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Original Article

Association Between Excess Sleep Duration and Risk of Stroke: A Population-Based Study

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Abstract: ***Background:*** Excess sleep is associated with higher risk of stroke, but whether the risk is modified by age and if it remains elevated after accounting for the competing risk of death is not well understood. ***Methods:*** We used nine years of the Canadian Community Health Survey between 2000 to 2016 to obtain self-reported sleep duration and created a cohort of individuals without prior stroke, heart disease, or cancer. We linked to hospital records to determine subsequent admissions or emergency department visits for acute stroke until December 31, 2017. We used Cox proportional hazard models to determine the association between sleep duration and risk of stroke, assessing for modification by age and sex and adjusting for demographic, vascular, and social factors. We obtained cumulative incidence of stroke accounting for the competing risk of death. ***Results:*** There were 82,795 individuals in our cohort who met inclusion criteria and had self-reported sleep duration, with 1705 stroke events in follow-up. There was an association between excess sleep (≥10 h/night) and risk of stroke in those <70 years (fully adjusted hazard ratio 2.29, 95% CI 1.04–5.06), but not ≥70 years of age, with a similar association after accounting for the competing risk of death. ***Conclusion:*** Sleep duration ≥10 h/night is associated with increased risk of stroke in those <70 years of age. The findings support current guidelines for 7–9 h of sleep per night. Further research is needed to elucidate the relationship between sleep and cerebrovascular disease.

Résumé : Association entre des durées prolongées de sommeil et le risque d'AVC : une étude basée sur la population. ***Contexte :*** On le sait, les excès de sommeil sont associés à un risque accru d'AVC. Cela dit, on n'est pas encore certains si un tel risque peut évoluer en fonction de l'âge et s'il demeure élevé lorsqu'on tient compte du risque concurrent de décès. ***Méthodes :*** De 2000 à 2016, nous avons fait appel à neuf cycles de collecte de l'Enquête sur la santé dans les collectivités canadiennes pour obtenir des données portant sur la durée de sommeil déclarée par des patients. Cela nous a permis de constituer une cohorte de sujets sans antécédent d'AVC, de maladie cardiaque ou de cancer. Nous avons ensuite établi un lien avec des dossiers hospitaliers pour déterminer les admissions ultérieures ou les visites aux urgences pour un AVC aigu, et ce, jusqu'au 31 décembre 2017. À noter que nous avons utilisé des modèles à risque proportionnel de Cox afin de déterminer l'association entre la durée du sommeil et le risque d'AVC. À cet égard, nous avons évalué les modifications du risque en lien avec l'âge et le sexe et avons ajusté les facteurs démographiques, vasculaires et sociaux. Enfin, nous avons obtenu l'incidence cumulative de l'AVC en tenant compte du risque concurrent de décès. ***Résultats :*** Notre cohorte a compté 82 790 personnes répondant à nos critères d'inclusion et ayant signalé elles-mêmes la durée de leur sommeil. Au total, 1705 cas d'AVC ont été signalés lors d'un suivi. Une association entre une durée prolongée de sommeil (≥10 heures) et un risque d'AVC a été notée chez des personnes âgées de moins de 70 ans (rapport de risque entièrement ajusté = 2,29 ; IC 95 % 1,04–5,06) mais non pas chez celles âgées de 70 ans ou plus, une telle association s'étant avérée similaire même en tenant compte du risque concurrent de décès. ***Conclusion :*** Une durée de sommeil prolongée (≥10 heures) est donc associée à un risque accru d'AVC chez les personnes âgées de moins de 70 ans. Ces résultats vont dans le sens des recommandations actuelles qui préconisent de 7 à 9 heures de sommeil par nuit. Chose certaine, des recherches supplémentaires sont nécessaires pour élucider la relation qui existe entre le sommeil et les maladies cérébrovasculaires.

Keywords: Stroke; Sleep; Epidemiology

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Introduction

Divergence from the recommended 7–9 h of sleep duration has been associated with cardiovascular disease and mortality, with the suggestion of a J-shaped relationship.[1–4] Recently, an association between abnormal sleep duration and stroke incidence has been reported, especially excess sleep >9 h.[5–9]

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However, the results are inconsistent, with some studies and meta-analyses reporting no association between sleep duration and stroke risk.[10,11] In addition, older individuals have lower recommended and self-reported sleep duration,[12] and whether age modifies the association of abnormal sleep duration with stroke is not well understood despite the potential importance of age for the targeting of preventive efforts. Lastly, sleep duration is also associated with all-cause mortality,[13,14] which may bias estimates of stroke risk.

We sought to determine the association between sleep duration and stroke risk in a large Canadian population-based cohort, evaluate differences with age, and account for the competing risk of death.

Methods

Study Sample – Canadian Community Health Survey

The Canadian Community Health Survey (CCHS) is an annual cross-sectional survey, representing 97% of the Canadian household population aged 12 years and older.[15] The CCHS collects information about health status, health determinants, and health care utilization of the household population. The 3% of the general population that is excluded from the survey target population includes those living on Indigenous reserves, those living in foster care, full-time members of the Canadian Armed Forced, the institutionalized population, and the remote Région du Nunavik and Région des Terres-Cries-de-la-Baie-James.

Administrative Linkages

Linkages were performed by Statistics Canada and included the Canadian Institutes of Health Discharge Abstract Database (CIHI-DAD) for hospitalizations, the National Ambulatory Care Reporting System (NACRS) for emergency department visits, and the Canadian Vital Statistics Database (CVSD) for deaths.[16,17] The linkage subsample contained 85% of total CCHS respondents who agreed to have their responses linked to administrative records. We used CIHI-DAD, NACRS, and CVSD to determine stroke events and deaths after the survey response until December 31, 2017. All participants had a minimum of 1 year of full follow-up for events and were censored if alive on December 31, 2017.

Cohort

We used CCHS years 2000, 2007, 2008, and 2011–2016 to capture data on sleep duration and other baseline covariates. Sleep duration was an optional module in all years except 2000, meaning that it could be selected by some but not all provinces and territories. We excluded those under the age of 40 and those with a history of heart disease (self-report), cancer (self-report), or prior stroke (either administrative data diagnosis or self-report).

Exposure

Our main exposure was self-reported sleep duration. Participants were asked the number of hours spent sleeping per night. Time spent in daytime napping was not captured. We categorized sleep duration as <4 h, 4–6 h, 7–9 h, and ≥10 h/day, with excess sleep duration defined as ≥10 h/day, as the Canadian guidelines recommend 7–9 h of sleep per night for individuals <65 years of age.[18]

Covariates

Covariates were obtained from the CCHS, including age, sex, rural residence, and self-report of ethnicity, education level, total household income, marital status, body mass index, current smoking status, hypertension, diabetes, heart disease, cancer, arthritis, chronic obstructive pulmonary disease (COPD), migraine, and asthma. Categorization of the variables can be seen in Table 1. Due to known biases in self-report of body mass index, we employed a correction developed by the CCHS.[19]

Outcome

Our primary outcome was acute stroke (ischemic stroke or intracerebral hemorrhage [ICH]) at any time in follow-up, using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada* (ICD-10-CA) codes (ischemic stroke: I63.x, I64.x, H34.1; ICH: I61.x) and ICD-9 codes (ischemic stroke: 434.01, 434.11, 434.91, 436; ICH: 431). Our secondary outcome was death during follow-up.

Analysis

We first used Cox proportional regression models to obtain the hazard of stroke by category of sleep duration, censoring people at death or end of follow-up. We assessed for the presence of modification of the sleep duration-stroke association by age (<70 years and ≥70 years) and sex. As there was evidence of modification by age but not sex, we created age-specific stratified models.

In our simple model, we adjusted for sex only. In our vascular model, we adjusted for sex, body mass index, hypertension, diabetes, and smoking. In our full model, we adjusted for the above in addition to income quartile, rural residence, alcohol consumption, education, ethnicity, marital status, and other comorbidities (migraine, arthritis, COPD, and asthma). We evaluated the proportional hazards assumption by assessing the significance ($p < 0.05$) of an interaction term of sleep duration category and follow-up time.

We conducted three sensitivity analyses. First, we additionally adjusted for symptoms of depression (2 or more weeks of feeling sad, blue, or depressed in the past 12 months) in the sub-set of individuals in which this variable was available. Second, we changed the upper category of sleep duration to ≥9 h. Third, we evaluated the risk of ischemic stroke only; there were insufficient events for an analysis of ICH only.

Lastly, we conducted competing risk regression to confirm that the risk of stroke was elevated while accounting for the competing risk of death. We obtained subdistribution hazard ratios and generated cumulative incidence functions for the risk of stroke over follow-up time. We adjusted for the same factors as in previous models.

Analyses were done in the Prairie Regional Data Centre at the University of Calgary using Stata 16.0 (College Station, TX, USA). Threshold of significance for *p*-values was <0.05. Under Tri-Council guidelines, this analysis did not require approval by a research ethics board.

Results

Our total cohort comprised 82,795 people with self-reported sleep duration and without prior heart disease, cancer, or stroke. During a median follow-up time of 9.1 years (interquartile range [IQR] 3.2–16.6 years), there was a total of 1705 stroke events (88.3% ischemic). Among those with incident stroke, the median time from survey response until stroke was 7.5 years (IQR 3.8–12.3).

Baseline characteristics of the cohort weighted to the Canadian population are shown in Table 1. The proportion of individuals

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Table 1: Weighted percentage of baseline characteristics

Variable	Weighted percentage
Age <70	85.9
Age 70+	14.1
Females	53.2
Education	
Less than secondary school	20.2
Secondary school graduation	20.9
Post-secondary	58.9
Income	
Income quartile 1 (lowest)	23.8
Income quartile 2	21.1
Income quartile 3	31.8
Income quartile 4	23.3
Body mass index	
Underweight/normal	33.0
Overweight	39.2
Obese	27.8
Ethnicity	
Caucasian	73.4
Asian	6.5
First nations	2.6
Other	17.5
Marital status	
Married/common law	73.6
Single	8.1
Widowed/separated/divorced	18.3
Rural residence	19.0
Current smoking	
Daily	18.6
Occasionally	3.2
Not at all	78.3
Hypertension	21.0
Diabetes	6.9
COPD	1.8
Asthma	7.0
Arthritis	11.0
Migraine	9.7
Depression	13.2
Alcohol consumption	
0 drinks per day	77.0
1–2 drinks per day	20.2
>2 drinks per day	2.8
Sleep time categories	
<4 h	1.7
4–6 h	41.2
7–9 h	55.8
≥10 h	1.2

<70 years was 86% and the proportion of females was 53.2%. The majority of people had 7–9 h of sleep duration (55.8%), with a small proportion having ≥10 h of sleep duration (1.2%).

Weighted percentages of stroke events in follow-up are shown in Supplemental Table 1 and stratified by subgroup. The greatest increases in stroke rate occurred when comparing 7–9 h of sleep with ≥10 h of sleep in those <70 years of age (1.5% to 5.9%) and in females (2.0% to 6.9%; Supplementary Table 1).

In the simple Cox regression model, there was a significant interaction between sleep duration ≥10 h and age ($p = 0.030$), but not sex ($p = 0.27$). There was no evidence of violation of the proportional hazards assumption.

Among individuals <70, excess sleep was associated with higher long-term risk of stroke in the simple model (adjusted hazard ratio [aHR] 3.15, 95% CI 1.74–5.73), vascular model (aHR 2.77, 95% CI 1.35–5.70), and full model (aHR 2.26, 95% CI 1.02–5.00; Figure 1A–C). There was no association between excess sleep and risk of stroke in those ≥70 years (Figure 1). The results were consistent in a sensitivity analysis adjusting for symptoms of depression. The association did not persist when the highest category of sleep duration was changed to ≥9 h (Supplementary Table 2). When analyzing ischemic stroke only, there was a higher risk in the simple and vascular models, but the association was attenuated in the full model (Supplementary Table 3).

After accounting for the competing risk of death, there remained a significantly elevated risk and higher cumulative incidence of stroke in those with excess sleep and age <70 years (Figure 1D and Figure 2).

Discussion

We demonstrate that excess sleep duration ≥10 h is associated with increased long-term risk of stroke among individuals younger than 70 years old, and this risk remains elevated after accounting for the competing risk of death.

Our results are consistent with prior studies showing an increased risk of stroke with excess sleep time.[5–8,20,21] Some studies have suggested a J-shaped relationship, with low amounts of sleep also increasing risk.[22] While the point estimate of stroke risk for the category of <4 h sleep was elevated among individuals <70, it did not reach significance in our study. The mechanism of stroke with excess sleep and stroke is unknown. Long duration of sleep is associated with inflammatory biomarkers,[23,24] vascular risk factors,[25–27] carotid intimal thickness,[28] and white matter hyperintensities.[29] In addition, excess sleeping may be a surrogate for higher sedentary time, depression, sleep apnea, or low socioeconomic status, all of which have been linked to stroke and cardiovascular risk.[30–33] Our findings are consistent with guidelines recommending 7–9 h of sleep per night to promote optimal health.[18,34]

The reason for the observed age modification is unclear. Multiple studies have reported associations between sleep and hypertension that are attenuated in the elderly.[35–37] Similarly, among individuals <65 years, both short and long duration sleep was associated with excess mortality, but not in individuals 65 years and older.[38] These finding are also in line with prior studies showing the associations between vascular risk factors such as obesity or diabetes and adverse outcomes are also greater at younger age.[39,40] Total sleep duration is significantly shorter in elderly, and the overall dynamics and homeostasis of sleep differ compared to middle-aged and younger subjects.[41] Retirement also improves sleep quality, which may mitigate the impact of excess sleep duration.[42] However, our results are in contrast to two studies from

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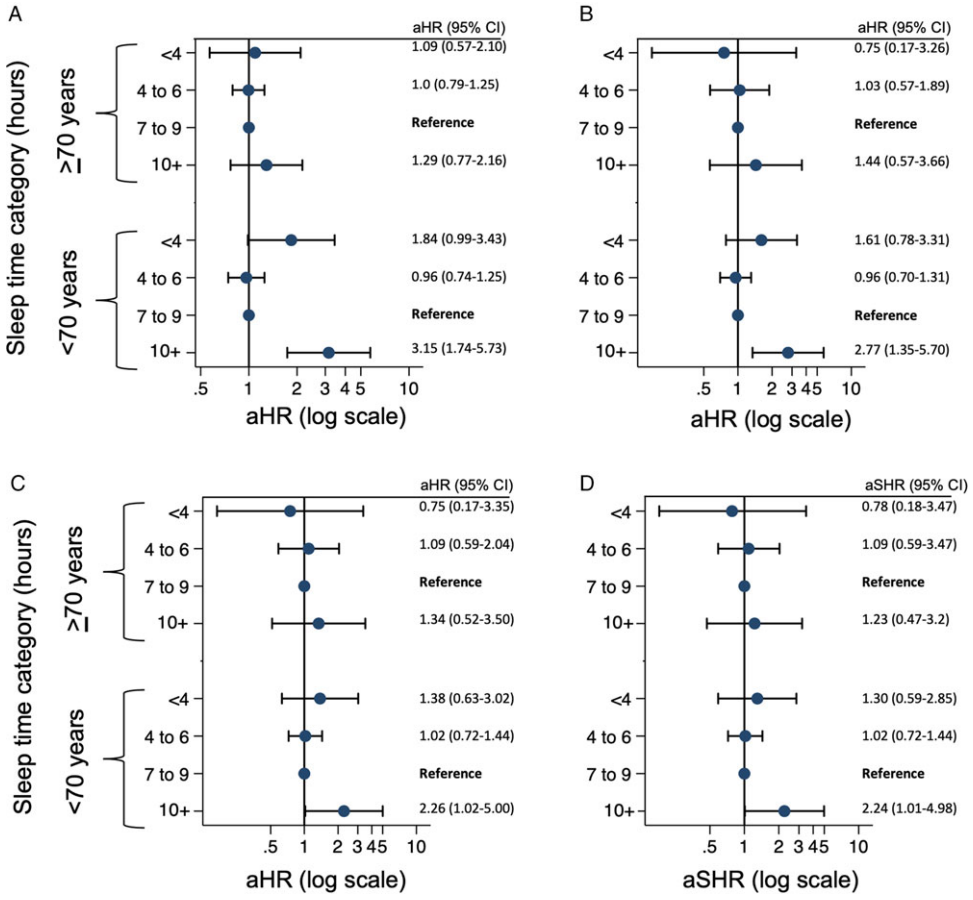


Figure 1: Association between categories of sleep duration and risk of stroke, stratified by age. Hazard ratios with 95% CIs are from Cox regression models (A, simple model; B, vascular model; C, full model), and subdistribution hazard ratios are from competing risk analysis (D, full model). There is a higher hazard of stroke in those <70 years old who report 10+ hours of sleep per night.

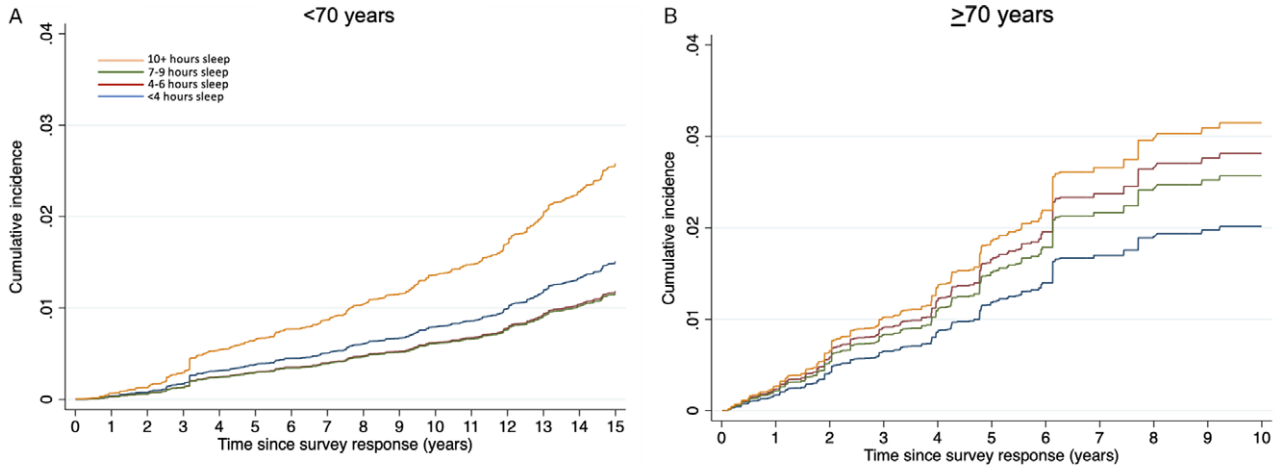


Figure 2: Cumulative incidence functions over years of follow-up for categories of sleep duration, stratified by age. Those ≥70 years have lower maximal follow-up time due to higher mortality. The greatest elevation in cumulative incidence of stroke occurs in individuals <70 years who report 10+ hours of sleep per night. Estimates obtained from fully adjusted competing risk regression models.

China showing the association of excess sleep and stroke was stronger at older age,[6,21] and may be due to variability in the population studied, amount of follow-up, or other study differences. We had a smaller number of individuals who were ≥70 years old and shorter follow-up time due to higher mortality, which may have limited our ability to detect an association in this age group.

There were some limitations to this study. First, we relied on self-reported sleep duration in the CCHS. Self-reported sleep duration overestimates sleep duration compared to objective measurements; therefore, the true threshold for increased risk may be lower than reported here.[43] Second, we relied on administrative data to measure stroke events, although the codes used have high validity in Canada.[44] Third, we had no assessment of sleep quality, sleep

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apnea, or mid-day napping. Lastly, there is the potential for residual confounding from many vascular and socioeconomic factors which may be related to both sleep duration and stroke risk.

In conclusion, excess sleep duration ≥10 h was associated with elevated stroke risk in those <70 years of age. The results support current guidelines for 7–9 h of sleep per night and suggest the need for further research on determining mechanisms of sleep-related cardio- and cerebrovascular disease.

Supplementary Material. To view supplementary material for this article, please visit https://doi.org/10.1017/cjn.2021.242

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Statement of Authorship. RJ was involved with conception, data analysis and interpretation, and drafting the article; SP, JW, and ES were involved with interpretation of results and critical revision of the article.

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