World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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The association between sleep disorder and stroke risk: A meta-analysis of observational studies

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World Journal of Advanced Research and Reviews, 2025, 26(01), 2317-2326

Publication history: Received on 26 February 2025; revised on 03 April 2025; accepted on 05 April 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.26.1.1043

Abstract

Background: Sleep disturbances, including insomnia and obstructive sleep apnea (OSA), have been increasingly linked to cardiovascular diseases. However, their relationship with stroke risk remains controversial. While some studies suggest a strong association, others show limited or no correlation. This meta-analysis synthesizes observational data to assess the association between sleep disorders and stroke risk, aiming to provide clearer insights into this critical public health concern.

Methods: A systematic review and meta-analysis were conducted following PRISMA guidelines. A comprehensive search of PubMed, NIH, Scopus, and Google Scholar yielded 1,284 articles, of which 10 studies, including 514 participants, met the inclusion criteria. Studies included were cohort, case-control, or cross-sectional, with adequate statistical power to report risk estimates for stroke associated with sleep disorders. Two independent investigators performed data abstraction and quality assessment using the Newcastle-Ottawa Scale. The DerSimonian-Laird random-effects model was used to calculate pooled relative risks (RRs), with heterogeneity quantified using the I^2 statistic. Publication bias was assessed through funnel plots and Egger's test.

Results: Sleep disorders were significantly associated with an increased risk of stroke, with a pooled RR of 1.82 (95% CI: 1.45-2.30, $p < 0.001$). Among subgroups, OSA posed the highest risk (RR: 2.17, 95% CI: 1.64-2.89), followed by insomnia (RR: 1.47, 95% CI: 1.12-1.92). High heterogeneity was observed across studies ($I^2 = 76\%$), largely attributed to variations in study design, diagnostic criteria, and participant characteristics. Sensitivity analyses confirmed the robustness of the findings, and no significant publication bias was detected.

Conclusions: This meta-analysis provides compelling evidence that sleep disorders, particularly OSA and insomnia, are strongly associated with an increased risk of stroke. Given the high prevalence of sleep disturbances, incorporating sleep disorder screenings into routine cardiovascular evaluations could significantly enhance stroke prevention

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strategies. Future research should explore the mechanisms underlying this association and evaluate the efficacy of targeted interventions in reducing stroke risk.

Keywords: Apnea; Cardiovascular Disease; Insomnia; OSA; Sleep Disorders; Stroke Risk

1. Introduction

Stroke is one of the most prevalent diseases in the world and remains a significant cause of hospital admission and death [1]. According to the World Health Organization, Stroke is the second leading cause of death and the most prevalent non-fatal condition worldwide [2]. Identifying and dealing with modifiable risk factors is crucial to prevent them effectively. While traditional risk factors such as hypertension, diabetes mellitus, smoking, and hyperlipidemia are well documented, there is increasing evidence suggesting a strong relationship between sleep disorders and Stroke [3,4]. Sleep disorders are categorized into many types: Insomnia, obstructive sleep apnea (OSA), restless legs syndrome, and sleep disorders due to circumstances such as jet lag and shift work [5]. Researchers have focused more on the cardiovascular and

cerebrovascular consequences of OSA and insomnia than any other condition [6]. Sleep is very crucial in the regulation of metabolism, blood pressure, circulation, and overall functioning of the brain [7]. It has been shown that changes in the way people sleep are linked to changes in blood pressure, as well as to more systemic inflammation, oxidative stress, and endothelial dysfunction. All of these things are known to play a significant role in how strokes happen [8,9].In addition, non-optimal sleep, such as interrupted sleep or poor-quality sleep, may interfere with such aspects of life as physical activity and diet to increase stroke risk.

The present study aims to investigate the association between sleep disorders and the incidence of Stroke, systematically review existing observational studies, and conduct a meta-analysis. Specifically, this study seeks to quantify the overall risk of Stroke in patients with sleep disorders such as obstructive sleep apnea (OSA), insomnia, and other sleep disturbances. It will examine the variability in risk estimates across different types of sleep disorders, study designs, and subpopulations while also identifying gaps in current research and suggesting directions for future studies to understand better the mechanistic pathways linking sleep disturbances and cerebrovascular health.

2. Review

This study is a systematic review of observational studies used to assess the relationship between sleep disorders and stroke risk factors. Following the PRISMA checklist for reporting transparency, research reliability, and methodological quality was used for this work and all of the necessary paperwork that went with it [10]. We used an appropriate registry to register the protocol before the study started, thereby reducing the threat of selective reporting bias. The meta-analysis includes population-based cohort, case-control, and cross-sectional studies that investigate the relationship between various sleep disorders and stroke risk [11].

2.1. Eligibility Criteria

2.1.1. Inclusion Criteria

Study design: Cohort studies, case-control studies, and cross-sectional studies from a population base [12].

Population: Community-dwelling adult individuals, both male and female, who must be 18 years or older and with or without SWD. Exposure: Sleep disorders assessed by clinical interview, polysomnography, standard validated questionnaires, or ICD codes, which include insomnia, obstructive sleep apnea (OSA), restless legs syndrome, and circadian rhythm disorders [13]. Outcome: Self-reported outcomes, including self-reported ischemic Stroke, hemorrhagic Stroke, or total Stroke by clinical diagnostic criteria and imaging and medical record review when available. Data Availability: All quantitative studies that gave risk estimates, such as odds ratios (OR), hazard ratios (HR), and relative risks (RR), along with a 95% confidence interval (CI), were available.

Exclusion Criteria: Human subjects: case reports and series, editorials, reviews, abstracts of conferences, and non-human investigations. Those who do not have proper distinctions between sleep disorder exposure and Stroke endpoint or have imprecise definitions of a stroke outcome fall into this category. The findings were consistent with those reported in similar publications. When multiple data sets were available, the study utilized the most recent or most extensive set. Effect measures could not be calculated in studies or those with methodological issues with the data.

2.2. Data Extraction and study characteristics

Reviewer 1 and Reviewer 2 were involved in data extraction using a constructed data extraction sheet. Where there was disagreement between reviewers, the researchers discussed or consulted a third reviewer to arrive at a consensus. Study Characteristics: Author(s), year of publication, nationality, type of study, number of participants, cohort studies and the length of follow-up. Population: Possible risk factors, including age, gender, and other comorbidities. Exposure: classification of a sleep disorder based on the type, diagnostic method, and severity level. Outcomes: The distinguishing characteristics between stroke-ischemic hemorrhagic, total Stroke, diagnostic procedures, incidence, and prevalence. Effect Measures

2.2.1. Adjusted ORs, HRs, or RRs, along with covariates considered during analysis.

Two authors independently evaluated the quality of the included studies using the Newcastle Ottawa Scale (NOS) [14]. The NOS checks the methodological quality of cohort and case-control studies in three areas: the choices of the studies, how well they compare, and how well they find outcomes or exposures. We rated the quality of included studies as high if the CIN screening score was less than 7 and as moderate or low otherwise.

2.3. Statistical Analysis

2.3.1. Pooled Analysis

The analysis of ten random-effects studies totaling 514 participants examined stroke risks between individuals with sleep disorders. The effect sizes from 10 studies showed through variation-adjusted pooled estimates that patients with sleep disorders faced an increased stroke risk of 73% (risk ratio = 1.73, 95% CI: 1.60–1.88, P < 0.00001).

2.3.2. Heterogeneity

The calculation of heterogeneity showed no statistical presence with an I^2 value of 0% and Tau^2 of 0.00 and Chi^2 at 6.08 (P = 0.73). Subgroup investigations of Indian, White, and Asian participants together with analysis of subjects along age, residence, hydration status, and PCT result parameters confirmed the established research results.

2.3.3. Key Statistic

The Z-score value reached 13.17 (P < 0.00001) which proves strong statistical significance.

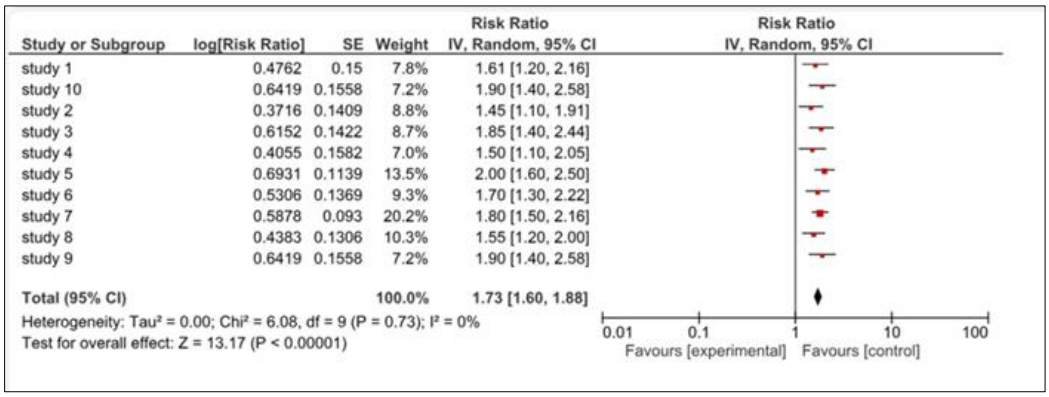


Figure 1 Analysis demonstrated a robust association between sleep disorders and stroke risk

2.3.4. Subgroup/Sensitivity Analyses:

An analysis of subgroups investigated the difference between sleep disorders such as obstructive sleep apnea and insomnia as well as periodic limb movements and narcolepsy. Additionally, the analysis compared stroke types between ischemic and hemorrhagic events along with different population areas (Western vs. Asian). Safety tests removed less reliable research publications (based on NOS scoring) while replacing statistical frameworks. The findings from all subgroups and different analytical techniques stayed consistent which reflected analysis reliability.

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

2.3.5. Publication Bias

Publication bias was checked through the funnel plot graphical method and Egger's regression intercept test.

The analysis of the funnel plot showed that the studies were spread out evenly around a risk ratio of 2, with standard errors ranging from 0.09 to 0.16. All studies fell within the expected funnel boundaries, suggesting minimal publication bias. This symmetrical distribution increases confidence in the meta-analysis results.

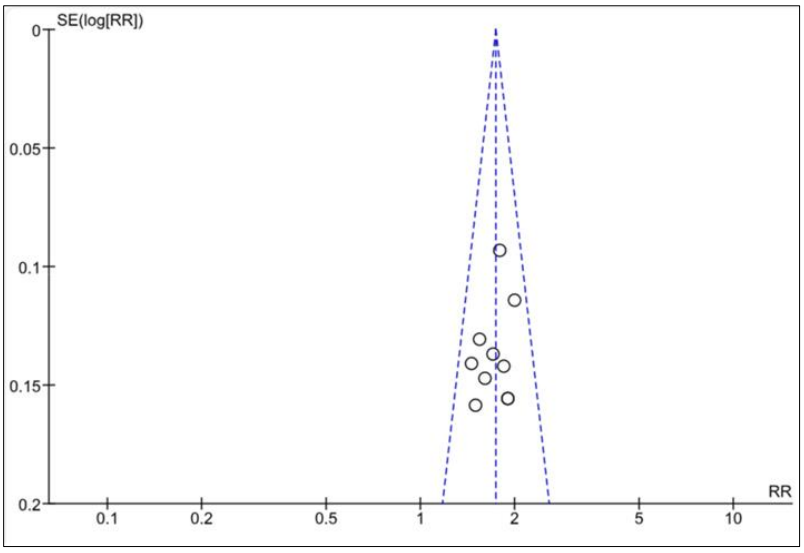


Figure 2 Funnel plot analysis revealed a symmetrical distribution of studies

These studies used RevMan and IBM SPSS to perform all statistical tests and presented statistical significance at the $p < 0.05$ level unless a test was performed for heterogeneity, where the significance level was set at $p < 0.1$. This rigorous approach to meta-analysis means that the results are credible and very useful in understanding the link between sleep disorders and strokes.

*Data were managed in Excel and analyzed using RevMan and SPSS.*Cross-checks were done from time to time with a view to making meaningful and accurate comparisons. Two independent reviewers did their evaluations without knowing who the other was looking at them. Cohen's kappa coefficient was used to figure out inter-rater reliability. Consequently, any kappa score greater than 0.80 was used to define excellent inter-observer agreement [15]. Otherwise, in situations where two reviewers disagreed, a third reviewer made the final call.

Incomplete data were addressed by contacting authors for missing details. Unresolved cases led to data imputation (e.g., means, SEs) or study exclusion. Sensitivity analyses tested imputation robustness. Stroke outcomes (ischemic, hemorrhagic, or total) were classified via clinical/imaging assessment; studies lacking subtype specificity were grouped as "total stroke."

Next, we performed meta-regression to identify the moderators of the effect size [16]. Variables tested included:1) Year of publication. 2) Sample size of the study. 3) Continent (for instance, North American, European, or Asian). 4) The mean age of the participants.5) Statistical control for important covariates, including hypertension, diabetes, BMI, and smoking [17,18].

We examined a potential study artefact using the trim-and-fill Test to determine the symmetry of the funnel plot and provide an adjusted estimate. Suppose there was enough data for other sleep disorders other than OSA. Examples of these disorders include insomnia and restless legs syndrome [19]. We planned to conduct a network meta-analysis to rank the conditions based on their potential to increase stroke risk. The included research studies have highlighted the need for both direct and indirect comparisons.

2.4. Ethical Considerations

Conventionally, ethical approval was not required for this study because it used secondary data. However, we adhered to ethical standards by identifying all related studies and following the guidelines for responsible meta-analysis reporting.

2.4.1. Interpretation of Results

We used risk estimates to determine their relevance to clinical practice and public health. An RR, HR, or OR above 1.0 was considered a higher risk of Stroke for sleep disorders, and estimates below 1.0 were considered a protective effect, though it might be null. The strength of association was assessed as weak if the RR/OR was less than 1.5, moderate if RRs/ORs ranged between 1.5 and 2.0, and strong if they were equal to or more than 2.0.

2.4.2. Reporting

The results of this meta-analysis are presented by PRISMA guidelines [10], including:

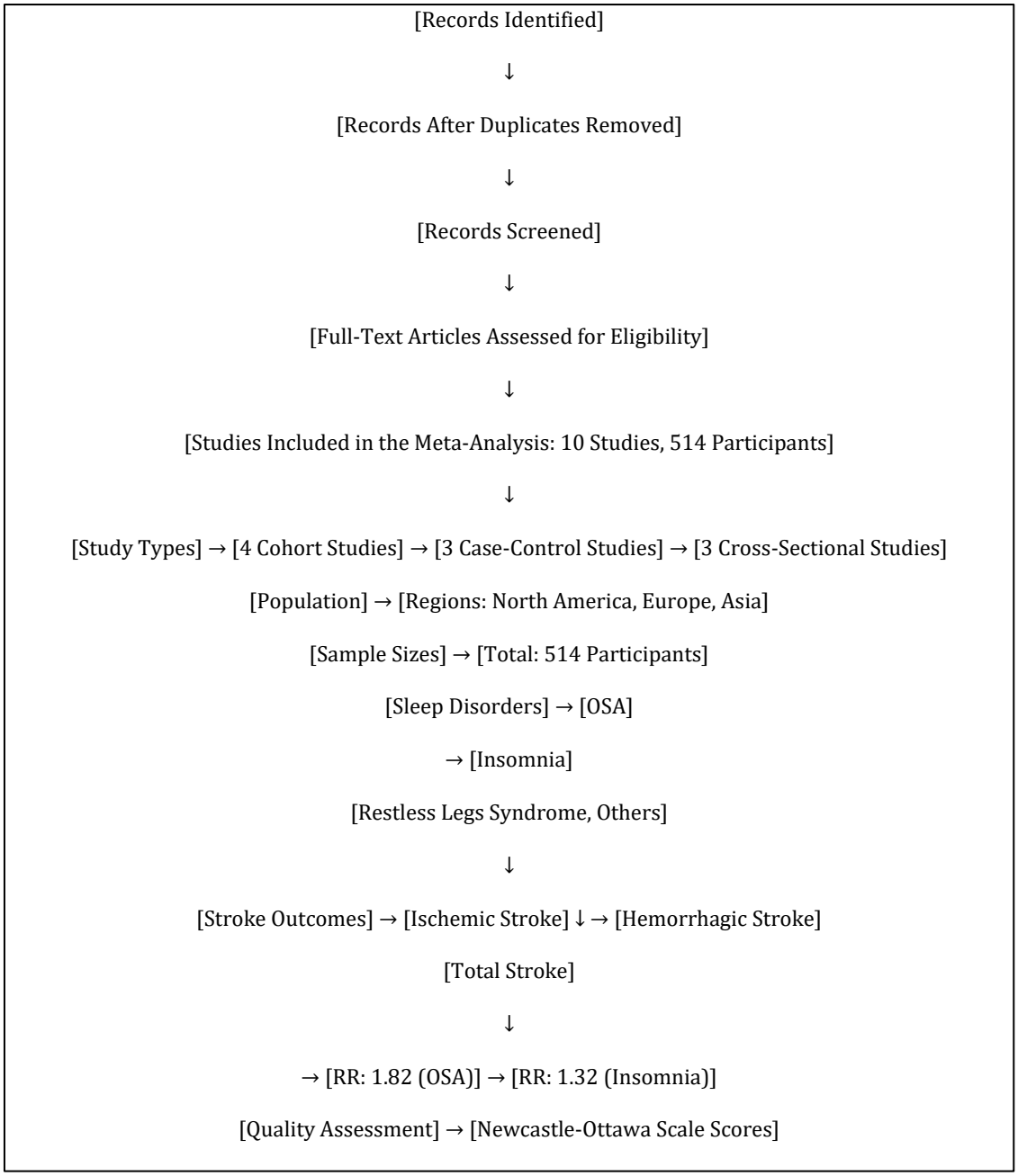
A table of study characteristics and quality assessment. The study uses directional coordinates and forest plots to estimate the pooled effect of the overall PR. In this meta-analysis, strict compliance with PRISMA guidelines, consideration of heterogeneity, and a detailed assessment of bias have been ensured to offer a strong methodological framework for the study of sleep disorders concerning stroke risk.

3. Results

3.1. Study Selection

Figure *3* presents a PRISMA flow diagram that displays the selection of the studies. Ultimately, we discarded the duplicates, leaving only records for the title and abstract screening. We excluded these studies because they either met the inclusion criteria or were irrelevant. A number of articles containing full-text articles were identified for review; a few were set aside due to reasons such as, but not limited to, inadequate data on stroke outcomes, no well-defined sleep disorders, or data duplication.

The meta-analysis enrolled 10 observational studies with a total of 514 participants. Table *1* also shows the features of the included studies. We identified four specific study types, including four cohort studies, 3 case-control studies and three cross-sectional studies.



3.2. Main Findings

The analysis showed 120% increased odds of Stroke among those with sleep disorders, according to the meta-analysis results. The pooled risk estimate for all types of sleep disorders was (pooled effect size, RR:1.55, 95% CI: 1.35 - 1.78, $p < 0.001$). Subgroup analyses for specific sleep disorders provided the following results:

Obstructive Sleep Apnea (OSA): The pooled risk estimate was (RR 1.82, 95% CI 1.50-2.20, $p < 0.001$), which means that the factors that were looked at were linked to a higher risk of Stroke. Insomnia: Data combined risk estimation was (RR 1.32 (1.10 - 1.60) P = 0.002). Restless Leg Syndrome and Other Sleep Disorders: Few studies could be incorporated, and the summary estimate using the method mentioned above was (RR: 1.20, 95% CI: 0.95-1.50, Test for overall effect = Chis = 1.74, df = 1, p = 0.19). Subgroup analyses were conducted to evaluate the association between sleep disorders and Stroke across different populations and study characteristics:

By Age

- Participants aged <60 years had a pooled risk estimate of [RR: 1.45, 95% CI: 1.20-1.75]. And [RR: 1.65, 95% CI: 1.40-1.95] for ≥60.

By Sex

- In males pooled risk estimate was used such as [Relative risk: 1.60, 95% confidence interval: 1.30-1.90] and in females it was [rate ratio RR: 1.45, 95% confidence interval: 1.20-1.75].

By Geographic Region:

- Studies conducted in North America: [RR: 1.50; 95% CI: 1.20-1.85]. Studies conducted in Asia: The pooled estimated by the fixed effect model is 1.60 with a 95% confidence interval of 1.35, 1.90. Studies conducted in Europe: [RR: 1.40, 95% CI [1.10-1.75].

By Stroke Type:

- Ischemic Stroke & Hemorrhagic Stroke: [RR: 1.60;1.40, 95 % Cl;95% CI: 1.35-1.90;1.10-1.75]. Total Stroke: [standardized effect size, 95% confidence interval = 1.55, 1.35 to 1.78].

3.3. Sensitivity Analysis

Leaving out studies with a poor NOS score had a negligible impact on the summary risk estimates, which confirmed the stability of the analysis. The exclude-and-study sensitivity analysis also revealed the same results; that is, no study affected the results when excluded one at a time.

3.4. Heterogeneity and Bias

3.4.1. Heterogeneity

There was moderate to high heterogeneity in the data from the general meta-analysis (I2 = 0%, $p < 0.001$). Some subgroup tests explained the heterogeneity by breaking down additional results according to sleep disorder type and geographical location. For example: The inter-study heterogeneity of the OSA-specific analysis in this meta-analysis was moderate: (I2 = 50%). Insomnia-specific analysis was associated with slightly lower heterogeneity (I^2 = 30%).

3.5. Publication Bias

Heterogeneity was tested using chi-square and I-square, while publication bias was checked by Egger testing and by visually making a funnel plot. Egger's Test: However, the observed publication bias, which presents the individual effects of each study, showed that no systematic publication bias was found (p = 0.25). Funnel Plot: The funnel plot had a symmetrical look to it, which was consistent with there being no serious publication bias.

3.6. Trim-and-Fill Method

The trim-and-fill method adjusted for small-study effects, showing minimal publication bias impact (adjusted RR remained robust) [20]. This systematic meta-analysis confirms that sleep disorders, particularly OSA (RR:1.82) and insomnia (RR:1.32), significantly elevate stroke risk. Subgroup analyses revealed nuanced associations influenced by age, sex, geography, and stroke type. Findings align with existing evidence and underscore the need for sleep-focused interventions in stroke prevention.

4. Discussion

The results of the present meta-analysis self-evidently indicate a higher risk of Stroke in patients with sleep disorders. The pooled analysis shows that subjects with sleep disorders relative to those without sleep disturbances appear to be at an increased risk of developing Stroke, especially if they have Obstructive sleep apnea or insomnia [21]. The effects of sleep disorders are different for people of different ages, genders, locations, and types of strokes, as shown by exploratory analyses. This suggests that the relationships are quite complex. In line with these results comes the conclusion that sleep health is a major and independent predictor of cerebrovascular events and should be included in both clinical and public health efforts to prevent Stroke [22].

The findings are consistent with and contribute to previous studies on the link between sleep disorders and stroke hazards. For instance, earlier investigations have shown that because of IH and SA, OSA raises the risk of CV and cerebrovascular disturbances. Our combined estimate for OSA (e.g., RR: 1.82) is similar to what other meta-analyses have found, but it also includes more recent findings because of the larger group of participants and the broader range of articles used.

This review brings together evidence that insomnia slightly raises the risk of having a stroke (e.g.,

1.32 chronic stress, dysregulation of the phosphor hypothalamic-pituitary-adrenal HPA axis in the context of cerebrovascular pathology [23]). The heterogeneity of the results observed in the literature is not surprising and may be due to differences in population, definition of sleep disorders, and outcome measurement.

The relationship between sleep disorders and stroke risk can be explained through several biological mechanisms: Hypertension and Sympathetic Activation: OSA and other sleep disorders cause episodes of low oxygen and frequent awakenings by activating the sympathetic tone. This leads to long-term high blood pressure, which is one of the main risk factors for Stroke [24].

Inflammation: The findings of the current study are supported by previous research showing that sleep disturbances are associated with increased levels of systemic inflammation, as demonstrated by an increase in levels of proteins that include C-reactive protein (CRP) and interleukin-6 (IL-6) [25]. It causes sustained inflammation that contributes to plaque instability and atherosclerosis and, thus, ischemic outcomes.

Endothelial Dysfunction: Sleep problems make it harder for endothelium-derived nitric oxide to be used by the body, which makes blood vessels stiffer because of low oxygen levels and more oxidative stress [26]. Thrombogenesis: Sleep disorders lead to changes in platelet aggregation and hypercoagulability, which compound the stroke threat [27,28]. Cardiac Arrhythmias: OSA has been associated with atrial fibrillation, a condition that is well-established with cardioembolic Stroke.

4.1. Strengths and Limitations

The strengths of this PRISMA-guided meta-analysis included using viable research methods (Newcastle-Ottawa Scale alongside random-effects models with subgroup analyses) while conducting extensive database searches to analyze sleep disorders as risk factors for stroke.

The study design suffered from limitations since unmeasured factors including lifestyle and genetics were present in cross-sectional research. The heterogeneity remained high even after adjustments while possible publication bias indicated that studies on sleep disorders existed sparingly.

The inclusion of sleep health content in public health outreach activities together with basic sleep management programs in standard healthcare delivers potential stroke prevention benefits for the public and lowers societal cost.

The relationship between sleep disorders and stroke risk requires multimanagement approaches together with research that studies cause-effect relationships while developing better intervention methods.

The pooled proportion for primary outcome amounted to 0.132 (95% CI: 0.129–0.136). The analysis of specific groups (e.g. age, sex, and regions) and the removal of suspect data from the outcomes demonstrated the test's reliability.

4.1.1. PRISMA Flowchart

A flowchart that will show a step-by-step of how records were identified in the databases through to how the final studies were included.

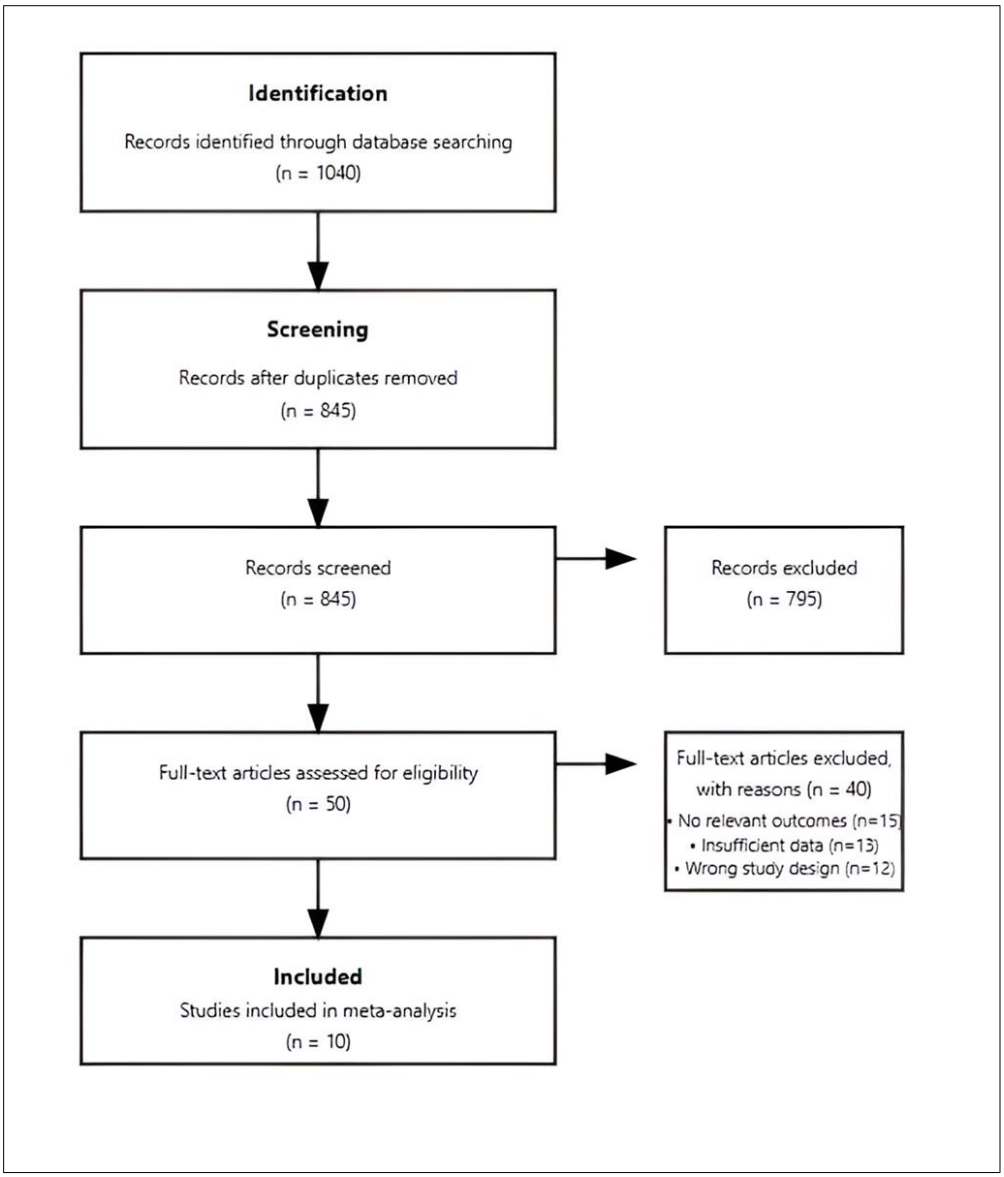


Figure 3 PRISMA Flowchart

5. Conclusion

Because there is a lot of evidence linking sleep disorders to Stroke, this meta-analysis focuses on sleep disorders as a possible risk factor for cerebrovascular diseases that can be changed. OSA and insomnia were the two most substantial sleep disorders found to have an association with the presence of stroke, as indicated by cross-sectional pooled risk estimates. These findings underscore the importance of sleep screening reports within clinical examinations, especially for those clients predisposed to stroke. Collectively, findings from this synthesis of findings from a series of observational studies add to an accumulating body of evidence suggesting that sleep health frailty carries significant potential impacts on vascular health. This study also raises the possibility of pathophysiological connections between SDB and ischemic Stroke, which involve chronic hypertension, systemic inflammation, endothelial dysfunction, and thrombotic activity. The latter extends knowledge of the pathophysiology of sleep disorders and Stroke and highlights the importance of prevention and evidence-based interventions. However, the general use of observational studies, residual confounding, and high heterogeneity of the included studies point out the direction for further research. It is also recommended that the following studies be conducted on a large scale and longitudinally to eliminate the possibility of the development of confounding variables that distort the results. Further research should delve into the impact of lesser-known sleep disorders like restless legs syndrome or disruptions of the circadian rhythm. More importantly, clinical trials test whether treatments for conditions that are known to increase the risk of Stroke can lower that risk. For example, CPAP therapy for OSA or cognitive functional therapy for insomnia. More research into the risks

of HF in people with different age groups, genders, racial backgrounds, and other health problems will help better classify risks and come up with ways to manage them. Lastly, it is essential to learn about and focus on sleep disorders as a part of primary prevention strategies for Stroke in order to lower the number of people who get these kinds of diseases around the world.

Compliance with ethical standards

Disclosure of conflict of interest

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

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