The association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses: a systematic review and meta-analysis

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Abstract

Background: Identifying patients with increased risk of suicidal behaviors is a constant challenge and concern for clinicians caring for patients with psychiatric conditions. We conducted a systematic review to assess the association between suicidal behaviors and sleep disturbances in psychiatric patients.

Methods: A systematic literature search of Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid PsycInfo, Ovid Cochrane Database of Systematic Reviews, Ovid Cochrane Central Register of Controlled Trials, and Scopus was conducted using earliest inclusive dates to 28 June 2013. Eligible studies were comparative observational studies that reported sleep disturbances in psychiatric patients and the outcome of interest (any type of suicidal behaviors). Pairs of reviewers extracted descriptive data, study quality, and outcomes. Odds ratios (OR) and 95% confidence intervals (CI) were pooled across studies using the random-effects model. Newcastle-Ottawa scale was used to critically appraise study quality.

Results: Nineteen studies met the inclusion criteria. Compared to those without sleep disturbances, patients with psychiatric diagnoses and co-morbid sleep disturbances were significantly more likely to report suicidal behaviors (OR = 1.99, 95% CI 1.72, 2.30, P < 0.001). The association was also demonstrated across several psychiatric conditions including depression (OR = 3.05, 95% CI 2.07, 4.48, P < 0.001), post-traumatic stress disorder (PTSD) (OR = 2.56, 95% CI 1.91, 3.43, P < 0.001), panic disorder (OR = 3.22, 95% CI 1.09, 9.45, P = 0.03), and schizophrenia (OR = 12.66, 95% CI 1.40, 114.44, P = 0.02). In subgroup analysis based on the type of sleep disorder, we also found suicidal behavior to be significantly associated with the presence of insomnia, parasomnias, and sleep-related breathing disorders, but not hypersomnias.

Conclusions: This systematic review and meta-analysis suggests that in patients with psychiatric diagnoses, sleep disturbances are associated with the increased risk of suicidal behaviors.

Keywords: Sleep disturbances, Suicidal behaviors, Systematic reviews, Meta-analysis

Background

Psychiatric patients are thought to be at high risk of suicidal behaviors. However, clinicians face challenges of identifying patients at risk [1]. The literature suggests that the severity of psychiatric illness is not always predictive of suicide attempts [2]; and the sensitivity and specificity of risk factors, including gender, prior suicide attempts, and suicidal ideations, remain low in predicting future suicide [3]. There is a great need to find additional risk factors. Given that sleep disturbances are fairly common in psychiatric patients, it is suggested that sleep disturbances may constitute a modifiable risk factor for suicidal behaviors [4,5].

Direct relationship between sleep disturbances and suicide has been evaluated in multiple studies. A recent systematic review and meta-analysis of 39 studies found patients with sleep problems had significantly increased risk of suicidal ideations, suicide attempts, and completed
suicides [6]. That study focused on the general population although it reported that depression did not moderate the association between sleep and suicide. However, other studies found significant associations between suicides and sleep disturbances among psychiatric patients. A study of 954 patients with affective disorders found that global insomnia was significantly associated with attempted suicide [1]. In another study, both insomnia and hypersomnia had prognostic significance in predicting suicide among patients with major depression [7]. Moreover, in an epidemiologic prospective study of 1,231 psychiatric outpatients, nocturnal sleep disturbances, particularly frequent insomnia and recurrent nightmares, were independently associated with enhanced suicidal risk [8].

Considering the lack of a systematic review that focuses on the effect of sleep on suicide risk in patients with psychiatric conditions and the conflicting results from the literature, we conducted this study to assess the association between suicidal behaviors and sleep disturbances in psychiatric patients.

Methods

A review protocol was developed at the beginning of this study. The reporting of this systematic review is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [9].

Inclusion and exclusion criteria

Eligible studies were comparative observational studies that reported sleep disturbances in psychiatric patients and the outcome of interest (any type of suicidal behaviors). We used the original study’s definition of sleep disturbances, which ranged from snoring, nightmares, hypersomnia insomnia, sleep panic attacks, and sleep deprivation. With respect to suicidal behaviors, we include suicide ideations, suicide attempts, completed suicides, and any other suicidal behaviors defined by the original studies. Studies were excluded if they did not report outcomes for psychiatric patients or did not provide sufficient data to quantitatively estimate the association between suicidal behaviors and sleep disturbances. We also excluded publications without original data (clinical reviews, editorials, letters, or erratum). No language or country restrictions were used.

Data sources and search strategy

An expert reference librarian and study authors with expertise in conducting systematic reviews developed the search strategy. A comprehensive search of databases from each database’s earliest inclusive dates to 26 June 2013 was conducted. The databases included Ovid Medline In-Process & Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid PsycInfo, Ovid Cochrane Database of Systematic Reviews, Ovid Cochrane Central Register of Controlled Trials, and Scopus. Controlled vocabulary, supplemented with keywords, was used to search for the concept areas: suicide, sleep disorders, and psychiatric conditions. The database search strategy is available in Additional file 1. We also searched additional references from a recent systematic review [6].

Study selection and data extraction

Reviewers working independently and in duplicate assessed each abstract for eligibility. Disagreements yielded an automatic inclusion into the following level of screening. Included studies were retrieved and full text screening commenced in duplicate as well. Disagreements at this level were resolved by discussion and consensus. Two reviewers working independently and in duplicate extracted baseline and outcome data and assessed the quality of each included study. A third reviewer compared the reviewers’ data and resolved inconsistencies by referring to the full text article.

Reviewers independently extracted study details from the full text articles, using a pilot-tested form. The following data were abstracted: study design, country, patient characteristics (sex, age), psychiatric diagnoses, sleep disturbances, and suicidal behaviors. We extracted numbers of patients with outcomes (suicidal behaviors) at the longest duration of complete follow-up.

Assessment of study quality and publication bias

Using the Newcastle-Ottawa scale, we assessed the quality of included observational studies by determining outcome ascertainment, adjustment for confounders, and proportion of patients lost to follow-up as well as sample selection. We assessed potential publication bias by visual inspection of funnel plots and the Egger’s regression asymmetry tests.

Statistical analysis

The outcome of interest was suicidal behaviors, including suicidal ideations, suicide attempts, and completed suicides. Outcomes were either dichotomized by the individual study or when presented as a scale, were converted to log transformed OR (logOR) based on the commonly used formula suggested by Borenstein et al. [10].

We pooled the logOR from all of the included studies using the DerSimonian & Laird random effects method with the estimate of heterogeneity from the Mantel-Haenszel model [11]. We conducted a priori planned subgroup analysis based on the type of suicidal behaviors (ideations, attempts, and completed suicides). We subsequently evaluated separately the different types of sleep disturbances (insomnia, hypersomnia, parasomnia, sleep-related breathing disorders, and mixed/unclear types) to further explore heterogeneity across studies. When one
study reported outcomes for multiple subgroups, these outcomes were pooled separately in each subgroup. When multiple outcomes were reported in one subgroup, we chose the one that clearly defined or objectively measured.

We used the $I^2$ statistic to measure heterogeneity across the studies. Statistical analyses were conducted using STATA version 12 (StataCorp, College Station, TX, USA) and R software version 3.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results
Description and quality of included studies
Our search identified 372 candidate references (Figure 1). After deleting duplicated studies and excluding irrelevant studies, 19 studies met the inclusion criteria and were included in this analysis. The characteristics of these studies are summarized in Table 1. Overall, 104,436 patients were included in this review. The average age was 49.4 years (range, 17-79 years). Fifty-eight percent of the patients were female. The average length of follow-up in the prospective studies was 9.9 years (range, 3 days - 27 years). Of 19 studies, 13 (68.4%) reported outcomes in depressive patients. The other psychiatric diagnoses included were post-traumatic stress disorder (PTSD), panic disorder, schizophrenia, and anxiety. Eleven studies (57.9%) were prospective studies, four (21.1%) were cross-sectional, and three (15.87%) were retrospective.

Figure 2 shows the quality indicators of the included studies. We found variable quality across studies. Most (68.4%) of the studies did not adjust for risk factors. However, 15 studies reported low risk of bias for the ascertainment of outcomes. Using the Egger regression asymmetry test and visual inspection of the funnel plot, we found potential publication bias in this body of evidence. Across the included studies, substantial heterogeneity was observed in most of the pooled outcomes (>50%) [28]. In summary, the risk of bias is moderate to high due to potential publication bias and substantial heterogeneity.

Figure 3 shows the pooled odds ratios (ORs) from all of the included studies. Compared to those without sleep disturbances, patients with psychiatric diagnoses and co-morbid sleep disturbances were significantly more likely to report suicidal behaviors (OR = 1.99, 95% CI 1.72, 2.30, $P < 0.001$). Regarding to specific psychiatric conditions, we found strong association between suicidal behaviors and sleep disturbances in depression (OR = 3.05, 95% CI 2.07, 4.48, $P < 0.001$), PTSD (OR = 2.56, 95% CI 1.91, 3.43, $P < 0.001$), panic disorders (OR = 3.22, 95% CI 1.09, 9.45, $P = 0.03$), and schizophrenia (OR = 12.66, 95% CI 1.40, 114.44, $P = 0.02$). Table 2 shows the pooled OR for different suicidal behaviors. Sleep disturbances were also significantly associated with suicide ideations, suicide attempts, and completed suicides. Subgroup analysis based on the type of sleep disturbance showed that insomnia, parasomnia, and sleep-related breathing disorders were significantly associated with increased risk of suicidal behaviors (Table 3). The only exception was hypersomnias (OR = 1.91, 95% CI: 0.60, 6.06, $P = 0.27$).

Discussion
We conducted a systematic review and meta-analysis to investigate the association between the presence of sleep disturbances and risk of suicidal behaviors in patients with psychiatric diagnoses. Nineteen studies with 104,436 patients were included in the analysis. We found significantly increased risk of suicidal behaviors among patients

Figure 1 Flow diagram for selection of studies included in the systematic review.
| Author, year | Study design | Patients (n) | Female (%) | Age (years) | Psychiatric diagnoses | Suicidal behaviors | Sleep disturbances |
|-------------|-------------|-------------|------------|-------------|----------------------|------------------|------------------|
| Agargun, 1997 [7] | Retrospective | 113 | 74% | Mean: 32.6 range: 18-70 | Major depression | Ideation | Insomnia and hypersomnia assessed by SCID-I |
| Li, 2010 [8] | Cross-sectional | 1,231 | 68.20% | Mean: 42.4, range 18-65 | Major depression, Bipolar, Other | Attempt | Self-reported insomnia and recurrent nightmares assessed by a questionnaire |
| McGirr, 2007 [12] | Prospective | 156 | 19.20% | Mean: 42.4 | Major depression | Completed suicide | Insomnia and hypersomnia assessed by SCID-I |
| Nrugham, 2008 [13] | Prospective | 2,464 | 50.80% | Mean age 13.7 | Depressive symptom and disorder | Ideation, attempt | Insomnia, hypersomnia, non-restorative sleep assessed by K-SADS and MFQ |
| Paffenbarger, 1994 [14] | Prospective | 21,582 | 0 | Range: 35-74 | Depressive disorder | Completed suicide | Insomnia defined as difficulty initiating or maintaining sleep, or non-restorative sleep causing impaired functioning or suffering that was long-lasting or demanded treatment and recorded from patients’ medical records |
| Pompili, 2009 [15] | Retrospective | 40 | 10% | Mean: 40 Range: 23-76 | Schizophrenia | Completed suicide | Self-reported insomnia assessed by a questionnaire |
| Sjostrom, 2009 [16] | Prospective | 165 | 78% | Range: 18-69 | Axis 1 DSM disorders | Attempt | Difficulties initiating sleep, problems maintaining sleep and early morning awakening assessed by USI |
| Agargun, 1997 [17] | Prospective | 41 | 76% | Mean: 34.6 SD: 10.8 | Major depression | SADS suicidality score | Subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, daytime dysfunction, and global severity measured by PSQI |
| Agargun, 1998 [18] | Prospective | 63 | 76% | Mean: 34.1 SD: 10.8 | Major depression | Ideation, attempts | Frequency of nightmares |
| Agargun, 1998 [19] | Unclear | 67 | 73.10% | Mean: 31.9 SD: 8.8 | Panic disorder | Ideation | Sleep panic and insomnia ascertained from SADS |
| Agargun, 2003 [20] | Prospective | 26 | 61.50% | Unclear | Major depression | HDRS suicide scores | REM latency, REM%, REM periods measured by three nights of polysomnography |
| Chellappa, 2007 [21] | Cross-sectional | 70 | 62.90% | Mean: 40.5 SD: 12.54 | Major depression | Ideation | Insomnia or excessive sleepiness assessed by the SHQ and ICSD |
| Krakow, 2000 [22] | Prospective | 153 | 100% | Mean: 36.4 SD: 11.1 | PTSD | Hamilton Depression and suicidality scores | SMD and SDB assessed by AASM 1997 and ASDA 1997 |
| Agargun, 2007 [23] | Retrospective | 100 | 52% | Mean: 32.1 SD: 10.7 | Unipolar major depression | Attempt | Nightmares assessed by ICSD-R; insomnia assessed by the HDRS items 6, 7, and 8 |
| Yoshimasu, 2006 [24] | Cross-sectional | 231 | 57.10% | Mean: 36.3 SD: 28.5 | Major depression | Ideation | Insomnia assessed by SDS, KMI, and patients’ three most painful complaints |
| Bjorgaard 2011 [25] | Prospective | 74,977 | 51% | Mean: 37.9 SD: 16.0 | Anxiety, depression | Completed suicide | Self-reported sleep difficulties assessed by a questionnaire |
Table 1 Basic characteristics of the included studies (Continued)

| Study       | Design       | Sample Size | %     | Mean (SD) | Condition                  | Symptoms and Measurements                                      |
|-------------|--------------|-------------|-------|-----------|----------------------------|-----------------------------------------------------------------|
| Li 2012 [26] | Prospective  | 419         | 81.80%| Mean: 44.6 SD: 10.4 | Major depression     | Ideation Insomnia, nightmares, and frequency of sleep disturbances measured by a questionnaire |
| Krakow 2011 [27] | Cross-sectional  | 1,584      | 55%   | Mean: 49.8 SD: 66.4 | Depression Attempt    | Sleep disturbances measured by SMH, ISI DDNSI, FOSQ, and TMB-10 |
| Fawcett, 1990 [1] | Prospective  | 954         | 58%   | Mean: 38.1 Range: 17-79 | Major affective disorder | Completed suicide Insomnia assessed by SADS |

AASM: American Academy of Sleep Medicine; ASDA: American Sleep Disorders Association; DDNSI: Disturbing Dream and Nightmare Severity Index; FOSQ: Functional Outcomes Sleep Questionnaire; HDRS: Hamilton Depression Rating Scale; ICSD: International Classification of Sleep Disorders diagnostic criteria for sleep disorders due to mood disorders; ICSD-R: International Classification of Sleep Disorders, revised; ISI: Insomnia Severity Index; KMI: Kyudai Medical Inventory; K-SADS: Kiddie-Schedule for Affective Disorders and Schizophrenia; MFQ: Mood and Feelings Questionnaire; PSQI: Pittsburgh Sleep Quality Index; PTSD: Post-traumatic stress disorder; REM: Rapid eye movement; SADS: Schedule for Affective Disorders and Schizophrenia; SCID-I: Structured Clinical Interview for DSM-IV-TR Axis I Disorders; SD: standard deviation; SDB: Sleep-disordered Breathing; SDS: Self-rating Depression Scale; SHQ: Sleep Habits questionnaire; SMD: Sleep-related Movement Disorders; SMH: Sleep Medicine History; TMB-10: Time Monitoring Behavior; USI: Uppsala Sleep Inventory.
with sleep disturbances and psychiatric diagnoses compared
to those without sleep disturbances.

Nevertheless, the causal role or mechanism of sleep
disturbances in suicidal behavior remains unclear. It is
suggested that sleep disturbances exacerbates psycho-
logical distress [4,5], rendering psychiatric patients more
vulnerable to suicidal behavior as a way to reduce or
escape from such distress. There is also evidence that
fatigue subsequent to sleep problems may impair prob-
lem solving and decrease emotion regulation increasing
one's risk for suicidal behavior through vulnerability to
impulsive behavior [29]. Other possibilities may include
changes in sleep architecture that render one vulnerable
to suicide. Certainly, future research is necessary to exam-
ine the specific mechanism of vulnerability because such
knowledge may lead to an effective intervention. Research
should establish whether there are specific problems in
sleep or sleep architecture that promotes vulnerability,
and should determine whether there are specific sleep
profiles (for example, nightmares, insomnia, early morning
awakening) that may discriminate between individuals
who are at risk to suicide behaviors and those who actually
complete suicide.

Clinical implications
Given the findings of this study, the presence of sleep
disturbances in individuals with psychiatric illness may
trigger the need for further evaluation of increased risk
for suicide. In particular, clinicians evaluating psychiatric
patients who report acute changes in sleep should be
aware that this may represent a specific vulnerability for
suicide, and a careful suicide risk assessment may be
warranted. Correspondingly, a comprehensive suicide risk
assessment may include an evaluation of sleep quality and
maintenance. Screening measures such as the Pittsburgh
Sleep Quality Index (PSQI) [30], which assesses sleep
quality, efficiency, duration, disturbances, and daytime
dysfunction, and has good reliability and validity in detect-
ing sleep problems, may assist in this effort. A suicide risk
assessment that includes evaluation of sleep disturbances
may not only add to the estimation of risk, but it may
also provide a potential target for intervention. This is
particularly promising given that many of the previously
established risk factors are person variables such as age,
type of psychiatric disorder, and family history of suicide
attempts, and thereby not amenable to intervention.

In terms of intervention, there is considerable evidence
for the efficacy of Cognitive Behavioral Therapy for Insom-
nia (CBT-I) with large effect sizes found in meta-analytic
studies [31]. Not only is CBT-I effective for treating pri-
mary sleep disorders, research examining CBT-I in patients
with major depression and co-morbid insomnia found that
the treatment led to improvements in both disorders [32].
Although CBT-I is considered to be a first-line treatment
for insomnia [33], pharmacological treatments may also be
given consideration for insomnia and other sleep problems.
However, caution should be taken as studies found
sedative-hypnotics were associated with increased suicidal

![Figure 2 Quality assessment of the included studies.](image-url)
behaviors [34-37]. A large cohort study demonstrated that receiving hypnotic prescriptions was associated with greater than three-fold increased hazards of death even when prescribed <18 pills/year. This association held in separate analyses for several commonly used hypnotics and for newer shorter-acting drugs [38].

Limitations and strengths
Strengths of the study include the comprehensive literature search, application of bias protection measures in the study selection, and careful evaluation of methodological quality. There are important limitations. Observational studies are subject to high risk of bias due to potential outcome confounding. Substantial heterogeneity was observed across the studies. Publication bias may have also affected our results. At last, we observed substantial variations of how the included studies define sleep disturbances and suicidal behaviors, and of how these studies measure them. All of the above may affect our findings. Based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, the strength of the current evidence is low due to potential publication bias and heterogeneity [39].

Table 2 Subgroup analysis based on suicidal behaviors

| Suicidal behaviors | OR | 95% CI | P value | I² |
|-------------------|----|--------|---------|----|
| Ideation          | 2.69 | 1.62, 4.48 | <0.001 | 73.5% |
| Attempt           | 4.36 | 2.28, 8.33 | <0.001 | 0.0% |
| Completed suicide | 1.59 | 1.17, 2.17 | <0.001 | 45.0% |

Figure 3 Forest plot of the association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses.

Table 3 Subgroup analysis based on sleep disturbance type

| Sleep disturbance type                     | Studies (n) | OR   | 95% CI   | P value | I²  |
|--------------------------------------------|-------------|------|----------|---------|-----|
| Insomnia                                   | 11          | 2.66 | 1.74, 4.07 | <0.001 | 75.4% |
| Hypersomnia                                | 3           | 1.91 | 0.60, 6.06 | 0.27    | 85.8% |
| Parasomnia                                 | 6           | 4.69 | 2.58, 8.51 | <0.001 | 0.0% |
| Sleep-related breathing disorder           | 1           | 2.56 | 1.91, 3.43 | <0.001 | n/a |
| Other/unclear                              | 7           | 4.16 | 1.96, 8.81 | <0.001 | 81.7% |

Sleep-related breathing disorder (SBD): only one study (Krakow, 2000) reported SBD and no objective test was used to confirm the diagnosis.
Conclusions
The current evidence and the results of this systematic review and meta-analysis suggest that in patients with psychiatric diagnoses, sleep disturbances are associated with the increased risk of suicidal behaviors.

Additional file

Additional file 1: Database search strategy.

Abbreviations
95% CI: 95% Confidence interval; CBT-I: Cognitive behavioral therapy for insomnia; GRADE: Grading of recommendations assessment development and evaluation; OR: Odds ratio; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; PSQI: Pittsburgh Sleep Quality Index; PTSD: Post-traumatic stress disorder.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
SM carried out study design, study screening, data extraction, quality appraisal, and drafted the manuscript. AK participated in study design, study screening, data extraction, and critically revised the manuscript. LS conducted data extraction, drafted, and critically revised the manuscript. LP designed the search strategy and revised the manuscript. ZW carried out study design, study screening, data extraction, quality appraisal, data analysis, and drafted the manuscript. KB participated in data extraction, quality appraisal, and critically revised the manuscript. MHM carried out study design, advised on all methodological issues, drafted, and critically revised the manuscript. SM and ZW had equal contributions to the manuscript. All authors approved the final version of this manuscript.

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