

Adherence to the dietary approaches to stop hypertension diet and risk of stroke

A meta-analysis of prospective studies

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Abstract

The Dietary Approaches to Stop Hypertension (DASH) diet has been shown to lower the risk of hypertension, but its role in the prevention of stroke remains in debate. We therefore conducted a meta-analysis to examine the association between DASH diet and incident stroke.

A systematic database search in PubMed and Embase was performed to identify eligible prospective studies. The study-specific relative risks (RRs) and 95% confidence intervals (CIs) were pooled using random-effect meta-analysis. Dose–response relationship between DASH diet score and risk of stroke was also assessed.

We included 12 prospective cohort studies comprising a total of 548,632 participants, with follow-up duration ranging from 5.7 to 24 years. Compared with lower adherence, higher adherence to the DASH diet was related to a reduced risk of developing stroke (RR 0.88, 95% CI 0.83–0.93). Such a benefit of DASH diet seemed to be greater in the Asian than in the Western populations (P for interaction = .037). Dose–response meta-analysis indicated a linear association of the DASH diet score with stroke (P for nonlinearity = .411), and each 4-points increment in the score conferred a risk reduction of 4% (RR 0.96, 95% CI 0.94–0.97) in total stroke events.

Our findings suggest that higher adherence to the DASH diet is associated with a decreased risk of stroke.

Abbreviations: CIs = confidence intervals, DASH = Dietary Approaches to Stop Hypertension, HRs = hazard ratios, NOS = Newcastle-Ottawa Scale, RRs = relative risks.

Keywords: diet, meta-analysis, risk factors, stroke

1. Introduction

Stroke, a severe cerebrovascular attack, is 1 of the leading causes of morbidity and mortality in the world.^[1] According to the World Health Organization, an estimated 6.7 million deaths in the year 2015 were attributable to stroke.^[2] Stroke also represents a main contributor to the long-term disability, with projections showing a staggering more than 200 million disability-adjusted life-years lost globally in 2030.^[3] Therefore, effective primary preventions are required to relieve the growing burden of stroke. Among the various preventive strategies, lifestyle modification, particularly a healthy diet, has gained increasing interests in recent years. For instance, epidemiological

findings have suggested that accordance to the Mediterranean diet or healthy Nordic diet was inversely correlated with incident stroke.^[4,5]

The Dietary Approaches to Stop Hypertension (DASH) diet was developed in 1997, emphasizing on 8 components: high consumption of fruits, vegetables, whole grains, low-fat dairy foods, legumes and nuts, and low intake of sodium, sweetened beverages, and red and processed meat.^[6] Clinical trials and observational studies have established that the DASH-style diet could lower blood pressure^[7] and reduce the incidence of hypertension^[8]—a major risk factor for stroke development. However, whether the DASH diet is associated with the risk of stroke remains, to date, in debate. This is due to the inconsistent results in epidemiological studies. Therefore, we conducted a meta-analysis of prospective cohort studies to determine the role of DASH diet in the prevention of stroke in general population. We hypothesized that higher adherence to the DASH diet may reduce the risk of future stroke events.

2. Materials and methods

2.1. Search strategy

This meta-analysis was carried out according to the Meta-analysis of Observational Studies in Epidemiology guideline.^[9] We systematically searched the PubMed and Embase databases through May, 2018 to identify eligible studies, using the Medical Subject Headings terms and free-text word as follows: (“stroke” OR “ischemic stroke” OR “cerebral infarction” OR “hemorrhagic stroke” OR “intracranial hemorrhage” OR “cerebrovascular”

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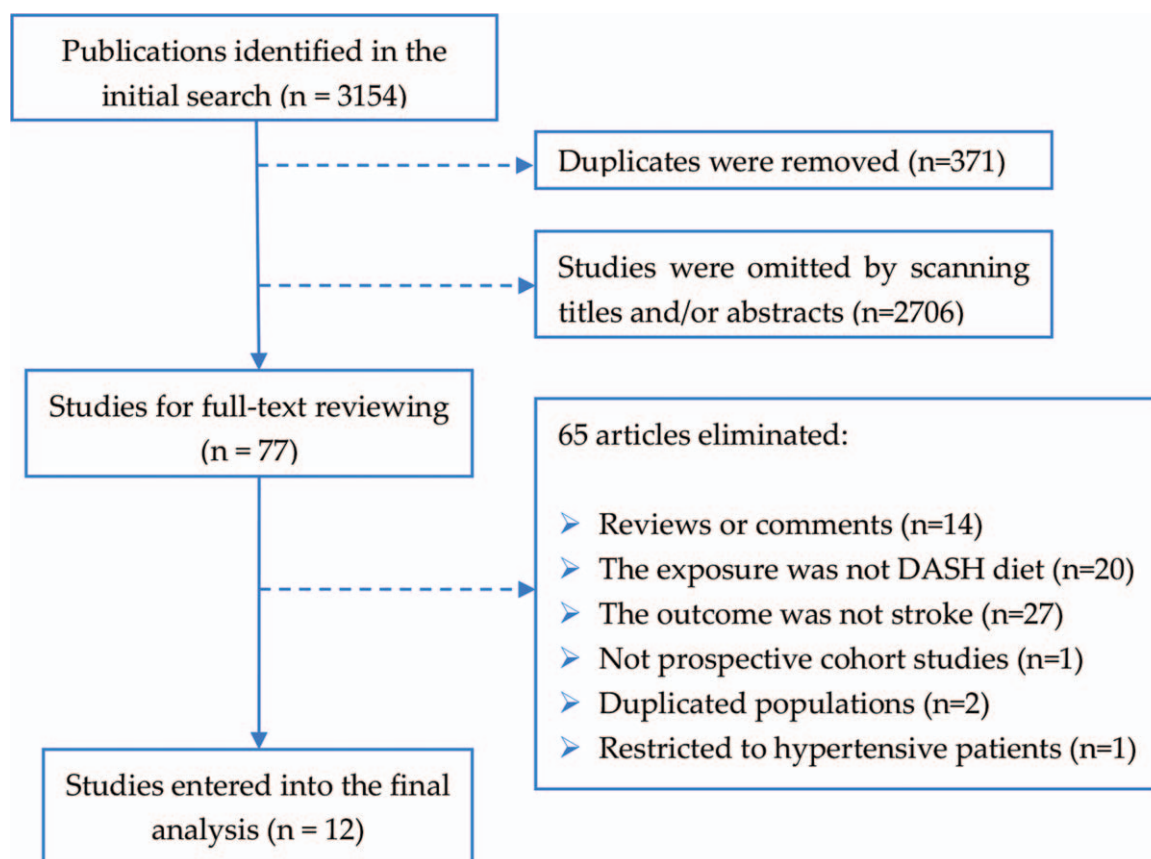


Figure 1. Flow diagram of study search process. A total of 12 prospective cohort studies were included in this meta-analysis.

OR “cardiovascular”) AND (“prospective” OR “follow-up” OR “cohort” OR “longitudinal”) AND (“Dietary Approaches to Stop Hypertension” OR “DASH” OR “dietary pattern” OR “dietary score” OR “dietary adherence” OR “dietary quality”). Detailed search strategies were shown in Table S1 (<http://links.lww.com/MD/C501>). In addition, the citation lists of retrieved publications were manually scrutinized to find potential complements.

2.2. Inclusion criteria

To be considered as eligible, the clinical studies should meet the following requirements: designed as prospective cohort studies; the exposure was DASH diet evaluated by the DASH diet score; the outcome was stroke incidence or stroke mortality; the risk estimates of stroke, such as relative risks (RRs) or hazard ratios (HRs), were present in the studies. For the studies included in dose-response meta-analysis, the RRs or HRs should be provided for ≥ 3 quantitative categories of the DASH diet score. Reviews, comments, abstracts, animal experiments, non-English articles, studies pertained to overlapping populations, and studies restricted to hypertensive patients were excluded.

2.3. Data extraction and quality assessment

In total, 2 reviewers independently recorded the study information, including study authors, publication year, location, the number of participants and cases, baseline age, gender, hypertension history, ascertainment of exposure and outcome, and confounders. The maximally adjusted risk effect sizes of stroke were also extracted

for pooling analysis. If necessary, the corresponding authors of the included studies were contacted for additional data. To evaluate the methodological quality of included studies, the Newcastle-Ottawa Scale (NOS)^[10] was used with 3 major respects: participants selection, between-groups comparability, and outcomes ascertainment. High-quality studies were defined as those with a NOS score ≥ 7 . Any disagreements between the 2 reviewers were handled by consulting with a third reviewer.

2.4. Statistical methods

In this meta-analysis, we reported the summary risk estimate as RR with its 95% confidence intervals (CIs). The study-specific risk effect sizes of stroke for the highest versus lowest categories of the DASH diet score were pooled using random-effect meta-analysis. Heterogeneity across the included studies were detected by the Cochrane Q test and measured by the I^2 statistic, with a value of $I^2 \geq 50\%$ indicating substantial heterogeneity. Stratified analyses were conducted based on stroke type (ischemic or hemorrhagic), sex (men or women), study location (US, Europe, or Asia), follow-up duration (< 10 or ≥ 10 years), and adjustment of hypertension history (yes or no). The differences between subgroups were confirmed with meta-regression analysis.^[11] To evaluate the stability of summary RRs, we carried out a sensitivity analysis by eliminating each study in sequence. Publication bias was examined by visual evaluation of funnel plots and by Egger test. If such bias was present, we further used the “trim and fill” approach to adjust it and then re-calculate the results.^[12]

Table 1
Baseline characteristic of included studies.

References	Publication year	Location	Sample size	Cases	Age (y)	Men (%)	HP (%)	Exposure	Outcome	FU (y)	NOS score
Agnoli et al ^[15]	2011	Italy	40681	178	37–75	31	37	FFQ	ICD-9 code	7.9	8
Aigner et al ^[16]	2018	US	172043	3548	45–75	47	38	FFQ	ICD-9 and ICD-10 codes	17.6	8
Chan et al ^[17]	2013	Hong Kong	2735	156	≥65	49	34	FFQ	ICD-9 code	5.7	7
Chiuve et al ^[18]	2008	US	43685	994	54	100	NA	FFQ	Medical records	16	8
Folsom et al ^[19]	2007	US	41386	236	55–69	0	0	FFQ	ICD-9 and ICD-10 codes	16	8
Fung et al ^[20]	2008	US	88517	3105	34–59	0	15	FFQ	Medical records	24	9
Jones et al ^[21]	2018	UK	23655	1011	39–79	46	19	FFQ	ICD-10 code	12.4	8
Larsson et al ^[22]	2016	Sweden	74404	4632	45–83	54	21	FFQ	ICD-10 code	11.9	8
Lin et al ^[23]	2013	Taiwan	2061	123	46	43	5	FFQ	ICD-9 code	12	7
Mertens et al ^[24]	2018	UK	1867	209	45–59	100	NA	FFQ	ICD-9 code	16.6	8
Struijk et al ^[25]	2014	Netherlands	33671	527	20–70	36	21	FFQ	ICD-9 and ICD-10 codes	12.2	8
Tikk et al ^[26]	2014	Germany	23927	551	35–64	46	NA	FFQ	ICD-10 code	12.7	8

FFQ=Food-Frequency Questionnaire; FU=follow-up; HP=hypertension; ICD=International Classification of Diseases; NA=not applicable; NOS=Newcastle-Ottawa Scale.

For better understanding of the association between adherence to the DASH diet and stroke risk, we also performed a dose–response meta-analysis. The studies that quantified the DASH diet score according to the 2006 DASH eating plan^[6] were included. A 4-knots (5th, 35th, 65th, and 95th percentiles) restricted cubic spline model was then estimated to test the nonlinearity hypothesis of the association.^[13] If the test was not statistically significant, the method of generalized least-squares for trend estimates^[14] was used to calculate the RR of stroke for each 4-points increase in the DASH diet score.

All data analyses were completed using STATA 13.0 (StataCorp, College Station, TX) and R 3.4.3 (The R Foundation for Statistical Computing, Vienna, Austria) software, and *P* values of <.05 were considered as the significant threshold.

2.5. Ethics statement

This study was a secondary analysis of human subject data published in the public domain, thus no ethical approval was needed.

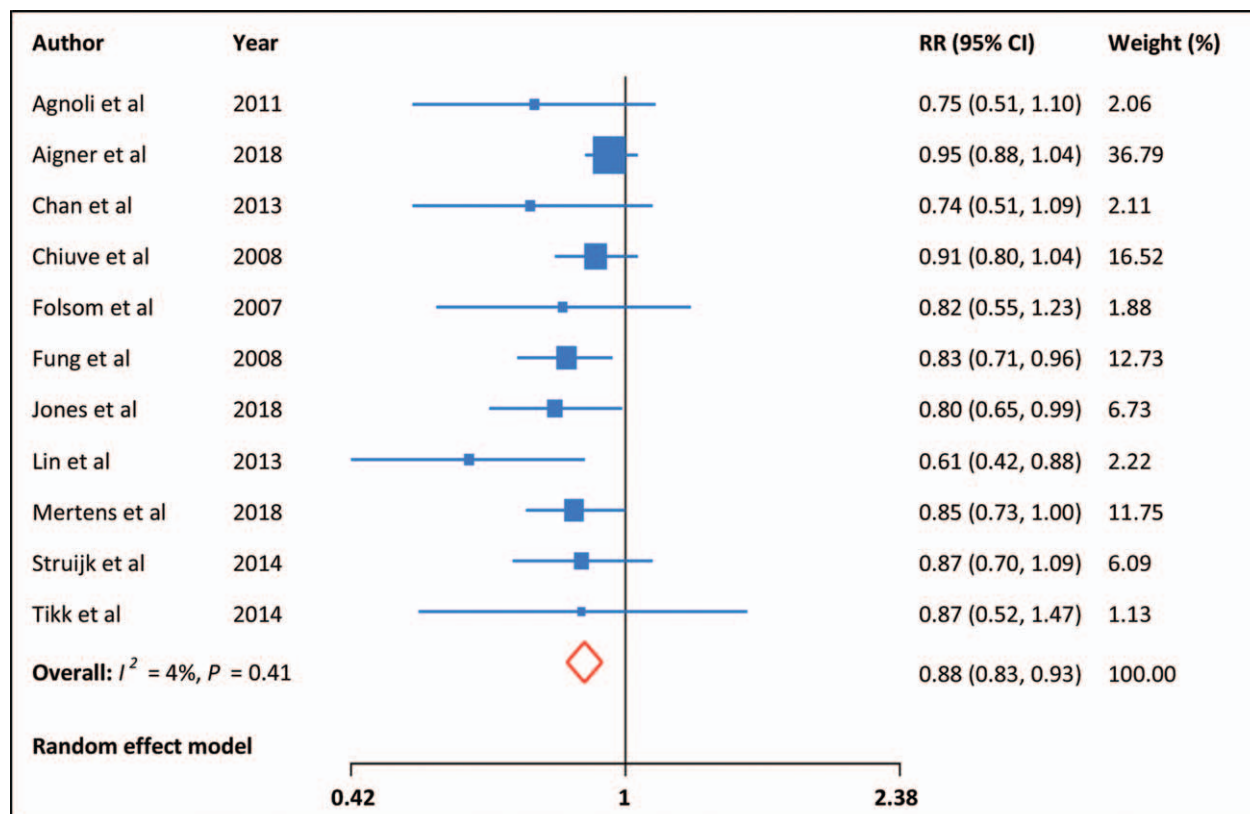


Figure 2. Highest versus lowest meta-analysis of adherence to the DASH diet and risk of stroke. The pooled result of 11 independent studies suggested that higher adherence to the DASH diet was associated with a lower risk of developing stroke. DASH=Dietary Approaches to Stop Hypertension.

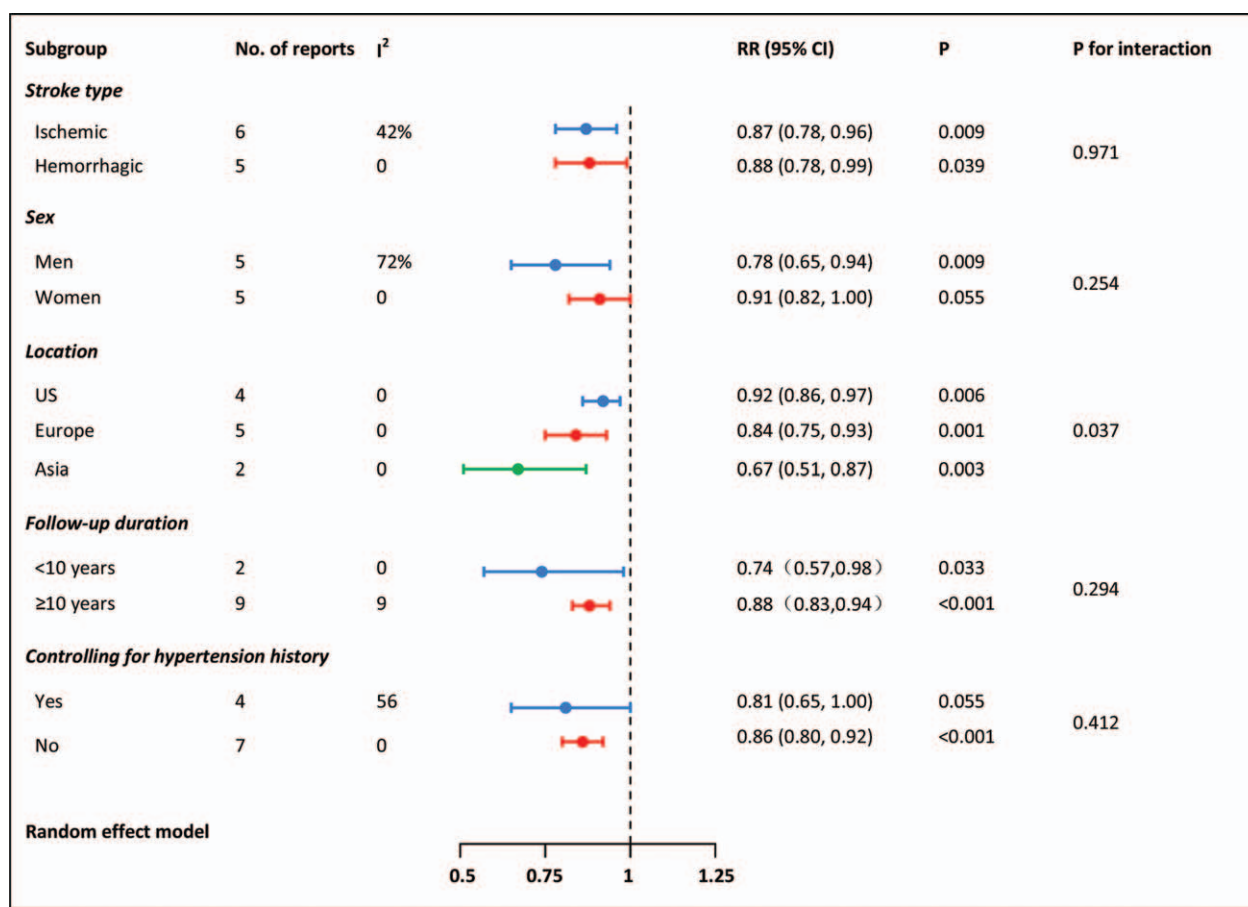


Figure 3. Subgroup analysis of adherence to the DASH diet and risk of stroke. The results suggested that the benefit of DASH diet appeared to be more pronounced in populations from Asia than from Western countries. DASH=Dietary Approaches to Stop Hypertension.

3. Results

3.1. Study search

A total of 3154 publications were documented during the preliminary search, of which 371 duplicates and 2706 irrelevant studies were removed. Among the remaining studies, 65 were further excluded after full-text reading. Finally, 12 prospective cohort studies^[15–26] published between 2007 and 2018 were included in the analysis (Fig. 1).

3.2. Baseline characteristics

The main details of the included studies were summarized in Table 1. Generally, the dataset comprised 548,632 participants, of whom 15,270 developed stroke during the follow-up time of 5.7 to 24 years. The baseline age ranged from 20 to 79 years, and men and hypertensive patients accounted for 31% and 25% of the total participants, respectively. Of the studies, most were conducted in the United States and Europe, and only 2 were from Asia. All studies evaluated the diet by food-frequency questionnaire, and stroke cases were identified using International Classification of Diseases codes or medical records. The most common factors controlled for in the studies were age, sex, smoking, alcohol use, body mass index, and energy intake (Table S2, <http://links.lww.com/MD/C501>). The NOS score of the included studies varied from 7 to 9, suggesting the presence of high methodological quality.

3.3. Highest versus lowest analysis

Eleven studies^[15–21,23–26] were included in the meta-analysis for total stroke, and no heterogeneity was found across them ($I^2 = 4\%$, $P = .41$). Compared with lower adherence, higher adherence to the DASH diet significantly decreased the risk of developing stroke (RR 0.88, 95% CI 0.83–0.93; Fig. 2). This benefit was not modified by the difference in stroke type, sex, follow-up duration, and adjustment of hypertension history. However, the risk reduction in stroke appeared to be more pronounced in populations from Asia than from Western countries (P for interaction = .037; Fig. 3). Sensitivity analysis by omitting studies one at a time had no influence on the final results. There was an indication of publication bias from the asymmetric funnel plot and Egger test ($P = .004$). After introducing the “trim and fill” strategy to adjust this bias, the overall RR maintained significant in favor of higher adherence to the DASH diet (RR 0.90, 95% CI 0.84–0.96; Fig. S1, <http://links.lww.com/MD/C501>)

3.4. Dose-response analysis

Seven cohorts from 6 studies^[15,20,21,24–26] were selected for the dose-response meta-analysis. There was no evidence of a curvilinear relationship between the DASH diet score and risk of total stroke (P for nonlinearity = .41). For each 4-points increase in the DASH diet score, the risk of stroke was reduced by 4% (RR 0.96, 95% CI 0.94–0.97; Fig. 4). For the 4 knots (5th, 35th, 65th, and 95th percentiles) of DASH diet score, the RR

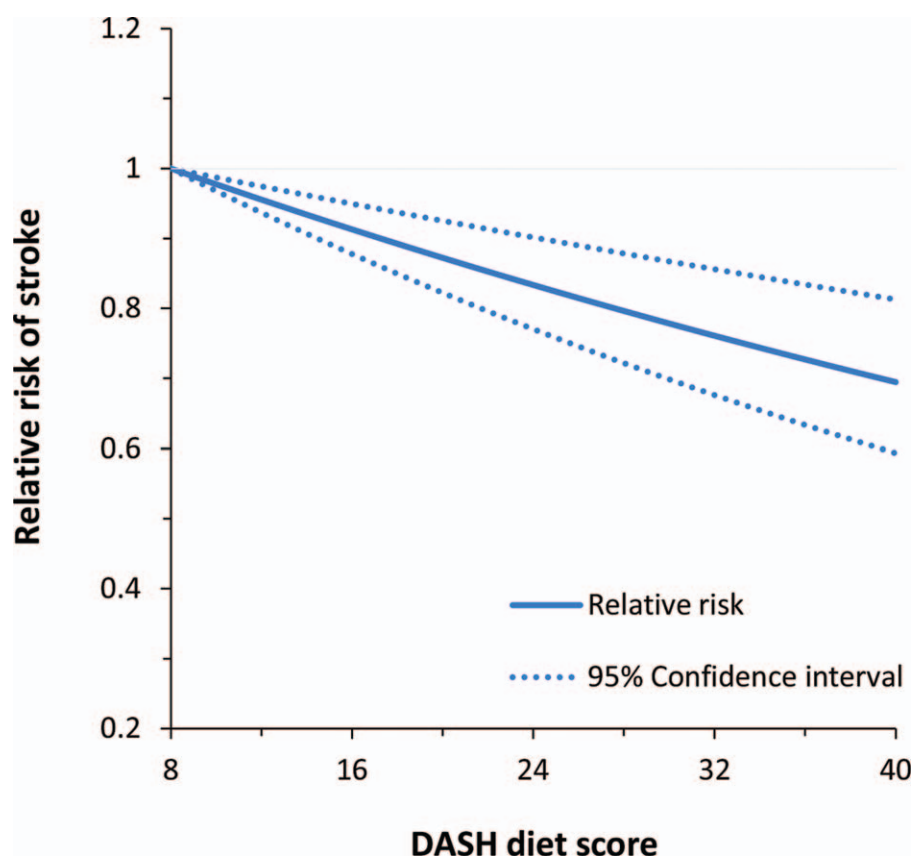


Figure 4. Dose–response meta-analysis of adherence to the DASH diet and risk of stroke. The results showed that there was an inversely linear association between DASH diet score and risk of stroke. DASH=Dietary Approaches to Stop Hypertension.

(95% CI) of stroke was 0.93 (0.91–0.96), 0.86 (0.80–0.92), 0.81 (0.74–0.89), and 0.74 (0.66–0.85), respectively.

4. Discussion

A healthy diet has been accepted as a critical preventive strategy against the development of stroke. In the present meta-analysis of 548,632 participants and 15,270 stroke cases, we found that higher adherence to the DASH diet was associated with a lower risk of developing stroke. Such a benefit of DASH diet seemed to be greater in the Asian than in the Western populations. In addition, dose–response meta-analysis suggested a linear correlation of DASH diet score with stroke risk, and every 4-points increase in the score lowered the risk of stroke by 4%.

Previous epidemiological studies have revealed the salutary effects of DASH diet on vascular disease. In a recent longitudinal study of 153,082 US veterans, the DASH diet score was inversely associated with the incidence of coronary artery disease (HR 0.82, 95% CI 0.75–0.89).^[27] Likewise, Niknam et al analyzed the data of 388 hospitalized patients in a case-control study, and found that a DASH-style diet could lower the prevalence of stroke (odds ratio [OR] 0.48, 95% CI 0.24–0.96).^[28] Apart from this, a previous meta-analysis by Salehi-Abargouei et al^[29] also reported an inverse relationship between DASH diet consumption and risk of stroke (RR 0.81, 95% CI 0.72–0.92). Nevertheless, that meta-analysis only included 3 studies^[15,19,20] for stroke, and no subgroup analysis was conducted. Our work summarized the data of 12 prospective cohort studies, thus providing more

comprehensive and reliable insights into the role of DASH diet in preventing stroke.

Several possible mechanisms may account for the causal relation of adherence to the DASH diet and stroke. In addition to the blood pressure-lowering effects, randomized trials also found that intervention with DASH diet improves lipid profiles and body weight,^[30,31] and all of these cardiometabolic risk factors have been linked to the pathology of stroke. Following a DASH diet has also been pointed out to decrease the risk of developing type 2 diabetes mellitus^[32] and metabolic syndrome,^[33] both of which may contribute to the development of ischemic stroke.^[34] Furthermore, a recent meta-analysis by Soltani et al^[35] showed that adherence to the DASH diet is effective in improving serum inflammatory biomarkers in adults, and potential profitable impacts of the DASH diet on reduced oxidative stress have also been described.^[36] Therefore, the association between DASH diet and stroke may be also mediated by its anti-inflammatory and antioxidative effects.^[37]

In addition to ischemic stroke, we observed that higher accordance to the DASH diet also benefited the prevention of hemorrhagic stroke. This finding has not been achieved in previous cohort studies,^[20,22] although elevated blood pressure is known to increase the incidence of cerebral hemorrhage.^[38] A possible explanation is the small number of hemorrhagic stroke cases in previous studies, which may hinder the detection of significance. Apart from this, a geographical difference was seen regarding the preventive effects of DASH diet on stroke, as the effects appeared to be greater in the Asian than in the US or European populations. For the Asian population in particular,

the management of hypertension is important because of the higher rate of stroke events than in Western countries.^[39] Also, the contribution of blood pressure for stroke events is greater among Asians compared with Caucasians.^[40] Of note, only 2 included studies were conducted in Asia, which may be inadequate to assess the ethnicity-specific healthy impacts of DASH diet. Future prospective studies are needed to address this issue.

There are some limitations that should be acknowledged. First of all, the recall and selection bias cannot be ignored owing to the observational design of the primary studies. However, we analyzed only the maximally adjusted RRs of prospective cohort studies, which may largely attenuate such bias. Secondly, due to the lack of data, we could not perform stratified analyses by some important confounders, such as age and body mass index. Thirdly, publication bias was detected in the pooling analysis of total stroke. Nevertheless, the result remained significant after the application of the “trim and fill” method, suggesting that our findings are less likely to be affected by the publication bias. Fourthly, as only 1 study^[21] has described the proportion of patients with blood pressure-lowering treatments, it is difficult to exclude the impacts of antihypertensive medication on the final results.

5. Conclusions

In summary, our study demonstrates that higher adherence to DASH diet is associated, in a dose-response pattern, with a decreased risk of stroke. Future large, prospective studies are warranted to confirm our findings, in particular, the geographic difference regarding the benefit of DASH diet in the prevention of stroke.

Author contributions

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