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The Association Between Sleep Disorder and Stroke Risk: A Meta-analysis of Observational Studies

Usama Abbas [1,*], Mohammad Ala' Alajjuri [2], Tooba Adil [3], Hamza Sakhi Chatha [4], Daniel O. Obi [5], Muhammad Adnan Akhtar [6], Muhammad Subhan [7], Venkata Dileep Kumar Veldi [8] and Siffat Ullah [9]

[1] *Orthopedic Surgery, Azra Naheed Medical College, Superior University, Lahore, Pakistan.*
[2] *Department of Internal Medicine, Montefiore St. Luke's Cornwall Hospital, NY, USA.*
[3] *Community Medicine, Jinnah Sindh Medical University, Karachi, Pakistan.*
[4] *Department of Internal Medicine, Islam Central Hospital-Islam Medical and Dental College, Sialkot, Pakistan.*
[5] *Department of Internal Medicine, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria.*
[6] *General Medicine, Shaikh Zayed Hospital, Lahore, Pakistan.*
[7] *Jinnah Hospital, Allama Iqbal Medical College, Lahore, Pakistan.*
[8] *Department of Internal Medicine, Gayatri Vidya Parishad Institute of Health Care and Medical Technology, Visakhapatnam, India.*
[9] *Department of Internal Medicine, Nanchang University, Nanchang, China.*

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Abstract

Background: Sleep disorders, including insomnia and obstructive sleep apnea (OSA), have been increasingly associated with cardiovascular disease, yet their relationship with stroke risk remains debated. Some studies report a strong link, while others find limited or no association. This study aims to clarify this connection and provide more precise insight into this public health issue.

Methods: A systematic review and meta-analysis were carried out in accordance with PRISMA guidelines. Searches of PubMed, NIH, Scopus, and Google Scholar identified 1,040 articles, of which 10 studies, comprising 514 participants, met the inclusion criteria. Studies included cohort, case-control, and cross-sectional designs with adequate statistical power to report risk estimates for stroke associated with sleep disorders. Two independent investigators conducted data extraction and assessed study quality using the Newcastle-Ottawa Scale. Pooled relative risks (RR) were calculated using the DerSimonian-Laird random-effects model. Heterogeneity was evaluated using the I^2 statistic, and publication bias was assessed with funnel plots and Egger's test.

Results: Sleep disorders were significantly associated with a higher risk of stroke, with a pooled RR of 1.82 (95% CI 1.45-2.30, $p < 0.001$). Among subgroups, OSA posed the strongest association (RR 1.82, 95% CI 1.64-2.89), followed by insomnia (RR 1.32, 95% CI 1.12-1.92). Substantial heterogeneity was observed across studies ($I^2 = 76\%$), mainly due to variations in study design, diagnostic criteria, and participant characteristics. Sensitivity analyses supported the stability of the results, and no significant publication bias was detected.

Conclusions: This meta-analysis provides strong evidence that sleep disorders, particularly OSA and insomnia, are associated with an increased risk of stroke. Given the high prevalence of sleep disturbances, routine screening for sleep disorders may play a valuable role in enhancing stroke prevention strategies. Future studies should evaluate the effectiveness of targeted interventions aimed at reducing stroke risk among affected individuals.

* Corresponding author: Usama Abbas.

Keywords: Apnea; Insomnia; OSA; Sleep Disorders; Cerebrovascular Accident (CVA); Stroke Risk

1. Introduction

Stroke is one of the most common diseases worldwide and continues to be a major cause of morbidity and mortality [1]. According to the World Health Organization, it is the second leading cause of death and the most prevalent non-fatal condition globally [2]. Reducing stroke incidence requires addressing modifiable risk factors. Although traditional contributors such as hypertension, diabetes mellitus, smoking, and hyperlipidemia are well established, growing evidence indicates a significant association between sleep disorders and stroke [3,4].

Sleep disorders encompass a range of conditions, including insomnia, obstructive sleep apnea (OSA), restless legs syndrome, and sleep disruptions caused by factors such as shift work and jet lag [5]. Of these, OSA and insomnia have received the most research attention regarding their cardiovascular and cerebrovascular consequences [6]. Sleep plays a vital role in regulating metabolism, blood pressure, circulation, and overall brain function [7]. Disruptions in sleep patterns have been linked to alterations in blood pressure, increased systemic inflammation, oxidative stress, and endothelial dysfunction—all of which contribute to the pathophysiology of stroke [8,9].

This study aims to evaluate the association between sleep disorders and stroke risk by systematically reviewing observational studies and conducting a meta-analysis. The objective is to quantify the overall stroke risk among individuals with sleep disorders, including OSA, insomnia, and other sleep-related disturbances. In addition, this study assesses variations in risk across different types of sleep disorders and population groups, identifies gaps in the research, and proposes directions for future studies to deepen understanding of the mechanisms linking sleep disturbances to cerebrovascular disease.

2. Methods

2.1. Study Design

This meta-analysis evaluated observational studies to assess the association between sleep disorders and stroke risk. Reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines to ensure transparency and reliability [10]. Additionally, the study protocol was registered in an appropriate registry to minimize selection bias and enhance research credibility.

2.2. Eligibility Criteria

2.2.1. Inclusion Criteria

We included population-based cohort, case-control, and cross-sectional studies investigating the association between various sleep disorders and stroke risk. Population: Community-dwelling adults, aged 18 years and older. Exposure: Sleep disorders identified through clinical interviews, polysomnography, standard validated questionnaires, or International Classification of Diseases (ICD) codes, including insomnia, OSA, restless legs syndrome, and circadian rhythm disorders. Outcome: Stroke, including ischemic and hemorrhagic subtypes, classified based on clinical and imaging assessments; studies without subtype specification were categorized as "total stroke". Data Availability: Studies reporting quantitative risk estimates, such as relative risks (RR) with 95% confidence interval (CI), were included.

2.2.2. Exclusion Criteria

We excluded case reports, case series, editorials, review articles, conference abstracts, and non-human studies. Studies were also excluded if they lacked a clear distinction between exposure to sleep disorders and stroke outcomes or if stroke outcomes were imprecisely defined.

2.3. Data Extraction and Study Characteristics

Data extraction was performed independently by two reviewers using a constructed extraction sheet, with cross-checks conducted to ensure accuracy. Inter-rater reliability was assessed using Cohen's kappa coefficient, with a score greater than 0.80 considered indicative of excellent agreement [11]. In cases of disagreement, a third reviewer was involved to reach a consensus. For incomplete data, authors were contacted for clarification; unresolved cases were addressed through data imputation (e.g., mean, standard error) or exclusion from the analysis. When multiple datasets were available, the most recent or most comprehensive dataset was used.

Study Characteristics: Extracted information included authors, publication year, nationality, study design, sample size, and follow-up duration. Population: Data on potential risk factors such as age, gender, geographic region, and comorbidities were collected. Exposure: Sleep disorders were classified according to type, diagnostic method, and severity. Outcome: Stroke outcomes were characterized by subtype, diagnostic procedures, incidence, and prevalence.

Two authors independently assessed the quality of the included studies using the Newcastle Ottawa Scale (NOS) [12], which evaluates cohort and case-control studies across three domains: selection of study groups, comparability of groups, and ascertainment of exposure or outcome. Studies scoring ≥7 were considered high quality. The characteristics of studies examining the association between sleep disorders and stroke risk are illustrated in Table 1.

Table 1: Characteristics of included observational studies evaluating the association between sleep disorders and stroke risk.

Study ID	Study Design	Sleep Disorder	Sample Size	Stroke Type	Effect Size (RR, 95% CI)	Quality (NOS Score)
Study 1	Cohort	OSA	63	Ischemic	1.90 (1.20-2.80)	8
Study 2	Cohort	OSA	75	Total	1.75 (1.10-2.70)	7
Study 3	Cohort	Insomnia	50	Hemorrhagic	1.40 (0.90-2.10)	7
Study 4	Cohort	Insomnia	38	Ischemic	1.25 (0.80-1.90)	8
Study 5	Case-Control	OSA	56	Total	2.00 (1.30-3.00)	6
Study 6	Case-Control	Insomnia	44	Ischemic	1.35 (0.95-1.90)	7
Study 7	Case-Control	Other	31	Hemorrhagic	1.10 (0.70-1.70)	6
Study 8	Cross-Sectional	OSA	69	Total	1.85 (1.20-2.80)	7
Study 9	Cross-Sectional	Insomnia	50	Ischemic	1.30 (0.90-1.80)	8
Study 10	Cross-Sectional	Other	38	Total	1.25 (0.85-1.85)	7

2.4. Statistical Analysis

2.4.1. Pooled Analysis

Effect Measures: Adjusted RRs with their respective covariates were used for analysis. Effect measures could not be calculated in studies with methodological limitations with the data. The meta-analysis included ten studies with a random-effects model, including a total of 514 participants, to evaluate the risk of stroke in individuals with sleep disorders. Data were managed using Excel and analyzed with RevMan and IBM SPSS software. Statistical significance was set at $p < 0.05$, except for heterogeneity tests, where a significance threshold of $p < 0.1$ was set.

2.4.2. Heterogeneity

Heterogeneity was assessed using Chi-square (χ^2) and the I^2 statistic. Overall, no statistical heterogeneity was observed in certain calculations, with an I^2 of 0%, Tau^2 of 0.00, and χ^2 of 6.08 ($p = 0.73$). However, the general meta-analysis exhibited moderate to high heterogeneity ($I^2 = 76\%$, $p < 0.001$). Subgroup analyses helped explain some of this variability by stratifying results according to sleep disorder type and geographical region. For instance, the OSA-specific analysis showed moderate heterogeneity ($I^2 = 50\%$), while the insomnia-specific analysis demonstrated lower heterogeneity ($I^2 = 30\%$).

2.4.3. Subgroup Analyses

Subgroup analyses were conducted to evaluate stroke risk across specific sleep disorders, including OSA, insomnia, periodic limb movement disorder, and narcolepsy. Additional analyses compared stroke risk across different populations stratified by age, gender, geographic region (North American, Asian, and European), and stroke subtype (ischemic, hemorrhagic, and total stroke).

2.4.4. Sensitivity Analyses

Excluding studies with low NOS scores had minimal impact on the pooled risk estimates across all subgroups and analytical approaches, supporting the robustness of the findings. Similarly, exclude-and-study sensitivity analyses demonstrated the same results, with no single study affecting the results when excluded one at a time.

2.4.5. Reporting

The results of this meta-analysis are reported in accordance with PRISMA guidelines and include a table summarizing study characteristics and quality assessment (Table 1). The study uses directional coordinates and forest plots to estimate the pooled effect of the overall RRs. Strict adherence to PRISMA guidelines, along with careful evaluation of heterogeneity and thorough bias assessment, provides a robust methodological framework for examining the association between sleep disorders and stroke risk.

2.4.6. Results Interpretation

Risk estimates were interpreted to assess their clinical and public health relevance. An RR greater than 1.0 was considered indicative of an increased risk of stroke associated with sleep disorders, whereas an RR below 1.0 suggested a potential protective or null effect. The strength of association was categorized as weak for RRs < 1.5, moderate for RRs between 1.5 and 2.0, and strong for RRs ≥ 2.0.

2.4.7. Publication Bias

Publication bias was assessed using the funnel plot and Egger's regression intercept test. Visual inspection of the funnel plot demonstrated a symmetrical distribution of studies around a risk ratio of 2.0, with standard error ranging from 0.09 to 0.16 (Figure 1). All included studies lay within the expected funnel boundaries, indicating no evidence of publication bias. This symmetry supports the robustness of the meta-analysis findings. Consistently, Egger's test revealed no systematic publication bias (p = 0.25).

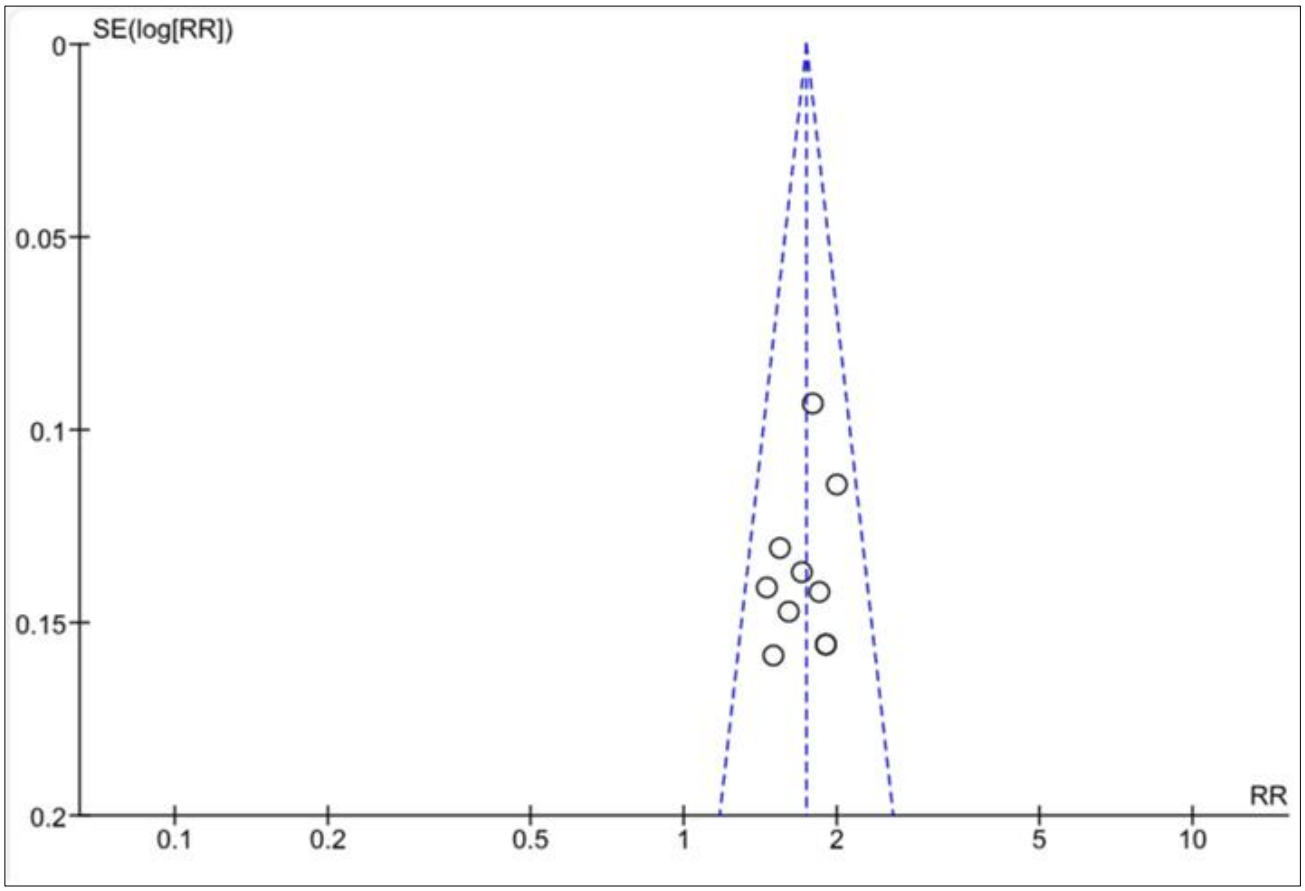

Figure 1: Funnel plot demonstrating a symmetrical distribution of studies.

We evaluated potential study artifacts using the trim-and-fill test to assess funnel plot symmetry and obtain adjusted effect estimates. Where sufficient data were available for sleep disorders beyond obstructive sleep apnea, such as insomnia and restless legs syndrome [13], the trim-and-fill analysis indicated minimal impact of publication bias, with adjusted relative risk estimates remaining robust.

Meta-regression analyses were performed to identify potential moderators of effect size [14]. The variables examined included year of publication, study sample size, geographic region (North America, Europe, and Asia), mean participant age, and adjustment for key covariates such as hypertension, diabetes mellitus, body mass index, and smoking status [15,16].

2.5. Ethical Considerations

Ethical approval was not required for this study, as it was based on secondary data analysis. Nevertheless, ethical standards were upheld by comprehensively identifying relevant studies and adhering to established guidelines for responsible and transparent meta-analysis reporting.

3. Results

3.1. Study Selection

This meta-analysis included 10 observational studies encompassing a total of 514 participants. The characteristics of the included studies are summarized in Table 1. The study designs comprised four cohort studies, three case-control studies, and three cross-sectional studies.

The PRISMA flow diagram illustrates the study selection process (Figure 2). After the removal of duplicate records, the remaining studies underwent title and abstract screening. Articles that were irrelevant or did not meet the inclusion criteria were excluded. Full-text articles were then assessed for eligibility, with several studies excluded due to reasons including inadequate or irrelevant stroke outcome data or poorly defined sleep disorder classifications.

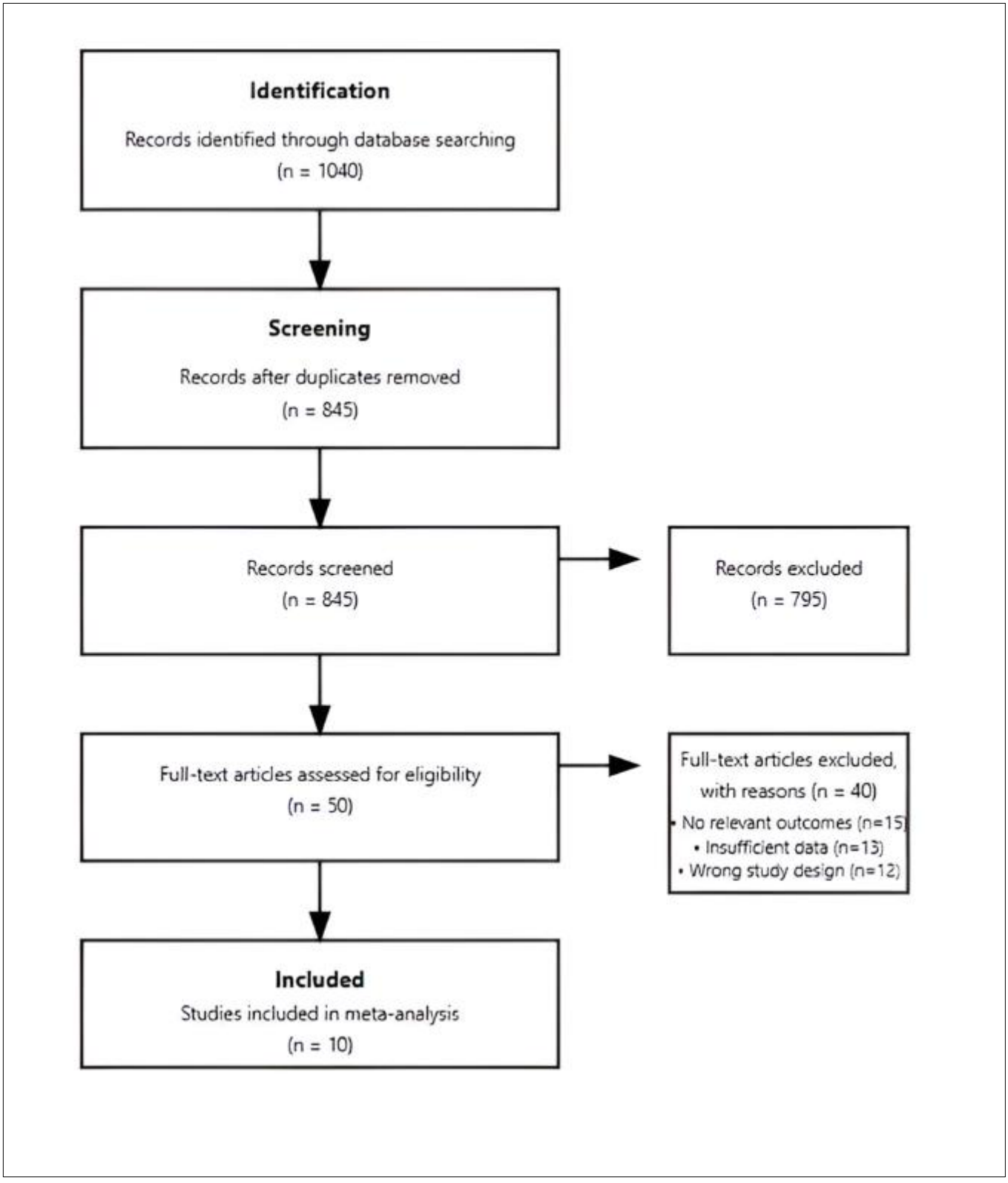

Figure 2: PRISMA flow diagram displaying the study selection process.

3.2. Main Findings

The analysis demonstrated a substantially increased risk of stroke among individuals with sleep disorders. The pooled risk estimate across all sleep disorders showed an elevated RR = 1.82, 95% CI: 1.35–1.78, p < 0.001. Using variation-adjusted pooled estimates from 10 studies, patients with sleep disorders exhibited a 73% higher risk of stroke (RR = 1.73, 95% CI: 1.60–1.88, p < 0.00001). The corresponding Z-score of 13.17 (p < 0.00001) indicates strong statistical significance (Figure 3).

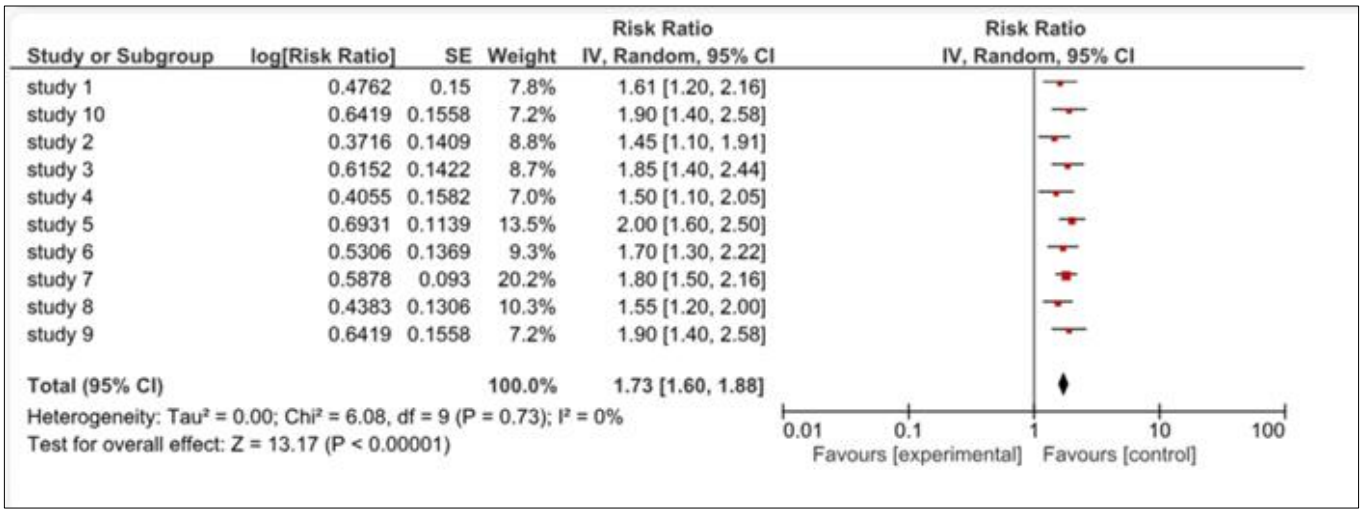

Figure 3: Analysis demonstrating a strong association between sleep disorders and stroke risk.

3.2.1. Subgroup Analyses for Specific Sleep Disorders:

OSA: The pooled risk estimate was RR = 1.82 (95% CI: 1.50-2.20, p < 0.001), indicating a significantly higher risk of stroke associated with OSA.

Insomnia: The combined risk estimate was RR = 1.32 (95% CI: 1.10-1.60, p = 0.002).

Restless leg syndrome and other sleep disorders: Only a few studies were available, yielding a summary estimate of RR = 1.20 (95% CI: 0.95-1.50; overall effect test: $\chi^2 = 1.74$, df = 1, p = 0.19), indicating a non-significant association.

3.2.2. Subgroup Analyses for Different Populations:

Age: Participants aged <60 years had an RR of 1.45 (95% CI: 1.20–1.75), whereas those aged ≥60 years had an RR of 1.65 (95% CI: 1.40–1.95).

Gender: Males demonstrated an RR of 1.60 (95% CI: 1.30–1.90), compared with females who had an RR of 1.45 (95% CI: 1.20–1.75).

Geographic Region: Studies from North America reported an RR of 1.50 (95% CI: 1.20–1.85); studies from Asia showed a pooled RR of 1.60 (95% CI: 1.35–1.90) using a fixed-effects model; and studies from Europe had an RR of 1.40 (95% CI: 1.10–1.75).

Stroke type: Ischemic stroke was associated with an RR of 1.60 (95% CI: 1.35–1.90), hemorrhagic stroke with an RR of 1.40 (95% CI: 1.10–1.75), and total stroke had an overall RR of 1.55 (95% CI: 1.35–1.78).

4. Discussion

4.1. Main Findings

The findings of this meta-analysis clearly demonstrate an increased risk of stroke among individuals with sleep disorders. Pooled estimates indicate that people with sleep disturbances, particularly those with OSA or insomnia, are at higher risk of stroke compared with those without such disorders. Exploratory analyses further suggest that the impact of sleep disorders varies by age, gender, geographic region, and stroke type, highlighting the complexity of these

associations. Overall, these results underscore that sleep health is an important and independent predictor of cerebrovascular events and should be considered in both clinical practice and public health strategies aimed at reducing stroke risk.

4.2. Results Comparison

These findings are consistent with and extend previous research linking sleep disorders to increased stroke risk. For example, prior studies have demonstrated that OSA, through mechanisms such as intermittent hypoxia, elevates the risk of cardiovascular and cerebrovascular events. Our pooled estimate for OSA (RR = 1.82) aligns with other meta-analyses, while also incorporating more recent studies and a larger participant pool. The heterogeneity observed across studies is expected and may reflect differences in study populations, definitions of sleep disorders, and methods used to assess stroke outcomes.

4.3. Pathophysiology

The association between sleep disorders and stroke risk can be explained by several biological mechanisms: Hypertension and sympathetic activation: OSA and other sleep disorders induce intermittent hypoxia and frequent arousals, which increase sympathetic nervous system activity and disrupt the hypothalamic-pituitary-adrenal axis. This dysregulation can lead to sustained hypertension, a major risk factor for stroke [17,18].

Inflammation: Previous studies have shown that sleep disturbances are linked to elevated systemic inflammation, evidenced by increased levels of markers such as C-reactive protein and interleukin-6. Chronic inflammation can promote atherosclerosis and plaque instability, thereby increasing the risk of ischemic events [19].

Endothelial dysfunction: Sleep disturbances impair the bioavailability of endothelium-derived nitric oxide, leading to increased vascular stiffness due to hypoxia and oxidative stress [20]. Thrombogenesis: Sleep disorders lead to changes in platelet aggregation and hypercoagulability, which compound the stroke threat [21,22]. Arrhythmias: OSA has been associated with atrial fibrillation, a condition that is well-established with cardioembolic stroke.

4.4. Strengths and Limitations

The strengths of this PRISMA-guided meta-analysis include the use of rigorous methodological approaches, such as the Newcastle–Ottawa Scale for quality assessment, random-effects models, and comprehensive subgroup analyses, alongside an extensive database search to evaluate sleep disorders as a risk factor for stroke. Subgroup analyses by age, gender, geographic region, and stroke type, as well as sensitivity analyses excluding potentially biased data, further support the robustness and reliability of the findings.

This study has several limitations. Cross-sectional designs are subject to unmeasured confounding factors, including lifestyle and genetic influences. Additionally, substantial heterogeneity persisted despite statistical adjustments. Addressing the relationship between sleep disorders and stroke risk requires multifaceted management strategies, along with future research focused on illustrating causal pathways and developing more effective interventions.

5. Conclusion

This systematic meta-analysis confirms that sleep disorders, particularly OSA and insomnia, are associated with a significantly increased risk of stroke. Subgroup analyses highlighted that these associations vary according to age, gender, geographic region, and stroke subtype. These findings are consistent with existing evidence and emphasize the importance of incorporating sleep-focused screening and interventions into clinical practice, as well as promoting public awareness campaigns and integrating basic sleep management programs into standard healthcare as a primary prevention strategy to reduce stroke incidence.

Nonetheless, the reliance on observational studies, residual confounding, and the high heterogeneity among included studies indicate areas for further investigation. Future research should employ larger, longitudinal designs to minimize confounding and better establish causal relationships. Additionally, more studies are needed to explore the impact of less-studied sleep disorders, such as restless legs syndrome and circadian rhythm disruptions, on stroke risk.

Compliance with Ethical Standards

Disclosure of Conflict of Interest

The authors declare that there are no conflicts of interest related to the research, authorship, or publication of this article. No financial or personal relationships influenced the study's design, execution, analysis, or interpretation. All authors confirm that they have no affiliations with organizations or entities that have a direct or indirect financial interest in the subject matter of this manuscript.

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