# A Systematic Review Assessing Bidirectionality between Sleep Disturbances, Anxiety, and Depression

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**Study Objectives:** To investigate whether sleep disturbances are bidirectionally related to anxiety and depression, and thus identify potential risk factors for each problem.

**Design:** A systematic review was conducted on 9 studies (8 longitudinal, 1 retrospective) that assessed bidirectionality between a sleep disturbance, and anxiety or depression. Treatment studies were excluded, along with those solely based on clinical samples or cohorts at high risk of suffering from a sleep disturbance, anxiety and depression. Eligible studies were identified by searching PubMed, PsychINFO, Embase, and Scopus databases, and reference lists of eligible studies. Publication dates ranged from the beginning of each database to December 2011.

**Measurements and Results:** Syntheses of longitudinal studies suggested insomnia and sleep quality were bidirectionally related to anxiety and depression, and depression/anxiety, respectively. Childhood sleep problems significantly predicted higher levels of depression and a combined depression/anxiety variable, but not vice-versa. A one-way relationship was found where anxiety predicted excessive daytime sleepiness, but excessive daytime sleepiness was not associated with depression.

**Conclusions:** Definitive conclusions regarding bidirectionality cannot be made for most sleep disturbances due to the small number and heterogeneity of cohort samples used across studies. Nevertheless, best available evidence suggests insomnia is bidirectionally related to anxiety and depression. Clinical and theoretical implications are discussed.

**Keywords:** Anxiety, depression, insomnia, sleep disturbances, systematic review

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## INTRODUCTION

Sleep disturbances encompass various potentially overlapping symptoms and disorders including insomnia, hypersomnia, excessive daytime sleepiness, circadian rhythm disturbance, and extrinsic sleep disorders (related to insufficient sleep and sleep hygiene). Sleep disturbances, anxiety and depression are common problems that lead to neuropsychological impairment,[1-3] alcohol and drug abuse,[4] and suicidal ideation.[5-7] Recent studies have established high comorbidity rates between sleep disturbances (such as insomnia, narcolepsy, sleep apnea, and circadian rhythm complaints), and depression and anxiety,[8-10] rates which vary across different anxiety disorders.[11] Longitudinal associations have also been established between sleep disturbances, anxiety, and depression.[12,13] Nevertheless, the etiological relationship between these problems remains unclear. Understanding the etiological relationship could help determine whether the onset of one is a risk-factor for the onset of the others, and inform public health campaigns and clinical interventions for each disorder.[11,14,15]

Research on bidirectionality can achieve such goals. Bidirectionality is established by accounting for the base rate of outcome variables,[16] considering whether a sleep disturbance independently predicts the onset of anxiety or depression, *and* whether anxiety or depression independently predicts the onset of a sleep disturbance.

Various studies have found a bidirectional relationship between sleep disturbances, anxiety and depression, suggesting that each contribute to the development and are a consequence of one another.[14,15,17] Other studies have suggested the existence of two distinct cause-effect associations, where anxiety predicts a sleep disturbance and a sleep disturbance predicts depression, but not vice-versa.[11,18] The inconsistent nature of the research may relate to variations of sleep disturbances that have been assessed across studies. The statistical significance and magnitude of the relationship between sleep disturbances, anxiety and depression differs across sleep and mental health variables (anxiety and depression),[18-21] which in turn may affect the results of bidirectionality studies. The current study, therefore, presents a systematic review that aims to determine whether a variety of sleep disturbances are risk factors for the development of anxiety or depression, and whether anxiety or depression are risk factors for the development of sleep disturbances.

## METHODS

### Data Sources and Study Selection

An extensive search of PubMed, PsychINFO, Embase, and Scopus was conducted using the following search terms in combinations specified for each database: (anxiety OR anxious* OR phobic OR phobia* OR psychological stress OR stress OR stresses OR internalization OR internalization OR obsessive compulsive OR asthenia OR depression OR depress* OR depressive disorder OR dysthym* OR seasonal affective disorder OR rumination) AND (sleep initiation and maintenance disorders OR sleep* OR insomnia OR early awakening OR early waking OR non-restorative OR non-restorative OR night waking). The Embase and Scopus searches also included the

**Table 1**—Items for quality assessment

1. Sampling procedure of cohort described?
2. Population characteristics described?
3. Inclusion and exclusion criteria described?
4. Studied population ≥ 75% of originally selected population?
5. Information about responders vs nonresponders
6. Lost to follow-up < 20%?
7. Information about completers vs noncompleters?
8. Are insomnia, anxiety and depression assessments for clinical diagnosis?
9. Same measures at both baseline and follow-up?
10. Are depression and anxiety assessed separately?
11. Does the sleep variable assess a specific sleep related problem?
12. Correction for potential demographic confounders?
13. Correction for circadian rhythm disorders, alcohol & drug use, exercise or caffeine intake?
14. Correction for other potential non-demographic confounders such as physical disorders or medication?
15. Are given data usable/transformable for meta-analysis?

following terms to account for the large number of search hits: NOT (neoplasm OR cancer OR tumor OR tumour OR carcinoma* OR oncolog* OR 'cardiovascular disease' OR dementia* OR Alzheimer* OR parkinson* OR therapy' OR 'psychiatric treatment' OR medicat* OR treatment). Publication dates for the searches ranged from the beginning of each database to December 2011, and all searches were limited to English and human studies. The Reference lists of retrieved studies were also assessed for other citations.

Studies were eligible if the following criteria was met: (1) Study assessed any sleep disturbance; (2) Study assessed an anxiety or depression variable; (3) Study reported a significance test when assessing bidirectionality; (4) Study accounted for baseline/previous sleep, anxiety or depression variable. Based on the recommendations of Jansson-Frojmark and Lindblom,[15] treatment studies, along with those who solely included clinical samples or cohorts at high risk of suffering from a sleep disturbance, anxiety, and depression were excluded due to the potential bias towards a stronger association between sleep disturbances, anxiety, and depression. The inclusion/exclusion criteria were developed by the primary author and reviewed by the secondary author.

### Quality Assessment

The methodological quality of the eligible studies was assessed by the first author who used a modified version of a 15-item checklist from a recent meta-analysis (Table 1).[22] Items 10 and 11 were included because the nature and magnitude of associations between sleep disturbances, anxiety, and depression often differs across sleep and mental health variables.[18-21] Sleep disturbances, anxiety and depression have been found to be associated with demographic information (e.g., age and gender),[23,24] circadian rhythm disorders,[25-27] alcohol and drug use,[4,28] exercise,[29,30] and caffeine,[31-33] thus providing the rationale behind items 12 and 13. Each item was labelled with a (+) or (-), depending on whether the study satisfied the criterion or not. A cutoff score was not used as a reference for

quality because such methods assign equal importance to all criteria. However, items were not weighted: the Cochrane Collaboration recommend against this method due to difficulties in justifying the weights assigned to each item.[34] Instead, quality was assessed along a continuum that ranged from 0-15, where lower scores indicated lower quality and higher scores indicated higher quality.

### Data Extraction and Synthesis

A coding form was developed to extract the following data from each study: geographical location of the study, sample size at baseline and follow-up, response rate, method of participant recruitment, method of data collection, use of medication, study methodology, possible biases, prediction and outcome variables, demographic statistics at baseline and (when available) follow-up, descriptive statistics for the variables of sleep disturbance, anxiety and depression, statistical analyses, variables controlled for, results, interpretation of results, author(s)' conclusions, and cited articles that were potentially relevant. Data extraction was conducted by the first author.

A meta-analysis could not be conducted due to the heterogeneous characteristics of the studies that met the inclusion criteria. Therefore, the research questions were analyzed by two narrative syntheses. The first presented an overall representation of the findings from each study, whereas the second compared results across different sleep variables.

## RESULTS

### Included and Excluded Studies

The PubMed, PsychInfo, Embase, and Scopus database searches identified 2,273, 2,352, 1,252, and 2,664 studies, respectively, and one study was identified from the reference searches. Ninety-three studies were selected as potentially relevant following the application of the inclusion criteria to the titles and abstracts. Most articles were excluded because they did not assess bidirectionality. Five studies[13,35-38] assessed bidirectionality but not between a sleep disturbance and anxiety or depression; one study assessed bidirectionality but used a cohort that was at risk for sleep disturbances, anxiety, and depression[39]; and one study did not report a significance test when assessing bidirectionality.[18] Therefore, 10 studies were eligible for analysis in the systematic review (12% of the original articles). Two eligible studies contained identical samples[40,41] and hence were collapsed into 1, leaving 9 independent studies that were included in the systematic review (refer to Figure 1 for a representation of the database searches and summary of the reasons for exclusion). Eligibility of each study was assessed by the first author.

Table 2 displays the general characteristics of each study. All studies were conducted between 2002 and 2010; 8 were longitudinal and prospective, and the other study was retrospective and cross-sectional. Studies were set in various countries; 2 in the USA, 2 in the UK, and 1 each in Switzerland, Sweden, Japan, South Korea, and the Netherlands. Sample populations also differed across studies; adolescents were assessed by 3 studies, adults by 2, and young adults, the elderly, child twin pairs, and adopted children were assessed by 1 study each. Participants were recruited by random selection in

3 studies, high schools in 2, and a 2-stage sampling procedure, the Colorado adoption agency, birth records, and a national registrations list of all community residents were used in 1 study each. Participants were recruited by self-report questionnaires in 4 studies (2 were postal surveys), interviews in 3 (2 were structured and 1 was semi-structured), parent reported questionnaires in 1, and parent reported and self-reported questionnaires in 1 study.
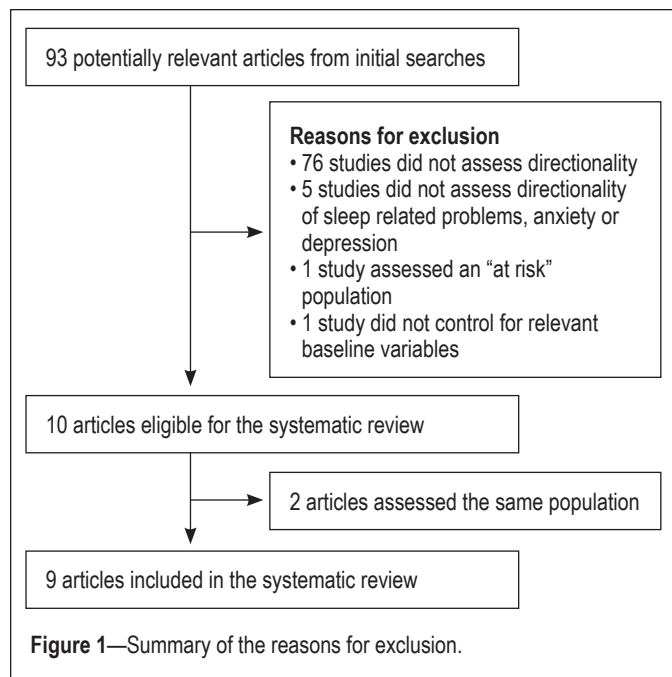
## Quality Assessment

Study quality ratings ranged from 7 to 13 (M = 9.9, SD = 1.9). All studies described the sampling procedure and population characteristics, used the same measures at baseline and follow-up, and gave data useable for a meta-analysis. Seven studies compared responders to non-responders and completers to non-completers, assessed a specific sleep disturbance, and corrected for potential demographic confounders; 6 studies retained 75% of the originally selected population and assessed depression and anxiety separately; 4 studies lost more than 20% of participants at follow-up; 3 studies described the inclusion and exclusion criteria, and corrected for other potential non-demographic confounders such as physical disorders; 2 studies assessed insomnia, anxiety, and depression according to a clinical diagnosis; 1 study corrected for alcohol and exercise; and no study corrected for circadian rhythm disorders, drug use, or caffeine intake (Table 3).

## Overall Synthesis

Table 4 presents the data for the overall synthesis. Four of the 9 independent studies supported the bidirectional theory,[14,15,17,42] 2 of which assessed insomnia, anxiety, and depression,[15,17] 1 assessed insomnia and depression,[42] and 1 assessed insomnia and mental health status.[14] The unidirectional theory discussed above was supported by 3 studies.[11,43,44] One study found 2 one-way relationships where anxiety predicted insomnia and insomnia predicted depression but not vice-versa[11]; the other reported that childhood sleep problems predicted depression but not vice-versa[43]; and the last suggested that childhood sleep problems predicted higher levels of depression/anxiety, but not vice-versa.[44] However, this does not necessarily support the unidirectional theory discussed above, as the mental health variable that was used (depression/anxiety) assessed anxiety and depression as a single construct rather than separate variables.

Two independent studies reported mixed results.[40,41,45] One study found no relationship between excessive daytime sleepiness and major depressive episodes or "pure insomnia" (insomnia without concurrent depression) and "pure depression" (depression without concurrent insomnia), a bidirectional relationship between insomnia and major depressive episodes, and a one-way relationship where anxiety predicted excessive daytime sleepiness.[40,41] The other found a bidirectional relationship between sleep quality and depression/anxiety and a one-way relationship between time in bed and depression/anxiety, where less time in bed at baseline predicted higher levels of depression/anxiety, but not vice-versa.[45] Therefore, 6 independent studies supported the bidirectional theory,[14,15,17,40-42,45] 5 supported a unidirectional relationship,[11,40,41,43-45] and 1 study did not find a significant relationship between excessive daytime sleepiness and major depressive episodes or "pure insomnia"



Figure 1—Summary of the reasons for exclusion.

93 potentially relevant articles from initial searches

**Reasons for exclusion**
- 76 studies did not assess directionality
- 5 studies did not assess directionality of sleep related problems, anxiety or depression
- 1 study assessed an "at risk" population
- 1 study did not control for relevant baseline variables

10 articles eligible for the systematic review

2 articles assessed the same population

9 articles included in the systematic review

and "pure depression."[40,41] Figure 2 depicts the number of studies and analyses that supported each type of relationship.

## Synthesis of Sleep Variables

Insomnia was the most commonly assessed sleep variable,[11,15,17,40,42] followed by childhood sleep problems,[43,44] sleep quality,[14,45] excessive daytime sleepiness,[41] and time in bed (Table 5).[45] Studies that assessed bidirectionality between anxiety, depression, and other common sleep disturbances such as sleep apnea were not found.

For insomnia, 3 of the 5 studies supported the bidirectional theory.[15,17,42] One study supported the unidirectional theory, where anxiety disorders predicted insomnia, which predicted major depressive disorder.[11] The remaining independent study reported several analyses across 6 time points over 20 years. No relationship was found in either direction between "pure insomnia" and "pure depression," along with a bidirectional relationship between insomnia and insomnia comorbid with depression across 5 separate bidirectional analyses over 20 years.[40] The same study also found conflicting results across these 5 analyses when assessing bidirectionality between "pure depression" and insomnia comorbid with depression (2 bidirectional relationships, a one-way relationship where insomnia comorbid with depression predicted pure depression but not vice-versa, and 2 relationships where no association was found in either direction). Finally, insomnia without concurrent depression predicted the development of depression at the interview directly following baseline and interviews at any given follow-up, whereas depression without concurrent insomnia predicted insomnia at the interview at any given time-point only.[40]

Regarding sleep quality, both studies found a bidirectional relationship, one with depression/anxiety[45] and the other with mental health status (a variable that contains a depression/anxiety scale).[14] Childhood sleep problems predicted depression and depression/anxiety but not vice-versa.[43,44] One study found that less time in bed at baseline is associated with more severe symptoms of depression/anxiety at follow-up, but not vice-versa.[45] Finally,

**Table 2**—General Characteristics of Each Study Included in the Systematic Review

| Study | Sample size | Study design | City/ Country | Population | Age range at baseline | Method of participant recruitment | Method of participant assessment | N time points (N years between follow up) |
|---|---|---|---|---|---|---|---|---|
| 40/41 | 457 | Longitudinal, Prospective | Switzerland | Young adults, representative, stratified sample | 20-21 | Two stage sampling procedure: (1) Participants were screened for health problems, (2) Those at risk for psychiatric syndromes were identified using a stratified sampling procedure and selected for interviews. Males recruited through conscription, females recruited through electoral register. Males were investigated in groups of 10, and females received postal surveys | Semi-structured interview | 6 (2, 5, 2, 5, 6) |
| 44 | 360 | Longitudinal, Prospective | USA | Adopted children | 4 | Participants recruited from the Colorado Adoption Project | Parent reported questionnaires | 2 (11) |
| 43 | 500 | Longitudinal, Prospective | Wales & England | Child twin pairs | 8 | Twin pairs identified through birth records. Parents were contacted by the UK Office for National Statistics after screening for infant mortality. | Questionnaires. Parent reported at baseline, and Self-report at follow up | 2 (2) |
| 15 | 1,498 | Longitudinal, Prospective | Sweden | Adult | 20-60 | Random selection, identified via public register | Self-report questionnaires, postal | 2 (1) |
| 11 | 1,014 | Cross-sectional, Retrospective | USA | Adolescents, metropolitan | 13-15 | Random selection, Youth-parents pairs identified from a 400,000 member Health Maintenance Organisation | Structured interviews | 1 (n/a) |
| 14 | 516 | Longitudinal, Prospective | Japan | Adolescents | 13-15 | High schools from metropolitan Tokyo | Self-report questionnaires | 2 (2) |
| 42 | 909 | Longitudinal, Prospective | South Korea | Elderly, general population | 65+ | All community residents within 2 geographic catchment areas (one urban, one rural) were identified and approached through national registration list. | Structured interview, home based | 2 (2) |
| 45 | 493 | Longitudinal, Prospective | Netherlands | Adolescents | 12-15 | High schools | Self-report questionnaires | 3 (1) |
| 17 | 1,589 | Longitudinal, Prospective | UK | Adults | 18+ | Random selection, adults registered to 1 of 5 general practices from urban and rural areas | Self-report questionnaires, postal | 2 (1) |

one study found a one-way relationship where anxiety predicted excessive daytime sleepiness, but no relationship between excessive daytime sleepiness and depression (i.e., excessive daytime sleepiness did not predict depression and vice-versa).[41]

## DISCUSSION

Each study included in the systematic review reported at least one significant relationship between a sleep disturbance, anxiety and/or depression, which further consolidates the notion of an association between these problems.[8,23,44] Interestingly, one study[41] found that anxiety predicted later excessive daytime sleepiness but no relationship between excessive daytime sleepiness and major depressive disorder symptoms, sug-

gesting that a bidirectional relationship is not consistent across mental health problems. This is surprising given the overlap of abnormalities in neurotransmitters and brain structures involved in problems with the sleep wake cycle, anxiety, and depression,[46-53] but Hasler and colleagues[41] suggested that the association between excessive daytime sleepiness and depression may be mediated by sleep disorder symptoms and co-morbid anxiety. More studies are needed to draw a definitive conclusion on whether excessive daytime sleepiness, anxiety, and depression are bidirectionally related.

Best available evidence suggests that insomnia is bidirectionally related to anxiety and depression. One retrospective study reported a one-way relationship where anxiety predicted

**Table 3**—Amount of studies (n) that met each criterion of quality assessment

| Criterion | Number (n) +, n/a | Studies |
|---|---|---|
| Sampling procedure of cohort described? | 9 | 11, 14, 15, 17, 40, 42-45 |
| Population characteristics described? | 9 | 11, 14, 15, 17, 40, 42-45 |
| Inclusion and exclusion criteria described? | 3 | 11, 15, 42 |
| Studied population ≥ 75% of originally selected population? | 6 | 14, 40, 42-45 |
| Information about responders vs nonresponders | 7 | 11, 15, 17, 40, 42, 44, 45 |
| Lost to follow-up < 20%? | 4 | 11, 15, 43, 45 |
| Information about completers vs noncompleters? | 7 | 11, 17, 40, 42-45 |
| Are insomnia, anxiety and depression assessments for clinical diagnosis? | 2 | 11, 42 |
| Same measures at both baseline and follow-up? | 9 | 11, 14, 15, 17, 40, 42-45 |
| Are depression and anxiety assessed separately? | 6 | 11, 15, 17, 40, 42, 44 |
| Does the sleep variable assess a specific sleep related problem? | 7 | 11, 14, 15, 17, 40, 42, 45 |
| Correction for potential demographic confounders? | 7 | 11, 14, 15, 17, 42, 44, 45 |
| Correction for circadian rhythm disorders, alcohol & drug use, exercise, or caffeine intake? | 1 | 42 |
| Correction for other potential non-demographic confounders, such as physical disorders or medication? | 3 | 14, 17, 42 |
| Are given data usable/transformable for meta-analysis? | 9 | 11, 14, 15, 17, 40, 42-45 |
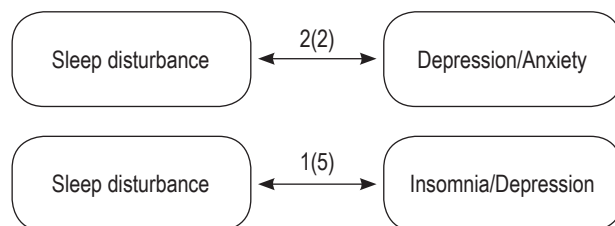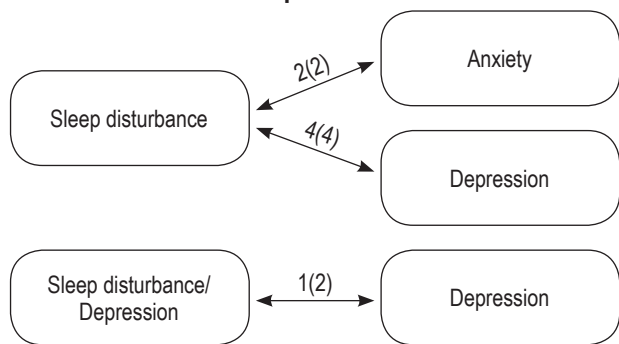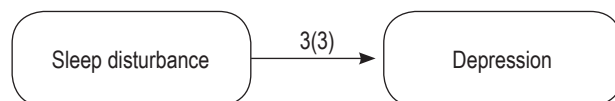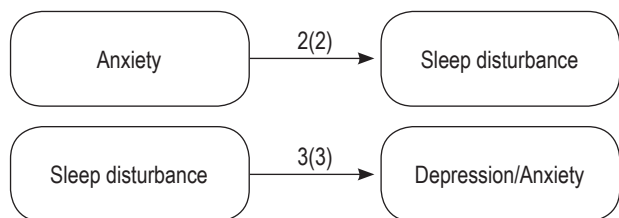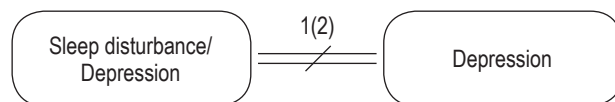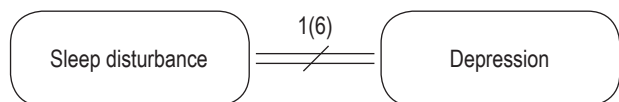


**Figure 2**—Summary of the total number of studies (analyses) that supported each type of relationship between sleep disturbances, anxiety and depression.

depression, but not vice-versa.[11] Conversely, four longitudinal studies found a bidirectional relationship between insomnia, anxiety and/or depression.[15,17,40,54] Due to the retrospective nature of, and hence the memory bias apparent in retrospective methodology,[55] longitudinal study designs allow for more ac-

curate causal inferences and reliable assessment of bidirectionality, and are therefore the preferred methodology for bidirectional studies.[14]

Interestingly, insomnia could predict depression more consistently than depression predicts insomnia. Buysse and col-

**Table 4**—Main findings from each study

| Study | Sleep variable (instrument name) | Mental health variables (instrument name) | Baseline/past variables accounted for | Results |
|---|---|---|---|---|
| 40, 41 | Insomnia – immediate follow up only (SPIKE[63]) | MDE – immediate follow up only (SPIKE[63]) | Concurrent MDE when predicting insomnia, and vice-versa. | Insomnia → immediate follow up depression. |
| | Insomnia – any follow up (SPIKE[63]) | MDE – any follow up (SPIKE[63]) | Concurrent MDE when predicting insomnia, and vice-versa. | Bidirectional: baseline variable and follow up at any time |
| | "Pure insomnia" (SPIKE[63]) | "Pure depression" (SPIKE[63]) | Only participants who reported no baseline symptoms of the outcome variable were included in the analysis. | 5 analyses, all no relationship |
| | "Pure insomnia" (SPIKE[63]) | Insomnia comorbid with depression (SPIKE[63]) | "Pure insomnia" refers to those without concurrent depression | 5 analyses, all bidirectional |
| | Insomnia comorbid with depression (SPIKE[63]) | "Pure depression" (SPIKE[63]) | "Pure depression" refers to those without concurrent insomnia | 5 analyses: 2 bidirectional, 2 no relationship, 1insomnia + depression → depression |
| | EDS (SPIKE[63]) | Cumulative MDE (SPIKE[63]), Cumulative Anxiety (SPIKE[63]) | Baseline EDS when assessing anxiety and depression as predictors, and vice-versa. Gender and stratified sampling for both analyses. | Anxiety → EDS. No relationship between EDS and MDE |
| 44 | Childhood sleep problems (CBC[64]) | Depression/Anxiety (CBC[64]) | Baseline depression/anxiety, when assessing childhood sleep problems as a predictor, and vice-versa. Adoptive status and child sex for both analyses. | Childhood sleep problems → Depression/Anxiety |
| 43 | Childhood sleep problems (CSHQ[65]) | Depression (CDI[66]) | When predicting depression: the effects of depression at age 8 on depression at age 10 and the association between sleep and depression at age 8. When predicting childhood sleep problems: the effects of childhood sleep problems at age 8 on childhood sleep problems at age 10 and the association between sleep and depression at age 8. | Childhood sleep problems → Depression |
| 15 | Insomnia (BNSQ[67] & USI[68]) | Depression (HADS[69]), Anxiety (HADS[69]) | Only participants who reported low or no symptoms of the outcome variable at baseline were included in analyses, e.g., if assessing anxiety as an outcome variable, only participants with low scores of anxiety were used. Age and gender were used as predictor variables for all analyses. | Bidirectional |
| 11 | Insomnia (DSM-IV)[70] * | Depression (DSM-IV)[70] *, Any Anxiety Disorder(DSM-IV)[70] * | Prior depression was controlled for in the insomnia – anxiety disorders models and prior anxiety disorders in the insomnia – depression models. Gender and race/ethnicity were also controlled for in each analysis. | Anxiety → Insomnia → Depression |
| 14 | Sleep quality (PSQI[71]) | Mental Health Status (GHQ-12)[72] | Only participants who did not report symptoms of the outcome variable at baseline were included in the analyses, e.g. only those without poor sleep quality were used when assessing sleep quality as an outcome variable. Predictor variables, gender, and lifestyle and contentment with daily life at baseline were used as covariates. | Bidirectional |
| 42 | Insomnia (10/66DDCRG)[73]* | Depression (GMS B3)[74]* | Only participants who did not report symptoms of the outcome variable at baseline were included in the analyses, e.g. those without insomnia at baseline were used when assessing insomnia as an outcome variable. Number of physical disorder, age, gender, education, housing, past occupation, current employment, living area, life events, social deficit, physical activity, organicity, anxiety, and daily drinking were controlled for in all analyses. | Bidirectional |
| 45 | Sleep quality (SQS)[75] | Depression/Anxiety (YSR)[76] | Time is included as a covariate, along with time 1, sleep quality, and mean time in bed. | Bidirectional |
| | Time in Bed (TBS)[45] | Depression/Anxiety (YSR)[76] | Time is included as a covariate, along with time 1, sleep quality, and mean time in bed. | Less time in bed → Depression/Anxiety |
| 17 | Insomnia (ISRS)[77] | Depression (HADS[69]), Anxiety (HADS[69]) | Only participants who did not report symptoms of the outcome variable at baseline were included in analyses, e.g., if assessing insomnia as an outcome variable, only participants who were not categorised as having insomnia were used. Age and gender were used as predictor variables for all analyses. Baseline covariates such as age, sex, social class and pain areas were also controlled for. | Bidirectional |

*Diagnosis. EDS, excessive daytime sleepiness; MDE, major depressive episode; SPIKE, The Structured Psychopathological Interview and Rating of Social Consequences of Psychic Disturbances for Epidemiology; CBC, Child Behavior Checklist; CSHQ, Child Sleep Habits Questionnaire; CDI, Child Depression Inventory; BNSQ, Basic Nordic Sleep Questionnaire; USI, Uppsala Sleep Inventory; HADS, Hamilton Anxiety Depression Scale; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders-IV; PSQI, Pittsburgh Sleep Quality Index; General Health GHQ, Questionnaire; 10/66DDCRG, 10/66 Dementia in Developing Countries Research Group; GMS B3, Geriatric Mental State diagnostic schedule; SQS, Sleep Quality Scale; YSR, Youth Self-report; TBS, Time in Bed Scale; ISRS, Insomnia Self-report Scale.

leagues[40] assessed bidirectionality over a 20-year period across six time-points. They found consistent bidirectional relationships between "pure insomnia" and insomnia comorbid with depression, yet conflicting relationships between "pure depression" and insomnia comorbid with depression. Such results

suggest that insomnia at baseline is a stronger and more persistent predictor of follow-up depression than baseline depression is of follow-up insomnia.

Various types of mechanisms may explain the bidirectional association between insomnia, anxiety and depression. Com-

**Table 5**—Comparison of study findings between sleep variables

| Sleep variables | Study | Mental health variable(s) | Study design | Results |
|---|---|---|---|---|
| Insomnia | 40, 41 | MDE | Longitudinal (immediate only) | Insomnia → immediate follow up depression |
| | 40, 41 | MDE | Longitudinal (any follow up) | Bidirectional |
| | 40, 41 | "Pure depression" | Longitudinal | All no relationship |
| | 40, 41 | Insomnia comorbid with depression | Longitudinal | All bidirectional |
| | 15 | Depression, Anxiety | Longitudinal | Bidirectional |
| | 42 | Depression* | Longitudinal | Bidirectional |
| | 17 | Depression, Anxiety | Longitudinal | Bidirectional |
| | 11 | Depression*, Anxiety* | Retrospective | Anxiety → Insomnia → Depression |
| Insomnia comorbid with depression | 40, 41 | "Pure depression" | Longitudinal | 2 bidirectional, 2 no relationship, 1 insomnia + depression → depression |
| EDS | 40/41 | MDE, Anxiety | Longitudinal | Anxiety → EDS, No relationship between EDS & major depression |
| Childhood sleep problems | 44 | Depression/Anxiety | Longitudinal | Childhood sleep problems → Depression/Anxiety |
| | 43 | Depression | Longitudinal | Childhood sleep problems → Depression |
| Sleep quality | 14 | Mental Health Status | Longitudinal | Bidirectional |
| | 45 | Depression/Anxiety | Longitudinal | Bidirectional |
| Time in bed | 45 | Depression/Anxiety | Longitudinal | Less time in bed → Depression/Anxiety |

*Diagnosis. EDS, Excessive Daytime Sleepiness; MDE, Major Depressive Episode.

mon neurobiological underpinnings (i.e., neurotransmitters and brain structures, discussed above) have been associated with insomnia, anxiety, and depression.[46-53] Batterham and colleagues[56] hypothesize there may also be biological factors such as increased inflammatory dysregulation in response to sleep disturbances[57] that are associated with anxiety[58] and depression.[59] Three other potential mechanisms discussed by Kaneita and colleagues,[14] which may coexist, include common factors (e.g., genetic, familial, social, or environmental) that independently contribute to the development of insomnia, anxiety and depression; insomnia, anxiety, and depression may be related, in which only the order of appearance of symptoms may alter; and insomnia, anxiety, and depression may be independent, but mutually influencing disorders.

A definitive conclusion is difficult to make regarding whether sleep disturbances, anxiety, and depression are bidirectionally related. Firstly, the small number of studies that assessed each sleep disturbance variable prevents an accurate representation of the true relationship between sleep disturbances, anxiety, and depression. Further longitudinal studies are needed to understand whether there is a bidirectional relationship between sleep disturbances, anxiety, and depression.

Secondly, sleep disturbance variables that were assessed by the studies in this systematic review were limited and sometimes problematic. Prevalent sleep disorders such as obstructive sleep apnea and circadian rhythm sleep disorders were not investigated, while insomnia symptoms such as problems with sleep latency, nighttime awakenings, and daytime functioning

deficits as a result of sleep were incorporated in the definition of sleep quality[14,45] and childhood sleep problems.[43,44] The definition of childhood sleep problems also incorporated other sleep disturbances such as nightmares, sleep duration, overtiredness, bedtime resistance, sleep anxiety, parasomnias, sleep disordered breathing, and daytime sleepiness. Therefore, implying differences in findings across sleep variables is problematic because distinctions between sleep variables are obscured and the definition of childhood sleep problems was overly inclusive. Future bidirectionality studies should focus on a broader range of clearly defined sleep disturbances that contain reasonable conceptual overlap.

Variables of anxiety and depression were also sometimes defined using conceptually overlapping and overly inclusive variables, along with non-diagnostic self-report questionnaires, and may variably reflect current diagnostic criteria. Such cases include a combined depression/anxiety variable, which assessed depression and anxiety as one construct. These inventories could mask potential differences in bidirectionality across variables, and are problematic because bidirectional inferences cannot be made about the relationship between sleep disturbances. Indeed, only two studies assessed diagnosed insomnia, anxiety, and depressive disorders.[11,42] Future studies should refrain from using overly inclusive variables, and use definitions based on established diagnostic criteria.

Moreover, bidirectionality between anxiety, depression, and different types of insomnia symptoms (i.e., sleep onset insomnia, early morning awakening) was not assessed. Recent

studies have suggested that the association between insomnia, anxiety and depression may differ across specific insomnia symptoms.[19,20] Therefore, it remains unclear whether anxiety and depression are bidirectionally related across insomnia symptoms. Further contributions to the field may consider different insomnia profiles.

Also, studies did not consider bidirectionality across different types of anxiety disorders. Johnson et al.,[11] found that comorbidity rates of insomnia vary across different subtypes. Future research can assess whether sleep disturbances are consistently bidirectionally associated with different anxiety profiles.

Furthermore, the samples used by the included studies were heterogeneous, assessing children, adolescents, young adults, adults, and the elderly. Recent evidence has suggested age may be related to types and prevalence rates of sleep disturbances,[60-62] rendering a comparison between studies potentially flawed at this time. The heterogeneous samples across studies also prevented the use of meta-analytic techniques to perform quantitative analyses.

Finally, important potential covariates were not controlled for. One study corrected for alcohol and exercise, but no study accounted for variables that have been associated with sleep disturbances, anxiety, and depression such as lifestyle factors, medical conditions, and other sleep disorders.[4,25-33] Bidirectionality is difficult to infer without controlling for such variables. Future research should account for variables such as circadian rhythm disorders, drug and alcohol use, caffeine intake, and exercise.

Although few conclusions can be made, this study contributes to the burgeoning understanding of the etiological relationship between, and prevention of anxiety, depression and various sleep disturbances. At the very least, patients who present with a sleep disturbance should also be assessed for anxiety and depression, and vice-versa.

Bidirectionality was found between insomnia, anxiety, and depression, suggesting that insomnia predicts and is predicted by anxiety and depression. Therefore, successful treatment of insomnia may prevent the onset of subsequent or exacerbation of comorbid anxiety or depression, and vice-versa.[14] Future research should consider the most appropriate and cost-effective targets of prevention and intervention for insomnia, anxiety and depression.

The unidirectional relationship between childhood sleep problems and depression suggests that some sleep disturbances may significantly contribute to depression, at least in children, but not vice-versa. Such conclusions should be treated with caution due to the limited research in this area, the overly inclusive nature of the childhood sleep problems variable, and the conceptual overlap with insomnia. Further research is needed to identify the specific sleep disturbance profiles that independently predict anxiety and depression.

In conclusion, due to the small number of studies in this area and the heterogeneity of cohort samples used across studies, few definitive conclusions about the bidirectionality of most sleep disturbances can be made. Best available evidence to date suggests depression bidirectional relationship between insomnia, anxiety, and depression, and further consolidates the association found between sleep disturbances, anxiety, and depression. Therefore, treatment of insomnia may prevent the development of anxiety and depressive disorders, and vice-versa. Future research should consider whether insomnia, anxiety, or depression should be targeted to ensure the most efficient and cost-effective method for prevention and intervention of these disorders.

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