neglect in adults with BD, as well as implications for treatment (Palagini et al., 2021; Daglas et al., 2014; McCraw and Parker, 2017; Novo et al., 2014; Hogg et al., 2024; Oymak Yenilmez et al., 2019; Schwarz et al., 2024; Ehrlich et al., 2023; Savitz et al., 2008; Jansen et al., 2016; Janiri et al., 2015; Upthegrove et al., 2015; Pavlova et al., 2018; Fowke et al., 2012; Watson et al., 2014; Cakir et al., 2016; Cascino et al., 2021; Aas et al., 2017; Hosang et al., 2018; Li et al., 2014; Etain et al., 2010; Garno et al., 2005; Etain et al., 2013). The included studies reported that childhood emotional abuse and neglect in BD adults is associated with a wide variety of negative impact across multiple domains of psychopathology including worsened long-term functional outcomes, the severity of affective symptoms, maladaptive coping styles and behaviour, poor memory functioning, increased suicidality and impulsiveness, increased vulnerability to traumatic experiences and comorbidities such as anxiety disorders, poor treatment response, emotional blunting and dysregulation, and poor social skills. (Palagini et al., 2021; Daglas et al., 2014; McCraw and Parker, 2017; Oymak Yenilmez et al., 2019; Schwarz et al., 2024; Ehrlich et al., 2023; Savitz et al., 2008; Jansen et al., 2016; Janiri et al., 2015; Upthegrove et al., 2015; Pavlova et al., 2018; Fowke et al., 2012; Watson et al., 2014; Cakir et al., 2016; Cascino et al., 2021; Aas et al., 2017; Hosang et al., 2018; Li et al., 2014; Etain et al., 2010; Garno et al., 2005; Etain et al., 2013).

Palagini et al. (2021) reported that early life emotional stress correlates with insomnia symptoms ($a = 1.1$, standard error (SE) $a = 0.20$), hopelessness ($Z = 3.2$, $SE = 0.02$, $p = 0.001$), and depressive symptoms ($Z = 2.72$, $SE = 0.17$, $p = 0.006$), with insomnia mediating the relationship between early life emotional stress, hopelessness, and depressive symptoms in adults with BD. Furthermore, Daglas et al. (2014) revealed that direct personal trauma (e.g. sexual, physical, and emotional maltreatment) in adults with BD, when compared to adults without a history of direct personal trauma, is strongly correlated with worsened depressive symptoms, as measured by the Montgomery–Åsberg Depression Rating Scale (MADRS) (13.19 ± 4.94 vs. 9.88 ± 6.24, $p = 0.02$), as well as worsened affective symptoms in general, as measured by the Brief Psychiatric Rating Scale (BPRS) (61.9 ± 13.88 vs. 58.74 ± 11.97, $p = 0.33$). Additionally, Cakir et al. (2016) reported that persons with BD who reported a lifetime suicide attempt had significantly higher childhood emotional neglect CTQ scores than those who did not ($t = -1.99$, $df = 133$, $p = 0.043$).

We identified two studies that reported on the efficacy of treatments for adults with BD who have reported childhood emotional abuse or neglect (Novo et al., 2014; Hogg et al., 2024). Both studies evaluated the effects of eye movement desensitization and reprocessing therapy (EMDR) in adults with BD who were exposed to trauma. In the study conducted by Novo et al. (2014), 20 adults with BD and subsyndromal mood symptoms were randomized into an EMDR or treatment-as-usual (TAU) group. The EMDR group received 14 to 18 EMDR sessions over 12 weeks, and the effects of this therapy on BD symptoms were assessed at baseline, 2, 5, 8, 12, and 24 weeks. Between baseline to week 12, the EMDR group demonstrated significant improvements in comparison to the TAU group specifically in the Young Mania Rating Scale ($F = 14.41$, $p = 0.004$), Hamilton Depression Rating Scale ($F = 23.86$, $p = 0.001$), Clinical Global Impression-mania ($F = 9.22$, $p = 0.018$), and Clinical Global Impression-depression ($F = 5.32$, $p = 0.047$). However, these differences did not persist between 12 and 24 weeks.

Separately, Hogg et al. (2024) randomly assigned 77 adults with BD and trauma-related symptoms to receive 20 weekly sessions of EMDR or supportive therapy (ST). At 12-month follow-up, the EMDR group had significantly greater improvements in depressive symptoms ($t = 4.252$, $p = 0.0006$, *Cohen's d* $= 0.905$) and manic symptoms ($t = 2.248$, $p = 0.027$, *Cohen's d* $= 0.444$) as well as functioning. Furthermore, both EMDR and supportive therapy (ST) did not increase relapse or dropout rates among the participants.

Taken together, Novo et al. (2014) and Hogg et al. (2024) suggest that EMDR may be an effective treatment method for adults with BD who have experienced childhood emotional abuse, neglect, and general traumatic experiences. EMDR has been demonstrated to reduce the severity of affective and trauma-related symptoms, as well as improve functioning (Novo et al., 2014; Hogg et al., 2024).

3.6. Clinical impact of childhood sexual abuse in adults with bipolar disorder

From the included studies, 20 studies investigated the clinical impact of childhood sexual abuse on adults with BD (Chessen et al., 2011; Daglas et al., 2014; Ihme et al., 2022; Palagini et al., 2021; Schwarz et al., 2024; Savitz et al., 2008; Jansen et al., 2016; Janiri et al., 2015; Upthegrove et al., 2015; Pavlova et al., 2018; McIntyre et al., 2008; Conus et al., 2010; Cakir et al., 2016; Cascino et al., 2021; Hyun et al., 2000; Hosang et al., 2018; Li et al., 2014; Garno et al., 2005; Erten et al., 2014; Etain et al., 2013).

Hyun et al. (2000) evaluated 142 adults with BD and 191 adults with unipolar depression over a 2-year period with a semi-structured clinical interview. Results from a Chi-square analysis revealed a statistically

Table 2
Risk of Bias Assessment Using the Cochrane Risk of Bias Assessment Tool for Randomized Trials (RoB2).

Study	Item														Overall Quality Rating
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Guillen-Burgos et al. (2025)	✓	✓	NR	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	Good
Katz et al. (2024)	✓	✓	NA	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Rowe et al. (2024)	✓	✓	✓	✓	NR	✓	NR	NA	✓	✓	✓	✓	✓	✓	Fair
Wrobel et al. (2022)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Ehrlich et al. (2023)	✓	✓	✓	✓	✓	X	✓	✓	✓	X	✓	X	NR	NR	Fair
Schwarz et al. (2024)	✓	✓	✓	NR	✓	✓	✓	NR	NR	✓	✓	X	✓	✓	Fair
Lu et al. (2009)	✓	NR	NR	NA	NR	✓	X	NR	✓	✓	✓	X	✓	✓	Fair
Rosenberg et al. (2004)	X	X	X	X	X	✓	✓	✓	✓	✓	✓	X	✓	✓	Poor
Leverich and Post (2006)	✓	✓	✓	NR	NR	X	NR	✓	NR	NR	✓	✓	✓	NR	Poor
Oymak Yenilmez et al. (2019)	✓	✓	✓	✓	✓	X	✓	✓	✓	NR	✓	✓	✓	✓	Good
Miller et al. (2018)	✓	✓	X	✓	✓	✓	✓	✓	✓	✓	✓	X	X	✓	Fair
Nishith et al. (2024)	X	X	X	X	X	✓	X	NR	NR	✓	✓	X	✓	✓	Poor
Hogg et al. (2024)	✓	✓	✓	X	✓	✓	X	✓	NR	✓	✓	✓	✓	✓	Good
Novo et al. (2014)	✓	✓	NR	X	X	✓	✓	✓	NA	✓	✓	✓	✓	✓	Fair
Frost et al. (2020)	✓	✓	NR	NA	X	✓	NR	NR	NA	✓	✓	✓	✓	NA	Fair
McCraw and Parker (2017)	✓	✓	NR	✓	X	✓	✓	✓	✓	X	✓	X	NA	✓	Fair
Chessen et al. (2011)	✓	✓	✓	NR	NR	✓	NR	NR	✓	NR	✓	X	NR	✓	Fair
Schneeberger et al. (2014)	X	NR	NR	NR	NR	✓	✓	✓	NR	NR	✓	NR	✓	✓	Poor
Daglas et al. (2014)	✓	✓	NR	NR	NR	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Palagini et al. (2021)	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	✓	X	✓	Good
Savitz et al. (2008)	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	✓	✓	✓	Good
Jansen et al. (2016)	✓	✓	✓	✓	✓	NA	✓	✓	✓	X	✓	NR	✓	✓	Good
Janiri et al. (2015)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	Good
Upthegrove et al. (2015)	✓	✓	NR	✓	NR	✓	✓	✓	✓	✓	✓	NR	NA	✓	Fair
Pavlova et al. (2018)	✓	✓	✓	NR	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
McIntyre et al. (2008)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	Good
Fowke et al. (2012)	✓	✓	NR	✓	✓	✓	✓	✓	✓	NA	✓	NR	✓	✓	Good
Conus et al. (2010)	✓	✓	✓	✓	NR	✓	✓	✓	✓	✓	✓	NR	✓	✓	Good
Watson et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓	NA	✓	✓	✓	✓	Good
Cho et al. (2021)	✓	✓	✓	✓	✓	✓	✓	✓	✓	X	✓	✓	✓	✓	Good
Cakir et al. (2016)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	Good
Cascino et al. (2021)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Hyun et al. (2000)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Aas et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Hosang et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	Good
Li et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Etain et al. (2010)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Etain et al. (2017)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Garno et al. (2005)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	Good
Xie et al. (2018)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	NR	✓	✓	Good
Erten et al. (2014)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good
Etain et al. (2013)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Good

Note: #1 = Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?; #2 = Was the method of randomization adequate (i.e., use of randomly generated assignment)?; #3 = Was the treatment allocation concealed (so that assignments could not be predicted)?; #4 = Were study participants and providers blinded to treatment group assignment?; #5 = Were the people assessing the outcomes blinded to the participants' group assignments?; #6 = Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?; #7 = Was the overall drop-out rate from the study at endpoint 20 % or lower of the number allocated to treatment?; #8 = Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?; #9 = Was there high adherence to the intervention protocols for each treatment group?; #10 = Were other interventions avoided or similar in the groups (e.g., similar background treatments)?; #11 = Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?; #12 = Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80 % power?; #13 = Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?; #14 = Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?

significant higher incidence of sexual abuse in adults with BD compared to adults with unipolar depression ($X^2 = 5.72$, $df = 1$, $p < 0.02$) and also found a significantly elevated sexual abuse rate in female subjects as opposed to male ($X^2 = 15.61$, $df = 1$, $p < 0.001$). Chessen et al. (2011) investigated 74 randomly selected patients who had been enrolled for at least two years in an outpatient clinic and revealed that 93.3 % of participants had experienced either physical or sexual assault in the past, but 59 % of the same pool of participants reported their history of assault was not addressed during treatment. However, the study was limited because a comorbid diagnosis of substance use disorder was not excluded, resulting in possible confounding variables not being addressed.

Daglas et al. (2014) reported a past exposure rate to trauma in adults with first-episode psychotic mania to be 48 % ($p = 0.02$). The CTQ has often been a measure to capture rates of sexual abuse in trauma related research including BD (Ihme et al., 2022; Schwarz et al., 2024). Schwarz et al. (2024) reported that in 103 adults with BD, there was no association between a history of sexual abuse and functional outcomes. However, it is noted that history of sexual abuse was categorized in the same group as other types of trauma as measured by the CTQ, which may affect how subtypes of trauma are interpreted in this analysis. The report by Ihme et al. (2022) clearly defined sexual abuse as "any sexual contact between the child and an older individual, regardless of whether the child was forced or not". A univariate analysis revealed that sexual abuse was associated with suicide attempters, ($p = 0.025$). However, a Bivariate Spearman's rho analysis following the univariate analysis displayed a weak relationship between sexual abuse scores obtained from the CTQ and avoidance scores obtained from the Experience in Close Relationships Inventory-Revised (ECR-R), as well as with suicide attempts. The study concluded sexual abuse was not highly inter-

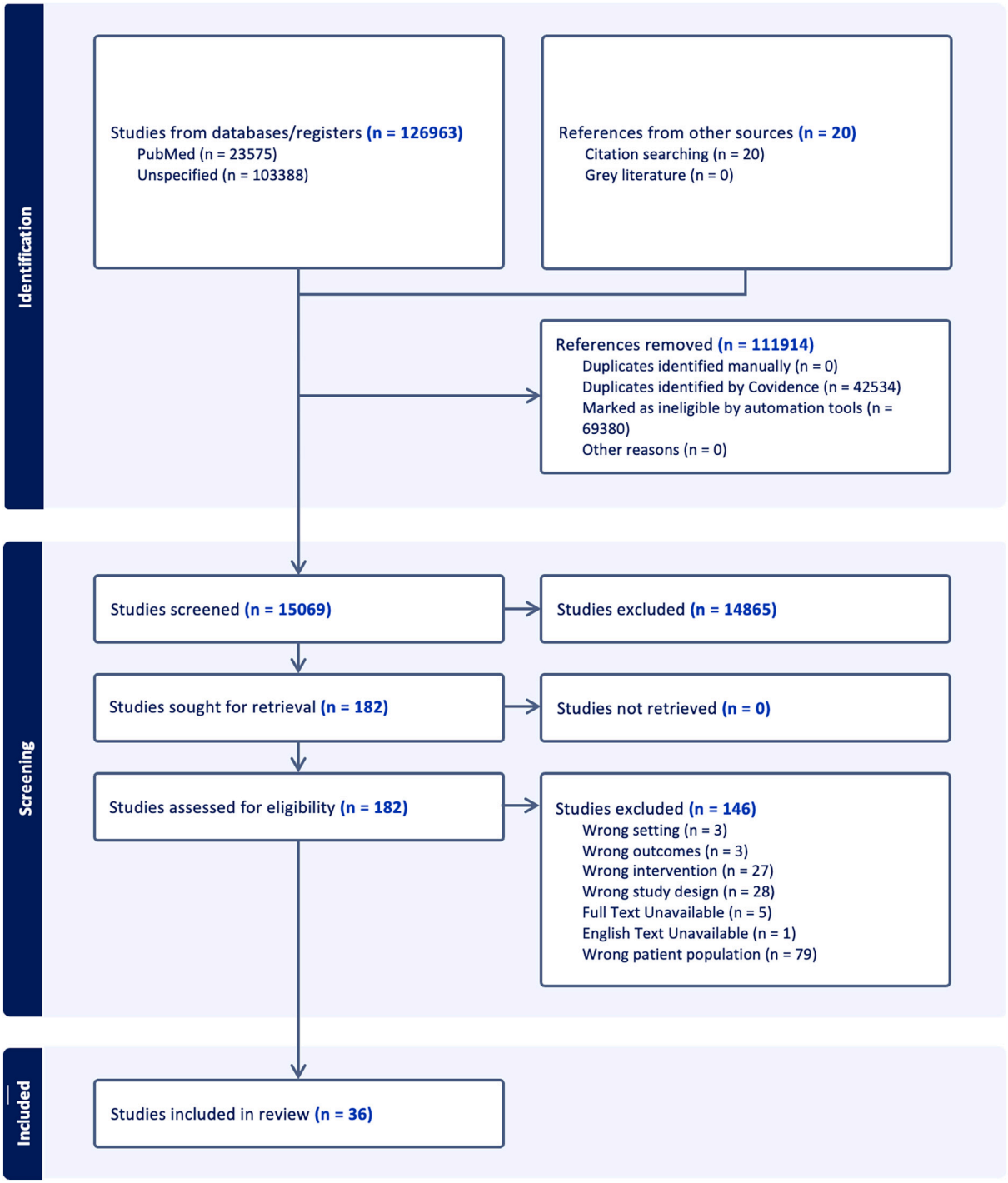

Fig. 1. PRISMA Flow Diagram of Study Selection Process.

correlated and medium correlated with avoidant attachment tendencies, depression scores and suicidal behaviour, along with the other subtypes of childhood trauma. Palagini et al. (2021) reported that insomnia symptoms mediated the association between a reported childhood history of trauma and depressive symptoms and suicidality in the adult living with BD.

Most studies that we identified did not report outcomes specifically as it relates to sexual abuse and instead most studies included sexual abuse in the category of physical assault. For instance, Watson et al. (2014) reported that a childhood history of emotional neglect but not sexual abuse was associated with an adult diagnosis of BD.

3.7. Clinical impact of comorbid PTSD in adults with bipolar disorder

From the included studies, three studies investigated the clinical impact of comorbid PTSD in adults with BD (Guillen-Burgos et al., 2025; Katz et al., 2024; Frost et al., 2020). Frost et al. (2020) investigated manic and depressive symptoms in 81 participants, 27 of whom had a comorbid diagnosis of PTSD and 54 who did not. The study reported higher current depressive symptoms in adults with comorbid BD and PTSD as compared to those without PTSD. However, no significant difference was found between the two groups for mania symptoms.

The study conducted by Guillen-Burgos et al. (2025) specifically evaluated the efficacy of lithium treatments in 34 adults with BD and

comorbid PTSD. They administered 600 mg of lithium once daily for 7 days, after which doses were adjusted based on the clinician's criteria to a maximum of 1800 mg. Similarly, an initial dose of 50 mg of quetiapine was split into two doses per day, adjusted depending on the clinician's judgment up to 800 mg. They found that lithium paired with quetiapine resulted in an 85 % reduction ($p = 0.021$) in the risk of mood episodes recurring compared to using only mood stabilizers (MS). However, there was insufficient evidence to compare the effect of monotherapy versus combination therapy in adults with BD and comorbid PTSD. The study conducted by Katz et al. (2024) examined the efficacy of prolonged exposure therapy (PE) on 32 adults with comorbid BD and PTSD. 10 sessions were administered twice weekly for 5 weeks following the prolonged exposure (PE) manual. This study reported a decrease of $M = 26.79$ ($p < 0.001$) in PCL-5 test scores assessing PTSD symptoms after 10 sessions of PE treatment, demonstrating the feasibility and efficacy of administering PE to adults with comorbid diagnoses of BD and PTSD.

4. Discussion

The findings from our systematic review indicate that trauma is prevalent among adults with BD. In addition, the findings herein indicate that a history of trauma is negatively associated with measures of illness and quality of life, including illness presentation, progression, comorbidity treatment, and poorer clinical outcomes (Rosenblat et al., 2020; McIntyre et al., 2012; Post, 2021; Manno et al., 2006). Specifically, BD has been linked to higher rates of childhood trauma and experiences of physical or sexual assault in adulthood (McCraw and Parker, 2017). Adults with BD also report more frequent exposure to stressful life events compared to those with major depressive disorder (MDD), such as interpersonal conflicts, relationship breakdowns, legal problems, financial hardship, and substance use issues (McCraw and Parker, 2017). However, no significant gender differences were found between the rates of exposure to trauma in adults with BD (McCraw and Parker, 2017). Additionally, a majority of those with BD who have been exposed to trauma do not meet the criteria for a formal diagnosis of PTSD (McCraw and Parker, 2017).

Childhood trauma, specifically emotional abuse and neglect, has consistently been associated with increased severity of affective symptoms, greater suicidality and impulsiveness, maladaptive coping strategies, poor memory and social functioning, and reduced responsiveness to treatment in persons with BD (Palagini et al., 2021; Daglas et al., 2014; McCraw and Parker, 2017; Oymak Yenilmez et al., 2019; Schwarz et al., 2024; Ehrlich et al., 2023). Similarly, experiences of childhood physical abuse and neglect are common among adults with BD and are linked to greater vulnerability to affective instability, comorbid anxiety disorders, impulsivity, suicidality, and poor functional outcomes (Lee and Park, 2016; McCraw and Parker, 2017; Oymak Yenilmez et al., 2019; Park, 2017; Schwarz et al., 2024; Wrobel et al., 2022). However, there is little evidence on whether this category of childhood maltreatment impacts treatment response, warranting future research to investigate childhood maltreatment as a potential mediator or moderator of treatment response in persons with BD.

Childhood sexual abuse is prevalent in persons with BD; however, there is limited evidence reporting on the association between sexual abuse and clinical outcomes in this patient population (Chessen et al., 2011; Daglas et al., 2014). Available evidence suggests that sexual trauma highly correlates with incident psychopathology, comorbidities, and negative impact on BD outcomes, potentially through increasing oxidative stress and damage. For example, Eriksen et al. (2022) found that adults with affective disorders who experienced sexual abuse had higher levels of urinary 8-oxodG ($B = 1.033$, $p = 0.032$) and 8-oxoGuo ($B = 1.009$, $p = 0.398$), which are biomarkers of oxidative DNA and RNA damage.

Among those with BD and comorbid PTSD, comorbid PTSD is associated with a heightened likelihood of experiencing depressive episodes when compared to those without comorbid PTSD, though it does not appear to be correlated with changes in the likelihood of experiencing manic symptoms (Frost et al., 2020).

With respect to therapeutic considerations, PE may be an effective form of psychotherapy as it has demonstrated efficacy in alleviating trauma-related symptoms in adults with comorbid PTSD and BD (Katz et al., 2024). EMDR has been shown to be significantly effective at reducing the severity of affective and trauma-related symptoms in adults with BD who have experienced trauma, as well as ST, however, neither have shown to decrease rates of dropout or relapse (Novo et al., 2014; Hogg et al., 2024).

Complex PTSD (CPTSD), recognized in the International Classification of Diseases 11th Revision (ICD-11), results from chronic exposure to trauma such as childhood abuse or enslavement. (World Health Organization, 2019). While CPTSD shares symptoms with PTSD, including flashbacks and hypervigilance, CPTSD is more strongly linked to emotional dysregulation, feelings of shame, and difficulty maintaining relationships. (World Health Organization, 2019). Additionally, children and adolescents exposed to chronic trauma are more likely to develop CPTSD compared to adults, and the condition is often more difficult to treat than PTSD (World Health Organization, 2019). Due to the close overlap in key features between Borderline Personality Disorder (BPD) and CPTSD, there remains controversy on whether CPTSD should be recognized as a separate diagnosis. Furthermore, there exist diagnostic challenges in differentiating BDII and BPD, given the high prevalence of trauma exposure in both conditions. As a result, the overlapping core symptoms of BPD, BDII, and CPTSD which causes a challenge when differentiating the three conditions in adults impacted by trauma, potentially leading to misdiagnosis and treatment ramifications.

In a post-hoc analysis conducted by McIntyre et al. in 2012, childhood adversity was associated with components of metabolic syndrome in adults with mood disorders, including increased blood pressure and lowered HDL cholesterol levels (McIntyre et al., 2012). For instance, 45.28 % ($p = 0.010$) of participants with a history of childhood sexual abuse met the criteria for obesity, and 76.32 % ($p = 0.074$) of participants with a history of childhood physical abuse had a trend towards overweight. Though the aforementioned study did not identify a correlation between childhood adversity and other select components of metabolic syndrome, several other studies support a correlation between experiences of childhood trauma and the development of type II diabetes mellitus as well as obesity, especially among those who report childhood physical abuse (Midei et al., 2010). Taken together, it is hypothesized that childhood adversity may both increase vulnerability to components of metabolic syndrome in adults with mood disorders, underscoring the broad-based risk imparted by childhood trauma.

Neuroimaging studies further support the link between trauma and altered brain function in BD. In adults with PTSD and BD, trauma has been associated with reduced structural integrity in brain areas involved in executive function, disrupted cortical-subcortical connectivity, and diminished activation in emotion regulation regions. (Hinojosa et al., 2024; Hull, 2002; Bremner, 2007; Kunimatsu et al., 2020). In children, trauma has been correlated with decreased amygdala and hippocampal volumes. However, there are a limited number of studies with sufficient sample sizes examining the neurodevelopmental impact of trauma in children, indicating the need for further research on childhood trauma (Hinojosa et al., 2024).

There are a number of methodological limitations that affect the interpretations of our findings. Primarily, there exists a paucity of evidence for the clinical impact of childhood sexual abuse in adults of BD, as well as limited studies examining the clinical impact of trauma on response to pharmacological treatment. There are also few studies reporting on the effectiveness of pharmacological treatments for adults with BD who are affected by trauma. Furthermore, there is a disproportionate focus on childhood trauma exposure, but relatively fewer studies reporting on the effects of trauma in adolescence, adulthood, or later in life. Additionally, several of the included studies did not

disaggregate specific types of trauma, but instead reported on the clinical impact of trauma in general, limiting the ability to identify the effect of each type of trauma on outcomes in adults living with BD. Moreover, scales and questionnaires used in the studies to assess trauma varied significantly, making it difficult to compare reported outcomes in persons with trauma across studies. Additionally, there is a lack of research on the clinical impact of one traumatic event as compared to multiple or repeated traumatic events. Lastly, some included studies included populations with diagnoses other than BD, such as MDD or other mental disorders, which limits the ability to assess the effect of trauma in adults with BD specifically. For example, it remains a clinical challenge to differentiate BD from borderline personality disorder, as childhood trauma plays an important role in its etiology (Fowler et al., 2019; Li et al., 2025). The foregoing challenge in differentiating BD from other diagnostic groups contributes to a reduced ability to adequately investigate the effect of trauma in this patient population.

5. Conclusion

Findings from this systematic review indicate that trauma is a prevalent experience among adults living with BD, which significantly impacts several aspects of presentation, progression, treatment, and clinical outcomes. This review examines the prevalence of trauma, as well as the clinical impact of childhood physical, emotional, and sexual abuse, neglect, and comorbid PTSD in adults with BD. Further research vistas should seek to explore the effects of specific types of trauma across multiple facets of illness presentation and treatment outcomes in adults with BD.

CRediT authorship contribution statement

Kelei Xiao: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Hisham Sayed:** Writing – original draft, Formal analysis, Data curation. **Jason Xing:** Writing – original draft, Formal analysis, Data curation. **Xin Yi Zhang:** Writing – original draft, Formal analysis, Data curation. **Jeffrey Ai:** Writing – original draft, Formal analysis, Data curation. **Kayla M. Teopiz:** Writing – review & editing, Project administration, Conceptualization. **Roger Ho:** Writing – review & editing. Taeho Greg Rhee: Writing – review & editing. **Heidi Ka Ying Lo:** Writing – review & editing. **Hernan F. Guillen-Burgos:** Writing – review & editing. **Maj Vinberg:** Writing – review & editing. **Roger S. McIntyre:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization.

Author Statement

All authors have approved the final manuscript and note that this is our original work.

Declaration of competing interest

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