

# Childhood trauma and longitudinal clinical outcomes in bipolar affective disorder: a systematic review

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## Abstract

**Objective:** To review the literature regarding long-term effects of childhood trauma (CT) on the progression of bipolar affective disorder (BAD) in terms of affective symptomatology, depressive symptoms, hypomanic and manic symptoms, mood and activity instability, suicidality, hospitalisation, comorbidity, relapse, treatment response and remission, and functional outcomes.

**Methods:** The PubMed, MEDLINE, Embase, and PsycINFO databases were searched for English-language, longitudinal studies that investigated associations between CT and psychiatric outcomes in patients with BAD. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies.

**Results:** In total, 13 studies (involving 5418 patients) were included in the analysis. All 13 studies had a low risk of bias. Those with a history of CT had more severe manic symptoms, increased functional impairment, and higher risks of relapse, suicidality, and psychiatric comorbidities. However, findings related to depressive symptoms, hospitalisation, treatment response, and functional recovery were inconclusive. A history of physical or sexual abuse was associated with increased symptom severity, mood instability, and higher relapse risk.

**Conclusion:** CT remains a key determinant of BAD progression rather than just a risk factor for onset. The differential impacts of CT subtypes suggest distinct neurobiological and cognitive mechanisms, highlighting the need for personalised, trauma-informed interventions.

**Key words:** Adverse childhood experiences; Bipolar disorder; Child abuse

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## Introduction

Bipolar affective disorder (BAD) is a chronic psychiatric disorder, characterised by recurrent episodes of mania or

hypomania and depression,<sup>1</sup> with a global prevalence of approximately 4%.<sup>2</sup> It is associated with psychological distress, functional impairment, and reduced quality of life.<sup>3,4</sup>

Childhood trauma (CT) is defined as exposure to traumatic events before the age of 18 years, including abuse (emotional, sexual, or physical), neglect (emotional or physical), and household dysfunction (such as parental substance abuse, parental incarceration, domestic violence, separation, or bereavement), as well as other recognised adversities including bullying, community or collective violence, parental illness or death, child marriage, and trafficking.<sup>5,6</sup> Although the relationship between CT and BAD has been explored,<sup>7</sup> the long-term effects of CT on clinical course of BAD are less known.

CT is associated with increased severity of manic, depressive, and psychotic symptoms; increased risk of rapid cycling;<sup>8</sup> poorer cognitive function;<sup>9</sup> and elevated risks of suicidality and comorbid anxiety, alcohol misuse, and substance abuse disorders.<sup>8,10</sup> The findings of longitudinal studies of the broader psychiatric population suggest an adverse effect of CT on psychotic symptoms and suicidality.<sup>11,12</sup>

CT subtypes including physical abuse (PA), physical neglect (PN), emotional abuse (EA), emotional neglect

(EN), and sexual abuse (SA) have varying associations with brain deficits and psychopathologies.<sup>13-15</sup> Different subtypes of CT may exert distinct effects on BAD. Individuals with BAD who have experienced childhood PA may exhibit more severe manic and depressive episodes and an increased risk of suicidality.<sup>16,17</sup> Those with a history of childhood SA are more likely to experience rapid cycling, severe depressive symptoms, and elevated rates of self-harm and suicide attempts.<sup>17,18</sup> Childhood EA and EN are associated with greater mood instability, a more chronic illness course, and a higher likelihood of suicide attempts.<sup>16,19</sup> Therefore, this study aimed to review the literature regarding long-term effects of various CT subtypes on the progression of BAD in terms of affective symptomatology, depressive symptoms, hypomanic and manic symptoms, mood and activity instability, suicidality, relapse, treatment response and remission, hospitalisation, comorbidity, and functional outcomes.

## Methods

The guidelines provided in the Preferred Reporting Items for Systematic Reviews 2020 checklist were followed. The PubMed, MEDLINE, Embase, and PsycINFO databases<sup>20</sup> were searched using the following keywords: ‘childhood trauma’ OR ‘childhood adversity’ OR ‘childhood abuse’ OR ‘developmental trauma’ OR ‘early life stress’ OR ‘social stress’ OR ‘chronic stress’ OR ‘physical abuse’ OR ‘sexual abuse’ OR ‘emotional abuse’ OR ‘child neglect’ OR ‘childhood violence’ OR ‘family conflict’ OR ‘CTQ’ AND ‘bipolar affective disorder’ OR ‘bipolar disorder’ OR ‘bipolar’ AND ‘long term’ OR ‘longitudinal’.

The titles and abstracts of identified papers were screened by two medical students using the Rayyan platform. Reference lists of review papers were also screened. Inclusion criteria were English-language articles, longitudinal studies of patients with BAD, comparisons of outcomes within BAD populations, investigations of associations between CT and psychiatric outcomes, and the use of standardised assessment tools. Conference abstracts, non-peer-reviewed publications, dissertations, reviews, or meta-analyses were excluded.

The two medical students extracted relevant data using a standardised form. Any disagreements were resolved through discussion and, if necessary, by consulting a third reviewer for consensus. Extracted data included the five CT subtypes (PA, PN, EA, EN, and SA)<sup>21</sup> and clinical outcomes of psychotic symptoms, depressive symptoms, hypomanic and manic symptoms, illness severity, functional impairments, duration and frequency of hospitalisation, aggressiveness, rapid cycling, and suicide attempts.

Risk of bias was assessed by the two medical students using the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies.<sup>22</sup> The checklist includes 11 items assessing the clarity of the research question, study design, participant selection criteria, data collection

methods, and result analysis, as well as potential biases from confounding variables, loss to follow-up, and outcome measure reliability. Studies were categorised as low (<4 ‘no’ responses), moderate (4-7 ‘no’ responses), or high (≥8 ‘no’ responses) risk of bias. Any discrepancies were resolved through discussion with the research team.

## Results

Of 1175 studies identified, 282 were duplicates and the remaining 893 were screened, of which 13 (involving 5418 patients) met the inclusion criteria (Table 1).<sup>5,17,23-33</sup> The mean age of patients was 38.8 years and 54% were female. All 13 studies had a low risk of bias (Table 2). Outcomes of the 13 studies are summarised in Table 3.

### *Affective symptomatology*

Visioli et al<sup>32</sup> found that in patients with BAD, those with a history of SA (but not PA) was significantly associated with higher overall symptom severity and more illness episodes per year. Wrobel et al<sup>33</sup> found that those with a history of any CT had significantly higher scores on the Bipolar Inventory of Symptoms Scale and the Clinical Global Impression.

### *Depressive symptoms, hypomanic and manic symptoms, mood and activity instability*

Leverich et al<sup>17</sup> found increased severity of depressive symptoms in patients with a history of SA but not in those with a history of PA or those with no CT. However, Vaughn-Coaxum et al<sup>31</sup> found no significant effects of SA or PA on depressive symptom severity. Leverich et al<sup>17</sup> found significantly increased severity of hypomanic symptoms in those with a history of PA or SA. Visioli et al<sup>32</sup> found that a history of SA, but not PA, was significantly associated with more depressive and manic episodes per year and more time in hypomanic episodes but not in depressive episodes. von Hofacker et al<sup>26</sup> found that CT was positively associated with mood instability but not activity instability. Leverich et al<sup>17</sup> found significantly more rapid cycling, ultra-rapid cycling, and ultra-ultra-rapid cycling in patients with SA, and more ultra-rapid cycling in patients with PA. Brown et al<sup>5</sup> found that a history of PA increased the probability of rapid cycling, and that PA and SA were associated with rapid cycling.

### *Suicidality*

Leverich et al<sup>27</sup> found that patients with a history of PA or SA had significantly higher suicidality than those without a history of CT, and that patients with both PA and SA had higher suicidality than those with either PA or SA.

### *Relapse*

Dienes et al<sup>25</sup> demonstrated that those who experienced more severe CT were more likely to relapse when facing mild stress, compared with those who experienced mild or no CT.

**Table 1. Characteristics of the 13 included studies.**

Study	Sample size	Population	Age at admission, y	Female sex, %	Childhood trauma assessment tool	Childhood trauma subtype	Outcomes	Follow-up duration
Benarous et al, <sup>23</sup> 2017	81	Patients with a diagnosis of BAD I (a manic or mixed episode) at discharge (DSM-IV criteria)	15.7 ± 1.9	57.0	Adverse Childhood Experiences Scale, List of Threatening Experiences Questionnaire	CT	Treatment response, hospitalisation	From admission to discharge
Brown et al, <sup>5</sup> 2005	330	Veterans with BAD	46.6 ± 10.0	6.4	Structured Clinical Interview for DSM Disorders	Any abuse, PA, SA, combined abuse	Rapid cycling, hospitalisation	3 years
Cakir et al, <sup>24</sup> 2016	135	Patients with BAD I	40.6 ± 12.8	60.7	CTQ	CT, PA, PN, SA, EA, EN	Treatment response	1 year
Dienes et al, <sup>25</sup> 2006	64	Adults with BAD I	41.5 ± 12.4	50.0	Semi-structured interview for childhood adverse events that occurred up to 13 years of age	CT	Recurrence of symptoms	1 year (follow-up every 3 months)
von Hofacker et al, <sup>26</sup> 2024	258	Patients with BAD I or II, newly diagnosed within 2 years (ICD-10 criteria)	30.0 ± 9.2	68.2	CTQ	CT	Mood stability, activity stability (self-reported daily mood and activity level)	2 years
Leverich et al, <sup>17</sup> 2022	631	Outpatients with BAD I or II	41.0 ± 12.0	58.0	Questions regarding the occurrence of verbal, physical, or sexual abuse in childhood, adolescence, or adulthood	CT, PA, SA	Severity of mania (Young Mania Rating Scale) and depression (Inventory of Depressive Symptomatology), cycling, average time ill (as a percentage)	1-5.7 (mean, 2.8; median, 2.4) years
Leverich et al, <sup>27</sup> 2003	648	Patients with BAD I or II (DSM-IV criteria)	41.3	57.7	Questions regarding the occurrence of verbal, physical, or sexual abuse in childhood, adolescence, or adulthood	CT, PA, SA	Suicide rate	2.8 years
Neria et al, <sup>28</sup> 2005	109	First-admission BAD patients with psychosis diagnosed with structured interviews	15-54 for males and 16-57 for females	53.2	Post-traumatic stress disorder module of the Composite International Diagnostic Interview	CT	Remission	6 and 24 months
Sala et al, <sup>29</sup> 2014	2494: without childhood maltreatment (45.7%) and with one (23.7%), two (12.9%), and ≥3 (17.7%) types of childhood maltreatment.	Adults with lifetime BAD I and II (DSM-IV criteria)	40.3	56.8: 52.1, 57.0, 52.8, and 69.8 for those with none, 1, 2, and ≥3 types of abuse/neglect, respectively	Questions adapted from Adverse Childhood Experiences Scale, Conflict Tactics Scale, CTQ, and questions about SA	CT, PA, EA, PN, EN, SA	Comorbidity, anxiety disorders	Baseline and 36-month follow-up
Schwarz et al, <sup>30</sup> 2024	71	Patients with BAD	40.8 ± 12.5; 39.6 ± 11.6 for BAD and 43.3 ± 14.1 for unipolar depressive disorder	65.0: 60.6 for BAD and 75.0 for unipolar depressive disorder	CTQ	CT	Performance-based functioning: Assessment of Motor and Process Skills	Baseline and 6-month follow-up
Vaughn-Coaxum et al, <sup>31</sup> 2021	198	Youths from the Course and Outcome of Bipolar Youth study	12.2	43.9	A medical history questionnaire and a traumatic event screening questionnaire from the Kiddie Schedule for Affective Disorders and Schizophrenia	PA, SA	Depression symptom severity (12-item Kiddie Schedule for Affective Disorders and Schizophrenia, Depression Rating Scale)	A mean of every 7.2 months between 2000 and 2016
Visioli et al, <sup>32</sup> 2023	388	Adult outpatients with BAD (DSM-5-TR criteria)	48.6 for SA and 49.5 for PA	62.0	Child Abuse and Trauma Scale	PA, SA	Annual frequency of illness episodes (all episodes, depressive, hypomanic, and manic episodes) and the average total percentage of time ill and in episodes of mania, hypomania, or depression	Baseline and ≥12-month follow-up
Wrobel et al, <sup>33</sup> 2022	476: no CT (n = 225) and any CT (n = 251)	Adult outpatients with BAD I or II (DSM-IV-TR criteria)	38.9: 38.7 ± 13.0 for no CT and 39.0 ± 11.3 for any CT	59.3: 50.2 for no CT group and 67.3 for any CT group	A question in clinical interview: "Did the patient experience abuse during childhood?"	CT, PA, SA, EA	Functional impairment (Longitudinal Interval Follow-up Evaluation-Range of Impaired Functioning Tool) Symptom severity and reduction (Bipolar Inventory of Symptoms Scale and the Clinical Global Impression)	Baseline and weeks 12 and 24 Baseline and eight follow-up visits (at weeks 2, 4, 6, 8, 12, 16, 20, and 24)

Abbreviations: BAD = bipolar affective disorder, CT = childhood trauma, CTQ = Childhood Trauma Questionnaire, EA = emotional abuse, EN = emotional neglect, PA = physical abuse, PN = physical neglect, and SA = sexual abuse

**Table 2. Risk of bias of the 13 included studies based on the Joanna Briggs Institute Critical Appraisal Checklist for Cohort Studies.**

Study	Were the two groups similar and recruited from the same population?	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	Was the exposure measured in a valid and reliable way?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	Were the outcomes measured in a valid and reliable way?	Was the follow-up time reported and long enough for outcomes to occur?	Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?	Were strategies to address incomplete follow-up utilised?	Was appropriate statistical analysis used?
Benarous et al, <sup>23</sup> 2017	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	Yes
Brown et al, <sup>5</sup> 2005	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	Yes
Cakir et al, <sup>24</sup> 2016	Yes	Yes	Yes	No	NA	NA	Yes	Yes	No	NA	Yes
Dienes et al, <sup>25</sup> 2006	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	Yes
von Hofacker et al, <sup>26</sup> 2024	Yes	Yes	Yes	-	-	NA	Yes	Unclear	Unclear	No	Yes
Leverich et al, <sup>17</sup> 2022	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	No	NA	Yes
Leverich et al, <sup>27</sup> 2003	Yes	Yes	Yes	No	No	NA	Yes	Yes	Yes	Yes	Yes
Neria et al, <sup>28</sup> 2005	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	NA	Yes
Sala et al, <sup>29</sup> 2014	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	Yes
Schwarz et al, <sup>30</sup> 2024	Yes	Yes	Yes	-	-	NA	Yes	Yes	No	No	Yes
Vaughn-Coaxum et al, <sup>31</sup> 2021	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	NA	Yes
Visioli et al, <sup>32</sup> 2023	Yes	Yes	Yes	-	-	NA	Yes	Yes	No	No	Yes
Wrobel et al, <sup>33</sup> 2022	Yes	Yes	Yes	-	-	NA	Yes	Yes	Unclear	No	Yes

Abbreviation: NA = not applicable

**Treatment response and remission**

Neria et al<sup>28</sup> found that patients with CT were less likely to reach complete remission and took longer time to do so. However, Wrobel et al<sup>33</sup> found no significant differences in rates of improvement or symptom reduction during 24 weeks of treatment among patients with or without a history of SA, PA, or EA. Cakir et al<sup>24</sup> observed that individuals with BAD who responded well to treatment with valproate and carbamazepine had significantly lower scores on the

Childhood Trauma Questionnaire for those with a history of PA or EA, compared with poor responders, but no significant differences were found in other CT subtypes or in response to lithium treatment.

**Hospitalisation**

Brown et al<sup>5</sup> demonstrated that any CT was associated with more involuntary hospitalisations. However, Benarous et al<sup>23</sup> did not find an association between CT and duration of hospital stay.

Table 3. Outcomes of the 13 included studies.

Study	Outcome
<b>Affective symptomatology</b>	
Wrobel et al, <sup>33</sup> 2022	Participants with (vs without) a history of any CT (PA, SA, EA) had higher mean scores in the Bipolar Inventory of Symptoms Scale and the Clinical Global Impression at each visit (all $p < 0.05$ ), except for the 24-week follow-up visit.
Visioli et al, <sup>32</sup> 2023	A history of PA was not associated with the annual frequency of illness episodes and the average total percentage of time ill. A history of SA was associated with higher symptom severity at each visit, including more illness episodes/year ( $t = 3.00$ , $p = 0.003$ ).
<b>Depressive symptoms</b>	
Leverich et al, <sup>17</sup> 2022	Increasing severity of depression (measured by the Inventory of Depressive Symptomatology) was found in patients with SA (but not PA), compared with those without abuse ( $\chi^2 = 5.18$ , $p = 0.024$ ).
Visioli et al, <sup>32</sup> 2023	A history of PA was not associated with the annual frequency of illness episodes (all episodes, depressive, hypomanic, and manic episodes) and the average total percentage of time ill in depression. A history of SA was associated with more depressive episodes ( $t = 2.81$ , $p = 0.005$ ) but not the time in depressive episodes.
Vaughn-Coaxum et al, <sup>31</sup> 2021	No significant effects of PA and SA on depressive symptom severity (measured by the 12-item Schedule for Affective Disorders and Schizophrenia Depression Rating Scale).
<b>Hypomanic and manic symptoms</b>	
Leverich et al, <sup>17</sup> 2022	Increasing severity of mania (measured by the Young Mania Rating Scale) was found in patients with a history of PA ( $\chi^2 = 27.8$ , $p < 0.001$ ) or SA ( $\chi^2 = 27.8$ , $p = 0.002$ ), compared with those without a history of abuse.
Visioli et al, <sup>32</sup> 2023	A history of PA was not associated with the annual frequency of illness episodes (all episodes, depressive, hypomanic, and manic episodes) and the average total percentage of time in hypomania or mania. A history of SA was associated with manic or hypomanic episodes per year ( $t = 2.00$ , $p = 0.05$ ) and the percentage of time in a manic or hypomanic episode ( $t = 2.78$ , $p = 0.006$ ).
<b>Mood and activity instability</b>	
Leverich et al, <sup>17</sup> 2022	More rapid cycling was found in patients with a history of SA ( $\chi^2 = 8.84$ , $p = 0.034$ ). More ultra-rapid cycling was found in patients with a history of PA ( $\chi^2 = 8.49$ , $p = 0.046$ ), and SA ( $\chi^2 = 8.61$ , $p = 0.043$ ). More ultra-ultra-rapid cycling was found in patients with a history of SA ( $\chi^2 = 14.7$ , $p = 0.002$ ).
Brown et al, <sup>5</sup> 2005	PA had increased probability of a rapid cycling pattern of illness (OR = 1.96, 95% CI = 1.01-3.79, $p = 0.047$ ). Significant associations of PA and SA with rapid cycling.
von Hofacker et al, <sup>26</sup> 2024	Childhood Trauma Questionnaire score was positively associated with mood instability (B = 0.006, 95% CI = 0.000-0.012, $p = 0.031$ ) but not activity instability.
<b>Suicidality</b>	
Leverich et al, <sup>27</sup> 2003	Patients with a history of PA ( $p < 0.01$ ) and SA ( $p < 0.05$ ) showed higher suicidality than those without a history CT. Patients with a history of both PA and SA showed higher suicidality than those with a history of either PA or SA ( $p < 0.01$ ).
<b>Relapse</b>	
Dienes et al, <sup>25</sup> 2006	People with more severe early adversity (measured by the Structural Clinical Interview for DSM-IV) were more likely to experience a relapse when facing mild stress compared with those with mild or no early adversity.

Abbreviations: 95% CI = 95% confidence interval, BAD = bipolar affective disorder, CT = childhood trauma, EA = emotional abuse, EN = emotional neglect, OR = odds ratio, PA = physical abuse, PN = physical neglect, SA = sexual abuse

Table 3. (cont'd)

Study	Outcome
<b>Treatment response and remission</b>	
Cakir et al, <sup>24</sup> 2016	Good responders to treatment with valproate and carbamazepine had lower scores of PA ( $z = 2.18$ , $p = 0.029$ ) and EA ( $z = 2.10$ , $p = 0.036$ ), compared with poor responders. Good and poor responders to lithium treatment did not significantly differ in terms of PA, EA, PN, EN, or SA. Good and poor responders to treatment with valproate and carbamazepine did not significantly differ in terms of PN, EN, or SA.
Wrobel et al, <sup>33</sup> 2022	There was no significant difference between participants with and without a history of any CT subtype (PA, SA, EA) during the 24-week treatment in terms of the Bipolar Inventory of Symptoms Scale ( $\beta = -0.33$ , $p = 0.68$ ) and the Clinical Global Impression ( $\beta = 0.003$ , $p = 0.45$ ).
Neria et al, <sup>28</sup> 2005	Patients with a history of CT were less likely to reach complete remission or took longer time to do so, based on the World Health Organization classification of illness course (single episode/full remission vs multiple episodes/continuous illness) during the 24-month diagnostic conference.
<b>Hospitalisation</b>	
Benarous et al, <sup>23</sup> 2017	In patients with BAD I, a longer duration of hospital stay was not noted in those with a history of CT, compared with those without a history of CT.
Brown et al, <sup>5</sup> 2005	Any CT was associated with more involuntary hospitalisations (OR = 2.37, 95% CI = 1.10-5.14, $p = 0.029$ ), compared with those not reporting abuse.
<b>Comorbidity</b>	
Sala et al, <sup>29</sup> 2014	Dose-response relationships were found between the number of CT subtypes and the incidence of anxiety disorders ( $\chi^2 = 23.87$ , $p < 0.001$ ), substance use disorder ( $\chi^2 = 21.69$ , $p < 0.001$ ), and nicotine dependence ( $\chi^2 = 7.54$ , $p = 0.0061$ ).
<b>Functional outcomes</b>	
Benarous et al, <sup>23</sup> 2017	In patients with BAD-1, those with a history of CT ( $n = 16$ ) had better treatment response ( $p = 0.034$ ) in terms of changes in the Global Assessment Functioning Scale from admission to discharge than those with no history of CT ( $n = 61$ ).
Schwarz et al, <sup>30</sup> 2024	CT was a predictor of the Assessment of Motor and Process Skills ( $\beta = -0.244$ , $p < 0.05$ ), with more CT predicting less improvement in functioning ( $p < 0.05$ ).
Wrobel et al, <sup>33</sup> 2022	Participants with (vs without) a history of any of PA, SA, or EA had higher mean scores in the Longitudinal Interval Follow-up Evaluation-Range of Impaired Functioning Tool at weeks 12 and 24 (all $p < 0.05$ ). There was no significant difference between participants with and without a history of any CT during the 24 weeks of treatment ( $\beta = 0.01$ , $p = 0.56$ ).

### Comorbidity

Sala et al<sup>29</sup> found a significant dose-response relationship between the number of CT subtypes and the incidence of anxiety disorders, substance use disorder, and nicotine dependence.

### Functional outcomes

Wrobel et al<sup>33</sup> found that individuals with a history of PA, SA, or EA exhibited greater functional impairment in work performance, interpersonal relationships, living skills, and life satisfaction at 12- and 24-week follow-up, compared with those without such history. Benarous et al<sup>23</sup> found that patients with a history of CT demonstrated greater treatment response from admission to discharge. In contrast, Wrobel et al<sup>33</sup> found no significant differences in

functional improvement over a 24-week treatment period between those with and without any CT. Schwarz et al<sup>30</sup> found that CT was predictive of poorer improvement in motor and process skills.

### Discussion

Patients with a history of CT have more severe and volatile manic and depressive symptoms and greater functional impairment, as well as elevated risks for relapse, suicidality, and psychiatric comorbidities. However, associations between CT and hospitalisation, treatment response, and functional recovery remain inconclusive. Subtypes PA and SA are consistently associated with more severe symptoms, greater mood instability, and

an elevated risk of relapse. These findings demonstrate that such adverse effects persist longitudinally, affecting the clinical course of BAD. Individuals with BAD and a history of CT are at higher risk of suicidality, psychiatric comorbidities, and functional impairment, and have more severe and unstable symptoms.<sup>8,12,34,35</sup> Cognitive theories of childhood maltreatment-related psychopathology propose that trauma-induced cognitive distortions and maladaptive schemas, such as self-blame and abandonment schemas, may lead to heightened mood instability and worsened clinical outcomes.<sup>36,37</sup> For individuals with BAD, these negative self-schemas may exacerbate symptom severity and complexity. Given the high prevalence of CT in patients with BAD,<sup>38</sup> targeted, trauma-focused interventions may be of particular benefit.

CT is consistently associated with increased risks of suicidality, relapse, and comorbid psychiatric disorders.<sup>12,34,35</sup> However, each of these outcomes was supported only by a single study. CT is associated with more frequent hospitalisation but not the length of hospital stays.<sup>39,40</sup> This discrepancy may be due to the larger sample size in studies of hospitalisation frequency ( $n = 330$ ) compared to those analysing hospitalisation duration ( $n = 81$ ). This highlights the need for standardised methodologies and larger, well-controlled studies.

Regarding treatment response and remission, although one study found that individuals with a history of CT were less likely to achieve complete remission and took longer time to do so,<sup>28</sup> another found no significant differences in improvement rates.<sup>33</sup> This variability may be due to sample differences, treatment protocols, and the inclusion of various CT subtypes. Pharmacological treatment outcomes were also mixed, particularly in studies that examined the differential impact of CT subtypes.<sup>24</sup> This suggests that CT may influence treatment response in a subtype-specific manner, further emphasising the importance of individualised, trauma-informed treatment approaches for BAD.

The impact of CT on functioning may evolve over time. A short-term study found better functioning for those with CT (though the sample size was small [ $n = 16$ ]), whereas a longer-term study found that a history of any of PA, SA, or EA was associated with more impaired functioning. This suggests that CT might initiate early engagement in recovery, but adverse effects emerge over time, probably due to chronic stress responses or maladaptive coping mechanisms developed in early life. Interestingly, CT does not appear to significantly affect functional recovery,<sup>41</sup> although specific CT subtypes (PA, SA, and EA) were associated with greater functional impairment. This suggests a possible homogeneous effect of various CT subtypes on functional outcomes.<sup>42</sup>

The distinct impact of particular CT subtypes on the clinical course of BAD suggests that different neurobiological and psychological mechanisms may underlie these relationships. PA and SA are consistently associated with increased symptom severity, mood instability, rapid cycling, and relapse risk, likely due to

heightened emotional dysregulation. These types of CT are strongly associated with hyperactivation of stress-response systems, particularly the hypothalamic-pituitary-adrenal axis, which is essential in regulating stress reactivity and emotional stability.<sup>17,18</sup> Chronic hypothalamic-pituitary-adrenal axis dysregulation, often observed in survivors of PA and SA, may contribute to the persistent mood instability and heightened vulnerability to stressors seen in patients with BAD and a history of CT. EA is hypothesised to play a role in shaping core cognitive processes such as self-esteem, identity development, and interpersonal functioning.<sup>43</sup> These cognitive and relational disruptions may be particularly relevant in BAD, as individuals with EA histories often exhibit insecure attachment patterns, which can impair emotional regulation, exacerbate interpersonal conflicts, and reduce resilience to stress.

Although there may be individual effects of CT subtypes, it is important to recognise the influence of abuse as a whole, as individuals often experience multiple types of abuse.<sup>44</sup> Brown et al<sup>5</sup> examined the impact of 'any abuse' and 'combined abuse' to determine synergistic or cumulative effects of different CT subtypes on the clinical course of BAD. Their findings emphasise the need for personalised, trauma-informed interventions, such as emotional regulation and stress response modulation for patients with PA and SA, and cognitive restructuring and interpersonal support for patients with EA.

There are several limitations to this review. The number of studies included was small. Only peer-reviewed English-language articles were included; relevant studies in other languages or the grey literature were excluded. The scarcity of long-term studies limits the strength of the findings, which rely on data from few studies. The inherent complexity of CT prohibits distinct conclusions regarding any one subtype. A lack of standardisation in assessing and quantifying CT complicates comparisons between studies. Some assessments of CT focus solely on abuse- and neglect-related trauma, overlooking the broader spectrum of traumatic experiences. The variability in instruments used to assess outcome measures highlights the fragmented nature of the current review. Many studies treat CT as a general construct, potentially obscuring distinct subtype effects; although some studies do differentiate between subtypes, most focus on PA and SA and often overlooks EA and EN. Sample heterogeneity may complicate interpretation. Life factors such as occupational and interpersonal issues may also contribute to BAD outcomes over time. Relying on retrospective self-reporting of CT raises concerns about recall bias; however, recall bias in CT reporting was found to have little effect on validity of findings.<sup>45</sup> Future research should adopt prospective designs, corroborative data sources, standardised measures, and a wide variety of CT subtypes to improve comparability and reliability. Incorporating genetics, environmental influences, and personality and lifestyle factors may help to identify how impairments arise and inform preventive and interventional strategies.

## Conclusion

PA and SA are consistently associated with greater symptom severity, mood instability, and relapse risk. Although the evidence of CT on hospitalisation, treatment response, and functional recovery remains inconclusive, CT remains a key determinant of BAD progression rather than just a risk factor for onset. The differential impacts of CT subtypes suggest distinct neurobiological and cognitive mechanisms, highlighting the need for personalised, trauma-informed interventions.

## Contributors

All authors acquired the data, designed the study, analysed the data drafted the manuscript, critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

As editor of the journal, SKWC was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## References

1. Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. *Lancet* 2016;387:1561-72. [Crossref](#)
2. Ketter TA. Diagnostic features, prevalence, and impact of bipolar disorder. *J Clin Psychiatry* 2010;71:e14. [Crossref](#)
3. McIntyre RS, Berk M, Brietzke E, et al. Bipolar disorders. *Lancet* 2020;396:1841-56. [Crossref](#)
4. Zarate CA Jr, Tohen M, Land M, Cavanagh S. Functional impairment and cognition in bipolar disorder. *Psychiatr Q* 2000;71:309-29. [Crossref](#)
5. Brown GR, McBride L, Bauer MS, Williford WO; Cooperative Studies Program 430 Study Team. Impact of childhood abuse on the course of bipolar disorder: a replication study in U.S. veterans. *J Affect Disord* 2005;89:57-67. [Crossref](#)
6. Thurston C, Murray AL, Franchino-Olsen H, Meinck F. Prospective longitudinal associations between adverse childhood experiences and adult mental health outcomes: a protocol for a systematic review and meta-analysis. *Syst Rev* 2023;12:181. [Crossref](#)
7. Aas M, Henry C, Andreassen OA, Bellivier F, Melle I, Etain B. The role of childhood trauma in bipolar disorders. *Int J Bipolar Disord* 2016;4:2. [Crossref](#)
8. Agnew-Blais J, Danese A. Childhood maltreatment and unfavourable

- clinical outcomes in bipolar disorder: a systematic review and meta-analysis. *Lancet Psychiatry* 2016;3:342-9. [Crossref](#)
9. Barczyk ZA, Foulds JA, Porter RJ, Douglas KM. Childhood trauma and cognitive functioning in mood disorders: a systematic review. *Bipolar Disord* 2023;25:263-77. [Crossref](#)
10. Daruy-Filho L, Brietzke E, Lafer B, Grassi-Oliveira R. Childhood maltreatment and clinical outcomes of bipolar disorder. *Acta Psychiatr Scand* 2011;124:427-34. [Crossref](#)
11. Trotta A, Murray RM, Fisher HL. The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. *Psychol Med* 2015;45:2481-98. [Crossref](#)
12. Zatti C, Rosa V, Barros A, et al. Childhood trauma and suicide attempt: a meta-analysis of longitudinal studies from the last decade. *Psychiatry Res* 2017;256:353-8. [Crossref](#)
13. Cai J, Li J, Liu D, et al. Long-term effects of childhood trauma subtypes on adult brain function. *Brain Behav* 2023;13:e2981. [Crossref](#)
14. Cassiers LL, Sabbe BG, Schmaal L, Veltman DJ, Penninx BW, Van Den Eede F. Structural and functional brain abnormalities associated with exposure to different childhood trauma subtypes: a systematic review of neuroimaging findings. *Front Psychiatry* 2018;9:329. [Crossref](#)
15. Curran E, Adamson G, Rosato M, De Cock P, Leavey G. Profiles of childhood trauma and psychopathology: US National Epidemiologic Survey. *Soc Psychiatry Psychiatr Epidemiol* 2018;53:1207-19. [Crossref](#)
16. Etain B, Aas M, Andreassen OA, et al. Childhood trauma is associated with severe clinical characteristics of bipolar disorders. *J Clin Psychiatry* 2013;74:991-8. [Crossref](#)
17. Leverich GS, McElroy SL, Suppes T, et al. Early physical and sexual abuse associated with an adverse course of bipolar illness. *Biol Psychiatry* 2002;51:288-97. [Crossref](#)
18. Maniglio R. The impact of child sexual abuse on the course of bipolar disorder: a systematic review. *Bipolar Disord* 2013;15:341-58. [Crossref](#)
19. Erten E, Funda Uney A, Saatçioğlu Ö, Özdemir A, Fistikçi N, Çakmak D. Effects of childhood trauma and clinical features on determining quality of life in patients with bipolar I disorder. *J Affect Disord* 2014;162:107-13. [Crossref](#)
20. Page MJ, McKenzie J, Bossuyt P, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. [Crossref](#)
21. Bernstein DP, Fink L, Handelsman L, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *Am J Psychiatry* 1994;151:1132-6. [Crossref](#)
22. JBI. Checklist for Cohort Studies. Critical Appraisal tools for use in JBI Systematic Reviews. Accessed 7 February 2025. Available from: [https://jbi.global/sites/default/files/2020-08/Checklist\\_for\\_Cohort\\_Studies.pdf](https://jbi.global/sites/default/files/2020-08/Checklist_for_Cohort_Studies.pdf)
23. Benarous X, Raffin M, Bodeau N, Dhossche D, Cohen D, Consoli A. Adverse childhood experiences among inpatient youths with severe and early-onset psychiatric disorders: prevalence and clinical correlates. *Child Psychiatry Hum Dev* 2017;48:248-59. [Crossref](#)
24. Cakir S, Tasdelen Durak R, Ozyildirim I, Ince E, Sar V. Childhood trauma and treatment outcome in bipolar disorder. *J Trauma Dissociation* 2016;17:397-409. [Crossref](#)
25. Dienes KA, Hammen C, Henry RM, Cohen AN, Daley SE. The stress sensitization hypothesis: understanding the course of bipolar disorder. *J Affect Disord* 2006;95:43-9. [Crossref](#)
26. von Hofacker AJ, Faurholt-Jepsen M, Kjaerstad HL, et al. Predictors of mood and activity instability in participants with newly diagnosed bipolar disorder: exploratory findings from a prospective cohort study. *J Affect Disord Rep* 2024;15:100708. [Crossref](#)
27. Leverich GS, Altshuler LL, Frye MA, et al. Factors associated with suicide attempts in 648 patients with bipolar disorder in the Stanley Foundation Bipolar Network. *J Clin Psychiatry* 2003;64:506-15. [Crossref](#)
28. Neria Y, Bromet EJ, Carlson GA, Naz B. Assaultive trauma and illness course in psychotic bipolar disorder: findings from the Suffolk County Mental Health Project. *Acta Psychiatr Scand* 2005;111:380-3. [Crossref](#)
29. Sala R, Goldstein BI, Wang S, Blanco C. Childhood maltreatment and the course of bipolar disorders among adults: epidemiologic evidence

- of dose-response effects. *J Affect Disord* 2014;165:74-80. [Crossref](#)
30. Schwarz R, Miskowiak KW, Kessing LV, Vinberg M. Clinical and personal predictors of functioning in affective disorders: exploratory results from baseline and 6-month follow-up of a randomised controlled trial. *J Psychiatr Res* 2024;175:386-92. [Crossref](#)
  31. Vaughn-Coaxum RA, Merranko J, Birmaher B, et al. Longitudinal course of depressive symptom severity among youths with bipolar disorders: moderating influences of sustained attention and history of child maltreatment. *J Affect Disord* 2021;282:261-71. [Crossref](#)
  32. Visioli C, Tondo L, Miola A, Pinna M, Contu M, Baldessarini RJ. Early sexual or physical abuse in female and male mood disorder patients. *J Psychiatr Res* 2023;167:125-31. [Crossref](#)
  33. Wrobel AL, Jayasinghe A, Russell SE, et al. The influence of childhood trauma on the treatment outcomes of pharmacological and/or psychological interventions for adolescents and adults with bipolar disorder: a systematic review and meta-analysis. *J Affect Disord* 2022;296:350-62. [Crossref](#)
  34. Boukidi H, Ballouk H, Sabir M, Ait Bensaïd N, Elomari F. Childhood trauma in bipolar disorder: experience of Arrazi hospital. *Eur Psychiatry* 2024;67(S1):S430. [Crossref](#)
  35. Li XB, Liu JT, Zhu XZ, Zhang L, Tang YL, Wang CY. Childhood trauma associates with clinical features of bipolar disorder in a sample of Chinese patients. *J Affect Disord* 2014;168:58-63. [Crossref](#)
  36. Ehlers A, Clark DM. A cognitive model of posttraumatic stress disorder. *Behav Res Ther* 2000;38:319-45. [Crossref](#)
  37. Marziano V, Ward T, Beech AR, Pattison P. Identification of five fundamental implicit theories underlying cognitive distortions in child abusers: a preliminary study. *Psychol Crime Law* 2006;12:97-105. [Crossref](#)
  38. Quidé Y, Tozzi L, Corcoran M, Cannon DM, Dauvermann MR. The impact of childhood trauma on developing bipolar disorder: current understanding and ensuring continued progress. *Neuropsychiatr Dis Treat* 2020;16:3095-115. [Crossref](#)
  39. Du Rocher Schudlich T, Youngstrom EA, Martinez M, et al. Physical and sexual abuse and early-onset bipolar disorder in youths receiving outpatient services: frequent, but not specific. *J Abnorm Child Psychol* 2015;43:453-63. [Crossref](#)
  40. Watson S, Gallagher P, Dougall D, et al. Childhood trauma in bipolar disorder. *Aust N Z J Psychiatry* 2014;48:564-70. [Crossref](#)
  41. Conus P, Cotton S, Schimmelmann BG, et al. Pretreatment and outcome correlates of past sexual and physical trauma in 118 bipolar I disorder patients with a first episode of psychotic mania. *Bipolar Disord* 2010;12:244-52. [Crossref](#)
  42. Carr CP, Martins CM, Stingel AM, Lemgruber VB, Juruena MF. The role of early life stress in adult psychiatric disorders. *J Nerv Ment Dis* 2013;201:1007-20. [Crossref](#)
  43. Riggs SA. Childhood emotional abuse and the attachment system across the life cycle: what theory and research tell us. *J Aggress Maltreat Trauma* 2010;19:5-51. [Crossref](#)
  44. Chartier MJ, Walker JR, Naimark B. Separate and cumulative effects of adverse childhood experiences in predicting adult health and health care utilization. *Child Abuse Negl* 2010;34:454-64. [Crossref](#)
  45. Fergusson DM, Horwood LJ, Boden JM. Structural equation modeling of repeated retrospective reports of childhood maltreatment. *Int J Methods Psychiatr Res* 2011;20:93-104. [Crossref](#)