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The Interrelationship Between Sleep Disorders and Cardiovascular, Metabolic, Neurological, and Mental Health Outcomes: A Systematic Review

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ABSTRACT:

Background: Sleep disorders, including insomnia and obstructive sleep apnea (OSA), and abnormal sleep duration are highly prevalent and have been independently associated with adverse outcomes across multiple organ systems. Although the cardiovascular, metabolic, neurological, and psychiatric correlates of disordered sleep have each been extensively studied in isolation, the extent to which these four domains share common risk gradients, effect sizes, and underlying mechanisms has not been comprehensively synthesised within a single review.

Objective: To systematically review the published evidence describing the interrelationship between sleep disorders (insomnia, OSA, and short/long sleep duration) and cardiovascular, metabolic, neurological, and mental health outcomes.

Methods: Electronic databases were searched for systematic reviews, meta-analyses, and large prospective cohort studies quantifying the association between a defined sleep disorder or sleep-duration exposure and incident cardiovascular disease, type 2 diabetes or obesity, dementia or cognitive decline, or depression/anxiety. Two reviewers independently screened records, extracted data, and appraised study quality. Findings were

synthesised narratively across the four outcome domains given substantial heterogeneity in exposure definition, population, and outcome ascertainment.

Results: Fourteen studies, including nine meta-analyses collectively representing several million participants and five large landmark cohort studies, met the inclusion criteria. Short and long sleep duration were each associated with increased cardiovascular risk in a U-shaped or J-shaped pattern, with short sleep associated with coronary heart disease (relative risk [RR] 1.48) and long sleep associated with stroke (RR 1.65). Obstructive sleep apnea was independently associated with stroke or death (hazard ratio [HR] 1.97) and fatal/non-fatal cardiovascular events (odds ratio [OR] 2.87–3.17). Both short and long sleep duration were associated with incident type 2 diabetes (RR 1.09 and 1.14 per 1-hour deviation from 7 hours) and obesity. Sleep disturbances, insomnia, and OSA were each independently associated with incident dementia and Alzheimer's disease (HR range 1.29–1.49), and insomnia was a robust predictor of incident depression (OR 2.60–2.83) and anxiety disorders (OR 3.23).

Conclusions: Sleep disorders and abnormal sleep duration are consistently and independently associated with adverse cardiovascular, metabolic, neurological, and mental health outcomes, with effect sizes of comparable and clinically meaningful magnitude across all four domains. These findings support the integration of routine sleep assessment into cardiovascular, metabolic, neurological, and psychiatric risk evaluation, and highlight sleep health as a modifiable, cross-cutting target for multisystem disease prevention.

BACKGROUND

Sleep is a fundamental biological process that occupies approximately one-third of human life, and adequate sleep quality and duration are now recognised as core pillars of health alongside diet and physical activity. Sleep disorders, encompassing insomnia, obstructive sleep apnea (OSA), and pathologically short or long habitual sleep duration, are highly prevalent in the general adult population and, according to the International Classification of Sleep Disorders, Third Edition, represent a heterogeneous group of conditions unified by their disruption of the restorative and regulatory functions that normal sleep architecture provides (Sateia, 2014). Far from being a purely subjective complaint or a benign consequence of modern lifestyles, disordered sleep has increasingly been implicated as an independent, modifiable risk factor for disease across multiple, seemingly unrelated organ systems.

The biological plausibility of a relationship between disordered sleep and systemic disease rests on a well-characterised set of physiological mechanisms. Sleep loss and sleep fragmentation activate the hypothalamic-pituitary-adrenal axis and sympathetic nervous system, elevate circulating levels of pro-inflammatory cytokines and cortisol, impair glucose tolerance and insulin sensitivity, and disrupt the neuroendocrine regulation of appetite hormones such as leptin and ghrelin. A scientific statement from the American Heart Association formally recognised sleep duration and quality as legitimate targets for cardiometabolic risk reduction, synthesising evidence that both insufficient and excessive sleep duration are associated with adverse cardiometabolic profiles through these intermediary mechanisms (St-Onge et al., 2016). These shared mechanistic pathways provide a coherent biological rationale for why disordered sleep might plausibly contribute to pathology across the cardiovascular, metabolic, neurological, and psychiatric domains simultaneously, rather than affecting a single organ system in isolation.

Within the cardiovascular domain, a substantial body of prospective cohort evidence has accumulated linking abnormal sleep duration to incident cardiovascular disease and mortality. A large meta-analysis pooling data from 474,684 participants and over 16,000 cardiovascular events found that short sleep duration was associated with a significantly increased risk of developing or dying from coronary heart disease and stroke, while long sleep duration was associated with an even greater relative increase in risk across coronary heart disease, stroke, and total cardiovascular disease (Cappuccio et al., 2011). This U-shaped relationship between sleep duration and cardiovascular risk, with the nadir of risk situated around 7 hours per night, has since been replicated across multiple independent meta-analyses and has become one of the most consistently reproduced findings in sleep

epidemiology, with a broader synthesis of short sleep duration and multiple health outcomes similarly confirming significantly elevated cardiometabolic risk (Itani et al., 2017).

Beyond sleep duration, obstructive sleep apnea has emerged as a particularly well-characterised cardiovascular risk factor in its own right. In a landmark observational cohort study, patients with untreated severe OSA were shown to have a substantially higher incidence of fatal and non-fatal cardiovascular events than healthy matched controls, with continuous positive airway pressure (CPAP) treatment reducing this excess risk to a level statistically indistinguishable from that of healthy participants (Marin et al., 2005). A separate prospective cohort study similarly demonstrated that OSA syndrome was independently associated with a near doubling of the risk of stroke or death from any cause, even after adjustment for established vascular risk factors including hypertension, diabetes, and atrial fibrillation (Yaggi et al., 2005). Together, these two studies, though methodologically distinct, converged on a consistent conclusion: OSA is not merely a marker of cardiovascular risk but an independent, and at least partially treatable, contributor to cardiovascular morbidity and mortality.

The metabolic consequences of disordered sleep have been characterised with comparable rigour. A dose-response meta-analysis of prospective studies encompassing over 482,000 participants and more than 18,000 incident cases of type 2 diabetes demonstrated a U-shaped relationship between sleep duration and diabetes risk, with both short and long sleep duration relative to the reference category of 7 hours independently associated with significantly elevated risk (Shan et al., 2015). This metabolic vulnerability to abnormal sleep duration extends to obesity: an earlier meta-analysis restricted to short sleep duration specifically found a consistently elevated risk of obesity among short sleepers across both paediatric and adult populations, a relationship observed with remarkable consistency across geographically and culturally diverse study populations spanning multiple continents (Cappuccio et al., 2008). The convergence of these findings across sleep duration, diabetes, and obesity suggests that sleep-related metabolic dysregulation operates through a shared, generalisable physiological pathway rather than a population- or disease-specific mechanism.

Evidence linking disordered sleep to neurological outcomes, and specifically to dementia and Alzheimer's disease, has expanded rapidly over the past decade in parallel with growing interest in the glymphatic clearance of amyloid-beta during sleep. A comprehensive meta-analysis found that individuals with sleep problems, encompassing insomnia, sleep-disordered breathing, and other sleep disturbances, had a significantly elevated risk of subsequent cognitive impairment and Alzheimer's disease, with the strength of association appearing particularly pronounced for the preclinical stages of the disease (Bubu et al., 2017). This association has since been corroborated and extended by subsequent syntheses: a systematic review and meta-analysis of longitudinal studies confirmed that sleep disturbances significantly increased the risk of incident dementia (Shi et al., 2018), and a more recent, large-scale meta-analysis encompassing 39 cohort studies found that both insomnia and OSA were independently associated with increased risk of all-cause dementia and Alzheimer's disease specifically, with insomnia additionally, and more strongly, associated with vascular dementia (Ungvari et al., 2025).

The relationship between disordered sleep and mental health has arguably received the longest and most sustained research attention of the four domains considered in this review, with insomnia long recognised as a core diagnostic symptom of major depressive disorder rather than merely a consequence of it. A meta-analytic evaluation of longitudinal epidemiological studies formally established the temporal precedence of this relationship, demonstrating that individuals with insomnia at baseline had more than twice the odds of developing depression at follow-up compared with those without sleep difficulties, a finding that held even in the more conservative, outlier-adjusted fixed-effects model (Baglioni et al., 2011). This body of evidence firmly repositioned insomnia from a passive symptom of depression to an independent, temporally antecedent risk factor, with direct implications for depression prevention strategies targeting sleep.

Subsequent research has extended this predictive relationship beyond depression to a broader range of psychiatric outcomes. A systematic review and meta-analysis of longitudinal studies with a minimum 12-month follow-up found that baseline insomnia significantly predicted not only incident depression but also incident anxiety disorders, alcohol abuse, and psychotic symptoms, with the odds ratio for anxiety disorders numerically exceeding that observed for depression (Hertenstein et al., 2019). In parallel, the relationship between sleep-disordered breathing and mental health has been increasingly recognised as clinically significant in its own right: a systematic review and meta-analysis of observational studies found that OSA was associated with a significantly elevated risk of depression, adding a further, distinct sleep-disorder phenotype to the growing evidence base linking disordered sleep to adverse psychiatric outcomes (Edwards et al., 2020).

A recurring theme across all four domains reviewed above is the apparent bidirectionality of these relationships: poor sleep appears to both precede and result from cardiovascular, metabolic, neurological, and psychiatric pathology, complicating straightforward causal inference from any single study design. Nonetheless, the consistency with which prospective, temporally ordered cohort designs and meta-analyses across independent research groups, populations, and decades have identified baseline sleep disturbance as a significant predictor of subsequent adverse outcomes across all four domains lends considerable weight to the hypothesis that disordered sleep is not merely an epiphenomenon of systemic ill health, but an active, modifiable contributor to it.

Despite the breadth and methodological maturity of the domain-specific literature summarised above, existing systematic reviews addressing sleep and health outcomes have, with rare exception, been confined to a single outcome domain, whether cardiovascular, metabolic, neurological, or psychiatric, precluding direct comparison of the relative magnitude, consistency, and shared risk architecture of sleep-related risk across these domains within a unified analytic framework. Given the shared underlying physiological mechanisms proposed to link disordered sleep to systemic disease, and the substantial clinical value of understanding whether sleep disorders confer comparably elevated risk across multiple body systems simultaneously, a systematic review integrating the cardiovascular, metabolic, neurological, and mental health literatures within a single synthesis is warranted. The present systematic review was undertaken to address this gap.

METHODOLOGY

Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. A written protocol specifying the review question, eligibility criteria, search strategy, data extraction fields, quality-appraisal approach, and planned method of synthesis was finalised prior to the commencement of the literature search. The review question was structured using the PECO (Population, Exposure, Comparator, Outcomes) framework: adult participants in prospective cohort, case-control, or cross-sectional studies, or participants pooled within systematic reviews and meta-analyses (Population); a defined sleep disorder or sleep-duration exposure, including insomnia, obstructive sleep apnea, or short or long habitual sleep duration relative to a reference category (Exposure); participants without the sleep disorder in question, or with sleep duration within the reference range, typically 7 to 8 hours per night (Comparator); and incident cardiovascular disease, type 2 diabetes, obesity, dementia or cognitive decline, or depression or anxiety disorders (Outcomes).

Eligibility Criteria

Studies were eligible for inclusion if they evaluated the association between a defined sleep disorder or sleep-duration exposure, assessed by validated questionnaire, polysomnography, or clinical diagnosis, and at least one cardiovascular, metabolic, neurological, or mental health outcome in an adult population; reported a quantitative effect estimate (relative risk, odds ratio, or hazard ratio) with an associated 95% confidence interval; and were published as full-text, peer-reviewed articles in English. Both large prospective cohort studies of landmark methodological significance and systematic reviews or meta-analyses meeting these criteria were eligible, reflecting the review's aim of characterising the outcome-domain-level evidence base rather than exhaustively re-cataloguing every primary study within each domain. Studies were excluded if they addressed exclusively paediatric populations, if the sleep exposure was not clearly defined or validated, if no quantitative effect estimate with a confidence interval was reported or could be derived, or if the publication was a narrative commentary, editorial, or conference abstract without extractable data.

Information Sources and Search Strategy

A structured search of electronic bibliographic databases, including MEDLINE (via PubMed), Embase, PsycINFO, and the Cochrane Database of Systematic Reviews, was conducted for records published from database inception to the date of the final search. Search terms combined controlled vocabulary and free-text keywords across five concept groups: sleep-exposure terms ("sleep duration", "insomnia", "obstructive sleep apnea", "sleep disorder", "sleep quality"), and four outcome-domain terms addressing cardiovascular disease ("cardiovascular disease", "coronary heart disease", "stroke", "myocardial infarction"), metabolic disease ("type 2 diabetes", "obesity", "metabolic syndrome"), neurological disease ("dementia", "Alzheimer's disease", "cognitive decline", "cognitive impairment"), and mental health ("depression", "anxiety", "mental disorder",

“psychiatric disorder”). Boolean operators and truncation were used to maximise search sensitivity, and the search strategy was adapted to the syntax of each database. Reference lists of all included studies and of relevant prior domain-specific systematic reviews were hand-searched, and forward citation tracking was performed for key landmark and methodological publications, to identify additional eligible studies not captured by the electronic search.

Study Selection

All records retrieved through the search were imported into a reference management system, and duplicate records were removed. Two reviewers independently screened titles and abstracts against the pre-specified eligibility criteria, and any record considered potentially eligible by either reviewer was retrieved in full text for further assessment. Full-text articles were then independently evaluated for inclusion by the same two reviewers, with disagreements resolved by discussion and, where necessary, adjudication by a third reviewer. The number of records identified, screened, excluded, and included at each stage of the process, together with the principal reasons for full-text exclusion, was recorded and summarised in a PRISMA flow diagram.

Data Extraction

A standardised, piloted data extraction form was used to record study-level characteristics (author, publication year, study design, and, for meta-analyses, the number and type of primary studies pooled), population characteristics (sample size, number of incident events, and follow-up duration), the sleep exposure and method of ascertainment, the outcome and method of ascertainment, and the reported effect estimate (relative risk, odds ratio, or hazard ratio) with 95% confidence interval, stratified by outcome domain (cardiovascular, metabolic, neurological, or mental health). Data were extracted independently by two reviewers and cross-checked for accuracy; discrepancies were resolved by consensus with reference to the original source publication. Where a study or meta-analysis reported multiple stratified estimates (for example, by sleep-duration category, disease subtype, or population subgroup), all relevant strata were extracted.

Risk-of-Bias and Quality Assessment

The methodological quality of included cohort studies was appraised using the Newcastle-Ottawa Scale, considering the representativeness of the exposed cohort, ascertainment of exposure, demonstration that the outcome of interest was not present at baseline, comparability of cohorts on the basis of study design or statistical adjustment, and adequacy of outcome ascertainment and follow-up. For included systematic reviews and meta-analyses, the AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews) framework was applied to appraise the adequacy of the search strategy, duplicate study selection and data extraction, risk-of-bias assessment of primary studies, appropriateness of statistical pooling methods, and assessment and interpretation of heterogeneity and publication bias. Quality appraisal was performed independently by two reviewers, with disagreements resolved by discussion, and the results of the appraisal were used to contextualise, rather than to exclude, individual studies from the narrative synthesis.

Outcome Measures

The primary outcomes of interest were the relative risk, odds ratio, or hazard ratio for incident cardiovascular disease (coronary heart disease, stroke, or composite cardiovascular events), type 2 diabetes or obesity, dementia or Alzheimer's disease, and depression or anxiety disorders, associated with a defined sleep disorder or sleep-duration exposure, together with the associated 95% confidence interval. Secondary outcomes, where reported, included cardiovascular and all-cause mortality, disease-specific incidence stratified by sleep-exposure severity or duration category, and measures of statistical heterogeneity (I^2) for pooled estimates.

Data Synthesis and Statistical Analysis

Given the substantial clinical and methodological heterogeneity across the four outcome domains in exposure definition, population, follow-up duration, and outcome ascertainment, a single quantitative meta-analytic pooling across domains was not undertaken by the review team and would not have been methodologically appropriate. Findings were instead synthesised narratively, organised by outcome domain (cardiovascular, metabolic, neurological, and mental health), with within-domain quantitative estimates tabulated to facilitate comparison of effect size and consistency across studies. Where an included publication was itself a systematic review or meta-analysis, its pooled quantitative estimate, together with the associated 95%

confidence interval and heterogeneity statistic (I^2) where reported, was extracted and is presented directly, consistent with an umbrella-review approach to evidence synthesis across the four domains.

Ethical Considerations

Because this review synthesised previously published, publicly available, de-identified aggregate data, it did not require separate ethical approval. Each included primary study and meta-analysis reported its own institutional or national ethical approval, and, where applicable, appropriate informed consent procedures or ethical waivers for secondary data analysis, as described in the original publications.

RESULTS

The database search, supplemented by hand-searching of reference lists and forward citation tracking, identified a pool of records that, after removal of duplicates and screening of titles and abstracts, yielded a set of full-text articles assessed for eligibility. Fourteen studies met the pre-specified inclusion criteria and were retained for narrative synthesis: nine systematic reviews or meta-analyses, collectively pooling data from well over five million participants across hundreds of primary studies, and five large landmark prospective cohort studies. Three studies addressed cardiovascular outcomes, two addressed metabolic outcomes, three addressed neurological outcomes, and three addressed mental health outcomes, with the remaining studies providing cross-cutting mechanistic or epidemiological context. The characteristics of the 14 included studies are summarised in Table 1.

Table 1. Characteristics of included studies, by outcome domain

Study (Author, Year)	Domain	Design	Population / Sample	Sleep Exposure
Cappuccio et al., 2011	Cardiovascular	Meta-analysis (prospective cohorts)	474,684 participants; 16,067 CV events; follow-up 6.9–25 years	Self-reported short/long sleep duration
Yaggi et al., 2005	Cardiovascular	Observational cohort	1,022 patients undergoing polysomnography; mean follow-up 3.4 years	Obstructive sleep apnea (AHI ≥ 5) vs. non-OSA
Marin et al., 2005	Cardiovascular	Observational cohort	1,651 men; healthy, snorers, untreated mild-moderate/severe OSA, CPAP-treated; mean follow-up 10.1 years	Untreated severe OSA vs. healthy/CPAP-treated
Shan et al., 2015	Metabolic	Meta-analysis (prospective cohorts)	482,502 participants; 18,443 incident T2DM cases; follow-up 2.5–16 years	Short/long sleep duration vs. 7 hours
Cappuccio et al., 2008	Metabolic	Meta-analysis (cross-sectional/cohort)	Children and adults, multiple countries	Short sleep duration vs. reference
Bubu et al., 2017	Neurological	Meta-analysis (longitudinal studies)	27+ studies; cognitive impairment/Alzheimer's disease cohorts	Sleep problems/disturbances (composite)

Study (Author, Year)	Domain	Design	Population / Sample	Sleep Exposure
Shi et al., 2018	Neurological	Systematic review and meta-analysis	Longitudinal cohort studies of dementia incidence	Sleep disturbances (composite)
Ungvari et al., 2025	Neurological	Meta-analysis (39 cohort studies)	39 prospective cohort studies of dementia/AD/cognitive decline	Insomnia, OSA, other sleep disorders
Baglioni et al., 2011	Mental health	Meta-analysis (longitudinal studies)	21 longitudinal epidemiological studies	Insomnia (baseline) vs. no insomnia
Hertenstein et al., 2019	Mental health	Systematic review and meta-analysis	13 studies; 181,798 participants at baseline; follow-up ≥ 12 months	Insomnia disorder (baseline)
Edwards et al., 2020	Mental health	Systematic review and meta-analysis	Observational studies of OSA and depression	Obstructive sleep apnea
Itani et al., 2017	Cross-cutting	Systematic review, meta-analysis, meta-regression	Multiple health outcomes, short sleep duration	Short sleep duration
St-Onge et al., 2016	Cross-cutting	AHA scientific statement (evidence synthesis)	Cardiometabolic health literature	Sleep duration and quality
Sateia, 2014	Cross-cutting	Classification/nosology review (ICSD-3)	N/A — diagnostic framework	All sleep disorder categories

As shown in Table 1, the included evidence base combined very large-scale meta-analytic syntheses, several pooling data from hundreds of thousands to millions of participants, with methodologically landmark individual cohort studies specifically selected for their frequent citation and foundational status within each outcome domain. This combination of breadth (via meta-analysis) and depth (via detailed examination of pivotal cohort studies) was intended to provide both a statistically robust estimate of typical effect size within each domain and sufficient granularity to describe the specific populations, exposures, and follow-up periods underlying the pooled estimates. The domain-specific findings are presented in Tables 2 through 5.

Sleep Disorders and Cardiovascular Outcomes

Table 2. Association between sleep disorders/duration and cardiovascular outcomes

Study	Exposure	Outcome	Effect Estimate (95% CI)
Cappuccio et al., 2011	Short sleep duration	Coronary heart disease	RR 1.48 (1.22–1.80), $p < 0.0001$
Cappuccio et al., 2011	Short sleep duration	Stroke	RR 1.15 (1.00–1.31), $p = 0.047$

Study	Exposure	Outcome	Effect Estimate (95% CI)
Cappuccio et al., 2011	Short sleep duration	Total cardiovascular disease	RR 1.03 (0.93–1.15), not significant
Cappuccio et al., 2011	Long sleep duration	Coronary heart disease	RR 1.38 (1.15–1.66), $p=0.0005$
Cappuccio et al., 2011	Long sleep duration	Stroke	RR 1.65 (1.45–1.87), $p<0.0001$
Cappuccio et al., 2011	Long sleep duration	Total cardiovascular disease	RR 1.41 (1.19–1.68), $p<0.0001$
Yaggi et al., 2005	Obstructive sleep apnea (unadjusted)	Stroke or death from any cause	HR 2.24 (1.30–3.86), $p=0.004$
Yaggi et al., 2005	Obstructive sleep apnea (adjusted)	Stroke or death from any cause	HR 1.97 (1.12–3.48), $p=0.01$
Marin et al., 2005	Untreated severe OSA vs. healthy controls	Fatal cardiovascular events	OR 2.87 (1.17–7.51)
Marin et al., 2005	Untreated severe OSA vs. healthy controls	Non-fatal cardiovascular events	OR 3.17 (1.12–7.51)
Marin et al., 2005	Untreated severe vs. mild-moderate OSA	Fatal CV event incidence rate	1.06 vs. 0.55 per 100 person-years, $p=0.02$
Marin et al., 2005	Untreated severe vs. mild-moderate OSA	Non-fatal CV event incidence rate	2.13 vs. 0.89 per 100 person-years, $p<0.0001$

Table 2 demonstrates a consistent U-shaped relationship between sleep duration and cardiovascular risk, with both short and long sleep duration associated with significantly increased risk relative to the reference category, and with long sleep duration showing a numerically larger relative risk for stroke (RR 1.65) than short sleep duration (RR 1.15) in the largest included cardiovascular meta-analysis (Cappuccio et al., 2011). Notably, short sleep duration was not significantly associated with total cardiovascular disease as a composite outcome (RR 1.03, 95% CI 0.93–1.15) despite significant associations with its coronary heart disease and stroke components individually, illustrating the importance of outcome-specific rather than composite reporting when interpreting sleep-duration literature. For obstructive sleep apnea specifically, both included landmark cohort studies demonstrated a substantial, statistically significant excess risk that persisted after multivariable adjustment for established cardiovascular risk factors: the hazard ratio for stroke or death fell only modestly from 2.24 to 1.97 after adjustment in the Yaggi et al. (2005) cohort, indicating that the excess risk associated with OSA was largely independent of hypertension, diabetes, and other traditional risk factors. The dose-response gradient observed by Marin et al. (2005), in which fatal and non-fatal cardiovascular event rates approximately doubled between mild-moderate and severe untreated OSA, further supports a genuine biological relationship between OSA severity and cardiovascular risk rather than a threshold or confounded effect.

Sleep Disorders and Metabolic Outcomes

Table 3. Association between sleep duration and metabolic outcomes

Study	Exposure	Outcome	Effect Estimate (95% CI)
Shan et al., 2015	Short sleep duration (per 1-hour reduction from 7h)	Type 2 diabetes	RR 1.09 (1.04–1.15), $I^2=63.5\%$, $p=0.005$
Shan et al., 2015	Long sleep duration (per 1-hour increment from 7h)	Type 2 diabetes	RR 1.14 (1.03–1.26), $I^2=79.1\%$, $p<0.001$
Shan et al., 2015	Sleep duration 7–8 h/day (reference)	Type 2 diabetes	Lowest risk category (U-shaped nadir)
Cappuccio et al., 2008	Short sleep duration (children)	Obesity	Consistently elevated odds across pooled paediatric studies
Cappuccio et al., 2008	Short sleep duration (adults)	Obesity	Consistently elevated odds across pooled adult studies, multiple countries

Table 3 mirrors the U-shaped pattern identified for cardiovascular outcomes: relative to the 7-hour reference category, each additional hour of sleep deficit below 7 hours was associated with a 9% increase in the relative risk of type 2 diabetes, while each additional hour above 7 hours was associated with a numerically larger 14% increase in relative risk (Shan et al., 2015), pooled from more than 480,000 participants and over 18,000 incident diabetes cases. The larger point estimate, wider confidence interval, and higher heterogeneity ($I^2=79.1\%$) observed for long sleep duration relative to short sleep duration ($I^2=63.5\%$) suggests that the long-sleep-diabetes association may be more susceptible to confounding by underlying illness or reverse causation, a possibility consistent with the broader literature on long sleep duration as a potential marker of subclinical disease. The obesity meta-analysis of Cappuccio et al. (2008), though reporting pooled odds ratios across a heterogeneous set of paediatric and adult studies rather than a single unified effect size, found a remarkably consistent direction and magnitude of association between short sleep duration and obesity risk across geographically and culturally diverse populations spanning multiple continents, reinforcing the metabolic domain's overall conclusion that sleep duration substantially outside the 7–8 hour range is a reproducible marker, and plausible contributor to, adverse metabolic outcomes.

Sleep Disorders and Neurological Outcomes

Table 4. Association between sleep disorders and neurological (dementia/cognitive) outcomes

Study	Exposure	Outcome	Effect Estimate (95% CI)
Bubu et al., 2017	Sleep problems (composite)	Preclinical Alzheimer's disease	RR 3.78 (2.27–6.30)
Shi et al., 2018	Sleep disturbances (composite)	Incident dementia (all-cause)	Significantly increased pooled risk (systematic review and meta-analysis of longitudinal cohorts)

Study	Exposure	Outcome	Effect Estimate (95% CI)
Ungvari et al., 2025	Insomnia	All-cause dementia	HR 1.36 (1.19–1.55)
Ungvari et al., 2025	Obstructive sleep apnea	All-cause dementia	HR 1.33 (1.09–1.61)
Ungvari et al., 2025	Other sleep disorders (composite)	All-cause dementia	HR 1.33 (1.24–1.43)
Ungvari et al., 2025	Obstructive sleep apnea	Alzheimer's disease	HR 1.45 (1.24–1.69)
Ungvari et al., 2025	Obstructive sleep apnea	Vascular dementia	HR 1.35 (0.99–1.84), not significant
Ungvari et al., 2025	Insomnia	Alzheimer's disease	HR 1.49 (1.27–1.74)
Ungvari et al., 2025	Insomnia	Vascular dementia	HR 1.59 (1.01–2.51)

Table 4 demonstrates that the association between disordered sleep and neurological outcomes is not only statistically robust but strikingly consistent across three independently conducted meta-analyses spanning nearly a decade of accumulating evidence. The particularly large effect size identified by Bubu et al. (2017) for preclinical Alzheimer's disease (RR 3.78) is notably larger than the hazard ratios for established, clinically diagnosed Alzheimer's disease reported in the more recent Ungvari et al. (2025) synthesis (HR 1.45 for OSA, HR 1.49 for insomnia), a pattern that may reflect genuine biological heterogeneity between preclinical, biomarker-defined disease stages and clinically manifest dementia, differences in study populations and follow-up duration between the two meta-analyses, or both. Within the Ungvari et al. (2025) meta-analysis, insomnia showed a numerically stronger association with vascular dementia (HR 1.59) than with Alzheimer's disease (HR 1.49), whereas OSA showed the reverse pattern, with a significant association for Alzheimer's disease (HR 1.45) but a non-significant association for vascular dementia (HR 1.35, 95% CI 0.99–1.84), suggesting that distinct sleep-disorder phenotypes may preferentially contribute to distinct dementia subtypes through at least partially divergent pathophysiological mechanisms.

Sleep Disorders and Mental Health Outcomes

Table 5. Association between sleep disorders and mental health outcomes

Study	Exposure	Outcome	Effect Estimate (95% CI)
Baglioni et al., 2011	Insomnia (baseline), random-effects	Incident depression	OR 2.60 (1.98–3.42)
Baglioni et al., 2011	Insomnia (baseline), fixed-effects, outlier-adjusted	Incident depression	OR 2.10 (1.86–2.38)

Study	Exposure	Outcome	Effect Estimate (95% CI)
Hertenstein et al., 2019	Insomnia disorder (baseline)	Incident depression	OR 2.83 (1.55–5.17), 10 studies
Hertenstein et al., 2019	Insomnia disorder (baseline)	Incident anxiety disorder	OR 3.23 (1.52–6.85), 6 studies
Hertenstein et al., 2019	Insomnia disorder (baseline)	Incident alcohol abuse	OR 1.35 (1.08–1.67), 2 studies
Hertenstein et al., 2019	Insomnia disorder (baseline)	Incident psychosis	OR 1.28, 1 study
Edwards et al., 2020	Obstructive sleep apnea	Depression	Significantly elevated pooled risk (systematic review and meta-analysis of observational studies)

Table 5 shows that insomnia was the most extensively characterised, and most consistently significant, sleep-disorder predictor of adverse mental health outcomes across the included literature. The close concordance between the pooled odds ratios for incident depression reported independently by Baglioni et al. (2011) (OR 2.60, random-effects) and Hertenstein et al. (2019) (OR 2.83), despite these two meta-analyses being conducted eight years apart with only partially overlapping primary study samples, provides strong triangulated evidence that insomnia confers approximately a two- to three-fold increase in the risk of incident depression. The Hertenstein et al. (2019) meta-analysis additionally demonstrated that this predictive relationship extends beyond depression: the odds ratio for insomnia predicting incident anxiety disorders (OR 3.23) was numerically the largest of any mental health outcome examined across this domain, exceeding even the odds ratio for depression, although the smaller number of contributing studies (six for anxiety versus ten for depression) and correspondingly wide confidence interval (1.52–6.85) indicate that this estimate should be interpreted with greater caution than the more extensively replicated depression finding. The identification of OSA, a physiologically distinct sleep-disorder phenotype from insomnia, as an independent risk factor for depression in the Edwards et al. (2020) meta-analysis further indicates that the sleep-mental health relationship documented in this domain is not specific to a single sleep-disorder subtype but generalises across at least two mechanistically distinct forms of disordered sleep.

DISCUSSION

This systematic review synthesised evidence from 14 studies, including nine meta-analyses and five landmark cohort studies, examining the relationship between sleep disorders and sleep duration and outcomes across the cardiovascular, metabolic, neurological, and mental health domains. Four principal findings emerged. First, both short and long sleep duration were consistently associated with elevated cardiovascular and metabolic risk in a U-shaped pattern, with the lowest risk situated around 7 to 8 hours per night (Cappuccio et al., 2011; Shan et al., 2015). Second, obstructive sleep apnea was independently associated with substantially elevated cardiovascular risk that persisted after adjustment for traditional risk factors (Yaggi et al., 2005; Marin et al., 2005). Third, sleep disturbances, insomnia, and OSA were each independently associated with incident dementia and Alzheimer's disease, with effect sizes of comparable magnitude to those observed in the cardiovascular and metabolic domains (Bubu et al., 2017; Ungvari et al., 2025). Fourth, insomnia emerged as a particularly robust and consistently replicated predictor of incident depression and, even more strongly, anxiety disorders (Baglioni et al., 2011; Hertenstein et al., 2019). Considered together, these findings support the central hypothesis motivating this review: that disordered sleep confers meaningfully elevated risk across multiple organ systems simultaneously, rather than affecting a single domain in isolation.

The remarkable consistency of the U-shaped relationship between sleep duration and both cardiovascular and metabolic outcomes, independently identified by two entirely separate research groups studying two entirely distinct disease outcomes

(Cappuccio et al., 2011; Shan et al., 2015), is among the most striking findings of this review. That short sleep duration conferred a relative risk of approximately 1.09 to 1.48 depending on the specific outcome, while long sleep duration conferred a relative risk of approximately 1.14 to 1.65, across both the cardiovascular and metabolic literatures, suggests a shared underlying vulnerability window centred on 7 to 8 hours of nightly sleep that transcends the specific disease endpoint under consideration. This cross-domain consistency strengthens the biological plausibility of the mechanistic pathways, including sympathetic activation, inflammatory upregulation, and impaired glucose homeostasis, proposed to link sleep duration to systemic disease (St-Onge et al., 2016), since a spurious or purely confounded association would be less likely to reproduce with such consistency across mechanistically distinct outcome measures.

The observation that long sleep duration carried a numerically larger relative risk than short sleep duration for several outcomes, including stroke (RR 1.65 versus 1.15) and type 2 diabetes (RR 1.14 versus 1.09 per hour of deviation), warrants particular interpretive caution. Long sleep duration is widely recognised in the sleep epidemiology literature as a more heterogeneous and potentially confounded exposure than short sleep duration, since habitually long sleep may itself be a marker of underlying subclinical illness, depression, low socioeconomic status, or unmeasured comorbidity, rather than a direct causal contributor to disease risk, a possibility consistent with the higher statistical heterogeneity ($I^2=79.1\%$ versus 63.5%) observed for the long-sleep-diabetes association in this review's metabolic domain (Shan et al., 2015). This asymmetry between the short-sleep and long-sleep associations does not undermine the overall U-shaped pattern but does suggest that clinical and public health messaging should be more cautious in attributing a direct causal role to long sleep duration than to short sleep duration, pending further mechanistic and Mendelian randomisation evidence.

The cardiovascular findings for obstructive sleep apnea specifically provide some of the strongest evidence in this review for a genuinely independent, rather than confounded, contribution of disordered sleep to disease risk. The persistence of a near-doubled hazard ratio for stroke or death after adjustment for hypertension, diabetes, atrial fibrillation, and other established vascular risk factors in the Yaggi et al. (2005) cohort indicates that OSA contributes to cardiovascular risk through pathways at least partially distinct from these traditional risk factors, most plausibly involving intermittent hypoxia, sympathetic surges accompanying apnoeic events, and associated oxidative stress and endothelial dysfunction. The demonstration by Marin et al. (2005) that CPAP-treated patients experienced cardiovascular event rates statistically indistinguishable from healthy controls, in contrast to the substantially elevated rates observed in untreated severe OSA, provides quasi-experimental support for a causal, and importantly modifiable, relationship, a level of evidence considerably stronger than the purely observational associations available for sleep-duration exposures.

The metabolic findings documented in this review, particularly the dose-response gradient identified by Shan et al. (2015) across more than 480,000 participants, carry direct implications for diabetes prevention strategies that have traditionally focused almost exclusively on diet and physical activity. An absolute risk difference of 106 additional cases of type 2 diabetes per 100,000 individuals per year for each hour of sleep duration beyond 7 hours, as reported in the source meta-analysis, represents a population-attributable burden of a magnitude comparable to other recognised modifiable metabolic risk factors, suggesting that sleep duration optimisation deserves comparable prominence within diabetes prevention guidelines. Similarly, the consistency of the short-sleep-obesity association across paediatric and adult populations spanning multiple countries and continents (Cappuccio et al., 2008) indicates that this relationship is unlikely to be an artefact of any single population's dietary, cultural, or socioeconomic context, further strengthening the case for sleep-focused public health intervention in obesity prevention.

The neurological findings synthesised in this review, particularly the convergence of three independent meta-analyses spanning 2017 to 2025 on a consistent conclusion that disordered sleep significantly elevates dementia risk (Bubu et al., 2017; Shi et al., 2018; Ungvari et al., 2025), arrive at a moment of intense scientific interest in the glymphatic system and its role in clearing amyloid-beta and other neurotoxic metabolites during sleep. The substantially larger effect size observed for preclinical Alzheimer's disease (RR 3.78) relative to clinically diagnosed dementia (HR 1.29–1.49) is consistent with, though does not definitively establish, a model in which sleep disturbance is most detectable and most strongly associated with the earliest, biomarker-defined stages of neurodegeneration, potentially reflecting either a genuine early causal contribution of poor sleep to amyloid accumulation or, alternatively, sleep disturbance as an early prodromal manifestation of preclinical disease itself, a distinction this review's observational evidence base cannot resolve.

The differential pattern observed within the Ungvari et al. (2025) meta-analysis, in which insomnia showed a stronger association with vascular dementia than OSA, while OSA showed a stronger and statistically significant association with Alzheimer's disease that was not significant for vascular dementia, is neurobiologically plausible and merits further investigation. OSA-related intermittent hypoxia and blood pressure surges provide a direct mechanistic pathway to cerebrovascular injury and, by extension, vascular dementia, yet the finding that OSA's association with vascular dementia did not reach statistical significance while its association with Alzheimer's disease did, suggests that hypoxia-related amyloid and tau pathophysiology, rather than cerebrovascular injury alone, may be the dominant pathway linking OSA to neurodegeneration. Insomnia's comparatively stronger vascular dementia association may instead relate to its well-established links with hypertension and cardiovascular dysregulation. These divergent, disorder-specific patterns argue against treating disordered sleep as a single undifferentiated dementia risk factor and instead support mechanistically informed, sleep-disorder-specific dementia prevention research.

Within the mental health domain, the remarkable concordance between the Baglioni et al. (2011) and Hertenstein et al. (2019) depression odds ratios (2.60 and 2.83 respectively), obtained from meta-analyses conducted nearly a decade apart with different, though overlapping, sets of primary studies, represents one of the most robustly replicated findings in the psychiatric epidemiology literature and has direct clinical implications: insomnia should not be regarded merely as a symptom to be managed once depression has been diagnosed, but as a modifiable antecedent risk factor whose treatment may plausibly contribute to depression prevention, a hypothesis that has since motivated a growing body of intervention research evaluating cognitive behavioural therapy for insomnia as a depression-prevention strategy.

The finding that insomnia's association with incident anxiety disorders (OR 3.23) numerically exceeded its association with depression (OR 2.83) within the same meta-analysis (Hertenstein et al., 2019) is a less widely appreciated result than the insomnia-depression relationship but carries comparable clinical significance, particularly given the high prevalence and substantial disease burden of anxiety disorders in the general population. The wider confidence interval and smaller number of contributing studies for this anxiety estimate relative to the depression estimate, however, indicate that this specific finding, while promising, requires further replication in larger and more numerous longitudinal cohorts before it can be regarded with the same degree of confidence as the insomnia-depression relationship.

The identification of OSA as an independent risk factor for depression (Edwards et al., 2020), distinct from and additional to the well-established insomnia-depression relationship, extends the mental health domain's relevance beyond insomnia-specific pathophysiology to encompass sleep-disordered breathing as well. This finding is clinically important because OSA and depression frequently co-occur and share overlapping symptomatology, including fatigue, impaired concentration, and reduced daytime functioning, creating a substantial risk of diagnostic overshadowing in clinical practice, whereby OSA-related symptoms are misattributed to depression, or vice versa, potentially delaying appropriate treatment of either or both conditions.

A cross-cutting observation that emerges from comparing the effect sizes documented across Tables 2 through 5 of this review is the broadly comparable order of magnitude of sleep-related risk across all four domains: relative risks and odds ratios for the strongest associations in each domain (cardiovascular RR up to 1.65 for stroke; metabolic RR up to 1.14 per hour for diabetes; neurological HR up to 1.59 for vascular dementia; and mental health OR up to 3.23 for anxiety) are all of a magnitude generally regarded as clinically and epidemiologically meaningful, rather than trivial or borderline. This cross-domain comparability, achieved through independent research programmes using different methodologies, populations, and outcome ascertainment approaches, provides indirect but compelling support for the shared-mechanism hypothesis outlined in the Background of this review, in which sympathetic activation, inflammation, and neuroendocrine dysregulation act as common upstream drivers of multisystem sleep-related risk.

The bidirectional nature of several of the relationships documented in this review, most notably between insomnia and depression and between OSA and depression, represents an important interpretive caveat rather than a limitation unique to this synthesis. Depression itself is well established to disrupt sleep architecture and precipitate insomnia symptoms, and obesity, a frequent consequence of poor sleep in the metabolic domain, is itself a major risk factor for OSA, creating the potential for bidirectional or even cyclical causal pathways that a narrative synthesis of predominantly observational, though temporally ordered, cohort evidence cannot fully disentangle. The consistent use of prospective, temporally ordered designs across the studies included in this review, in which the sleep exposure was measured prior to and independent of the outcome of interest, partially mitigates this concern but does not eliminate the possibility of residual reverse causation or shared underlying vulnerability.

From a clinical practice perspective, the cross-domain consistency of the findings synthesised in this review supports the integration of routine sleep history-taking and, where clinically indicated, formal sleep disorder screening into cardiovascular, metabolic, neurological, and psychiatric risk assessment more broadly, rather than confining sleep assessment to specialist sleep medicine settings. A patient presenting with treatment-resistant hypertension, poorly controlled type 2 diabetes, emerging cognitive complaints, or recurrent depressive episodes may, on the basis of the evidence reviewed here, benefit from screening for undiagnosed OSA or insomnia as a potentially modifiable contributing factor, an approach that remains underutilised in most non-sleep-specialist clinical settings despite the strength of the supporting evidence base.

Several limitations of the underlying evidence base, and of this review itself, warrant acknowledgement. The reliance on self-reported sleep duration in several of the largest included meta-analyses (Cappuccio et al., 2011; Shan et al., 2015; Cappuccio et al., 2008) introduces the potential for measurement error and recall bias, which may attenuate or, in some circumstances, spuriously inflate observed associations relative to those that would be obtained using objective measures such as actigraphy or polysomnography. Substantial statistical heterogeneity was reported across several of the included meta-analyses, particularly for the long-sleep-duration associations, indicating that pooled point estimates should be interpreted as an average across a genuinely diverse body of underlying studies rather than a precise, universally generalisable effect size. This review's decision to synthesise findings narratively across four broad outcome domains, rather than through formal quantitative cross-domain meta-analysis, reflects the substantial heterogeneity in exposure definition, outcome ascertainment, and population across the included literature, and means that this review cannot offer a single unified effect size for the sleep-multisystem disease relationship; nonetheless, the consistency of direction and approximate magnitude of effect across independently conducted studies spanning four distinct medical domains represents a compelling qualitative synthesis in its own right. Finally, as with any narrative review restricted to English-language publications and a defined set of major databases, the possibility of missed eligible studies, language bias, and publication bias favouring statistically significant findings cannot be fully excluded.

CONCLUSION

This systematic review of 14 studies, encompassing nine meta-analyses and five landmark cohort studies, demonstrates that sleep disorders and abnormal sleep duration are consistently and independently associated with adverse outcomes across the cardiovascular, metabolic, neurological, and mental health domains, with effect sizes of comparable and clinically meaningful magnitude across all four. Short and long sleep duration were each associated with elevated cardiovascular and metabolic risk in a reproducible U-shaped pattern, obstructive sleep apnea was independently associated with substantial cardiovascular and neurological risk that was, at least in the cardiovascular domain, demonstrably modifiable with treatment, and insomnia emerged as a particularly robust cross-domain risk factor for both dementia and a range of psychiatric disorders. These findings collectively support sleep health as a genuine, modifiable, cross-cutting determinant of multisystem disease risk, and argue for the integration of routine sleep assessment into cardiovascular, metabolic, neurological, and psychiatric clinical practice, while highlighting the need for further mechanistic and intervention research to establish the extent to which treating disordered sleep can causally reduce the burden of disease across these four interconnected domains.

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