

Resilience in Bipolar Disorder and Interrelationships With Psychopathology, Clinical Features, Psychosocial Functioning, and Mediational Roles: A Systematic Review

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ABSTRACT

Objective: A systematic review was conducted to examine resilience in bipolar disorder (BD) and its relationship to demographic, psychopathology, illness features, and psychosocial functioning.

Data Sources: A literature search was conducted from database inception to August 2022 using PubMed, Web of Science, EMBASE, and PsycINFO. Reference lists were also manually searched for relevant articles.

Study Selection: Studies were included if they involved patients with a primary diagnosis of BD, were published in English, and measured resilience using a clearly defined rating scale. Studies were excluded if they were case reports, systematic reviews, or conference articles. Of the initial 100 records screened after duplicates were removed, 29 articles were finally included in the systematic review.

Data Extraction: Information extracted included the number and type of subjects, socio-demographic characteristics, resilience scale(s) used, and relevant clinical correlates.

Results: Higher resilience in BD was associated with specific psychopathology (lower severity of depressive and psychotic symptoms; less rumination, hopelessness, impulsivity, and aggression; fewer depressive episodes and suicide attempts), clinical features (self-directed temperament, less childhood trauma, and positive attitudes toward pharmacologic treatment), social factors (better social support and family organization), and psychosocial functioning (better quality of life, social functioning, personal recovery, and spiritual well-being). Resilience also mediated pathways between childhood trauma, depression, and quality of life.

Conclusions: Based on resilience models, BD patients can be helped to better manage challenges and stressors and bolster internal compensatory factors and external protective factors during the course of their illness.

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Bipolar disorder (BD), an affective disorder affecting more than 1% of the world's population,¹ is characterized by recurrent episodes of hypomania, mania, or depression, which can be interspersed with intervals of euthymia.^{2,3} Due to its potential chronicity, BD has a significant impact on various aspects of family, work, social functioning, and quality of life,⁴ thus making it one of the top 5 psychiatric conditions exacting the greatest burden of illness.⁵ In recent years, the topic of resilience in serious mental illnesses has been of increasing interest.⁶ While resilience has been described as the process of adaptation when faced with significant sources of stress (including mental health problems), trauma, threats, or adversities,⁷ it is also seen as a dynamic multidimensional construct that is derived from a balance between vulnerability and protective factors.⁸ Patients with BD face considerable stress and adversity related to symptomatology, clinical course, and psychosocial functioning. Any significant compromises in adaptation can influence the longitudinal illness trajectory and outcomes. Thus, a better understanding of resilience and associated vulnerability and protective factors (related to demographic, clinical, functioning, and recovery features) can potentially assist in early identification of profiles of patients who may require more assistance to foster resilience and improve management of BD.^{9,10}

Earlier studies and reviews have examined the role of resilience in major psychiatric disorders such as schizophrenia and found the relevance of addressing associated vulnerability factors in resilience-targeted interventions.^{11–14} In comparison, there are fewer studies that assess resilience in patients with BD, and, to the best of our knowledge, there has been no systematic review of extant studies to date. In light of this, we sought to systematically review existing empirical studies that focus on resilience in BD and examine the interrelationships between resilience and aspects pertaining to demographic, psychopathology, illness features, psychosocial functioning, and the mediational role of resilience in BD.

METHODOLOGY

Data Collection and Search Strategy

We separately screened the abstracts of potentially relevant studies based on the inclusion and exclusion

Clinical Points

- A better understanding of resilience and associated vulnerability and protective factors in bipolar disorder can assist in early identification of profiles of patients who may require greater attention to improve clinical management of their condition.
- Based on our review findings and resilience models, patients with bipolar disorder can be helped to better manage challenges and stressors and bolster internal compensatory factors and external protective factors during their illness course.

criteria below. The search lists were then compared against each other, and any discrepancies were resolved through discussion, ensuring agreement among all authors before inclusion in the review. We included relevant empirical studies based on a search that was conducted from inception to August 2022 of digital databases including PubMed, Web of Science, EMBASE, and PsycINFO. An example of the detailed search strategy used for one of the databases (Web of Science) is as follows: TI = (((“bipolar disorder”) OR (mania) OR (hypomani*) OR (manic-depress*)) AND (resilien*)) OR AB = (((“bipolar disorder”) OR (mania) OR (hypomani*) OR (manic-depress*)) AND (resilien*)). A total of 1,225 studies were acquired, including 271 from PubMed, 285 from Web of Science, 446 from EMBASE, and 223 from PsycINFO before the removal of duplicates. In addition, 11 were acquired from manually searching reference lists. Duplicates were removed before the full text versions of articles were screened for eligibility. A total of 29 studies were subsequently included in the data synthesis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for this study is shown in Figure 1.¹⁵

Inclusion and Exclusion Criteria

The inclusion criteria for empirical studies were (1) participants included patients who had a primary diagnosis of BD, (2) resilience was measured by a clearly defined rating scale, and (3) articles were published in English. Studies were excluded if they were case reports, systematic reviews, or conference articles.

Data Analyses and Interpretation

For each empirical study, extracted information included the number and type of subjects, socio-demographic characteristics, resilience scale(s) used, and main relevant clinical correlates. The extracted variables were then organized into a table for data analyses and interpretation by all authors and readers. The quality of included cross-sectional studies was assessed using the modified Newcastle-Ottawa Scale.^{16,17}

RESULTS

Overall, 29 studies were included in this review, and the main findings are summarized in Table 1. The majority of

the studies (23/29, 79.3%) were cross-sectional in nature except for 2 (1 was an intervention study, and the other, a longitudinal study),^{38,43} and a preponderance of the studies were conducted in Europe (19/25, 76.0%), followed by Asia (6/29, 20.7%) and Americas (3/29, 10.3%) and in both Europe and Asia (1/29, 3.45%). The sample size of BD patients in the studies varied from 10 to 246, with a preponderance of studies (20/29, 69.0%) below sample size of 100. Based on 20 studies, the overall proportion of female BD subjects was 55.5% (1,235/2,226). Five studies did not provide sex proportions of BD subjects. The mean age of the entire sample of BD subjects (N = 2,143) included in this review was 40.0 years based on 23 out of 29 studies. Six studies did not provide mean age of BD subjects. The mean duration of illness was 15.2 years based on 14 out of 29 studies. Fifteen studies did not provide mean duration of illness.

Quality Assessment

The quality of cross-sectional studies included was satisfactory (Table 2), with the lowest scoring studies (5 out of a maximum possible score of 9) often not controlling for confounding factors in their analyses. All cross-sectional studies employed validated measurement tools for the diagnosis of BD in their participants, and the assessment of the outcome of interest (ie, resilience levels) through the use of self-report questionnaires was awarded 1 point in our modified version of the Newcastle-Ottawa Scale given that it is a subjective construct that cannot be validated through objective means such as reference to medical records.

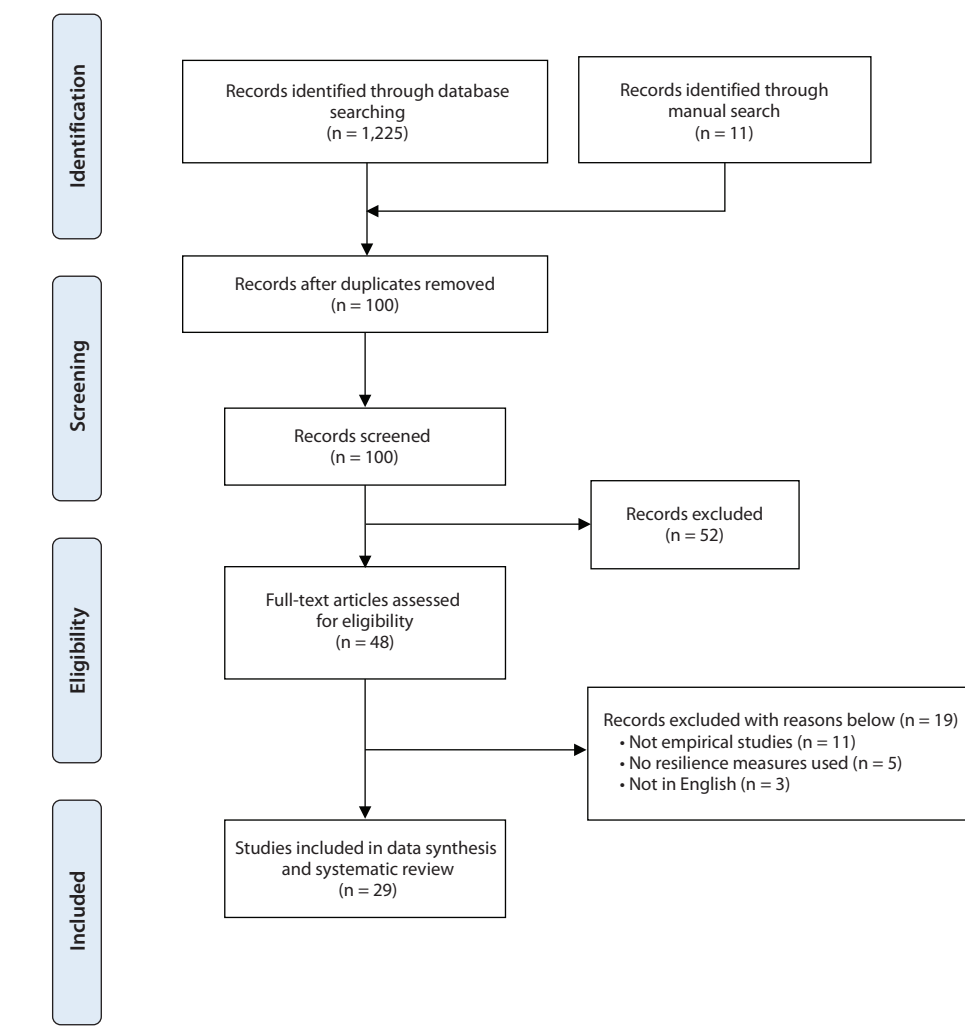
Resilience and Demographic Factors

For sex, higher resilience scores were found to be associated with female sex in one study,²⁵ but no sex association was found in another study.³¹ Regarding age, 3 out of 6 studies reported that higher resilience was associated with both younger²⁵ and older^{12,35} age, while no such association was found in 3 other studies.^{31,34,41} Mixed findings were observed regarding the relationship between educational level and resilience. Two out of 3 studies found that fewer²⁹ and more⁴¹ years of education were associated with higher levels of resilience, while 1 study³⁵ found no such association. No significant association was found between resilience level and socio-economic status.³⁵

Resilience and Psychopathology

Higher levels of resilience were associated with lower severity of depression in several studies,^{12,18,24–26,29,34,44} less rumination,²³ lower level of hopelessness,¹² better self-esteem,¹² fewer depressive episodes,^{22,41} less suicidal ideation,^{18,19,27} and fewer suicide attempts.^{22,29} Higher resilience was also associated with decreased psychotic symptoms²⁶ and lower aggression and impulsivity scores.^{29,41} There was no significant association between resilience and manic features,^{12,25} insight,^{12,29} general psychiatric symptoms,²⁵ or cognitive functioning.³⁶

Figure 1. PRISMA Chart of Studies Included in the Review



Resilience and Clinical Features

Two out of 3 studies found that an older age at onset of BD^{31,35} was associated with higher resilience, while 1 study⁴¹ found no such association. For intelligence quotient (IQ), higher resilience score was associated with higher IQ in 1 study²⁵ but not in another study.¹² In terms of temperament, lower resilience was associated with anxious,^{24,26,29,42} avoidant,²⁴ irritable,²⁹ cyclothymic,^{26,29} novelty seeking,³³ and harm avoidance³³ temperament types. Conversely, higher resilience was associated with hyperthymic,^{24,29} self-directed,³³ and cooperative³³ temperaments. Higher resilience was also associated with less negative perception regarding pharmacologic treatments.¹² Regarding stigma, Post et al⁶ found that lower self-stigma and greater stigma resistance were associated with higher resilience, but this was not significant in another study.¹² Of note, higher resilience levels were associated with less childhood trauma,^{24,30} abuse (emotional, sexual), and emotional neglect.⁴² No significant association was found between resilience level and smoking history,³¹ alcohol use,^{29,31} duration of illness,^{12,35,41} or previous hospitalizations.^{12,31}

Resilience and Social Factors

Better perceived social support, including from family and friends, was found to be associated with a higher level of resilience.^{21,31} Higher resilience was also found to be associated with greater pursuit of hobbies and conduct of home tasks, better family organization and functioning, and a less controlling family environment.^{21,26}

Resilience and Psychosocial Functioning and Personal Well-being

A number of studies found that higher resilience was associated with better quality of life.^{25,28,38–40} In addition, earlier studies found that higher resilience was associated with better psychosocial functioning,^{12,21,34,44} better personal recovery,²⁰ and overall,⁴⁴ as well as spiritual, well-being, but not attendance of religious services.³⁷

Mediational Pathways Involving Resilience

Resilience was found to mediate various pathways. Resilience partially mediates the effect of childhood trauma on the onset of BD and the severity of depression.³⁰ In a

Table 1. Summary of Main Findings of the Included Studies

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Palagini et al ¹⁸ (2022a) Italy	<u>Diagnosis</u> BD1 in current depressive episode: 48.9% (92/188) BD2 in current depressive episode: 51.1% (96/188) <u>Age (mean ± SD)</u> 46.4 ± 13.0 y <u>Sex</u> F: 43.0% (81/188) M: 57.0% (107/188) <u>DI</u> 18.4 ± 11.5 y	RSA	Early Trauma Inventory Insomnia Severity Index Scale for Suicide Ideation Beck Depression Inventory-II YMRS	Patients with insomnia had lower overall resilience and poorer ability to plan ahead and formulate clear goals (Planned Future subscale RSA) and were less likely to be goal- or routine-oriented (Structured Style subscale RSA) Passive suicidal ideation was correlated with low total resilience scores Active suicidal ideation was correlated with low total resilience scores and low scores in Planning Future and Structured Style subscales (RSA) Insomnia was a mediator between early life stress and total resilience scores, as well as between total resilience and suicide risk	↑Resilience a/w ↓Insomnia ↓Suicidal ideation
Palagini et al ¹⁹ (2022b) Italy	<u>Diagnosis</u> BD1 with current depressive episode: 48.7% (96/197) BD2 with current depressive episode: 51.3% (101/197) <u>Age (mean ± SD)</u> 46.4 ± 13.0 y <u>Sex</u> F: 42.6% (84/197) M: 57.4% (113/197) <u>DI (mean ± SD)</u> 18.2 ± 11.5 y	RSA	Biological Rhythms Interview of Assessment in Neuropsychiatry (BRIAN) • > 40 = circadian rhythm disorder • 5 domains: Sleep, Activity, Social life, Eating pattern, Chronotype Difficulties in Emotion Regulation Scale (DERS) • 6 subscales: Non-acceptance of emotion, Difficulties engaging in goal-directed behaviors, Impulse control difficulties, Limited access to effective regulatory strategies, Reduced emotional clarity, Lack of emotional awareness Scale for Suicide Ideation Beck Depression Inventory-II YMRS	Patients with circadian rhythm disorders had lower total resilience scores and lower scores on Planned Future and Structured Style subscales (RSA) Suicidal risk (total Scale for Suicide Ideation) was correlated with low total resilience scores and low scores on the Planned Future subscale (RSA) Low total resilience was related to total chronobiological dysrhythmicity (BRIAN) and limited access to effective regulatory strategies (DERS)	↑Resilience a/w ↓Circadian rhythm disorders ↓Depressive symptoms ↓Suicide risk ↓Difficulties in emotion regulation through access to effective regulatory strategies
Echezarraga et al ²⁰ (2022) Spain	<u>Diagnosis</u> BD in (hypo)mania phase: 56.7% (55/97) BD in depression phase: 12.4% (12/97) BD in euthymia phase: 30.9% (30/97) <u>Age (mean ± SD)</u> 45.0 ± 10.7 y <u>Sex</u> F: 63.9% (62/97) M: 36.1% (35/97) <u>DI</u> • Not provided	RBD • 5 factors: self-management of BD, turning point, self-care, self-confidence, interpersonal support	Brief-QoL BD Bipolar Recovery Questionnaire (BRQ) Work and Social Adjustment Scale (WSAS)	Self-confidence (RBD) moderated relationship between hypomania/depression and work and psychosocial functioning impairment (WSAS) Self-management (RBD) moderated the relationship between hypomania and personal recovery (BRQ) Self-management and self-care (RBD) were positively associated with personal recovery (BRQ) Resilience not directly associated with QoL or with work and psychosocial functioning impairment (WSAS)	↑Resilience a/w ↑Personal recovery

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])		Resilience scale used		Other scales used		Main findings		Summary
	Diagnosis	Age (mean $\pm$ SD)	CD-RISC	CD-RISC	Family Assessment Device (FAD) Functioning Assessment Short Test (FAST)	Other scales used	Lower resilience (CD-RISC) in BD than HC Worse family functioning (FAD) correlated with poorer resilience (CD-RISC) Worse psychosocial functioning (FAST) correlated with poorer resilience (CD-RISC) Better social support (SSRS) correlated with better resilience (CD-RISC)	Resilience a/w $\uparrow$ Family functioning $\uparrow$ Psychosocial functioning $\uparrow$ Social support	
Dou et al ²¹ (2022) China	BD: 78.1% (246/315) HC: 21.9% (69/315) Age (mean $\pm$ SD) BD: 28.4 $\pm$ 11.9 y HC: 31.3 $\pm$ 9.3 y Sex BD F: 63.4% (156/246) BD M: 36.6% (90/246) HC F: 60.9% (42/69) HC M: 39.1% (27/69) DI (mean $\pm$ SD) 7.6 $\pm$ 8.0 y				Autonomy Occupational functioning Cognitive functioning Financial issue Interpersonal relationships Leisure time Social Support Rating Scale (SSRS) Beck Scale for Suicide Ideation YMRS 17-item HDRS				
Fernández-Rocha et al ²² (2021) Spain	BD1: 67.4% (58/86) BD2: 16.3% (14/86) BD with mixed phase: 10.5% (9/86) BD not specified: 5.8% (5/86) Age (mean $\pm$ SD) 47.9 $\pm$ 12.4 y Sex F: 39.5% (34/86) M: 60.5% (52/86) DI (mean $\pm$ SD) 22.0 $\pm$ 12.8 y			CD-RISC	NA		No significant differences in resilience between the BD subtypes Those who had attempted suicide recorded lower resilience Resilience is inversely associated with a greater number of depressive episodes	$\uparrow$ Resilience a/w $\downarrow$ Depressive episodes $\downarrow$ Suicide attempts	
Aslan and Baldwin ²³ (2021) United Kingdom	Unipolar depression: 33.3% (50/150) BD: 33.3% (50/150) HC: 33.3% (50/150) Age (mean $\pm$ SD) Unipolar depression: 31.9 $\pm$ 11.35 y BD: 37.3 $\pm$ 14.3 y HC: 28.8 $\pm$ 8.8 y Sex Unipolar depression • F: 68.0% (34/50) • M: 32.0% (16/50) BD • F: 72% (36/50) • M: 28% (14/50) HC • F: 70% (35/50) • M: 30% (15/50) DI • Not provided		BRS		Ruminative Response Scale-Short Form Positive Beliefs about Rumination Scale Negative Beliefs about Rumination Scale Emotion Regulation Questionnaire • Two dimensions: cognitive reappraisal and expressive suppression Stroop Test Trail Making Test A and B • Two parts (A and B)		BD patients had higher resilience than unipolar depression group Negative correlation between rumination and resilience in BD and unipolar depression	$\uparrow$ Resilience a/w $\downarrow$ Rumination	

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Citak and Erten ²⁴ (2021) Turkey	<u>Diagnosis</u> BD1 90.9% (100/110) BD2 9.1% (10/110) <u>Age (mean ± SD)</u> 37.2 ± 10.6 y <u>Sex</u> F: 59.1% (65/110) M: 40.9% (45/110) <u>DL (mean ± SD)</u> 11.0 ± 7.82 y	RSA	HDRS YMRS Childhood Trauma Questionnaire-Short Form Experiences in Close Relationships-revised (ECR-R)	Emotional abuse scores negatively associated with resilience Resilience scores were negatively associated with attachment-related anxiety and avoidance Impact of childhood trauma on resilience was partly mediated by attachment-related anxiety and avoidance	↑Resilience a/w depressive symptoms (HDRS scores) ↓Total childhood trauma scores ↓Attachment-related anxiety and avoidance behavior (ECR-R) Attachment-related anxiety and avoidance behavior (ECR-R) mediated effect of childhood trauma on resilience
Nunes and da Rocha ²⁵ (2021) Brazil	<u>Diagnosis</u> BD: 18.5% (71/384) MDD: 52.1% (200/384) SCZ: 29.4% (113/384) <u>Age (mean ± SD)</u> Overall: 43.4 ± 15.1 BD: 43.5 ± 16.1 MDD: 45.7 ± 15.2 SCZ: 39.4 ± 13.6 <u>Sex</u> Overall: • F: 55.5% (213/384) • M: 45.5% (171/384) BD: • F: 67.6% (48/71) • M: 32.4% (23/71) MDD: • F: 65.0% (130/200) • M: 35.0% (70/200) SCZ: • F: 31.0% (35/113) • M: 69.0% (78/113) <u>DL (median, percentiles 25–75)</u> Overall: 8 (2–20) BD: 11 (3.0–21.0) MDD: 4.5 (1.0–15.3) SCZ: 11.5 (6.8–23.0)	RS—Brazilian adapted version • 2 domains: Personal Competence, Acceptance of Life and Self	World Health Organization QOL-Brief Form (WHOQOL-BREF) Global Assessment of Functioning Scale (GAF) Clinical Global Impression (CGI) Cumulative Illness Rating Scale (CIRS) HDRS YMRS Brief Psychiatric Rating Scale	Resilience negatively correlated with overall depressive symptoms and Acceptance of Life and Self domain No significant correlation between overall general psychiatric symptoms and resilience No significant correlations between resilience and clinical severity (CGI), global assessment of function (GAF), manic symptoms (YMRS), impairment of health state (CIRS) In BD, resilience is predicted by female gender, younger age, higher IQ, and lower educational level Overall resilience positively correlated with overall and all domains of QoL (physical, psychological, social, environmental)	↑Resilience (Acceptance of Life and Self) a/w ↓Overall depressive symptoms ↑General QoL and all subdomains (physical, psychological, social, environmental)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Post et al ⁶ (2021) Germany	Diagnosis BD1: 100.0% (60/60) Age (mean $\pm$ SD) 43.2 $\pm$ 11.0 y Sex F: 58.3% (35/60) M: 41.7% (45/60) DI (mean $\pm$ SD) 11.1 $\pm$ 10.3 y	RS-25	MADRS YMRS Personal and Social Performance Scale Cannon-Sporr Premorbid Adjustment Scale Internalized Stigma of Mental Illness scale • 2 subscales: self-stigma, stigma resistance	Resilience correlated negatively with self-stigma and positively with stigma resistance	$\uparrow$Resilience a/w $\downarrow$Self-stigma $\uparrow$Stigma resistance
Verdolini et al ²⁶ (2021) Spain	Diagnosis Psychiatric patients: 32.8% (174/530) • Anxiety and depressive disorders: 24.1% (42/174) • SCZ and BD: 71.8% (125/174) • Others: 4.02% (7/174) Unaffected relatives: 15.7% (83/530) HC: 51.5% (237/530) Age • Not provided Sex Psychiatric patients: • F: 59.8% (104/174) • M: 40.2% (70/174) Unaffected relatives: • F: 75.9% (63/83) • M: 24.1% (20/83) HC: • F: 86.5% (205/237) • M: 13.5% (32/237) DI • Not provided	BRS	Study-customized survey with 9 broad topics • Depression and anxiety • Trauma experiences • Psychotic-like experiences • Affective temperament • Perceived family environment • Cognition • Cognitive reserve • Physical aggressiveness	In psychiatric patients, the strongest predictor of poor state resilience was depressive symptoms In all subgroups, poor state resilience was associated with depressive and negative psychotic-like experiences In psychiatric patients, cohesion and organization in the family were associated with good state resilience Affective temperament and state resilience Across all subgroups, anxious and cyclothymic temperaments were significantly associated with poor state resilience, while hyperthymic temperament was associated with good state resilience In psychiatric patients, the association between poor state resilience and depressive symptoms was partially mediated by all affective temperaments (cyclothymic, dysthymic, irritable, anxious), with dysthymic temperament showing the strongest effect	Associations with poor state resilience: $\uparrow$Depressive symptoms $\uparrow$Negative psychotic-like experiences $\uparrow$Anxious and cyclothymic temperament Associations with good state resilience: $\uparrow$Pursuit of hobbies or conducting home tasks $\uparrow$Cohesion and organization in family environment $\uparrow$Good state resilience $\uparrow$Hyperthymic temperament Effect of poor state resilience on depressive symptoms mediated by affective temperaments

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Masi et al ²⁷ (2020) Italy	Diagnosis BD and ASD with severe suicidal ideation or attempt (BD-ASD-S): (17/52) BD and ASD without suicidal ideation or attempt (BD-ASD-noS): (17/52) BD without ASD and with severe suicidal ideation or attempt (BD-noASD-S): (18/52) Age (mean ± SD) • BD-ASD-S: 14.53 ± 2.03 y • BD-noASD-S: 14.78 ± 1.86 y • BD-ASD-noS: 14.94 ± 2.22 y Sex BD-ASD-S: • F: 17.6% (3/17) • M: 82.4% (14/17) BD-noASD-S: • F: 66.7% (12/18) • M: 33.3% (6/18) BD-ASD-noS: • F: 41.2% (7/17) • M: 58.8% (10/17) DI • Not provided	READ • 5 subscales: personal competence, social competence, structured style, family cohesion, social resources	Child Behavior Checklist Columbia–Suicide Severity Rating Scale Multi-Attitude Suicide Tendency Scale (MAST) • 4 attitudes: attraction to life, repulsion by life, attraction to death, and repulsion by death Barratt Impulsiveness Scale-11 • 3 subscales: attentional, motor, non-planning	BD-ASD-S scored higher than BD-noASD-S on Personal Competence subscale (READ) Personal Competence and Structured Style (READ) were negatively correlated with repulsion by life (MAST), while Social Resource subscale (READ) was negatively correlated with attraction to death (MAST)	↑Personal Competence and Structured Style (READ) a/w ↓Repulsion to life (MAST) ↑Social resources (READ) a/w ↓Attraction to death (MAST)
Pardeller et al ²⁸ (2020) Germany	Diagnosis • BD1: 7.41% (10/135) • MDD: 37.0% (50/135) • HC: 55.6% (75/135) Age (mean ± SD) BD1 + MDD: 45.1 ± 12.4 y HC: 42.7 ± 12.0 y Sex BD1 + MDD: • F: 60.0% (36/60) • M: 40.0% (24/60) HC: • F: 61.3% (46/75) • M: 38.7% (29/75) DI • Not provided	RS-25 • 2 subscales: acceptance of self and life, personal competence	MADRS WHOQOL-BREF • 5 domains: global QoL, physical health, psychological health, social relationships, and environment	Mean degree of resilience (RS-25) was significantly lower in patients compared to HC BD1 + MDD group had significant positive correlation between resilience (RS-25) and the WHOQOL-BREF domains global QoL, psychological health, and environment Resilience mediated the effect of diagnostic group (BD1 + MDD vs HC) on QoL global score	↑Resilience a/w ↑Global QoL, psychological health, and environment subdomains Resilience partially mediated the effect of BD diagnosis on QoL

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])		Resilience scale used		Other scales used		Main findings		Summary
	Diagnosis	Age (mean $\pm$ SD)	RSA—Turkish version	perception of the self, perception of the future, structured style, social competence, social resources, family cohesion	Schedule for Assessment of Temperament and San Diego Autoquestionnaire	Barratt Impulsiveness Scale (BIS-11)	Resilience (total RSA) negatively correlated with number of depressive episodes and number of suicide attempts	Resilience a/w	
Şenormancı et al ²⁹ (2020) Turkey	BD1: 100.0% (142/142)	37.8 $\pm$ 12.3 y	6 subscales:		Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire	3 subscales: motor, attentional, non-planning	Resilience (total RSA) negatively correlated with aggression (total AQ, anger, hostility, physical aggression subscales) and impulsivity (attentional impulsivity and total BIS-11)	↑Resilience a/w ↓Depressive episodes ↓Suicide attempts ↓Aggression ↓Impulsivity hyperthymic temperament	
	Sex	F: 49.3% (70/142) M: 50.7% (72/142)			Buss-Perry Aggression Questionnaire (AQ)	4 subscales: physical aggression, verbal aggression, anger, hostility	Resilience (total RSA) positively correlated with hyperthymic temperament and negatively associated with cyclothymic, depressive, irritable, anxious temperament	↓Resilience a/w cyclothymic, depressive, irritable, anxious temperament	
	DI	11.7 $\pm$ 9.5 y			Michigan Alcoholism Screening Test		No association between resilience and insight or alcohol consumption	No association between resilience and insight or alcohol consumption	
Vieira et al ³⁰ (2020) Brazil	Diagnosis	BD: 7.2% (90/1244) MDD: 25.5% (317/1244) HC: 67.3% (837/1244)	RS-25		Childhood Trauma Questionnaire (CTQ)		Negative correlation between childhood trauma (CTQ) and resilience (RS-25) in MDD and BD	↑Resilience a/w ↓Childhood trauma (CTQ)	
	Age (mean $\pm$ SD)	BD: 25.8 $\pm$ 2.11 y MDD: 26.0 $\pm$ 2.13 y HC: 25.9 $\pm$ 2.16 y			MADRS		Resilience (RS-25) mediates relationship between childhood trauma (CTQ) and diagnosis and severity of mood disorders	Resilience mediates effect of childhood trauma on diagnosis and severity of MDD and BD	
	Sex	F: 58.0% (721/1244) M: 42.0% (523/1244)			Alcohol, Smoking and Substance Involvement Screening Test				
	DI	• Not provided							
Uygun et al ³¹ (2020) Turkey	Diagnosis	BD: 75.0% (90/120) HC: 25.0% (30/120)	RSA		Multidimensional Scale of Perceived Social Support (MSPSS)	3 sources: family, friends, a special person	Social support (MSPSS) and resilience (RSA) scores were significantly lower in BD vs HC	↑Resilience a/w later age at onset of BD	
	Age (mean $\pm$ SD)	BD: 37.3 $\pm$ 11.6 y HC: 35.3 $\pm$ 10.2 y					In BD group, weak correlation was found between resilience (RSA) and age at onset	↑Perceived social support from family, a special person, and friends (MSPSS)	
	Sex	F: 70.0% (63/90) M: 30.0% (27/90)					In BD group, resilience (RSA) was correlated with social support from family, a special person and friends (MSPSS)		
	DI	• Not provided							

(continued)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Sánchez et al ³² (2019) US	Diagnosis MDD: 38.1% (74/194) BD: 35.6% (69/194) SCZ: 25.8% (50/194) Age • Not provided Sex F: 53.1% (103/194) M: 45.9% (89/194) Transgender: 0.5% (1/194) Nil response: 0.5% (1/194) DI • Not provided	BRS	World Health Organization Disability Assessment Schedule 2.0 (WHO-DAS-2) • 6 domains: communication, mobility, self-care, interpersonal interactions and relationships, life activities, participation Perceived Social Self-Efficacy scale Adaptation to Disability Scale-Revised-23 Multidimensional Scale of Perceived Social Support • 3 sources: family, friends, significant other Satisfaction with Life Domains Scale (SLDS)	Resilience (BRS) was not found to mediate the relationship between functional disability (WHO-DAS-2) and QoL (SLDS)	Resilience did not mediate relationship between functional disability and QoL
Sivri et al ³³ (2019) Turkey	Diagnosis SCZ: 9.4% (16/171) BD: 19.9% (34/171) MDD: 24.0% (41/171) Anxiety disorder: 11.1% (19/171) Alcohol/substance use: 19.9% (34/171) Other disorders: 15.8% (27/171) Age • Not provided Sex F: 43.9% (75/171) M: 56.1% (96/171) DI • Not provided	RSA • 6 dimensions: structured style, perception of the future, family cohesion, perception of the self, social competence, social resources	Temperament and Character Inventory (TCI) • 4 temperaments: novelty seeking, harm avoidance, reward dependence, persistence • 3 characters: self-directedness, cooperativeness, self-transcendence Symptom Checklist (SCL-90-R) • 10 basic symptom clusters: somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, other symptoms	Negative correlation between resilience (RSA) and novelty seeking and harm avoidance (TCI) Positive correlation between resilience (RSA) and persistence (TCI) Positive correlations between resilience (RSA) and self-directedness and cooperativeness (TCI) Persistence, self-directedness, and self-transcendence (TCI) predicted overall resilience scores (RSA) Severity of psychopathology (total SCL-90-R) negatively predicted resilience (total RSA)	↑Resilience a/w ↓Severity of psychopathology (SCL-90-R) ↓Novelty seeking and harm avoidance (TCI) ↑Self-directedness and cooperativeness (TCI) ↑Persistence, self-directedness, and self-transcendence (TCI) predicts ↑resilience
Bozikas et al ³⁴ (2018) Greece	Diagnosis BD1: 45.0% (36/80) BD2: 5.0% (4/80) HC: 50.0% (40/80) Age (mean ± SD) BD: 42.1 ± 9.70 y HC: 42.1 ± 9.99 y Sex BD: • F: 70.0% (28/40) • M: 30.0% (12/40) HC: • F: 70.0% (28/40) • M: 30.0% (12/40) DL (mean ± SD) 11.1 ± 9.44 y	CD-RISC	MADRS YMRS Mini International Classification of Functioning, Disability and Health rating of activities and participation in mental illnesses (Mini-ICF-APP)	BD had lower resilience levels (CD-RISC) vs HC Negative correlation between resilience levels (CD-RISC) and depressive symptoms (MADRS) and social functioning deficit (Mini-ICF-APP)	↑Resilience a/w ↓Depressive symptoms (MADRS) ↓Impairment in social functioning (mini-ICF-APP)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Camardese et al ⁴³ (2018) Italy	<u>Diagnosis</u> BD1: 50.0% (15/30) - Euthymic: 6 - Depressed: 9 BD2: 50.0% (15/30) - Euthymic: 9 - Depressed: 5 <u>Age (mean ± SD)</u> For all patients: 46.1 ± 10.4 y Euthymic: 47.0 ± 11.1 y Depressed: 45.3 ± 10.0 y <u>Sex</u> Euthymic: - F: 53.0% (8/15) - M: 47.0% (7/15) Depressed: - F: 47.0% (7/15) - M: 53.0% (8/15) <u>DL (mean ± SD)</u> - Not provided	CD-RISC	YMRS 21-item HDRS Hamilton Anxiety Rating Scale Questionario per la Valutazione della Conoscenza e dell'Apprendimento per il Disturbo Bipolare Questionnaire to assess knowledge and learning	Longitudinal study 37 recruited, 32 completed program, and 30 returned for follow-up visit after 1 year Significant improvement in resilience (CD-RISC) in all patients without significant differences between euthymic and depressed patients	A mixed psychoeducation and psychosocial intervention was efficacious in improving resilience
Chung et al ⁴⁵ (2018) Korea	<u>Diagnosis</u> BD: 6.12% (77/1259) - BD1: 67.5% (52/77) - BD2: 32.5% (25/77) MDD: 17.9% (224/1259) HC: 76.1% (958/1259) <u>Age (mean ± SD)</u> BD: 41.6 ± 12.5 y MDD: 49.6 ± 15.2 y HC: 25.9 ± 6.7 y <u>Sex</u> BD: - F: 68.8% (53/77) - M: 31.2% (24/77) MDD: - F: 80.4% (180/225) - M: 19.6% (44/225) HC: - F: 53.4% (512/958) - M: 46.6% (446/958) <u>DL (mean ± SD)</u> BD: 11.5 ± 10.2 y MDD: 7.0 ± 9.7 y	CD-RISC	Composite Scale of Morningness 3 types: morning, intermediate, evening	Resilience scores (CD-RISC) were significantly lower in patients with MDD/BD vs HC BD1 subgroup had significantly higher resilience (CD-RISC) than the BD2 subgroup MDD and BD patients had higher resilience (CD-RISC) with older age Older illness onset age of MDD and BD groups was associated with greater resilience (CD-RISC) Duration of illness and the number of mood episodes of MDD and BD groups were not correlated with resilience (CD-RISC)	$\uparrow$ Resilience a/w $\uparrow$ Age $\uparrow$ Age at BD onset

(continued)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Deng et al ³⁶ (2018) China	Diagnosis BD: 20.4% (34/167) SCZ: 48.5% (81/167) HC: 31.1% (52/167) Age (mean ± SD) BD: 22.7 ± 2.90 y SCZ: 22.8 ± 3.94 y HC: 22.1 ± 2.25 y Sex BD: • F: 50.0% (17/34) • M: 50.0% (17/34) SCZ: • F: 35.8% (29/81) • M: 64.2% (52/81) HC: • F: 57.7% (30/52) • M: 42.3% (22/52) DI (mean ± SD) BD: 38.1 ± 46.7 y SCZ: 33.4 ± 35.9 y	CD-RISC	Information subscale of Wechsler Adult Intelligence Scale-Chinese Revised (WAIS-CR) Tests of verbal fluency (VF) N-back task (N-back) Scale for Assessment of Positive Symptoms Scale for Assessment of Negative Symptoms HDRS YMRS	BD and SCZ groups had lower resilience (CD-RISC) vs HC Resilience (CD-RISC) was positively correlated with all 3 cognitive measures (VF, N-back, WAIS-CR) in the entire sample All 3 cognitive measures (WAIS-CR, VF, N-back) do not mediate relationship between diagnostic subgroups and resilience (CD-RISC)	↑ Resilience a/w ↑ Cognitive functioning (WAIS-CR, VF, N-back)
Echezarraga et al ⁴⁴ (2018) Spain	Diagnosis Timepoint 1: • BD1: 100.0% (125/125) Timepoint 2: • BD1: 100.0% (63/63) Age (mean ± SD) Timepoint 1: 46.1 ± 10.9 y Timepoint 2: 45.1 ± 11.1 y Sex Timepoint 1: • F: 62.1% (77/125) • M: 37.9% (48/125) Timepoint 2: • F: 58.1% (36/63) • M: 41.9% (27/63) DI • Not provided	RBD 5 factors: self-management of BD, turning point, self-care, self-confidence, interpersonal support	Bipolar Recovery Questionnaire (BRQ) Internal States Scale (ISS) 4 subscales: activation, well-being, psychopathology, depression The Work and Social Adjustment Scale Brief-QoL.BD	Resilience (RBD) positively correlated with well-being (ISS), personal recovery (BRQ), and QoL (Brief-QoL.BD) Resilience (RBD) was negatively related to psychosocial functioning deficit (The Work and Social Adjustment Scale) and depression (ISS)	↑ Resilience a/w ↑ Personal recovery (BRQ) and well-being (ISS) ↓ Depression (ISS) and ↑ Psychosocial functioning (Work and Adjustment Scale)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Mizuno et al ³⁷ (2018)	Diagnosis BD1: 32.5% (120/369) Paranoid SCZ: 30.3% (112/369) HC: 37.1% (137/369) Age (mean $\pm$ SD) Austria: • BD1: 43.2 $\pm$ 11.0 y • SCZ: 44.1 $\pm$ 10.6 y • HC: 42.7 $\pm$ 12.0 y Japan • BD1: 50.2 $\pm$ 13.8 y • SCZ: 45.9 $\pm$ 10.0 y • HC: 41.0 $\pm$ 17.6 y	RS-25	Religiosity questionnaire designed by Miller et al • Assessed 3 areas: denomination, attendance of religious services, personal importance of religion Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being Scale (FACIT–Sp) • 2 subscales: meaning/peace, faith Personal and Social Performance Scale PANSS MADRS YMRS	Attendance and importance of religious/spiritual activities were not associated with resilience (RS-25) in patients with SCZ or BD1 Strong positive correlation between spiritual well-being (FACIT–Sp) and resilience (RS) in combined patient group	↑Resilience a/w ↑Spiritual well-being for combined patient group (BD1 + SCZ) Religious attendance and religious importance not correlated with resilience
Sex					
Austria	• BD1: – F: 58.3% (35/60) – M: 41.7% (25/60) – SCZ: – F: 48.1% (25/52) – M: 51.9% (27/52) • HC: – F: 62.3% (48/77) – M: 37.7% (29/77)				
Japan	• BD1: – F: 53.3% (32/60) – M: 46.7% (28/60) • SCZ: – F: 63.3% (38/60) – M: 36.7% (22/60) • HC: – F: 50.0% (30/60) – M: 50.0% (30/60)				
DL (mean $\pm$ SD)					
Austria	• BD1: 11.3 $\pm$ 10.3 y • SCZ: 15.1 $\pm$ 10.5 y				
Japan	• BD1: 15.8 $\pm$ 10.5 y • SCZ: 18.9 $\pm$ 10.6 y				

(continued)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [D/I])	Resilience scale used	Other scales used	Main findings	Summary
Post et al ³⁸ (2018) Germany	Diagnosis BD1: 43.8% (60/137) HC: 56.2% (77/137) Age (mean $\pm$ SD) BD1: 42.9 $\pm$ 11.1 y HC: 42.8 $\pm$ 12.1 y Sex BD1: • F: 58.0% (35/60) • M: 42.0% (25/60) HC: • F: 65.0% (50/77) • M: 35.0% (27/77) DI (mean $\pm$ SD) BD1: 11.6 $\pm$ 10.2 y	RS-25	MADRS YMRS Internalized Stigma of Mental Illness scale Berliner Lebensqualitätsprofil (BELP) • German version of the Lancashire Quality of Life Profile • Nine domains: work/occupation, leisure time, financial situation, housing, personal safety, family life, friends, physical health, mental health	BD patients had lower resilience (RS-25) vs HC Positive correlations between resilience (RS-25) and QoL (BELP subscales of overall QoL, work/occupation, leisure time, friends, physical health, and mental health)	↑Resilience a/w ↑Overall QoL and QoL subscales of work/occupation, leisure time, friends, physical health, and mental health (BELP)
Lee et al ³⁹ (2017) Korea	Diagnosis BD1: 30.1% (41/136) BD2: 14.7% (20/136) BD-NOS: 5.15% (7/136) HC: 50.0% (68/136) Age (mean $\pm$ SD) BD: 38.1 $\pm$ 11.3 y HC: 38.4 $\pm$ 11.9 y Sex BD: • F: 44.9% (31/69) • M: 55.9% (38/69) HC: • F: 47.8% (33/69) • M: 52.9% (36/69) DI • Not provided	CD-RISC	WHOQOL-BREF • 4 subscales: physical, psychological, social, environmental • 2 questions: overall QoL, general health Barratt Impulsivity Scale • 3 subscales: attention, motor, non-planning	BD patients had lower resilience vs HC Resilience (CD-RISC) was positively correlated with overall QoL and all its subscales in the BD group	↑Resilience a/w ↑Overall QoL and all its subdomains (WHOQOL-BREF)

(continued)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Hofer et al ⁴⁰ (2017) Austria	Diagnosis BD1: 31.7% (60/189) SCZ: 27.5% (52/189) HC: 40.7% (77/189) Age (mean ± SD) BD1: 43.2 ± 11.0 y SCZ: 44.1 ± 10.6 y HC: 42.8 ± 12.1 y Sex BD1: • F: 58.0% (35/60) • M: 42.0% (25/60) SCZ: • F: 48.0% (25/52) • M: 52.0% (27/52) HC: • F: 62.0% (48/77) • M: 38.0% (29/77) DL (mean ± SD) BD1: 11.6 ± 10.2 y SCZ: 15.4 ± 10.5 y	RS-25	WHOQOL-BREF • 4 subscales: physical, psychological, social, environment PANSS MADRS YMRS	BD patients had lower resilience (RS-25) vs HC Resilience (RS-25) was associated with better QoL (WHOQOL-BREF)	↑ Resilience a/w ↑ QoL (WHOQOL-BREF)
Mizuno et al ¹² (2016) Japan	Diagnosis BD: 33.3% (60/180) SCZ: 33.3% (60/180) HC: 33.3% (60/180) Age (mean ± SD) BD: 50.2 ± 13.8 y SCZ: 45.9 ± 10.0 y HC: 41.0 ± 17.6 y Sex BD: • F: 53.3% (32/60) • M: 46.7% (28/60) SCZ: • F: 63.3% (38/60) • M: 36.7% (22/60) HC: • F: 50.0% (30/60) • M: 50.0% (30/60) DL (mean ± SD) BD: 15.8 ± 10.5 y SCZ: 18.9 ± 10.6 y	RS-25	PANSS MADRS YMRS Personal and Social Performance Scale (PSP) Premorbid Adjustment Scale Japanese Adult Reading Test Insight and Treatment Attitudes Questionnaire Drug Attitude Inventory (DAI) Hopelessness Scale (HS) Internalized Stigma of Mental Illness Scale WHOQOL-BREF Rosenberg Self-esteem Scale (RSES) Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale (FACIT-Sp)	In BD group, self-esteem (RSES), spirituality (FACIT-Sp), QoL (WHOQOL-BREF), social functioning (PSP), age, and drug attitude (DAI) showed significant positive correlations with resilience (RS-25) In BD group, hopelessness (HS) and depression (MADRS) showed significant negative correlations with resilience (RS-25)	↑ Resilience a/w ↑ Self-esteem (RESES) ↑ Spirituality (FACIT-Sp) ↑ Social functioning (PSP) ↑ Drug attitude (DAI) ↓ Hopelessness (HS) ↓ Depressive symptoms (MADRS)

(continued)

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Table 1 (continued).

Studies	Study population (diagnosis, age, sex, duration of illness [DI])	Resilience scale used	Other scales used	Main findings	Summary
Choi et al ⁴¹ (2015) Korea	<u>Diagnosis</u> BD1: 29.0% (36/124) BD2: 16.1% (20/124) BD-NOS: 4.84% (6/124) HC: 50.0% (62/124) <u>Age (mean ± SD)</u> BD: 37.0 ± 10.9 y HC: 37.1 ± 11.0 y <u>Sex</u> BD: • F: 56.4% (35/62) • M: 43.5% (27/62) HC: • F: 56.4% (35/62) • M: 43.5% (27/62) <u>DI (mean ± SD)</u> BD: 12.3 ± 9.1 y	CD-RISC	Barrett Impulsivity Scale (BIS) • 3 subscales: attention, motor, non-planning Clinical Global Impression (CGI)	BD had significantly lower resilience (CD-RISC) and higher impulsivity (BIS) vs HC Degree of impulsivity (BIS), number of depressive episodes, (CES-D) and non-remission status (CGI) were negatively correlated with resilience (CD-RISC) for the BD group Length of education was positively correlated with resilience (CD-RISC) for the BD group No significant associations between resilience (CD-RISC) and age, age at onset, or duration of illness for the BD group	↑ Resilience a/w ↑ Length of education ↓ Degree of overall impulsivity (BIS) ↓ Severity of illness Remission status (CGI) ↓ Number of depressive episodes for BD group
Kesebir et al ⁴² (2015) Turkey	<u>Diagnosis</u> BD1: 100.0% (100/100) <u>Age (mean ± SD)</u> BD1: 32.7 ± 13.2 y <u>Sex</u> F: 54.0% (54/100) M: 46.0% (46/100) <u>DI</u> • Not provided	RSA—Turkish version	Turkish version of the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Autoquestionnaire (TEMPS-A) • 5 temperaments: depressive, hyperthymic, irritable, cyclothymic, anxious temperament Childhood Trauma Questionnaire (CTQ)	Lower resilience (RSA) associated with childhood trauma (CTQ) Higher sexual abuse, emotional abuse, neglect (CTQ), and anxious temperament (TEMPS-A) predicted lower resilience (RSA)	↑ Resilience a/w ↓ Childhood trauma (CTQ) in BD ↓ Anxious temperament (TEMPS-A) in BD with childhood trauma

Abbreviations: a/w = associated with, ASD = autism spectrum disorder, BD1 = bipolar type 1, BD2 = bipolar type 2, BD-NOS = bipolar not otherwise specified, Brief-QoL-BD = Brief Quality of Life in Bipolar Disorder, BRS = Brief Resilience Scale, CD-RISC = Connor-Davidson Psychological Resilience Scale, DI = duration of illness, F = female, HC = healthy controls, HDRS = Hamilton Depression Rating Scale, M = male, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = major depressive disorder, PANSS = Positive and Negative Syndrome Scale, RBD = Resilience Questionnaire for Bipolar Disorder, READ = Resilience Scale for Adolescents, RS = Resilience Scale, RS-25 = 25-Item Resilience Scale, RSA = Resilience Scale for Adults, SCZ = schizophrenia spectrum disorder, SD = standard deviation, QoL = quality of life, WHOQOL-BREF = World Health Organization QOL-Brief Form, YMRS = Young Mania Rating Scale.

Table 2. Assessment of Quality of Included Cross-Sectional Studies Using the Modified Newcastle-Ottawa Scale^a

Author (year)	Selection (out of 5) ^b			Comparability (out of 2)			Total score (out of 9)
	Representativeness of sample	Sample size	Ascertainment of exposure	Nonrespondents	Outcome (out of 2)	Assessment of outcome	
Palagini et al ¹⁸ (2022)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(Comparability between responders and nonresponders not established)	** (Controlled for current pharmacologic treatments, suicidal attempts, and illness duration)	* (Self-report)	8
Palagini et al ¹⁹ (2022)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(Comparability between responders and nonresponders not established)	** (Controlled for current pharmacologic treatments and illness duration)	* (Self-report)	8
Echezarraga et al ²⁰ (2022)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age, gender, marital status, education level, and employment status)	* (Self-report)	8
Dou et al ²¹ (2022)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age and gender)	* (Self-report)	7
Fernández-Rocha et al ²² (2021)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	6
Aslan and Baldwin ²³ (2021)	(No description of sampling strategy)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for duration of illness and illness age of onset)	* (Self-report)	6
Citak and Erten ²⁴ (2021)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	6
Nunes and da Rocha ²⁵ (2021)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the characteristics of the nonresponders)	** (Controlled for several clinical variables)	* (Self-report)	7
Post et al ⁶ (2021)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	5
Verdolini et al ²⁶ (2021)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for variables related to COVID-19 and subgroup)	* (Self-report)	8

(continued)

Table 2 (continued).

Author (year)	Representativeness of sample	Selection (out of 5) ^b		Ascertainment of exposure	Nonrespondents	Comparability (out of 2)			Total score (out of 9)
		Sample size	Average in the target population/ non-random sampling			The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled	Assessment of outcome	Statistical test	
Masi et al ²⁷ (2020)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for mean age and frequency of BP types)	* (Self-report)	* (Clearly described and appropriate)	7
Pardeller et al ²⁸ (2020)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age, sex, education)	* (Self-report)	* (Clearly described and appropriate)	7
Şenormancı et al ²⁹ (2020)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	* (Clearly described and appropriate)	5
Vieira et al ³⁰ (2020)	* (Truly representative of the average in the target population/ random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the characteristics of the nonresponders)	** (Controlled for sex, skin color, socioeconomic status, suicide risk)	* (Self-report)	* (Clearly described and appropriate)	8
Uygun et al ³¹ (2020)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age, gender, age at onset)	* (Self-report)	* (Clearly described and appropriate)	7
Sánchez et al ³² (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	* (Clearly described and appropriate)	5
Sivri et al ³³ (2019)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the characteristics of the nonresponders)	* (Controlled for effect of psychopathology)	* (Self-report)	* (Clearly described and appropriate)	6
Bozikas et al ³⁴ (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	** (Validated measurement tool)	(Comparability between responders and nonresponders not established)	** (Controlled for years of education and duration of illness)	* (Self-report)	* (Clearly described and appropriate)	8
Chung et al ³⁵ (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for several clinical and demographic variables)	* (Self-report)	* (Clearly described and appropriate)	7
Deng et al ³⁶ (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for years of education, gender, marital status, employment)	* (Self-report)	* (Clearly described and appropriate)	7
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Table 2 (continued).

Author (year)	Representativeness of sample	Sample size	Ascertainment of exposure	Nonrespondents	Comparability (out of 2)			Total score (out of 9)
					The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled	Assessment of outcome	Statistical test	
Mizuno et al ³⁷ (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	* (Controlled for age)	* (Self-report)	* (Clearly described and appropriate)	7
Post et al ³⁸ (2018)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age, sex, education)	* (Self-report)	* (Clearly described and appropriate)	8
Lee et al ³⁹ (2017)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for several clinical and demographic variables)	* (Self-report)	* (Clearly described and appropriate)	7
Hofer et al ⁴⁰ (2017)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	* (Controlled for education)	* (Self-report)	* (Clearly described and appropriate)	6
Mizuno et al ¹² (2016)	* (Somewhat representative of the average in the target population/ non-random sampling)	* (Justified and satisfactory)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for age, marital situation, working situation)	* (Self-report)	* (Clearly described and appropriate)	8
Choi et al ⁴¹ (2015)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	** (Controlled for occupation, length of education)	* (Self-report)	* (Clearly described and appropriate)	7
Kesebir et al ⁴² (2015)	* (Somewhat representative of the average in the target population/ non-random sampling)	(Not justified)	** (Validated measurement tool)	(No description of the response rate or the characteristics of the nonresponders)	(Not controlled for)	* (Self-report)	* (Clearly described and appropriate)	5

^aAsterisks indicate the number of stars earned in each area on the Newcastle-Ottawa Scale.

study of BD patients experiencing a depressive episode, resilience partially mediated the effects of depression on quality of life.²⁸ Citak and Erten²⁴ investigated the mediating role of attachment patterns on resilience and found the effect of childhood trauma on resilience to be partially mediated by attachment-related anxiety and avoidance. Additionally, affective temperaments (anxious, irritable, dysthymic, and cyclothymic) were found to partially mediate the effect of depressive symptoms on resilience.²⁶ Sánchez et al³² found that resilience did not mediate the effect of functional disability in BD on quality of life.

DISCUSSION

There were several main findings. The majority of studies (92.0%) were cross-sectional in design and were mainly conducted in Europe (64.0%). Second, higher resilience level in BD was associated with specific psychopathology (such as lower severity of depressive symptoms and psychotic symptoms; less rumination and hopelessness; better self-esteem; less impulsivity, aggression, and suicidal ideation; and fewer depressive episodes and suicidal attempts), clinical features (self-directed temperament, less childhood trauma, and positive attitudes toward pharmacologic treatment), social factors (better social support and family organization), and psychosocial functioning (better quality of life, social functioning, personal recovery, and spiritual well-being). Third, resilience mediated and mitigated the relationship between specific clinical features (such as depression and childhood trauma) and negative outcomes (such as increased severity of depression and poorer quality of life).

We noted mixed findings for several factors with regard to the directionality and significance of relationship with resilience, such as age, years of education, IQ, and self-stigma. This may be explained by the “differential susceptibility” or “developmental plasticity” hypothesis, which states that specific biological or environmental conditions do not necessarily fall neatly into either the “risk” or “resilience” category but may give rise to both greater risk and greater resilience depending on different gene-environment interactions.⁴⁵ Genes that increase one’s vulnerability to adversity (eg, greater stress reactivity) may also simultaneously increase their susceptibility to be positively influenced by environmental support and enrichment.^{46,47}

In view of the multifaceted findings from the review, a framework of resilience models by Fergus et al⁴⁸ that includes the Challenge, Compensatory, and Protective models is used to integrate these findings.

Challenge Model

First, the Challenge model proposes that extreme stressors can affect an individual’s adaptation to adverse conditions. In the context of our findings, some of these stressors can include the nature and severity of psychopathology (such as depressive, ruminative, psychotic, impulsive, and aggressive features; suicidal ideation; frequency of depressive episodes or suicidal attempts) and history of childhood trauma.

Earlier reports have found depressive ruminations to be negatively correlated with emotional regulation and cognitive reappraisal.^{23,49,50} Major depression²⁵ and comorbid depressive symptoms in other conditions such as psychotic spectrum disorders^{51–53} and addictive disorders⁵⁴ have also been associated with lower resilience. Psychotic symptomatology was associated with lower level of resilience in psychotic disorders,¹³ which is in keeping with our findings in this review. Reducing severity of depressive symptoms, ruminations, and psychotic symptoms can thus potentially alleviate stress, improve cognitive appraisal, and allow better adaptation to the illness.⁵⁵ A theory-driven network analysis has also supported the idea that depressive symptoms, poor resilience, and internal feelings of entrapment were among the many significant contributors to suicidal ideation in young adults,⁵⁶ which highlights the potential interactional role between symptomatology and resilience in BD.

We found that lower level of resilience was associated with childhood trauma, emotional/sexual abuse, and emotional neglect. These findings are consistent with previous findings in which the presence of childhood trauma in BD patients adversely affected resilience and triggered increased depressive symptoms.⁵⁷ In the presence of childhood trauma and emotional abuse, the formation of an insecure attachment pattern may affect early life experiences that are crucial for development of resilience in adulthood^{58,59} and influence coping when faced with future adversities.⁶⁰

Compensatory Model

Second, the Compensatory model proposes that certain internal, promotive factors can help individuals compensate and overcome adversity and prevent a negative outcome.⁴⁸ Some relevant internal, promotive factors include lower level of hopelessness,⁶¹ better sense of self-esteem, personal attitudes toward pharmacologic treatment, and temperament or personality features. Low self-esteem was associated with greater depression severity in bipolar depression⁶² and also with lower resilience in another cohort of adult subjects with spina bifida,⁶³ thus highlighting that intrapersonal factors are crucial in influencing the level of adaptation to challenging conditions including diagnosis of BD. Patients found it cathartic to be able to give a name to their condition, which helped them to see it for what it was and accept it.⁶⁴ Educating themselves on their illness and increasing their awareness of symptoms allowed them to feel empowered to make decisions including their treatment even within their limitations, which can help in relapse prevention.⁶⁴ Patients also described how having a naïve hopefulness for the future was crucial for promoting resilience.⁶⁴

With regard to personality, we found that irritable, anxious, and cyclothymic temperaments were associated with lower levels of resilience,^{26,29} whereas a self-directed temperament was associated with higher resilience.³³ Previous studies have found that cyclothymic and anxious temperaments were associated with increased stress reactivity in daily life.⁶⁵ Cyclothymic temperaments were also associated with increased psychological distress,⁶⁶ thus

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underscoring the need to identify BD patients with such personality profiles.

Protective Factor Model

Third, the Protective model refers to protective factors that moderate the exposure to stressors by neutralizing (protective-stabilizing model) or diminishing (protective-reactive model) the effect of an adversity.⁴⁸ In our review, possible protective factors included better social and family organization. Regarding social support, previous studies among non-psychiatric populations^{67,68} found that with better perceived social support, individuals may feel less overwhelmed by the emotional burden of a stressor, which provided a sense of optimism in the face of adversity. With respect to family organization, there are data to suggest that better family organization was associated with a more positive family environment,⁶⁹ while negative family dynamics (poor cohesion, organization) were related with worse functional outcomes in the context of psychiatric disorders.²⁶ In addition, a controlling parental environment was found to be associated with increased risk of overall psychiatric symptoms in children,⁷⁰ which can increase stress levels and affect resilience, as seen from the Challenge model of resilience. Of note, with better family dynamics and organization, there can be timely provision of social and financial resources, which serve as a protective factor in the face of stress and adversity.⁶⁹

Our finding of the association between better spiritual well-being and higher resilience levels was consistent with the findings of a previous study conducted within a non-psychiatric population.⁷¹ In the context of spirituality and religiosity, it was thought that the presence of support from a like-minded community can foster a sense of belonging, hope, and meaning and enhance religious coping, which in turn facilitates adaptation to a stressful condition.⁷²

Resilience Scales

The inclusion of different scales by various authors has been utilized to identify a mix of internal and external factors that could improve the individual's ability to cope with stress and which are relevant to the construct of resilience in BD.

First, scales that have identified mainly internal protective factors include the Connor-Davidson Resilience Scale (CD-RISC), Resilience Scale (RS), and Brief Resilience Scale (BRS). CD-RISC serves to measure 5 components of resilience, which include Personal competence, Trust/Tolerance/Strengthening effects of stress, Acceptance of change and secure relationships, Control, and Spiritual influences.⁷³ RS serves to measure the individual's personal competence and acceptance of self and life, which are positive personality characteristics that strengthen adaptation to stress. The 5 themes evaluated include equanimity, perseverance, self-reliance, meaningfulness, and existential aloneness.⁷⁴ BRS is a 6-item questionnaire that measures the perceived ability to bounce back from stress.⁷⁵ Factors identified with these scales include self-confidence and competence, spirituality, and positive personality features,

which are internal attributes that help improve individual resilience.

Second, scales that have identified both internal and external protective factors include Resilience Scale for Adults (RSA), Resilience Scale for Adolescents (READ), and Resilience to Bipolar Disorder (RBD). RSA examines the interpersonal and intrapersonal protective factors that help facilitate adaptation to psychosocial adversities. Factors evaluated include personal strength, social competence, structured style, family cohesion, and social resources.⁷⁶ While CD-RISC, RSA, and BRS have been developed for use in the adult population,⁷⁴ READ serves to evaluate factors improving resilience in the target population aged 13–15. Components evaluated include external support systems, family support and cohesion, and personal attitudes and behavior.⁷⁷ RBD is used to identify factors that aid adaptation to stress specifically in BD patients. Attributes developed during the course of BD were evaluated; they include Self-management, Turning point, Self-care, Self-confidence, and Interpersonal support.⁷⁸ External factors identified with this scale include family organization and social support, while internal factors identified include self-care and confidence, which are beneficial in strengthening resilience.

Of note, despite the different resilience scales employed by the studies included in this review, these scales captured internal and external factors that can contribute to or impede the adaptation to stressors. This is regardless of whether the scale was originally developed for use in the general or clinical population. Although there are some factors in the RBD unique to the clinical population (eg, Self-management, Turning point), other factors overlap with those captured in scales for the general population as well (eg, Self-care, Self-confidence, and Interpersonal support). Hence, this suggests that inquiring about these factors in the clinical setting is likely to be beneficial not only for patients currently experiencing stressors and in clinical relapse, but also for holistic case formulation for patients in remission.

Clinical Implications

These findings have several key clinical implications. First, there is a need for greater awareness and identification of BD patients with clinical profiles that may be associated with lower resilience. Such clinical factors include greater severity of illness, poor attitude toward treatment, underlying temperaments (anxious/cyclothymic/irritable), a history of childhood trauma, and having poor social support, among others. Specific clinical measures including better stabilization of symptomatology and psychoeducation about pharmacotherapy and non-pharmacologic treatment options. Additional support from social agencies can be provided to assist these individuals with BD, while those with higher resilience should be empowered and equipped with resources to better manage their own condition. Second, in line with the Challenge model, there is a need to identify and manage potential stressors such as the treatment and better stabilization of depressive, psychotic, aggressive, impulsive,

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and suicidal symptoms. Clinicians should regularly review suicide risk and appropriately address childhood trauma where needed through a multidisciplinary approach, which includes psychotherapeutic approaches and ensuring the presence of long-term support. Third, in line with the Compensatory model, mental health professionals may use the therapeutic relationship to improve patients' self-esteem and empower them to be involved in management decisions about their own condition. This could also include helping them understand their own temperament or personality and the way it affects interpersonal relationships and interactions with others. Fourth, in line with the Protective model, mental health professionals may seek to strengthen the social support of the BD patient via family and community resources. Family members can be offered family psychoeducation to help them better appreciate and understand the challenges faced by BD patients and consider ways to support them.⁷⁹

Limitations and Future Directions

First, the majority were cross-sectional studies with modest sample size, which limited our ability to determine a causal relationship between resilience and its clinical correlates. More longitudinal studies are warranted to examine how the relationships between resilience and other

clinical correlates change over time with treatment within a larger cohort of patients. Second, most studies on resilience in BD were conducted on middle-aged adult patients, and future studies may consider extension to younger and older BD subjects. Third, patients in these included studies mostly had a longer duration of illness; hence, more studies on early onset BD cases would proffer insights into trajectory of resilience over illness course. Fourth, few studies examined factors such as patients' intercurrent life events, interaction with the health care system, and relevant occupational factors. Fifth, data are sparse on biological factors underlying resilience and treatments focusing on resilience, and thus future studies could examine biological factors affecting resilience as well as effectiveness of resilience-targeted interventions.

In conclusion, our review found that resilience in BD was associated with specific symptomatology, illness features, social factors, and psychosocial functioning. Resilience also mediated pathways between childhood trauma, depression and negative outcomes. In the context of Challenge, Compensatory, and Protective resilience models, BD patients can be helped to better manage their stressors and strengthen internal compensatory factors and external protective factors within their illness course.

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