Boulevard of Broken Rhythms: A systematic review and meta-analysis on the relationship between sleep disturbances and suicidal behavior in bipolar disorder

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Abstract

Background: Among the clinical features of bipolar disorder (BD), sleep disturbances are highly prevalent and persist across all phases of the illness, from onset to acute and inter-episodic periods. Substantial evidence suggests that sleep disturbances may function as proximal triggers for suicidal behavior, independent of other underlying psychiatric conditions. Although suicide is a major clinical concern in BD, the interplay between sleep disturbances and suicidality remains incompletely understood.

Methods: We conducted a systematic review and meta-analysis (SRMA) following the PRISMA guidelines. We performed a comprehensive search across PubMed, PsycINFO, and SCOPUS, including all studies reporting an association between sleep disturbances and suicidal behavior in BD. A total of sixteen reports, comprising fourteen cross-sectional studies and two longitudinal studies, were included in this SRMA.

Results: Among individuals with BD, sleep disturbances were associated with increased odds of lifetime suicidal behaviors (OR= 1.51, 95%CI= 1.23, 1.86) and a history of suicide attempts was associated with significantly elevated odds of experiencing sleep disturbances (OR= 1.37, 95% CI= 1.21, 1.55). In addition, poor sleep quality as measured by the Pittsburgh Sleep Quality Index positively correlated with suicidality (r= 0.24, 95%CI= 0.10, 0.36).

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Conclusions: These results highlight the link between sleep disturbances and suicidal tendencies in individuals with BD. Prompt recognition and treatment of sleep disturbances could be crucial for averting or reducing suicidal behaviors in this population.

Keywords: bipolar disorder, sleep disturbances, suicidal ideation, suicidal attempts, insomnia

1. Introduction

Bipolar disorder (BD) is a chronic and severe illness stemming from the complex interaction between genetic, neurobiological, and environmental factors [1-3]. Among the neurobiological systems altered in BD, sleep/wake and circadian rhythms are affected, showing a strong overlap with disturbances in energy levels that are central to the disorder [4]. Sleep disturbances are part of the diagnostic criteria for BD [5] and structurally contribute to its clinical course and outcome, as they often persist in inter-episodic phases, thus contributing to relapses [6]. They also typically precede the onset of BD [7]. Regrettably, insomnia is often neglected as a symptom target in the management of affective disorders [8].

People with BD present a substantially increased risk of death by suicide, reportedly 10-to 30-fold higher than in the general population [9]. The rate of attempted suicide is also very high, with a lifetime risk of approximately 30-50% for people with BD [10]. In addition, suicide attempts (SA) are often more lethal in patients with BD than in those with other psychiatric disorders [11]. Suicidal thoughts and behaviors are strongly associated with depressive or mixed mood episodes, and with depressive illness onset [9, 12, 13]. Other established correlates of suicidality include male gender, younger age, age at illness onset, family history of suicide, previous SA, comorbid personality disorders, anxiety disorders, alcohol and substance use, and worse quality of life [9, 14-16].

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Notably, sleep disturbances, which are strongly linked to suicidal ideation and behavior in the general population [17], also play the aforementioned, significant role in BD exacerbating mood instability, leading to increasing suicide risk.

Until now, the existing literature on this topic appears unclear due to the often heterogeneous definitions of both sleep disturbances and suicidal outcomes, which may encompass a wide and heterogeneous range of phenomena. Also, a lack of control for relevant confounders complicates the overall understanding of the possible relationship between SA, sleep disturbances and BD.

This systematic review and meta-analysis addresses this gap by evaluating and quantifying the association between sleep disturbances and suicidality in individuals with BD.

2. Methods

The current SRMA followed the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) 2020 guidelines [18] and a registered protocol (PROSPERO-ID: CRD42023421381). The PRISMA checklist, the original protocol, and detailed deviations from the original protocol are reported in the Supplementary materials—Appendix 1 and 2.

2.1 Search strategy

The PsycINFO, PubMed, and Scopus databases were systematically searched from inception until May 13th, 2024 (search strings are available in Supplementary Materials, Appendix 3). The references of the included articles, books, and other pertinent materials were manually searched and inspected to identify additional original studies that were not captured by the search strings.

2.2 Eligibility criteria

The inclusion criteria were original articles that: (a) were published in peer-reviewed journals; (b) included individuals diagnosed with BD according to any edition of the Diagnostic and

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Statistical Manual of Mental Disorders (DSM) [19] or the International Statistical Classification of Diseases and Related Health Problems (ICD) [20]; (c) evaluated sleep disturbances in people with suicidality or suicidality in people with sleep disturbances; and (d) reported quantitative data about these association. Studies were eligible for inclusion if they examined sleep disturbances (e.g., insomnia, nightmares, extended sleep onset latency, wakefulness after sleep onset, reduced total sleep time, decreased sleep efficiency, or poor sleep quality) and suicidality (e.g., ideation, planning, attempts, or completed suicide), regardless of the specific definitions used. Only studies including BD patients as both cases and controls (e.g., BD patients with vs. without sleep disturbances or suicidality) were eligible. Both observational (cross-sectional and longitudinal) and interventional studies were eligible for inclusion, but only baseline data were considered in longitudinal and interventional studies in order to minimize the potential confounding effects of treatment, follow-up duration and time-varying exposures. No language or age restrictions were applied. Studies were excluded if they were: (a) reviews, clinical cases, abstracts, letters to the editor, conference proceedings, or study protocols; and (b) only included non-human samples.

2.3 Study selection and data extraction

After excluding irrelevant articles by title and abstract based on previously defined inclusion and exclusion criteria, potentially eligible articles were examined by reading their full texts. Data extraction included, when available: first author, year of publication, geographical region and country, study design, diagnostic criteria employed and (semi)structured interview used, study setting, age group of participants (categorized as children/adolescents, adults, elderly, or mixed), definition of cases (people with sleep disturbances or people with suicidality) and definition of controls (people without sleep disturbances or people with suicidality), mean age of cases and

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controls, number and percentage of females in both groups, the number and percentage of individuals diagnosed with BD-I among cases and controls, and the percentage of euthymic, depressed, or (hypo)manic, or mixed patients for cases and controls, pharmacological treatment for both cases and controls, the mean duration of illness and SD for cases and controls, and the percentage of BD familiarity among cases and controls, as well as the percentage of suicide familiarity among cases and controls, broad outcome (suicidality in people with sleep disturbances and sleep disturbances in people with suicidality), specific definition of the outcome (as detailed above), information regarding the time frame of suicidality when available, distinguishing between lifetime suicidality and current suicidality, details regarding the assessment method for suicidality (clinical diagnosis, standardized scale, clinical records), details regarding the assessment method for sleep disturbance (self-report, validated scale, or objective measures such as polysomnography (PSG) or actigraphy), number of individuals with and without sleep disturbances or number of individuals with or without suicidality, mean scores and standard deviation (SD) obtained on severity scale for the outcome of interest for cases and controls, statistics that quantify association between outcomes and predictors (correlation coefficients, odds ratios (ORs), or standardized mean differences (SMDs)). When information was not available, we contacted the authors to request relevant data.

Two investigators (CP and MB) conducted all steps described independently. Discrepancies were resolved by consensus with the third author (VO or MDP).

2.4 Quality control

Two investigators (CP and MB) independently assessed the Risk of Bias using the "Newcastle-Ottawa Scale" (NOS) [21]. Discrepancies were resolved by consensus with the third author (VO

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or MDP). The obtained scores were converted according to the standards set by the "Agency for Healthcare Research and Quality" (AHRQ) as previously described [22].

2.5 Statistical analysis

Statistical analyses were conducted using R version 4.3.1 [23], and separate random-effect meta-analyses (restricted maximum-likelihood estimator) [24] were performed using the metaphor R-package [25]. SMDs, ORs, and Pearson's r coefficients with 95% confidence intervals (CI) were used to calculate effect sizes for continuous and dichotomous outcomes and correlations, respectively.

The results were visualized using jungle plots, which display SMDs, ORs, correlation coefficients and 95% CI each outcome [26].

Heterogeneity was evaluated using Cochran's Q test and I^2 statistic. If heterogeneity was detected (Cochran's Q p-value$<$ 0.10 or $I^2 >$ 50%), meta-regressions were conducted according to predefined predictors (i.e., mean age, percentage of females, percentage of BD-I, percentage of euthymic patients, percentage of patients with depressive episode and percentage of patients with (hypo-)manic episode).

Leave-one-out sensitivity analysis, excluding one study at a time from the main analysis, was used to investigate the influence of each study on the overall effect size estimation. Publication bias was examined using funnel plots and Egger's test [27] when at least ten studies were available.

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3. Results

3.1 Study characteristics

The overall study selection process is shown in the PRISMA flowchart in Figure 1. The literature search identified 828 records, which became 714 after supervised removal of duplicates. Of these, 652 were excluded from the title and abstract screening, and 46 were excluded after reading the full text. Sixteen studies [28-43] fulfilled our inclusion criteria, and were included in the quantitative synthesis. A comprehensive list of the excluded studies, with the respective reasons for their exclusion, is provided in the Supplementary Materials – Appendix 4.

The included studies were published between 2012 and 2022, with six studies from Europe, five from North America, two from Asia, two from Africa, and one multicenter study (i.e., from multiple sites in Europe, Africa, and the Middle East). Fourteen studies used a cross-sectional design and two studies were longitudinal [31, 43]. The sample sizes across the studies varied from 8 to 16,411, encompassing a total of 19,084 individuals with BD. A comprehensive overview of the included studies is provided in Table 1.

For a thorough understanding of the scales used to assess suicidality and sleep disturbances included in the quantitative analysis, and additional information such as illness duration, family history of suicide and psychiatric disorders, and current treatment, please refer to Supplementary Materials-Appendix 5 and 6.

3.1.1 Suicidality in patients with BD and sleep disturbances

A total of eleven studies [28, 32, 33, 36-43] on patients with sleep disturbances were included, comprising a total of 18,420 participants (3,692 cases and 14,728 controls). The overall mean age was 36.25 years (SD= 18.88), and 56.73% of the participants were female.

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Three studies evaluated sleep quality using validated scales [28, 33, 36]. Three studies assessed general sleep disturbances, with one using a validated scale [43] and two relying on clinical assessment [32, 42]. Regarding insomnia, two studies used validated scales [39, 40], while one study assessed insomnia and hypersomnia clinically [38]. Two studies focused exclusively on nightmares, one with a clinical assessment and the other one with a validated scale [37, 41]. Six studies clinically evaluated suicidal ideation or attempts [28, 33, 36, 38, 42, 43], considering both lifetime and current instances. Four studies assessed current suicidality using validated scales [37, 39-41]. One study used medical records to assess completed suicides [32].

According to the NOS scale, four studies were rated as "Good," five as "Fair," and two as "Poor." For more information, please refer to Supplementary Material – Appendix 7.

3.1.2 Sleep disturbances in patients with BD and suicidality

Three studies [29, 32, 34] focusing on BD patients with suicidality (either current or lifetime) were included. The total number of participants was 16,666 (13,412 cases and 3,254 controls). The overall mean age was 48 years (SD= 11.2), with 57% female participants.

Two out of the three studies clinically assessed lifetime suicidality [29, 34]. One study evaluated current suicidal ideation using a validated scale [34]. Another study consulted medical records for suicide attempts [32]. Two studies assessed sleep as using validated scales [29, 34], one of them used actigraphy data [29] and the third one used clinical assessment without scales [32].

Two studies were rated as "Good" quality and one as "Fair". For more information, please refer to Supplementary Material – Appendix 7.

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3.1.3 Correlations between sleep disturbances and suicidality

Three studies reported correlation data between sleep disturbances and suicidality [30, 31, 35], with a total sample size of 322 participants. The mean age was 35.98 years (SD= 12.83), and 42.37% were female. Two studies provided objective sleep data using actigraphy and polysomnography [30, 31], while suicidality was assessed using validated clinical scales. The quality of the three studies were rated as "Poor".

3.2 Meta-analyses results

The main meta-analytic results are presented in Table 2. Jungle plots of the main results are presented in Figure 2. Forest plots and further details of the leave-one-out sensitivity analyses and meta-regressions are reported in Supplementary Materials-Appendix 8.

3.2.1 Suicidality in patients with BD and sleep disturbances

3.2.1.1 Lifetime suicidality

Sleep disturbances were associated with significantly higher lifetime suicidality (OR= 1.51, 95%CI= 1.23, 1.86, p-value <0.001, I^2= 20.1%). The leave-one-out sensitivity analysis did not show a significant influence of single studies on the overall results.

3.2.1.2 Current suicidality

No significant results were observed (OR= 2.52, 95%CI= 0.93, 6.81, p-value= 0.07, I^2= 36.1%). The meta-analysis became significant when two studies were excluded in the leave-one-out sensitivity analysis.

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3.2.1.3 Suicidality scores on assessment scales

Patients with sleep disturbances presented significantly higher scores at suicidality assessment scales (SMD= 0.79, 95%CI= 0.53, 1.05, p-value <0.01, I^2 = 0%).

3.2.2 Sleep disturbances in patients with BD and suicidality

3.2.2.1 Current sleep disturbances

SA were significantly associated with the presence of sleep disturbances (OR= 1.37, 95%CI= 1.2, 1.55, p-value <0.01, I^2= 0%).

3.2.2.2 Daytime sleepiness

No significant association was observed between suicide attempts and daytime sleepiness measured by the Epworth scale (ESS) (SMD= -0.12, 95%CI= -0.44, 0.21, p-value = 0.49, I^2= 39.8%).

3.2.2.3 Sleep quality

Poorer sleep quality, measured by Pittsburgh Sleep Quality Index (PSQI), was significantly associated with SAs (SMD= 0.42, 95%CI= 0.12, 0.73, p-value<0.01, I^2= 30.9%).

3.2.3 Correlations between sleep disturbances and suicidality

3.2.3.1 Association between sleep quality and suicidal ideation

A significant positive correlation was found (r= 0.24, 95%CI= 0.10, 0.36, p-value<0.01, I^2 = 66.67%). Leave-one-out sensitivity analysis did not show a significant influence of single studies on the overall results. Meta-regression analyses indicated a significant dependence on age (β= 0.014, 95%CI= 0.001, 0.028, p-value= 0.05). No significant differences were observed in terms of gender, bipolar disorder diagnosis, or affective state.

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3.2.3.2 Association between total sleep time and suicidal ideation

No significant correlation between suicidal ideation and total hours of sleep in BD was identified (r= 0.06, 95% CI: -0.29, 0.41, p-value = 0.73, I^2 = 58.6%).

3.2.4 Publication bias

Since none of the meta-analyses included the minimum of 10 studies, publication bias could not be assessed [44].

4. Discussion

The present SRMA aimed to assess the association between sleep disturbances and suicidality in individuals diagnosed with BD. Overall, we found a significant association between sleep disturbances and suicidality in BD in both directions: individuals with BD who report sleep disturbances (i.e., insomnia, hypersomnia, nightmares) have increased odds of suicidal behavior (lifetime suicidal attempts or suicidal ideation), while those with a history of suicide attempts are more likely to experience sleep disturbances. Additionally, poor sleep quality, as measured with PSQI, positively correlated with suicidal ideation and SAs.

Our findings align with previous SRMAs conducted in populations with unipolar major depression [45], as well as in other psychiatric diagnoses such as schizophrenia, anxiety, panic disorder [46, 47] and in general population [48, 49], where sleep disturbances were consistently linked to suicidality.

In BD, both insomnia and hypersomnia are clinically relevant. While insomnia is often the focus of suicide risk, hypersomnia, a common feature of atypical depression, is frequently underestimated [50]. Atypical depressive features are more prevalent in BD and have been

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associated with increased suicide risk [51]. Additionally, hypersomnia in BD is also linked with increased illness severity, a higher frequency of mood episodes, prolonged depressive or (hypo)manic phases, and psychiatric comorbidities [38]. Furthermore, genetic studies suggest that both suicidality and hypersomnia may share underlying proinflammatory pathways [52]. Thus, despite hypersomnia might be perceived as a less worrisome symptom when assessing suicide risk, it still should be routinely evaluated [53].

Interestingly, individuals with atypical depression may also exhibit elevated levels of emotion dysregulation [54]. Emotion dysregulation is a transdiagnostic construct characterized by difficulty in understanding, accepting, and regulating emotions [55, 56]. It is highly prevalent in BD and correlates with both depressive and (hypo)manic symptoms [57]. Emotion dysregulation worsens when sleep disturbances are present, increasing impulsivity and elevating the risk of suicide [58]. More precisely, rumination is the emotion regulation strategy most strongly associated with symptoms of BD [59], mediating between sleep and suicidality [60]. In line with this, neuroimaging studies support that sleep deprivation disrupts emotion-regulating neural circuits, whilst heightened emotional arousal negatively affects sleep [61]. So, emotion dysregulation would act as a state-dependent- and sleep-dependent- factor increasing the vulnerability to suicidal behavior, particularly in BD, where impulsivity and risk-taking are core and prevalent features [39, 62]. In addition to these state-dependent factors, individuals with BD also present stable, trait-like factors (i.e. affective temperaments) contributing to the likelihood for suicide. Temperaments such as irritable, cyclothymic, depressive, and anxious have been associated with impulsivity and mood instability [63–65]. These characteristics may interact with environmental stressors such as sleep disturbances, exacerbating emotion dysregulation and promoting both self- and hetero-aggressive behaviors.

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Along with sleep disturbances, broader circadian rhythm disruption represents another key trait-related framework in BD.

Circadian rhythms are regulated by feedback loops involving the commonly defined “clock genes” [63], which orchestrate not only the sleep-wake cycle but also metabolic and neurophysiological processes [64, 65]. Polymorphic variations in clock genes are significantly associated with BD [66, 67], and linked to greater severity and recurrence of mood episodes [68-70]. Importantly, several clock genes relate to key biomarkers for the prediction of suicidality [71], such as *CLOCK* and *ARNTL* (also known as *BMAL1*). Animal studies reinforce this connection: in CLOCK mutant rodents, circadian disruption is associated with increased activity in the ventral tegmental area, leading to manic-like behaviors [72]. This circadian misalignment alters dopamine dysregulation, representing a possible neurobiological substrate for suicidality in BD [73].

Although our SRMA did not reveal significant differences between BD-I and BD-II in terms of sleep disturbances and suicidality, prior literature suggests that may differ in relevant clinical features, including patterns of sleep dysregulation and risk profiles for suicidal behavior. In BD-I, suicide risk has been more consistently associated with insomnia, particularly difficulties initiating sleep and associated daytime impairments such as anhedonia [74]. Some studies also report higher rates of hypersomnia in BD-I which may reflect a real clinical feature, measurement limitations in detecting hypersomnia or treatment-related aspects [75]. Conversely, in BD-II, suicide risk appears more strongly linked to evening chronotype, emotional dysregulation, childhood trauma, and low resilience [76]. This pattern aligns with the circadian vulnerability model, in which eveningness constitutes a transdiagnostic marker of emotional instability [77]. Finally, the presence of mixed features across BD subtypes is consistently

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associated with more severe clinical outcomes, including rapid cycling, substance use comorbidity, and elevated suicide risk [13].

Another aspect to take into account in the relationship between sleep and suicidality in BD is the potential moderating role of age. Our meta-regression analysis indicated that the association between poor sleep quality and suicidality becomes stronger with increasing age. This pattern aligns with prior longitudinal and clinical studies emphasizing the relevance of sleep disturbances in suicide risk among older adults [78], possibly due to the cumulative burden of chronic sleep disruption, comorbid medical conditions, or reduced resilience.

According to our results, sleep contribute to shaping the clinical cascade leading to suicidal behavior in BD, so that their early detection is crucial. Clinicians must not underestimate any complaints and should always thoroughly explore sleep patterns, ideally with validated scales. Prospective, real-time monitoring of sleep, circadian rhythms has the potential to enhance standard clinical care in the near future. The use of technology and wearable devices alongside ecological momentary assessment tools (e.g., mobile-based self-report systems) offers a promising approach to accurately catch sleep, energy and mood fluctuations [79].

Although treatment considerations fall outside the scope of this review, the clinical relevance of managing sleep disturbances in the context of suicidality in BD warrants some considerations. Lithium remains the most robust pharmacological agent with dual effects on sleep regulation and suicide prevention [53, 80]. A syndrome-based pharmacological approach, tackling both sleep and mood fluctuations, seems the most rationale approach to sleep alterations in BD, so that the same considerations in the general management of BD are due, such as caution in the use of antidepressant and the unwarranted use of benzodiazepines for chronic insomnia [2, 81, 82]. Non-pharmacological interventions such as sleep hygiene education, light therapy, and

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cognitive-behavioral therapy for insomnia (CBT-I) may complement standard treatment in BD [83, 84].

4.1 .Limitations

The present SRMA is the first to examine the relation between sleep disturbances and suicidality in individuals with BD. Our results must be considered in the light of some limitations.

The most important limitation is the overall scarcity of prospective studies on the topic, and only two longitudinal studies were included, so that whilst this SRMA univocally supports an association between sleep disturbances and suicidality in BD, the directionality of this relationship remains unclear. Undoubtedly, sleep disturbances act as proximal triggers anticipating suicidal behaviors, but they might also arise as downstream effects of depressive symptoms, or other clinical aspects.

These limitations reflect a technological barrier which digitals tools for ecological and continuous monitoring will hopefully help to bypass [85]. Furthermore, the evidence reviewed in this study could not differentiate between acute and euthymic phases of the disorder, or finer aspects in the clinical course, such as the predominant polarity of relapses. Also, most of the studies lack the control for comorbid somatic, psychiatric and substance use confounding conditions, which are all well- known factors associated with sleep disturbances and suicidality in general populations and in individuals with BD [86-88]. Comorbid sleep disorders are especially relevant unconsidered and underdiagnosed in psychiatric populations [89]. Additionally, the majority of the patients of the included studies were on medication, and its effects on sleep and suicidality may be a confounder [90]. Last, the lack of ethnic data restricts the generalizability of our findings, as the relationship between sleep disturbances and suicidal

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behavior in BD may vary across different ethnic and environmental contexts, as, suggestive evidence exists on the association of high temperature and suicidal behaviors [91].

Future research should aim to improve methodological rigor—particularly through the use of more prospective designs—and incorporate ecological, continuous assessments of sleep and activity patterns, which might allow to differentiate the broad definition of sleep disturbances into a meaningful and clinical-wise stratification [92-94]. This temporal distinction is clinically meaningful, as it informs whether sleep interventions may serve a preventive versus palliative function in suicide risk management. Integrating this bidirectional model into clinical frameworks could help both refine and redefine screening and treatment priorities.

4.2 Conclusions

This systematic review and meta-analysis found a significant association between sleep disturbances and suicidality in individuals with bipolar disorder, with the most consistent relationship observed between poor sleep quality and suicidal ideation. Future studies using standardized, multidimensional assessments of sleep and prospective designs are needed to clarify the temporal and physiopathological links between sleep alterations and suicidality in bipolar disorder, and digital innovation will likely allow to fill this gap both in research and clinical practice. Nonetheless, integrating structured sleep assessment into routine care may offer clinicians a practical and accessible opportunity to improve monitoring, guide timely interventions, and ultimately enhance the safety and well-being of individuals living with bipolar disorder.

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Conflict of interest

GF has received CME-related honoraria, or consulting fees from Angelini, Janssen-Cilag and Lundbeck.

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All the other authors have no conflict to declare.

Data Availability Statement

Requests to see any data that are not included in the article or the appendix should be directed to the corresponding author.

Declaration of Generative AI and AI- assisted technologies in the writing process

None.

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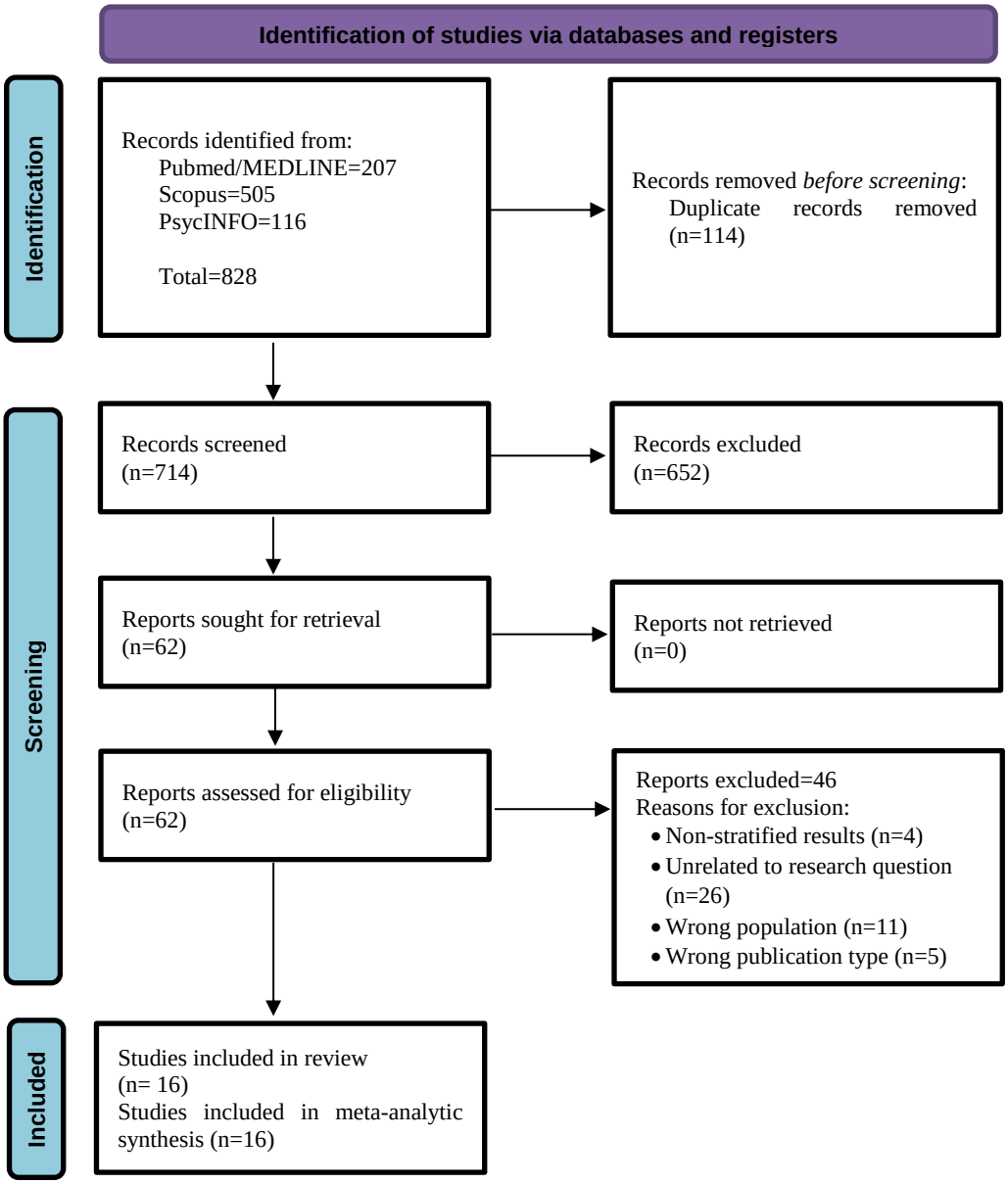
Figure n.1 - PRISMA flowchart, 2020 edition, adapted.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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Figure 2. Jungle plots summarizing the main effect sizes: A. Odds ratios (OR); **B.** Standardized mean differences (SMD); **C.** Correlation coefficients. Black-filled dots represent statistically significant comparisons, while white-filled dots indicate non-significant comparisons. Dot size corresponds to the sample size of each comparison.

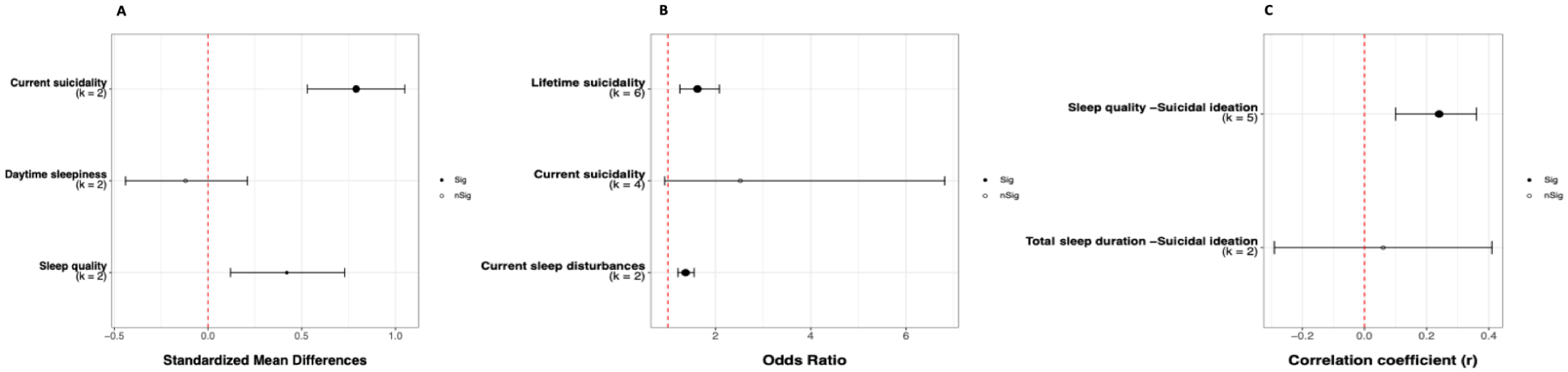

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Table 1 - Characteristics of the studies included in the systematic review and meta-analysis

Author, year, country	Study design	Setting	Diagnostic criteria	N (BD I %)		Mood state (%)		Mean age±SD % of females		Sleep assessment	Suicidality assessment	Outcome	Effect measures	Quality of the study (NOS)
				Cases *	Controls*	Cases *	Controls*	Cases *	Controls *					
(Aubert et al. 2016), France	Cross-sectional	Outpatients	DSM-IV (SCID)	199 (46.23 %)	294 (60.88%)	Euthymic (100%)	Euthymic (100%)	46 57.29%	43 54.76%	Actual sleep quality (PSQI)	Lifetime suicidality (clinical)	Suicidality	OR	6 (GOOD)
(Benard et al. 2019), France	Cross-sectional	Outpatients	DSM-IV (DIGS/SCID)	57 (72%)	90 (77%)	Euthymic (100%)	Euthymic (100%)	47.24±12.63 72%	44.77±12.95 54%	Sleep problems (PSQI, Berlin Questionnaire, ESS, Actigraphy fragmentation index)	Lifetime suicidal attempts (clinical)	Sleep problems	OR, SMD	6 (GOOD)
(Bernert et al. 2017), USA	Cross-sectional	NA	DSM-IV (SCID)	24 (NA)		Depressed (100%)		44.4±11.6 70.7%		Actual sleep duration (PSG-TST)	Actual suicidal ideation (HAM-D item 3)	-	Correlation	4 (POOR)

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(Bertrand et al. 2020), Canada	Longitudinal	Outpatients	DSM-V	76 (53%)		Euthymic (50%) Hypomanic (3.95%) Mixed (7.89%) Depressed (38%)		49 37.49%		Actual insomnia (AIS sleep, Actigraphy-TST)	Actual suicidal ideation (C-SSRS)	-	Correlation	6 (POOR)
(Bishop et al. 2020), USA	Cross-sectional	Outpatients	ICD-9	2212 (NA)	14199 (NA)	NA	NA	NA NA	NA NA	Actual sleep problems (clinical)	Actual suicidal attempts (register)	Suicidality	OR*	8 (GOOD)
				13308	3103	NA	NA	48.23 15.46%	50.01 16.37%			Sleep problems	OR	
(Esan and Fela-Thomas 2022), Nigeria	Cross-sectional	Outpatients	DSM-IV (SCID)	37 (100%)	39 (100%)	Euthymic (100%)	Euthymic (100%)	38.49±11.2 66.7%	39.67±11.1 58.6%	Actual sleep problems (PSQI)	Lifetime and actual suicidal attempts (clinical)	Suicidality	OR	6 (FAIR)
(Fekih-Romdhane et al. 2019), Tunisia	Cross-sectional	Outpatients	DSM-V	47 (100%)	61 (100%)	Euthymic (100%)	Euthymic (100%)	NA NA	NA NA	Actual daytime sleepiness (ESS), actual sleep quality (PSQI),	Lifetime suicidal attempts (clinical), actual suicidal ideation (HAM-D item)	Sleep problems	SMD	6 (FAIR)

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				108 (100%)		Euthymic (100%)		41.8±12.2 36.1%		Actual sleep quality (PSQI)	Actual suicidal ideation (HAM-D item)	-	Correlation	
(Hashmi et al. 2023), Pakistan	Cross-sectional	Outpatients	ICD-10	222 (92.8%)		NA		30.47±11.43 41%		Actual insomnia (clinical)	Actual suicidality (clinical)	-	Correlation	4 (POOR)
(Keskin, Tamam, and Ozpoyraz 2018), Turkey	Cross-sectional	Outpatients	DSM-IV-TR (SCID)	69 (78.3%)	53 (90.6%)	Euthymic (100%)	Euthymic (100%)	39.2±10.5 60.9%	38±11.3 67.9%	Sleep quality (PSQI)	Lifetime suicidal attempts (clinical)	Suicidality	OR	6 (FAIR)
(Marinova et al. 2014), Bulgaria	Cross-sectional	Inpatients	ICD-10	2	6	Depressed (100%)	Depressed (100%)	NA NA	NA NA	Nightmares (clinical)	Lifetime suicidal attempts (clinical), actual suicidality (HAM-D item)	Suicidality	OR	5 (POOR)
(Murru et	Cross-	Outpatient	DSM-V,	377	44 (NA)	Depress	Depresse	41.59±12.	46.98±12.	Insomnia /	Lifetime	Suicidali	SMD	8

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al. 2019), Spain, Bulgaria, Egypt, Morocco, Netherlands, Portugal, Russia, Turkey	sectional	s/ Inpatients	RDC	(NA)		ed (100%)	d (100%)	98 66.31%	62 65.9%	Hypersomnia (clinical)	suicidal attempts (clinical)	ty		(GOOD)
(Palagini et al. 2019), Italy	Cross-sectional	Inpatients	DSM-V (SCID)	54 (0%)	23 (0%)	Depressed Mixed (100%)	Depressed Mixed (100%)	47.6±12 62.3%	50.3±13 63.8%	Actual insomnia (ISI)	Actual suicidality (SSI)	Suicidality	SMD	6 (FAIR)
				77 (0%)		Depressed / Mixed (100%)		48.4±12.4 36.1%				-	Correlation	
(Palagini et al. 2022), Italy	Cross-sectional	Inpatients	DSM-V (SCID)	188 (48.9%)		Depressed (100%)		46.4±13 43%		Actual insomnia (ISI)	Actual suicidality (SSI)	Suicidality	SMD	7 (GOOD)
												-	Correlation	
(Stanley et al. 2017), USA	Cross-sectional	NA	DSM-IV	379 (100%)		Manic (100%)		10.2±2.7 53.8%		Actual nightmares (WASH-U-KSADS)	Actual suicidality (CDRS-R item 13)	Suicidality	OR	5 (POOR)

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(Stubbs et al. 2016), UK	Cross-sectional	Outpatients	DSM-IV	259 (NA)	NA	NA NA	Actual sleep problems (clinical)	Actual suicidal ideation (clinical)	Suicidality	OR*	5 (FAIR)
(Sylvia et al. 2012), USA	Longitudinal	Outpatients	DSM-IV (SCID)	73 (72.2%)	Euthymic (100%)	43.18±12.98 63.9%	Actual sleep problems (MADRS item 4)	Lifetime suicidal attempts (clinical)	Suicidality	OR*	6 (FAIR)

Notes: **AIS** - Abbreviated Injury Scale; **BD** - Bipolar Disorder; **CDRS-R** - Children's Depression Rating Scale-Revised; **C-SSRS** - Columbia Suicide Severity Rating Scale; **DIGS** - The Diagnostic Interview for Genetic Studies; **DSM** - Diagnostic and Statistical Manual of Mental Disorders; **ESS** - Epworth Sleepiness Scale; **HAM-D** - Hamilton Depression Rating Scale; **ICD** - International Statistical Classification of Diseases and Related Health Problems; **ISI** - Insomnia Severity Index; **MADRS** - Montgomery Asberg Depression Rating Scale ; **NOS** - Newcastle-Ottawa Scale; ; **PSG-TST** - Polisomnography-Total Sleep Time; **PSQI** - Pittsburgh Sleep Quality Index; **SCID** - Structured Clinical Interview for DSM Disorders; **SSI** - Scale for Suicide Ideation; **WASH-U-KSADS** - Washington University in St. Louis Kiddie Schedule for Affective Disorders and Schizophrenia. *Results only with the point estimate of the odds ratio.

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Table 2 – Results of the meta-analyses in detail

Outcome	Studies, n	Cases, n	Controls, n	OR	SMD	cor r	95% CIs	p-value	95% PIs	I^2(%)	tau^2	Q test p-value
Suicidality in patients with BD and sleep disturbances												
Lifetime suicidality	7	2969	14605	1.51			1.23, 1.86	**0**	0.09, 0.74	20.1	0.02	0.37
Current suicidality	4	677	45	2.52			0.93, 6.81	0.07	0.52, 12.13	36.08	0.39	0.19
Suicidality scores	2	172	93		0.79		0.53, 1.05	**3.53E-09**	0.53, 1.05	0	0	0.64
Sleep disturbances in patients with BD and suicidality												
Current sleep disturbances	2	13365	3193	1.37			1.21, 1.55	**3.75E-07**	1.21, 1.55	0	0	0.33
Daytime sleepiness	2	104	151		-0.12		-0.44, 0.21	0.49	-0.55, 0.32	39.8	0.02	0.20
Sleep quality	2	104	151		0.42		0.12, 0.73	**6.59E-03**	0.34, 0.81	30.93	0.02	0.23

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Correlations between sleep disturbances and suicidality												
Sleep quality – Suicidal ideation	5	671				0.24	0.10, 0.36	**6.27E-04**	-0.04, 0.53	66.67	0.02	0.01
Total sleep time – Suicidal ideation	2	100				0.06	-0.29, 0.41	0.73	-0.48, 0.61	58.6	0.04	0.12

Notes: CIs – Confidence Intervals; I^2 – Higgin and Thompson's I^2 estimating of the total heterogeneity; PIs – Prediction Intervals; Qp – p-value for the Cochran's Q-test of (residual) heterogeneity; OR-Odds Ratio; SMD – Standardized mean difference; tau^2 – between-study variance.

Significant results are depicted in bold.

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