Access this article online

Quick Response Code:

Website: http://www.braincirculation.org

DOI: 10.4103/bc.bc_7_24

The link between sleep duration and stroke risk

Yu Cheng[1,2], Yuchuan Ding[3], Ahmed Elmadhoun[4], Xunming Ji[5], Xiaokun Geng[1,2,3]

Abstract:

In this review paper, we explore the complex relationship between sleep duration and stroke risk, outlining the association of both insufficient sleep and excessive sleep with an increased risk of cerebrovascular diseases. We explore a U-shaped relationship between sleep duration and cardiovascular outcomes, including stroke. Our review explores findings from cohort studies, meta-analyses, and Mendelian randomization studies, highlighting the nuanced findings and identifying gaps in the current literature. We discussed the direct and indirect effects of sleep duration on stroke risk, considering factors such as atherosclerosis, atrial fibrillation, hypertension, and hyperlipidemia. We also discuss the methodological challenges inherent in current studies, such as the reliance on self-reported sleep measures and the need for more objective and comprehensive assessments. The paper emphasizes the importance of recognizing individual variations in optimal sleep duration and the potential confounding effects of sleep quality and other sleep-related disorders on stroke risk. Furthermore, we explore the potential mechanisms by which sleep duration may influence endothelial function, oxidative stress, and vascular compliance, suggesting areas for future investigation. The paper makes a compelling case for the inclusion of sleep duration as a key factor in stroke prevention strategies, recommending that healthcare professionals proactively assess and manage sleep patterns to mitigate stroke risk.

Keywords:

Cardiovascular health and neurovascular integrity, excessive and insufficient sleep, Mendelian randomization studies, observational

[1]Luhe Institute of Neuroscience, Capital Medical University, [2]Department of Neurology, Beijing Luhe Hospital, Capital Medical University, [5]Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing, China, [3]Department of Neurosurgery, Wayne State University School of Medicine, [4]Department of Biomedical Engineering, Wayne State University, Detroit, MI, USA

Address for correspondence:
Prof. Xiaokun Geng, Department of Neurology, Beijing Luhe Hospital, Capital Medical University, No. 82, Xinhua South Road, Tongzhou District, Beijing 101149, China.
E-mail: xgeng@ccmu.edu.cn

Submission: 13-02-2024
Revised: 04-11-2024
Accepted: 08-11-2024
Published: 21-03-2025

Introduction

Sleep duration, defined as the total amount of time spent sleeping within a 24-h period, is a critical component of overall health and well-being. The generally recommended healthy range for sleep duration is approximately 7–8 h per night.[1] Deviations from this range, such as excessive sleep (more than 9 h) and insufficient sleep (<6 h), have been increasingly recognized as potential risk factors for various health conditions. Clinically, variations in sleep duration are linked with several disorders including insomnia, hypersomnia, psychiatric conditions, and obstructive sleep apnea (OSA) syndrome, each contributing differently to an individual's sleep patterns and quality.[2,3]

In recent years, a growing body of investigation has begun to reveal the complex relationships between sleep duration, its quality, and cardiovascular health, particularly focusing on the incidence and prognosis of stroke.[1,3-9] This association is of significant interest given the prevalence and severity of stroke as a major health issue worldwide.[10] Stroke, characterized by the interruption of blood supply to the brain, can lead to lasting neurological damage, disability, and even death.[11] The role of sleep in this context is complex, encompassing direct physiological impacts on the brain and indirect effects mediated through other systemic health conditions.[12]

This review paper aims to provide a comprehensive overview of the existing evidence on the critical role of sleep in neurovascular health, identify gaps in

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Cheng Y, Ding Y, Elmadhoun A, Ji X, Geng X. The link between sleep duration and stroke risk. Brain Circ 2025;11:1-8.

our current understanding, and suggest directions for future research that could lead to better prevention and treatment strategies for stroke.

Sleep Duration and the Occurrence of Stroke

Previously, researchers noted the effect of sleep duration on cardiovascular diseases. However, the relationship between sleep duration and the risk of cardiovascular diseases remains to be not fully understood and is under exploration up to the present.[13] More recent studies demonstrated that both excessive and insufficient sleep are associated with an increased risk of cerebrovascular diseases in patients.[3,4,7,8] A meta-analysis and a prospective study identified a U-shaped relationship between sleep duration and cardiovascular diseases,[4,8] with stroke being the most prevalent cerebrovascular disease. Current research on the link between sleep duration and stroke primarily involves cohort studies, meta-analyses, and Mendelian randomization studies [Figure 1].

Cohort studies demonstrate that both excessive and insufficient sleep durations increase the risk of stroke.[1,3,7] These studies did not only link sleep duration with the overall incidence of stroke but also indicated that there is the relationship with the stroke subtype. These studies indicated that longer sleep heightens the risk of overall stroke and ischemic stroke, whereas inadequate sleep elevates the risk of hemorrhagic stroke.[3] While these studies have clearly identified changes in sleep duration occurring before the onset of stroke, cohort studies have several limitations. Clinical cohort studies are susceptible to confounding factors that may skew the outcomes.[14] For instance, many experiments fail to assess for variables such as sleep quality or other sleep patterns, which can significantly impact the outcome.[3,7] Recent observational studies have indicated that besides sleep duration, other factors such as daytime napping, insomnia, OSA, and poor sleep quality are all associated with an increased risk of stroke.[1,15-17] These factors not only impact stroke incidence but also affect sleep duration. Insomnia and daytime napping can lead to shorter sleep durations, whereas OSA and poor sleep quality are associated with longer sleep durations. Therefore, without adequate control for these confounding factors, populations with longer sleep durations are likely to have more individuals with OSA and poor sleep quality, whereas populations with shorter sleep durations may have more individuals with insomnia and daytime napping. The presence of confounding factors may exaggerate the impact of sleep duration on stroke incidence.

Moreover, alterations in sleep durations might also stem from pre-existing chronic health issues or cerebrovascular pathologies, which in turn could heighten the likelihood of stroke. Besides confounding factors, clinical cohort studies are also challenged by various other limitations that can impact the reliability of their findings. The

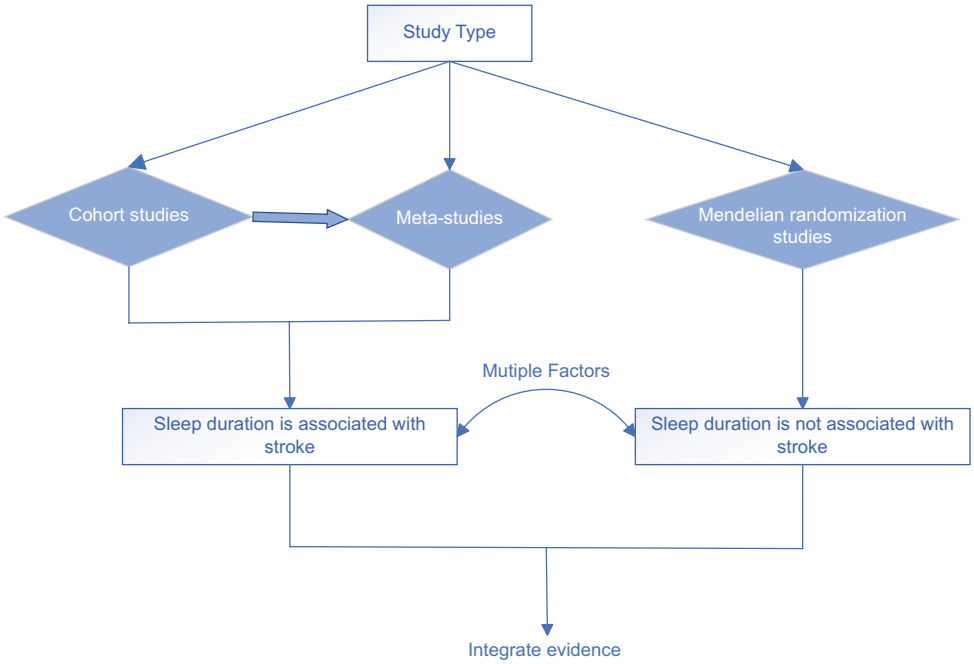

Figure 1: Research Methodologies and Outcomes in Stroke Studies. This diagram categorizes and compares different types of research methodologies: Cohort Studies, Meta-Analysis, and Mendelian Randomization Studies. It illustrates their findings on the association between sleep duration and stroke risk, highlighting studies where sleep duration is associated with stroke alongside those where no association was found. This visualization integrates evidence from multiple studies, factoring in various contributing elements to provide a comprehensive overview of the research landscape

majority of clinical studies lack standardized objective measurements for sleep duration and instead rely on data obtained through questionnaire surveys.[1,3,7] Self-reported sleep duration is often longer than objectively measured sleep duration and this trend is observed across different racial groups.[18,19] Self-reported sleep time is subjective and influenced by subjective feelings. Self-reporting suffers from issues such as recall bias, vague event definitions, background differences, and sleep disorders that may affect the assessment of sleep time.[20] To accurately assess sleep duration, an objective measurement of sleep time is needed. The most commonly used methods for evaluating objective sleep duration are polysomnography and actigraphy.[21] Furthermore, the majority of experiments did not examine natural short sleepers and long sleepers.[1,3,7] Due to individual differences, the assessment of sleep quantity should be based on the deviation from an individual's optimal sleep duration.[22]

Expanding on the findings from cohort studies, meta-analyses provide a broader perspective by including data from multiple studies. The results from these meta-analyses indicate how deviation from a standard 7-h nightly sleep duration, each hour increase or decrease in sleep significantly escalates the risk of stroke.[5,6] The meta-analysis similarly explored the influence of sleep duration on the occurrence of various subtypes of stroke; however, it arrived at a conclusion different from the cohort study.[2,3] The meta-analysis found that prolonged sleep duration increases the risk of hemorrhagic stroke, whereas insufficient sleep does not increase the risk of hemorrhagic stroke.[2] Meta-analyses offer more robust evidence than cohort studies by synthesizing data from multiple clinical investigations. This approach not only enhances the overall sample size, facilitating a more vigorous examination of the relationship between sleep duration and stroke but also standardizes the quality across studies, increasing the reliability of the findings. Despite these advantages over cohort studies, meta-analyses are not without limitations. The selection process may inadvertently exclude relevant studies, and these analyses are often vulnerable to various forms of bias – such as publication bias, time-lag bias, selective reporting bias, and language bias – which can skew the results and diminish the generalizability of the conclusions.[23]

Considering the limitations of cohort studies and meta-analysis, we explored another type of research studies. We reviewed Titova *et al*.'s Mendelian randomization study and Lu *et al*.'s Mendelian randomization study. Both studies found that there is no direct association between sleep duration and the occurrence of total stroke, as well as the occurrence of different subtypes of stroke.[3,24] In Lu *et al*.'s study, there is weak evidence suggesting that insufficient sleep increases the risk of cardioembolic stroke, whereas long sleep duration increases the risk of large artery stroke.[24] Conversely, in Titova *et al*.'s study, weak evidence suggests that shorter sleep duration increases the risk of large artery stroke.[3] In these Mendelian randomization study examining the relationship between sleep duration and cerebrovascular diseases, researchers chose genetic loci associated with sleep duration as the exposure factor to explore its relationship with stroke incidence. The process of genotype formation follows Mendel's second law of independent assortment of alleles, like the random allocation principle of a randomized controlled trial.[14] Therefore, Mendelian randomization studies not only can establish causal relationships but also can reduce the influence of confounding factors. However, the conclusions from Mendel's randomized study and observational study are inconsistent. Inconsistencies between Mendelian randomization studies and observational study results may indicate that the influence of sleep duration on stroke occurrence is determined by multiple factors. Mendelian randomization studies, while powerful, come with fundamental limitations. One significant restriction is the limited availability of single nucleotide polymorphisms, especially those linked to long sleep duration.[3,24] In addition, these studies often grapple with small sample sizes, which is particularly problematic in research involving hemorrhagic stroke samples.[3,24] These limitations can affect the robustness and generalizability of the findings. Studies have revealed that both excessively long and excessively short sleep durations are associated with an increased risk of stroke mortality.[2,25,26] Consequently, managing and regulating sleep duration could potentially enhance stroke prognosis.

Sleep Duration on Other Brain Pathology

Beyond its influence on stroke, sleep may also impact various other brain diseases, including Alzheimer's disease (AD), Parkinson's disease (PD), and cerebral small vessel disease.[27-29] The pathological hallmark of PD is the deposition of α-synuclein protein within neurons, resulting in neuronal death.[30] Reduced levels of misfolded alpha-synuclein (cerebrospinal fluid [CSF] α-syn) have been found in the CSF of PD patients.[31] Both excessively long and excessively short sleep durations can decrease CSF α-syn.[29] AD is pathologically characterized by the deposition of Aβ and tau proteins in the brain, where β-amyloid aggregates form extracellular plaques and tau proteins form neurofibrillary tangles within neurons.[32,33] In patients with AD, an increase in tau protein has been observed in CSF.[34] Short sleep duration increases tau protein in CSF.[35] As a result, monitoring and intervening in sleep duration could serve

as a practical and effective approach to prevent not only stroke but also other related diseases concurrently.

Mechanistic Studies on How Sleep Duration Affects Brain Pathology

While current exploration of the relationship between sleep and stroke incidence and prognosis remains at the level of correlation, a few studies delved into the mechanism underlying this relationship. Insufficient sleep not only directly affects stroke by altering cerebral blood vessels and blood flow, but it also indirectly influences stroke by increasing the incidence of atrial fibrillation, hypertension, hyperlipidemia, and hyperglycemia[36-41] [Figure 2].

Current studies suggest that insufficient sleep may lead to endothelial inflammation and oxidative stress, potentially resulting in endothelial procoagulant state and reduced production and bioavailability of nitric oxide (NO).[41-43] NO plays a crucial role in endothelial normal function, and insufficient sleep can impair NO-mediated vasodilation, leading to decreased vascular compliance.[40,44] Prolonged sleep deprivation can push the vascular system to a critical level, impairing functions like blood flow delivery.[45]

Besides sleep duration, sleep patterns can also lead to endothelial dysfunction or vascular structural damage.[41] However, the specific pathways through which sleep leads to endothelial and vascular dysfunction require further examination. In addition to the direct impact of sleep duration on stroke, insufficient sleep increases the incidence of atrial fibrillation, hypertension, hyperlipidemia, and hyperglycemia,[36-39] which may indirectly affect stroke incidents. Previous studies have demonstrated that atrial fibrillation, hypertension, hyperlipidemia, and hyperglycemia all elevate the risk of stroke.[39,46-50] Therefore, atrial fibrillation, hypertension, hyperlipidemia, and hyperglycemia may serve as intermediate factors mediating the influence of sleep duration on the incidence of stroke. Basic research examining the relationship between sleep duration and brain health has primarily concentrated on the effects of sleep deprivation and restriction.[42,51,52] However, there is a notable lack of studies exploring how prolonged sleep duration impacts brain function. Currently, animal studies on sleep duration and stroke face a significant challenge in establishing a mouse model for long sleep duration. This is due to challenges in identifying a simple and feasible external stimulus to increase the sleep duration of mice. Sleep deprivation, as a stressor, can induce physiological and psychological stress responses, thereby influencing the exploration of the relationship between sleep duration and stroke incidence.[53,54] Sleep deprivation is often caused by external stimuli, which can induce exogenous stress in mice. Physiological stress activates the hypothalamic–pituitary–adrenal axis, leading to increased secretion of cortisol.[55] Cortisol is a major stress hormone. Besides cortisol, during the stress process, levels of other hormones such as vasopressin, catecholamines, and aldosterone also increase.[55] The action of multiple hormones during stress responses leads to elevated blood sugar and blood pressure, increased coagulation, and compromised immunity in mice, all of which may increase the risk of stroke occurrence.[47,48,56]

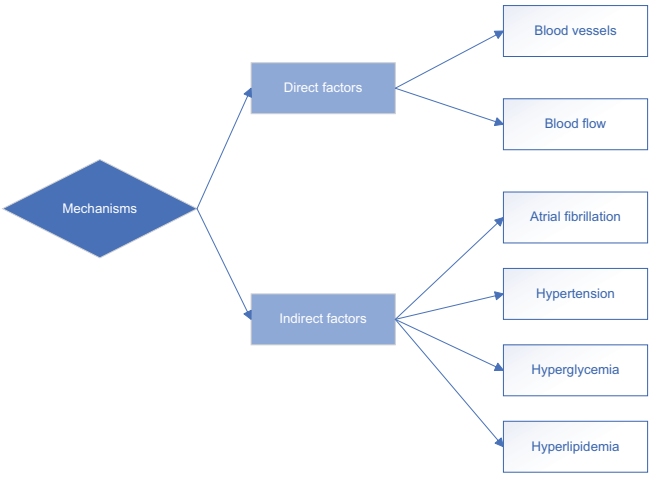

Figure 2: Mechanisms of Stroke-Related Complications. This flowchart delineates the direct and indirect pathways through which conditions such as hyperlipidemia, hyperglycemia, hypertension, and atrial fibrillation impact blood vessels and blood follow, contributing to the pathogenesis of stroke-related complications

In addition, sleep deprivation alters the homeostasis of sleep, causing psychological stress when mice cannot obtain sufficient sleep. Studies have shown that increased psychological stress can raise the risk of stroke.[54,57] Therefore, stress-induced responses can act as confounding factors when investigating the impact of sleep deprivation on stroke incidence. The physiological and psychological stress responses triggered by sleep deprivation may amplify the relationship between sleep duration and stroke incidence. Sleep regulation primarily relies on the activation and inhibition of sleep-active neurons.[58] To eliminate interference from external factors, sleep-active neuron activity can be modulated.[59] This modulation can be achieved through chemogenetics and optogenetics activation.[59,60] For example, modulating the activity of A2AR neurons in the nucleus accumbens through chemical genetics and optogenetics regulates sleep in mice.[60]

Regulation of sleep duration can also be manipulated genetically. The LKB1-SIK3-HDAC4-CREB pathway in neurons is known to modulate sleep duration.[61] Studies have shown that knocking out genes such as LKB1 or HDAC4 can lead to reduced sleep duration.[61] However, given the complexity of brain neural circuits, further

research is necessary to ascertain whether activating or inhibiting these neural circuits affects the production of stress hormones or influences the risk of stroke.

Additional Sleep-related Factors Impacting Stroke Risk

Not only does sleep duration affect the incidence of stroke but also sleep quality and sleep patterns can influence the occurrence rate of stroke. Recent observational studies have indicated that daytime napping, insomnia, OSA, and poor sleep quality are all associated with an increased risk of stroke.[1,15-17] Research has found that a healthy sleep pattern can reduce the incidence of stroke.[62,63] Furthermore, there may be mutual influences between sleep duration, sleep quality, and sleep patterns to increase stroke incidence.[7,64] The quality and pattern of sleep not only impact the occurrence of stroke but also have effects on AD and PD.[29,65,66] Research indicates that poor sleep quality and daytime sleepiness can lead to an increase in tau protein in CSF.[66] Daytime sleepiness, poor sleep quality, as well as both excessively long or short sleep durations, can result in a decrease in α-synuclein in the CSF.[29,65]

It is essential to comprehensively evaluate sleep duration, other sleep patterns, and sleep quality. Sleep assessment should undergo comprehensive evaluation from multiple perspectives. Currently, there are several sleep assessment questionnaires, including the Pittsburgh Sleep Quality Index for assessing sleep quality,[67] the Berlin Questionnaire and the STOP questionnaire for assessing OSA,[68] the Athens Insomnia Scale for assessing insomnia,[69] and the Epworth Sleepiness Scale for assessing excessive daytime sleepiness (EDS).[70] However, these questionnaires alone cannot comprehensively evaluate multiple sleep patterns and sleep quality. Recently, a Healthy Sleep Score has been proposed, which comprehensively considers factors such as sleep duration, insomnia, chronotype, snoring, and daytime sleepiness.[71] Aboubakari Nambiema researched the influence of the Healthy Sleep Score on stroke occurrence and found that higher scores and improvements in sleep scores were associated with a decreased incidence of stroke.[62]

Notably, epidemiological studies demonstrating that poor sleep is a risk factor for stroke are insufficient. In clinical practice, more objective evidence is needed to prove that sleep duration, sleep quality, and sleep patterns are risk factors for stroke. Researchers can also integrate neuroimaging, biochemical, and other relevant examinations to further elucidate the impact of sleep on stroke. White matter hyperintensities (WMHs) and fractional anisotropy (FA) are neuroimaging biomarkers of brain health.[72] Higher WMH and lower FA are both associated with increased stroke risk.[73,74] Both excessively long and short sleep durations are associated with WMHs and decreased FA values.[75,76] Not only is sleep duration associated with WMH but also poor sleep quality, delayed sleep onset, EDS, and snoring are also detrimental to white matter microstructure.[77] Neuroimaging biomarkers precede stroke occurrence and serve as strong predictors of stroke. Therefore, combining sleep assessment with neuroimaging may facilitate clinical practitioners in identifying brain abnormalities.

Perspective and Prospective

Current research on sleep duration remains insufficient. Although numerous clinical studies suggest that both excessively long and short sleep durations are associated with an increased risk of stroke, existing research often relies on self-reported sleep duration, lacking standardized and objective methods of measurement. Future research could assess the impact of objectively measured sleep duration on stroke occurrence and compare it with the effects of self-reported sleep duration on stroke incidence. In addition, it is critical for observational studies to control for confounding factors.

In addition to paying attention to the content and design of clinical research, it is also necessary to consider the strengths and limitations of different study designs. Both cohort studies and Mendelian randomization studies offer valuable insights but both have their strengths and limitations. Therefore, it is essential to integrate evidence from diverse study designs rather than solely relying on one type of study to infer the causal relationship between sleep duration and stroke incidence. Furthermore, while observational studies to explain the relationship between sleep duration and stroke incidence are insufficient, neuroimaging may be used to provide auxiliary evidence. In addition, sleep assessment should not be limited to sleep duration alone but should also consider factors such as sleep quality and other sleep patterns for comprehensive evaluation [Figure 3].

Given the established link between sleep duration and the incidence of stroke, clinical practitioners should pay attention to sleep duration, sleep quality, and sleep patterns. This approach will help in the assessment and potential reduction of stroke risk.

Author contributions

Yu Cheng: Writing - original draft; Yuchuan Ding: Writing - review and editing; Ahmed Elmadhoun: Writing - review and editing; Xunming Ji: Writing - review and editing; Xiaokun Geng: Writing - review and editing, Project administration.

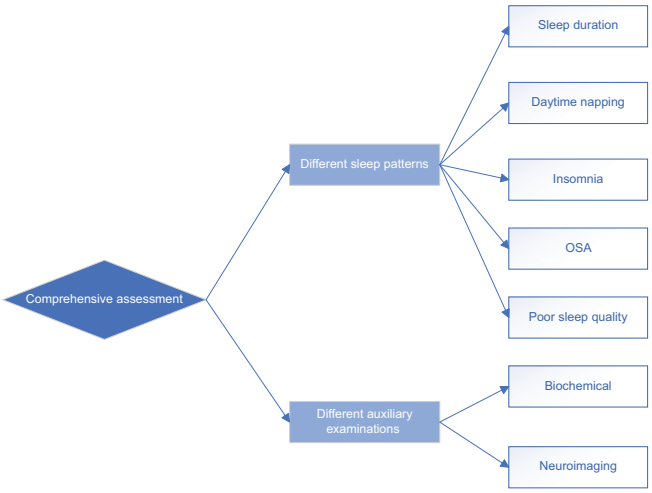

Figure 3: Comprehensive Assessment of Sleep Disorders. This diagram illustrates the various aspects of evaluating sleep disorders, including insomnia, obstructive sleep apnea, and other sleep-duration issues. It details different sleep patterns and the auxiliary examinations used in diagnosis, such as biochemical tests and neuroimaging. The figure highlights the interconnected nature of these assessments in identifying and addressing poor sleep quality. OSA: Obstructive sleep apnea

Ethical policy and institutional review board statement

Not applicable.

Data availability statement

Data sharing is not applicable to this article as no datasets were generated and/or analyzed during the current study.

Financial support and sponsorship

This work was partially supported by the Tongzhou Yunhe Talent Project (2024) and the Beijing Tongzhou District Financial Fund (2024).

Conflicts of interest

Xunming Ji is the Editor-in-Chief, Yuchuan Ding is an Associate Editor-in-Chief, Xiaokun Geng is the Executive Editor-in-Chief of *Brain Circulation*. The article was subject to the journal's standard procedures, with peer review handled independently of them and their research groups.

References

1. Zhou L, Yu K, Yang L, Wang H, Xiao Y, Qiu G, *et al*. Sleep duration, midday napping, and sleep quality and incident stroke: The Dongfeng-Tongji cohort. Neurology 2020;94:e345-56.
2. Wang H, Sun J, Sun M, Liu N, Wang M. Relationship of sleep duration with the risk of stroke incidence and stroke mortality: An updated systematic review and dose-response meta-analysis of prospective cohort studies. Sleep Med 2022;90:267-78.
3. Titova OE, Michaëlsson K, Larsson SC. Sleep duration and stroke: Prospective cohort study and Mendelian randomization analysis. Stroke 2020;51:3279-85.
4. Huang YM, Xia W, Ge YJ, Hou JH, Tan L, Xu W, *et al*. Sleep duration and risk of cardio-cerebrovascular disease: A dose-response meta-analysis of cohort studies comprising 3.8 million participants. Front Cardiovasc Med 2022;9:907990.
5. Li W, Wang D, Cao S, Yin X, Gong Y, Gan Y, *et al*. Sleep duration and risk of stroke events and stroke mortality: A systematic review and meta-analysis of prospective cohort studies. Int J Cardiol 2016;223:870-6.
6. He Q, Sun H, Wu X, Zhang P, Dai H, Ai C, *et al*. Sleep duration and risk of stroke: A dose-response meta-analysis of prospective cohort studies. Sleep Med 2017;32:66-74.
7. Ji A, Lou H, Lou P, Xu C, Zhang P, Qiao C, *et al*. Interactive effect of sleep duration and sleep quality on risk of stroke: An 8-year follow-up study in China. Sci Rep 2020;10:8690.
8. Chen Y, Kartsonaki C, Clarke R, Guo Y, Du H, Yu C, *et al*. Sleep duration and risk of stroke and coronary heart disease: A 9-year community-based prospective study of 0.5 million Chinese adults. BMC Neurol 2023;23:327.
9. Kwok CS, Kontopantelis E, Kuligowski G, Gray M, Muhyaldeen A, Gale CP, *et al*. Self-reported sleep duration and quality and cardiovascular disease and mortality: A Dose-response meta-analysis. J Am Heart Assoc 2018;7:e008552.
10. Lin X, Wang H, Huang S, Chen L, Yang S, Zhao P, *et al*. A reliable nonhuman primate model of ischemic stroke with reproducible infarct size and long-term sensorimotor deficits. Aging Dis 2023;14:245-55.
11. Eren F, Yilmaz SE. Neuroprotective approach in acute ischemic stroke: A systematic review of clinical and experimental studies. Brain Circ 2022;8:172-9.
12. Lo YJ, Mishra VK, Lo HY, Dubey NK, Lo WC. Clinical spectrum and trajectory of innovative therapeutic interventions for insomnia: A perspective. Aging Dis 2023;14:1038-69.
13. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: A systematic review and meta-analysis of prospective studies. Eur Heart J 2011;32:1484-92.
14. Larsson SC, Butterworth AS, Burgess S. Mendelian randomization for cardiovascular diseases: Principles and applications. Eur Heart J 2023;44:4913-24.
15. Mc Carthy CE, Yusuf S, Judge C, Alvarez-Iglesias A, Hankey GJ, Oveisgharan S, *et al*. Sleep patterns and the risk of acute stroke: Results from the interstroke international case-control study. Neurology 2023;100:e2191-203.
16. Guo C, Harshfield EL, Markus HS. Sleep characteristics and risk of stroke and dementia: An observational and Mendelian randomization study. Neurology 2024;102:e209141.
17. Xie C, Zhu R, Tian Y, Wang K. Association of obstructive sleep apnoea with the risk of vascular outcomes and all-cause mortality: A meta-analysis. BMJ Open 2017;7:e013983.
18. Cespedes EM, Hu FB, Redline S, Rosner B, Alcantara C, Cai J, *et al*. Comparison of self-reported sleep duration with actigraphy: Results from the hispanic community health study/study of latinos sueño ancillary study. Am J Epidemiol 2016;183:561-73.
19. Jackson CL, Patel SR, Jackson WB 2nd, Lutsey PL, Redline S. Agreement between self-reported and objectively measured sleep duration among white, black, Hispanic, and Chinese adults in the United States: Multi-ethnic study of atherosclerosis. Sleep 2018;41:zsy057.
20. Robbins R, Quan SF, Barger LK, Czeisler CA, Fray-Witzer M, Weaver MD, *et al*. Self-reported sleep duration and timing: A methodological review of event definitions, context, and timeframe of related questions. Sleep Epidemiol 2021;1:100016.
21. Lehrer HM, Yao Z, Krafty RT, Evans MA, Buysse DJ, Kravitz HM, *et al*. Comparing polysomnography, actigraphy, and sleep diary in the home environment: The Study of Women's Health Across the Nation (SWAN) sleep study. Sleep Adv 2022;3:zpac001.
22. Kohyama J. Which is more important for health: Sleep quantity

or sleep quality? Children (Basel) 2021;8:542.
23. Haidich AB. Meta-analysis in medical research. Hippokratia 2010;14:29-37.
24. Lu H, Wu PF, Li RZ, Zhang W, Huang G×. Sleep duration and stroke: A Mendelian randomization study. Front Neurol 2020;11:976.
25. Zhou B, Jiang C, Zhang W, Jin Y, Zhu T, Zhu F, *et al*. Association of sleep duration and napping with stroke mortality in older Chinese: A 14-year prospective cohort study of the Guangzhou biobank cohort study. Sleep Med 2023;101:384-91.
26. Kawachi T, Wada K, Nakamura K, Tsuji M, Tamura T, Konishi K, *et al*. Sleep duration and the risk of mortality from stroke in Japan: The Takayama cohort study. J Epidemiol 2016;26:123-30.
27. Shi L, Chen SJ, Ma MY, Bao YP, Han Y, Wang YM, *et al*. Sleep disturbances increase the risk of dementia: A systematic review and meta-analysis. Sleep Med Rev 2018;40:4-16.
28. Wang J, Chen X, Men X, Chen M, Tao J, Lu Z. Chronic insomnia is associated with higher circulating interleukin-8 in patients with atherosclerotic cerebral small vessel disease. Nat Sci Sleep 2020;12:93-9.
29. Wang XT, Liu FT, Bi YL, Shen XN, Xu W, Wang J, *et al*. Associations of sleep characteristics with alpha-synuclein in cerebrospinal fluid in older adults. Ann Clin Transl Neurol 2020;7:2026-34.
30. Dickson DW. Neuropathology of Parkinson disease. Parkinsonism Relat Disord 2018;46 Suppl 1:S30-3.
31. Nedelska Z, Ferman TJ, Boeve BF, Przybelski SA, Lesnick TG, Murray ME, *et al*. Pattern of brain atrophy rates in autopsy-confirmed dementia with Lewy bodies. Neurobiol Aging 2015;36:452-61.
32. Lane CA, Hardy J, Schott JM. Alzheimer's disease. Eur J Neurol 2018;25:59-70.
33. Kanuri SH, Sirrkay PJ. Profiling of microglial-originated microvesicles to unearthing their lurking potential as potent foreseeable biomarkers for the diagnosis of Alzheimer's disease: A systematic review. Brain Circ 2024;10:193-204.
34. Tapiola T, Alafuzoff I, Herukka SK, Parkkinen L, Hartikainen P, Soininen H, *et al*. Cerebrospinal fluid {beta}-amyloid 42 and tau proteins as biomarkers of Alzheimer-type pathologic changes in the brain. Arch Neurol 2009;66:382-9.
35. López-García S, Lage C, Pozueta A, García-Martínez M, Kazimierczak M, Fernández-Rodríguez A, *et al*. Sleep time estimated by an actigraphy watch correlates with CSF tau in cognitively unimpaired elders: The modulatory role of APOE. Front Aging Neurosci 2021;13:663446.
36. Lee DY, Jung I, Park SY, Yu JH, Seo JA, Kim KJ, *et al*. Sleep duration and the risk of type 2 diabetes: A community-based cohort study with a 16-year follow-up. Endocrinol Metab (Seoul) 2023;38:146-55.
37. Zhao J, Yang F, Zhuo C, Wang Q, Qu Z, Wang Q, *et al*. Association of sleep duration with atrial fibrillation and heart failure: A Mendelian randomization analysis. Front Genet 2021;12:583658.
38. He J, He Q. Association between sleep duration and hypertension among adults in Southwest China. Glob Heart 2022;17:10.
39. Abreu Gde A, Barufaldi LA, Bloch KV, Szklo M. A systematic review on sleep duration and dyslipidemia in adolescents: Understanding inconsistencies. Arq Bras Cardiol 2015;105:418-25.
40. Bain AR, Weil BR, Diehl KJ, Greiner JJ, Stauffer BL, DeSouza CA. Insufficient sleep is associated with impaired nitric oxide-mediated endothelium-dependent vasodilation. Atherosclerosis 2017;265:41-6.
41. Shah R, Shah VK, Emin M, Gao S, Sampogna RV, Aggarwal B, *et al*. Mild sleep restriction increases endothelial oxidative stress in female persons. Sci Rep 2023;13:15360.
42. Li X, Cao Y, Xu X, Wang C, Ni Q, Lv X, *et al*. Sleep deprivation promotes endothelial inflammation and atherogenesis by reducing exosomal miR-182-5p. Arterioscler Thromb Vasc Biol 2023;43:995-1014.
43. Janaszak-Jasiecka A, Siekierzycka A, Płoska A, Dobrucki IT, Kalinowski L. Endothelial dysfunction driven by hypoxia-the influence of oxygen deficiency on no bioavailability. Biomolecules 2021;11:982.
44. Cai Z, Wu C, Xu Y, Cai J, Zhao M, Zu L. The NO-cGMP-PKG Axis in HFpEF: From pathological mechanisms to potential therapies. Aging Dis 2023;14:46-62.
45. Bir SC, Kelley RE. Carotid atherosclerotic disease: A systematic review of pathogenesis and management. Brain Circ 2022;8:127-36.
46. Alshehri AM. Stroke in atrial fibrillation: Review of risk stratification and preventive therapy. J Family Community Med 2019;26:92-7.
47. Misgana S, Asemahagn MA, Atnafu DD, Anagaw TF. Incidence of stroke and its predictors among hypertensive patients in Felege Hiwot comprehensive specialized hospital, Bahir Dar, Ethiopia, a retrospective follow-up study. Eur J Med Res 2023;28:227.
48. Zhang Y, Gu S, Wang C, Liu D, Zhang Q, Yang M, *et al*. Association between fasting blood glucose levels and stroke events: A large-scale community-based cohort study from China. BMJ Open 2021;11:e050234.
49. Zhang w, LI Y, pang M, yue X. Causal relationship between hypertension and ischemic stroke: A two-sample Mendelian randomization study [J]. Brain Circ 2024;10:257-64.
50. Kasturiarachi BM, Saeed O, Gachechiladze L, Alsbrook D, Singh S, Zaid G, *et al*. The effects of stress hyperglycemia in diabetic and nondiabetic patients with large vessel occlusions undergoing mechanical thrombectomy. Brain Circ 2024;10:162-7.
51. Jiang J, Gan Z, Li Y, Zhao W, Li H, Zheng JP, *et al*. REM sleep deprivation induces endothelial dysfunction and hypertension in middle-aged rats: Roles of the eNOS/NO/cGMP pathway and supplementation with L-arginine. PLoS One 2017;12:e0182746.
52. Kristofikova Z, Sirova J, Klaschka J, Ovsepian SV. Acute and chronic sleep deprivation-related changes in n-methyl-d-aspartate receptor-nitric oxide signalling in the rat cerebral cortex with reference to aging and brain lateralization. Int J Mol Sci 2019;20:3273.
53. Nollet M, Wisden W, Franks NP. Sleep deprivation and stress: A reciprocal relationship. Interface Focus 2020;10:20190092.
54. Fayyaz AI, Ding Y. Mental stress, meditation, and yoga in cardiovascular and cerebrovascular diseases. Brain Circ 2023;9:1-2.
55. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, *et al*. Regulation of the hypothalamic-pituitary-adrenocortical stress response. Compr Physiol 2016;6:603-21.
56. Coelho MC, Santos CV, Vieira Neto L, Gadelha MR. Adverse effects of glucocorticoids: Coagulopathy. Eur J Endocrinol 2015;173:M11-21.
57. Reddin C, Murphy R, Hankey GJ, Judge C, Xavier D, Rosengren A, *et al*. Association of psychosocial stress with risk of acute stroke. JAMA Netw Open 2022;5:e2244836.
58. Bringmann H. Sleep-active neurons: Conserved motors of sleep. Genetics 2018;208:1279-89.
59. Bringmann H. Genetic sleep deprivation: Using sleep mutants to study sleep functions. EMBO Rep 2019;20:e46807.
60. Oishi Y, Xu Q, Wang L, Zhang BJ, Takahashi K, Takata Y, *et al*. Slow-wave sleep is controlled by a subset of nucleus accumbens core neurons in mice. Nat Commun 2017;8:734.
61. Zhou R, Wang G, Li Q, Meng F, Liu C, Gan R, *et al*. A signalling pathway for transcriptional regulation of sleep amount in mice. Nature 2022;612:519-27.
62. Nambiema A, Lisan Q, Vaucher J, Perier MC, Boutouyrie P, Danchin N, *et al*. Healthy sleep score changes and incident cardiovascular disease in European prospective community-based cohorts. Eur Heart J 2023;44:4968-78.
63. Fan M, Sun D, Zhou T, Heianza Y, Lv J, Li L, *et al*. Sleep patterns, genetic susceptibility, and incident cardiovascular disease: A prospective study of 385 292 UK biobank participants. Eur Heart J 2020;41:1182-9.
64. Li X, Pang X, Liu Z, Zhang Q, Sun C, Yang J, *et al*. Joint effect of

less than 1 h of daytime napping and seven to 8 h of night sleep on the risk of stroke. Sleep Med 2018;52:180-7.

65. Wang XT, Yu H, Liu FT, Zhang C, Ma YH, Wang J, *et al*. Associations of sleep disorders with cerebrospinal fluid α-synuclein in prodromal and early Parkinson's disease. J Neurol 2022;269:2469-78.
66. Sprecher KE, Koscik RL, Carlsson CM, Zetterberg H, Blennow K, Okonkwo OC, *et al*. Poor sleep is associated with CSF biomarkers of amyloid pathology in cognitively normal adults. Neurology 2017;89:445-53.
67. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
68. Solecka Š, Matler K, Kostlivý T, Kubec V, Tomášková H, Betka J. A comparison of the reliability of five sleep questionnaires for the detection of obstructive sleep apnea. Life (Basel) 2022;12:1416.
69. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens insomnia scale: Validation of an instrument based on ICD-10 criteria. J Psychosom Res 2000;48:555-60.
70. Goncalves MT, Malafaia S, Moutinho Dos Santos J, Roth T, Marques DR. Epworth sleepiness scale: A meta-analytic study on the internal consistency. Sleep Med 2023;109:261-9.
71. Wang Z, Yang W, Li X, Qi X, Pan KY, Xu W. Association of Sleep Duration, Napping, and Sleep Patterns With Risk of Cardiovascular Diseases: A Nationwide Twin Study. J Am Heart Assoc 2022;11:e025969.
72. Alhazmi FH, Alsharif WM, Alshoabi SA, Gameraddin M, Aloufi KM, Abdulaal OM, *et al*. Identifying cerebral microstructural changes in patients with COVID-19 using MRI: A systematic review. Brain Circ 2023;9:6-15.
73. Debette S, Markus HS. The clinical importance of white matter hyperintensities on brain magnetic resonance imaging: Systematic review and meta-analysis. BMJ 2010;341:c3666.
74. Evans TE, O'sullivan MJ, DE Groot M, Niessen WJ, Hofman A, Krestin GP, *et al*. White Matter Microstructure Improves Stroke Risk Prediction in the General Population. Stroke 2016;47: 2756-62.
75. Ning J, Zhang W, Chen SF, Li HQ, Wang RZ, Feng J, *et al*. Association of sleep behaviors with white matter hyperintensities and microstructural injury: A cross-sectional and longitudinal analysis of 26 354 participants. Sleep 2023;46:zsad020.
76. Clocchiatti-Tuozzo S, Rivier CA, Renedo D, Torres Lopez VM, Geer JH, Miner B, *et al*. Suboptimal sleep duration is associated with poorer neuroimaging brain health profiles in middle-aged individuals without stroke or dementia. J Am Heart Assoc 2024; 13:e031514.
77. Tsiknia AA, Parada HJR, Banks SJ, Reas ET. Sleep quality and sleep duration predict brain microstructure among community-dwelling older adults. Neurobiol Aging 2023, 125: 90-7.