

## SYSTEMATIC REVIEWS AND META-ANALYSES

## Sedentary behavior and the risk of stroke: A systematic review and dose-response meta-analysis



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## KEYWORDS

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**Abstract** *Background and aims:* The sedentary behavior in people's daily life has continued to increase in recent years, causing many studies to focus on its relationship with diseases. Several studies have shown that sedentary behavior is an independent risk factor for cardiovascular disease and metabolic disease. Therefore, we performed a meta-analysis to assess the association between sedentary behavior and the risk of stroke.

*Methods and results:* Two independent investigators searched for prospective cohort studies on the association between sedentary behavior and stroke risk, published before February 2022. We pooled adjusted effect size and performed the dose-response analysis by random-effect model. Seven studies with 677,614 participants and 15,135 stroke events during a median follow-up of 12.2 years were included. The pooled hazard ratio (HR) of stroke was 1.16 (95% confidence interval [CI]: 1.09–1.24) with no significant heterogeneity ( $I^2 = 0.0\%$ ,  $p$  for heterogeneity = 0.983). In dose-response analysis, a nonlinear association between sedentary behavior and stroke risk was discovered. Stroke risk began to increase when sedentary time exceeded 3.7 h/d (HR, 1.01; 95% CI, 0.97–1.05). And when reached 11 h/d, a significantly increased risk of stroke was observed (HR, 1.21; 95% CI 1.12–1.31).

*Conclusion:* A nonlinear association was found in the dose-response analysis, with increased risk only when sedentary time exceeded a certain level. Further research is needed to explain the biological mechanisms by which sedentary time above a certain threshold significantly increases stroke risk. (PROSPERO registration number: CRD42022311544)

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**Abbreviations:** MVPA, Moderate or vigorous physical activity; METs, Metabolic equivalents; CVD, Cardiovascular diseases; HR, Hazard ratio; RR, Relative risk; CI, Confidence interval.

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## 1. Introduction

Adherence to a healthy lifestyle can significantly reduce the risk of stroke.  $\geq 30$  min/day of moderate or vigorous physical activity (MVPA) is one of the core behaviors of a healthy lifestyle [1], and more physical activity is associated with a lower risk of stroke, especially ischemic stroke [2,3]. However, in 2016, 27.5% of adults worldwide do not

have sufficient activity (at least 150 min of moderate-intensity, or 75 min of vigorous-intensity physical activity per week, or any equivalent combination of the two) [4]. Therefore, it is particularly important to promote people to change their inactive lifestyles, such as increasing the amount of MVPA or reducing sitting time.

Physical inactivity is a modifiable risk factor for stroke [5], which contains two independent aspects of insufficient MVPA and prolonged sedentary behavior. Sedentary behavior is defined as any waking behavior characterized by an energy expenditure  $\leq 1.5$  metabolic equivalents (METs) while in a sitting or reclining posture (such as sitting, watching television, reclining, or lying) [4,6,7]. And sedentary time is used to assess sedentary behavior. Sedentary time has sustained growth in the United States over the past twenty years, with screen-based sedentary time significantly increasing among all age groups, especially in adults [8,9]. Several recent studies and meta-analyses have identified longer sedentary time was associated with a higher risk of cardiovascular diseases (CVD), independent of physical activity [10–13], and existed a nonlinear association [10]. But the association between sedentary time and the risk of stroke was not identified previously.

In recent years, there have been many prospective studies evaluating the relationship between sedentary behavior and stroke, including some high-quality studies with large sample sizes and long follow-up durations. However, the results of different studies were conflicting, and the quantitative risk for stroke associated with different levels of sedentary time is not known. Thus, in the present meta-analysis, the influence of sedentary behavior on stroke was evaluated. Meanwhile, the dose-response association between sedentary time and stroke risk was determined to provide recommendations for stroke prevention.

## 2. Methods

### 2.1. Search strategy

We followed the Meta-analysis of Observation Studies in Epidemiology (MOOSE) [14] and the standards of Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [15] to conduct the present research.

We searched for prospective cohort studies on the association between sedentary behavior and stroke risk, published before February 2022 in Pubmed, Web of Science, and Embase. The search terms used for Pubmed research were (stroke[Mesh] OR “cerebrovascular accident” OR “cerebrovascular disease” OR “brain vascular accident” OR apoplexy OR “cerebral hemorrhage” OR “cerebral infarction”) AND (“sedentary behavior[Mesh]” OR “behavior, sedentary” OR “sedentary behaviors” OR “sedentary lifestyle” OR “lifestyle, sedentary” OR “physical inactivity” OR “inactivity, physical” OR “lack of physical activity” OR “sedentary time” OR “sedentary times” OR “time, sedentary”) AND (“cohort studies[Mesh]” OR cohort OR “cohort analysis” OR prospective OR follow-up). The

same search terms were used to retrieve relative studies in Web of Science and Embase. To include eligible studies more comprehensively, the reference lists of included studies were individually reviewed.

### 2.2. Study selection

We included the studies that met the following criteria: 1) the study design was a prospective cohort study; 2) the study was published in the English language; 3) the exposure indicator was sedentary behavior, mainly measured by total sedentary time, sitting time and television viewing time; 4) the outcome was stroke; 5) hazard ratios (HRs) or relative risks (RRs) and 95% confidence intervals (CIs) of stroke were available. Studies were excluded if they were reviews, letters, commentaries, conference abstracts, case reports, cross-sectional studies, or case-control studies. If multiple articles were published from the same cohort, we included the study with the longest follow-up time. Two independent investigators screened all titles or abstracts initially and then filter out all the eligible studies based on full-text reviews. Any disagreement was resolved by discussion with a third investigator.

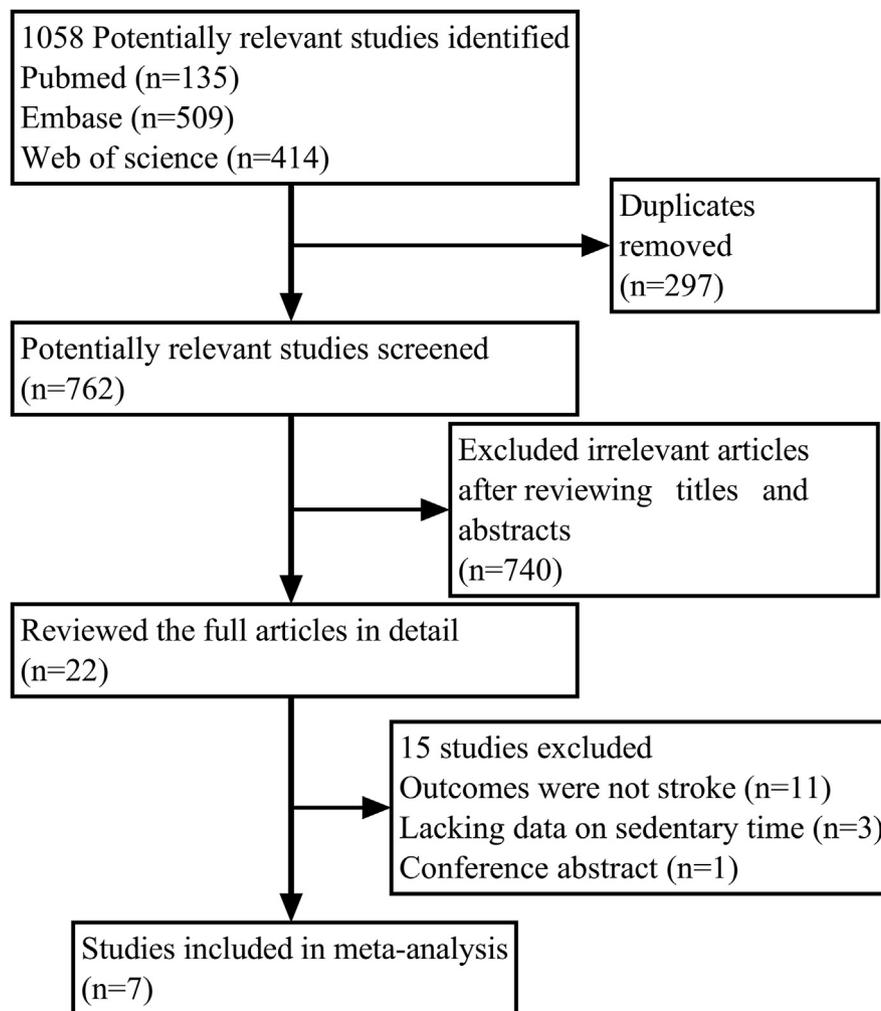
### 2.3. Data extraction and quality assessment

Two investigators of us extracted data from the selected studies independently, using a standard form. The information collected from each study was as followed: first author, publication year, country of the population, number of participants, follow-up time, age, sex, endpoints, number of events, sedentary behavior type, categories of sedentary time, adjusted covariates, and effect size (HRs or RRs) with 95% CIs. If multiple adjusted models existed in one study, we only extracted the effect size with the most adjusted covariates.

The quality of included studies was assessed by the Newcastle-Ottawa scale (NOS) [16], a nine-star scale for nonrandomized study quality assessment in meta-analyses. This scale grades the cohort studies on three fronts: selection, comparability, and outcome. Studies given more than six stars were considered high quality.

### 2.4. Statistical analysis

In the present meta-analysis, we considered that HRs and RRs were equivalent and used HRs as a common measure of the association between sedentary behavior and stroke risk. For each category, the average level of sedentary time was used to define the median sedentary time level. If the average duration was not reported, the midpoint of the upper and lower bounds for each category was calculated. For studies in which the highest category was open-ended, the width was equivalent to the interval between the midpoint and lower bound of the adjacent category. We extracted the HR with 95% CIs as the effect size to correspond to each category of sedentary time. If the study included more than one type of sedentary behavior, the



**Figure 1** Flow chart of study selection.

total sedentary time was prioritized for analysis. When studies reported stratified effect sizes, we combined these effect sizes with a fixed-effect model and then used the pooled HRs for the meta-analysis. The pooled HRs and 95% CIs for stroke risk associated with sedentary time were calculated by comparing the highest and lowest sedentary time categories using either a random-effects model in the presence of heterogeneity or a fixed-effect model without heterogeneity. Heterogeneity between studies was tested using the  $I^2$  and  $Q$  test ( $p < 0.10$  or  $I^2 > 50\%$  represented a significant heterogeneity) [17]. We used sensitivity analysis to confirm the stability of the meta-analysis, which removed one study at a time and then analyzed the remaining studies to determine whether the result would be significantly affected by the single study. We used Begg and Egger regression tests to assess publication bias.

Dose-response analysis included studies with three or more categories of sedentary time. A random-effects model was used in dose-response analysis to pool the

effect sizes [18]. We used the restricted cubic splines with three knots at fixed centiles (5%, 50%, and 95%) to explore the nonlinear association between sedentary behavior and stroke risk. A nonlinear probability value was calculated by testing the assumption that the coefficient of the spline transformation was equal to zero. Then the generalized least squares regression model was used to assess the linear trend [19]. Furthermore, we performed additional dose-response analyses to determine whether different types of sedentary behaviors had significantly different effects on stroke risk, depending on the subtypes of exposure factors used in the included studies.

Moreover, we performed subgroup analysis to explore the differences in the overall effects between each subgroup, which could also help determine the stability of the results. Subgroup analysis was based on location, number of stroke events, number of participants, age of participants, percentage of females, follow-up period, type of

**Table 1** Characteristics of studies included.

Author	Year	Country	Study population	Follow-up duration, y	Mean age	Female, %	Endpoint	No. of events
Joundi	2021	Canada	143,180	9.4	≥40	52.1	Total stroke	2965
McDonnell	2016	United States	22,257	7.1	64.9	55.5	Total stroke	727
Kim	2013	United States	134,596	13.7	58.6	54.4	Fatal stroke	1249
Patel	2018	United States	127,554	20.3	62.6	55.6	Fatal stroke	3239
Chomistek	2013	United States	71,018	12.2	63.1	100	Total stroke	2050
Liu	2020	China	93,110	5.8	52.8	60.6	Total stroke	2352
Ikehara	2015	Japan	85,899	19.2	57.3	58.1	Fatal stroke	2553
Author	Sedentary behavior type	Categories of sedentary time, h/d	Most adjusted HR by category (95% CI)	Covariates in the most adjusted model				
Joundi	Total sedentary behavior	1: <4 2: 4 to <6 3: 6 to <8 4: ≥8	1: 1 [Reference] 2: Not reported 3: Not reported 4: 1.11 (0.80–1.54)	Age, sex, rural residence, ethnicity, education level, income, marital status, alcohol consumption, BMI, smoking status, hypertension, diabetes, heart disease, cancer, migraine, arthritis, chronic obstructive pulmonary disease, and asthma BMI, waist circumference, systolic blood pressure, statin use, left ventricular hypertrophy, atrial fibrillation, alcohol use, smoking and diabetes Age, sex, race, education, employment status, smoking status, BMI, marital status, aspirin use, alcohol consumption, MVPA, American Cancer Society diet score, and comorbidity score Age, physical activity, race, education, income, marital status, smoking, family history of myocardial infarction, depression, alcohol intake, hours of sleep, intake of total calories, saturated fat, fiber, BMI, and history of hypertension, diabetes, or high cholesterol Age, sex, geographic region, education level, family history of CVD, urbanization, alcohol consumption, current smoking status, and MVPA Age, sex, BMI, smoking status, alcohol consumption, hours of exercise, hours of walking, perceived mental stress, presence of job, education level, fresh fish intake, sleep duration, depression symptoms, and histories of hypertension and diabetes Age, race/ethnicity, educational level, smoking status, diabetes and/or hypertension, energy intake, alcohol intake, physical activity, trend of hours for other sitting behaviors				
McDonnell	Television viewing	1: <2 2: 2 to <4 3: 4	1: 1 [Reference] 2: 1.13 (0.88–1.45) 3: 1.12 (0.85–1.48)					
Patel	Total sedentary behavior	1: <3 2: 3 to 5 3: ≥6	1: 1 [Reference] 2: 1.04 (0.96–1.12) 3: 1.15 (1.03–1.28)					
Chomistek	Total sedentary behavior	1: ≤5 2: 5.1 to 9.9 3: ≥10	1: 1 [Reference] 2: 1.03 (0.94–1.14) 3: 1.18 (1.04–1.34)					
Liu	Total sedentary behavior	1: <5 2: 5 to <8 3: 8 to <10 4: ≥10	1: 1 [Reference] 2: 1.00 (0.87–1.14) 3: 1.11 (0.96–1.28) 4: 1.19 (1.03–1.38)					
Ikehara	Television viewing	1: <2 2: 2 3: 3 4: 4 5: 5 6: ≥6	1: 1 [Reference] 2: 1.06 (0.93–1.19) 3: 0.98 (0.87–1.11) 4: 0.89 (0.76–1.03) 5: 1.06 (0.90–1.23) 6: 1.10 (0.92–1.32)					
Kim	Television viewing	1: <1 2: 1 to 4 3: ≥5	1: 1 [Reference] 2: 1.03 (0.85–1.24) 3: 1.25 (0.99–1.58)					

sedentary time, type of endpoint, and multivariable adjustment strategy. All data analyses were accomplished using STATA 14.0 and a probability level less than 0.05 was considered statistically significant.

### 3. Results

#### 3.1. Literature search

A total of 1058 relevant studies were retrieved from the three databases; after initially reviewing the title and abstract, 297 articles were excluded due to duplication and 740 articles because of irrelevance. We next reviewed the full text of the remaining 22 studies. We excluded eleven studies in which the outcome was not stroke, three studies in which lacked data on sedentary time, and one conference abstract. Finally, seven eligible studies [20–26] were

included in the final meta-analysis. The process of study selection was shown in Fig. 1.

#### 3.2. Study characteristics

The characteristics of the eligible studies are present in Table 1. The seven studies published between 2013 and 2021 included 677,614 participants (60.3% female and 39.7% male) and 15,135 stroke events during a median follow-up of 12.2 years. Of them, six studies [20–23,25,26] enrolled females and males, in which one [22] stratified the results by sex, and one [24] enrolled only females. The number of participants ranged from 22,257 to 143,180. Four studies [21–24] were conducted in the United States, two in Asia [25,26] (China and Japan), and one [20] in Canada. The endpoint events of four studies were total stroke (fatal or nonfatal stroke or both) and three were

**Table 2** NOS score of each study.

Author, year	Selection		Representativeness of Non-exposed Cohort	Representativeness of Exposed Cohort	Ascertainment of Exposure	Outcome Not Present at Beginning of Study	Comparability control for important factors <sup>a</sup>	Outcome		Total scores
	Representativeness of Exposed Cohort	Was Follow-up Long Enough?						Assessment of Outcome	Adequacy of follow-up	
Joundi, 2021	*	*	*	*	*	*	**	*	*	8
McDonnell, 2016	*	*	*	*	*	*	*	*	*	7
Kim, 2013	*	*	*	*	*	*	*	*	*	8
Patel, 2018	*	*	*	*	*	*	**	*	*	9
Chomistek, 2013	*	*	*	*	*	*	**	*	*	9
Liu, 2020	*	*	*	*	*	*	**	*	*	8
Ikehara, 2015	*	*	*	*	*	*	**	*	*	9

<sup>a</sup> A maximum of 2 stars can be allotted in this category, one for age, the other for sex and/or BMI (body mass index).

fatal stroke. In all included studies, sedentary behavior was assessed by a self-reported questionnaire. Three of the studies [20,24,25] were exposed to total sedentary behavior, and three [21,22,26] to television viewing. One study [23] assessed sedentary behavior by surveying participants' daily sleeping and five types of sitting time, including: 'sitting in a car or bus', 'sitting at work', 'sitting at meals', 'sitting watching television', and 'other leisure sitting activities (such as reading, playing cards, sewing)', which we also classify it as investigating total sedentary behavior. Physical activity was adjusted in five studies [22–26]. In most studies, adjusted covariates were age (n = 6), sex (n = 4), body mass index (BMI; n = 5), education level (n = 6), smoking and alcohol consumption (n = 7), and history of diabetes and/or hypertension (n = 4).

All studies had a score of seven or above and were considered high quality based on the NOS, which had a mean score of 8.3. The details of the quality assessment were exhibited in Table 2.

### 3.3. Sedentary behavior and stroke

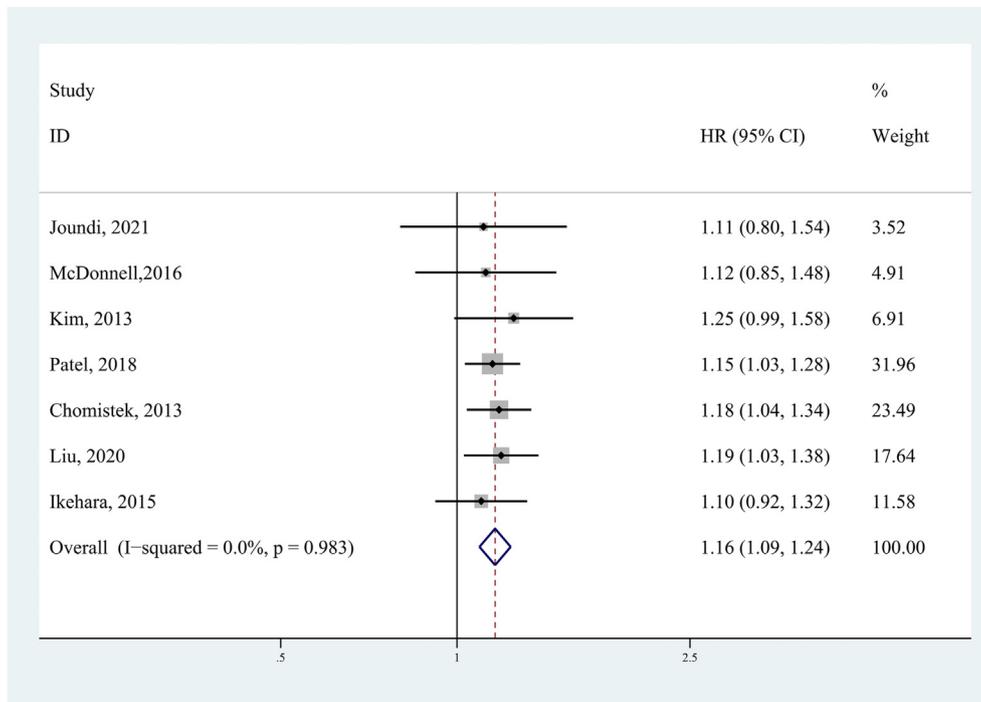
Figure 2 presents the multivariable-adjusted HR of stroke in relation to sedentary behavior from each study and the pooled HR. All seven eligible studies reported sedentary behavior as a risk factor for stroke, and three of them [23–25] were statistically significant. In the overall meta-analysis, participants in the highest category of sedentary time, compared with those in the lowest category, experienced an increased risk of stroke incidence (pooled HR, 1.16; 95% CI, 1.09–1.24). No significant heterogeneity was observed ( $I^2 = 0.0\%$ , p for heterogeneity = 0.983).

In the dose-response meta-analysis, six studies were included, and one study [20] was excluded because it did not provide HR for the intermediate category. The nonlinear association between sedentary behavior and risk of stroke was discovered (p for nonlinearity = 0.026). A non-statistically significant increased risk of stroke was observed when sedentary time exceeded 3.7 h/d (HR, 1.01; 95% CI, 0.97–1.05; p < 0.001). Notably, when sedentary time increased to 6.5 h/d, every additional hour increased stroke risk by 6% (HR, 1.06; 95% CI 1.01–1.11), and that became 21% when over 11 h/d (HR, 1.21; 95% CI 1.12–1.31) (Fig. 3).

### 3.4. Sensitivity analysis, publication bias, and subgroup analysis

The sensitivity analysis found that the pooled HRs were not influenced by a separate study, as the pooled HRs ranged from 1.15 to 1.17. Additionally, there was no significant publication bias tested by Begg and Egger regression (Begg P = 0.764; Egger P = 0.770).

Table 3 shows the results of the subgroup analysis. No significant differences in the correlation and direction of the association between sedentary behavior and stroke risk were observed in the subgroups based on location, number of stroke events, number of participants, age of



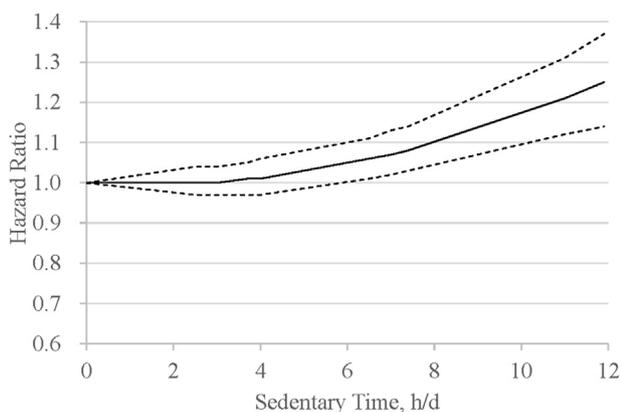
**Figure 2** Forest plot of sedentary behavior and risk of stroke.

participants, percentage of females, follow-up period, model whether adjusted for BMI and type of endpoint. However, we found that the association between sedentary behavior and stroke risk was not statistically significant in the subgroup without physical activity adjustment (HR, 1.12; 95%CI 0.90–1.36;  $p$  for test = 0.310). Furthermore, in the subgroup defined by sedentary behavior type, the pooled HR for where sedentary behavior was television viewing was 1.13 (95%CI, 0.98–1.30;  $p$  for test = 0.035), while the HR for total sedentary behavior was 1.17 (95% CI, 1.09–1.25;  $p$  for test < 0.001). In addition, we separately performed dose-response analyses of three

studies [23–25] reporting total sedentary behavior and three studies [21,22,26] reporting television viewing to determine nonlinear or linear associations between different types of sedentary behavior and stroke. The results showed a nonlinear dose-response association between total sedentary behavior and stroke risk similar to the overall analysis ( $p$  for nonlinearity = 0.049). The nonlinear association was also observed between television viewing and stroke, and an increased risk of stroke was found when it was longer than 7 h/d (HR, 1.16; 95% CI, 1.01–1.32;  $p$  for nonlinearity = 0.040). (Figs. 4 and 5).

#### 4. Discussion

To our knowledge, this is the first meta-analysis to assess the impact of sedentary behavior on the risk of stroke, involving 677,614 participants from seven cohorts, and including 15,135 stroke events. A positive association with no heterogeneity was found between sedentary behavior and stroke. This relationship was also present in each subgroup analysis, with no significant change in the correlation and no heterogeneity either, further confirm the robustness of our results. In addition, a dose-response meta-analysis was performed in which a nonlinear association between sedentary behavior and stroke risk was observed. When the sedentary time was shorter than 3.7 h/d, no significant change was observed in stroke risk. But when it was extended to 6.5 h/d, every additional hour was associated with a 6% increase in stroke risk. The very



**Figure 3** Dose-response relationship between sedentary behavior and the risk of stroke.

high level of sedentary behavior (>11 h/day) significantly increased the risk of stroke. This provides some evidence for future guidelines, which may have a greater impact on stroke beyond a certain threshold of sedentary behavior, and thus should pay more attention to reducing the higher level of sedentary behavior.

A nonlinear relationship between total sedentary behavior and stroke was shown in subgroup analyses by sedentary type and the corresponding dose-response analysis. We only observed a statistically significant increase in stroke risk for television viewing time over 7 h/d, with a slight reduction when it was less than or equal to 4 h/d. This difference may be due to two reasons, on the one hand, the assessment method of exposure is different, and on the other hand, it may be that among the studies we included, few studies reported watching television as sedentary behavior.

In three meta-analyses published in recent years, all reported a positive correlation between sedentary time and CVD risk [10,11,13]. In a dose-response meta-analysis published in 2016, there was a nonlinear association between sedentary behavior and CVD, with a nonsignificant increased risk observed when the sedentary time exceeded 6.8 h/d, and when above 10.04 h/d every additional hour caused an increase of CVD risk by 8% [10]. This is similar to the dose-dependent nonlinear association of sedentary behavior and stroke risk we found. Another

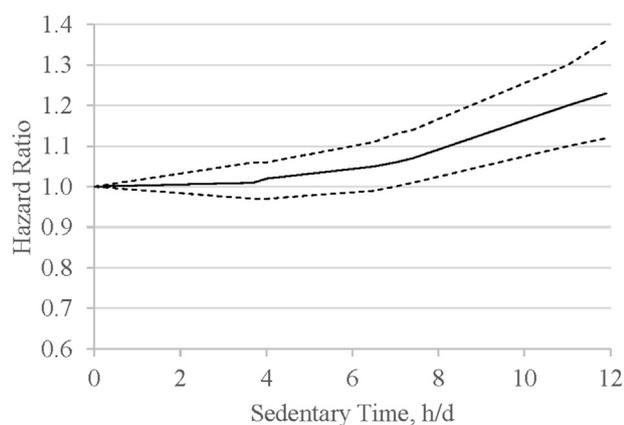
meta-analysis, published in 2018, described a non-linear relationship between both total sedentary behavior and television viewing and CVD risk with and without physical activity adjustment. Cardiovascular disease (CVD) is a general term for a group of diseases, including a variety of diseases such as heart failure, ischemic heart disease, and stroke. The present dose-response meta-analysis complements previous research to elucidate the impact of sedentary behavior on stroke.

It is well known that sedentary behavior is associated with chronic metabolic disease, for example, a meta-analysis has reported a positive linear association with the risk of type 2 diabetes [13], which may be due to lower insulin sensitivity in people who experience longer sedentary time [27]. There is also some epidemiological evidence that excessive sedentary behavior increases obesity risk [28]. These comorbidities may be a reason for an increased risk of stroke. However, the biological mechanism between sedentary behavior and stroke risk has not been elucidated. Several large population-based studies have shown that increased sedentary behavior may lead to telomere shortening [29,30], which played an important role in the development of many diseases, among which stroke is one [31]. In addition, it has been found that excessive sedentary time may be associated with increased inflammatory markers, such as adipokines and C-reactive protein [32,33]. The increase of these

**Table 3** Subgroup analysis of stroke risk.

	Number of studies	HRs (95%CI)	p for heterogeneity	I <sup>2</sup> (%)	p for test
Location					
US	4	1.17 (1.08–1.26)	0.916	0	<0.001
non-US	3	1.15 (1.03–1.28)	0.784	0	<b>0.011</b>
Events					
<2500	4	1.19 (1.09–1.29)	0.947	0	<0.001
≥2500	3	1.13 (1.04–1.24)	0.910	0	<b>0.006</b>
Participants					
<100,00	4	1.16 (1.07–1.26)	0.901	0	<0.001
≥100,000	3	1.16 (1.06–1.28)	0.785	0	<b>0.002</b>
Age					
<60	3	1.17 (1.06–1.30)	0.668	0	<b>0.002</b>
≥60	3	1.16 (1.07–1.25)	0.925	0	<0.001
% of female					
<60	5	1.14 (1.05–1.25)	0.962	0	<b>0.002</b>
≥60	2	1.18 (1.08–1.30)	0.932	0	<b>0.001</b>
Follow-up					
<10	3	1.18 (1.04–1.34)	0.893	0	<b>0.012</b>
≥10	4	1.16 (1.07–1.24)	0.893	0	<0.001
Exposure					
Total sedentary behavior	4	1.17 (1.09–1.25)	0.968	0	<0.001
Television viewing	3	1.15 (1.01–1.30)	0.686	0	<b>0.035</b>
Endpoint					
Total stroke	4	1.17 (1.07–1.28)	0.967	0	<0.001
Fatal stroke	3	1.15 (1.06–1.26)	0.697	0	<b>0.001</b>
Adjusted for physical activity					
Yes	5	1.17 (1.09–1.24)	0.923	0	<0.001
No	2	1.12 (0.90–1.36)	0.967	0	0.310
Adjusted for BMI					
Yes	5	1.15 (1.07–1.23)	0.977	0	<0.001
No	2	1.21 (1.07–1.37)	0.727	0	<b>0.003</b>

Boldface indicates statistical significance ( $p < 0.05$ ).

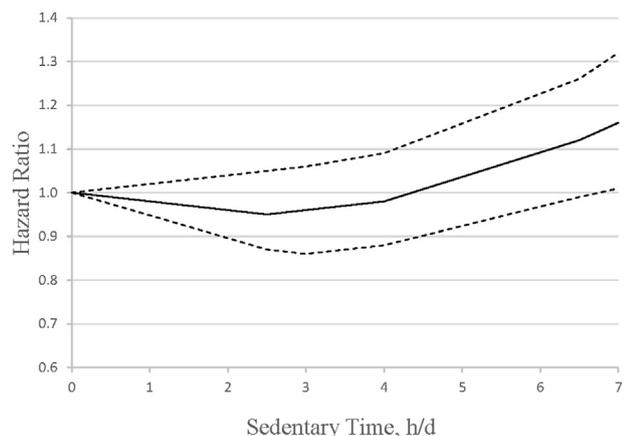


**Figure 4** Dose-response relationship between total sedentary behavior and the risk of stroke.

inflammatory markers damages the vascular endothelium, which may lead to the occurrence of stroke.

Our study had several advantages. Although there have been several previous meta-analyses evaluating the association between sedentary behavior and CVD, this is the first dose-response meta-analysis to specifically estimate its relationship with stroke risk. A positive association between sedentary behavior and stroke was found. In addition, an increasingly significant increase in stroke risk was reported with prolonged sedentary time. The cohort studies we included were high quality and most had large numbers of participants, making their results more convincing. In addition, we found no significant publication bias and heterogeneity. In subgroup and sensitivity analyses, no significant changes in the direction and magnitude of pooled HR were observed between sedentary behavior and stroke risk, which confirmed the robustness of this study's results.

The present study had a few limitations. First, sedentary behavior was measured by self-reporting rather than using accelerometers, which may have limited the power of this study to determine the association between sedentary behavior and stroke risk. In the future, it may be necessary



**Figure 5** Dose-response relationship between television viewing and the risk of stroke.

to use accelerometers to objectively measure sedentary time to reduce errors. Second, the self-reported questionnaires caused differences in measurement scales between studies. Some studies reporting total sedentary behavior did not differentiate between occupational and leisure time. Among the studies reporting television viewing, some studies did not determine whether they engaged in other activities, such as housework, etc., while watching television, which may be the reason why the pooled HR of the television viewing subgroup in our study was not statistically significant. Third, since only one of our included studies analyzed the joint effect of sedentary behavior and physical activity across different on stroke, no meta-analysis of the joint effect was performed. Therefore, it has not been determined whether the effect of exceeded sedentary behavior on stroke risk can be reduced by increasing the amount of physical activity at other times. Finally, only observational and English language studies were included in this study, thus the potential bias cannot be excluded.

## 5. Conclusion

In conclusion, this meta-analysis suggests a positive association between sedentary behavior and stroke risk. A nonlinear association was found in the dose-response analysis, with increased risk only when sedentary time exceeded a certain level (>3.7 h/d). And very high levels of sedentary time (>11 h/d) could significantly impact stroke risk. Further research is needed to explain the biological mechanisms by which sedentary time above a certain threshold significantly increases stroke risk.

## Funding

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## Authors' contributions

ZW and XJ contributed to the study design and data research. YL and CW contributed to study selection and quality evaluation. ZW and JL contributed to statistical analysis. ZW, XJ, LT and WT contributed to drafting of the manuscript and language modification.

## Declaration of competing interest

The authors declare they have no competing interests.

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