Dietary fiber intake and risk of first stroke: A systematic review and meta-analysis

Cover title: Dietary fiber and risk of stroke

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Abstract

Background and purpose:. Despite a decreasing trend of stroke incidence in industrialised countries, the high prevalence of stroke remains a concern for governmental bodies. Fiber intake is associated with reduced stroke risk in prospective studies, but no meta-analysis has been published to date.

Methods: Multiple electronic databases were searched for healthy participant studies reporting fiber intake and incidence of first haemorrhagic or ischemic stroke, published between January 1990 and May 2012.

Results: Eight cohort studies from the United States, Northern Europe, Australia and Japan met inclusion criteria. Total dietary fiber intake was inversely associated with risk of haemorrhagic plus ischemic stroke, with some evidence of heterogeneity between studies (I^2) (relative risk (RR) per 7g/day 0.93, 95% confidence intervals (CI) 0.88 to 0.98, I^2=59%). Soluble fiber intake, per 4g/day, was not associated with stroke risk reduction with evidence of low heterogeneity between studies RR 0.94 (95%CI: 0.88 to 1.01, I^2=21%). There were few studies reporting stroke risk in relation to insoluble fiber or fiber from cereals, fruit or vegetables.

Conclusions: Greater dietary fiber intake is significantly associated with lower risk of first stroke. Overall, findings support dietary recommendations to increase intake of total dietary fiber. However, a paucity of data on fiber from different foods precludes conclusions regarding the association between fiber type and stroke. There is a need for future studies to focus on fiber type and to examine risk for ischaemic and haemorrhagic strokes separately.

Introduction

Stroke and other cerebrovascular diseases are the second most common cause of death worldwide, and in 2008 accounted for 6.2 million deaths (11% of fatalities).[1] In many developed countries the incidence of stroke has declined, largely due to improvements in hypertension management. However, the absolute number of strokes continues to increase with the expansion of the aging population in these counties.[2] Data from the United States (US) suggests that 78% of strokes are first attacks[3] with ischaemic stroke being ten times more common than haemorrhagic stroke in most western countries.[4] Moreover, stroke is the leading cause of disability in many developed countries and its primary prevention should, therefore, be a key public health priority.[5]

Dietary fiber intake is associated with improvements in key modifiable risk factors for stroke, such as hypertension[6, 7] and hypercholesterolaemia.[8] Greater fiber intake is also associated with improvements in insulin resistance, which has been suggested as a mechanism for the development of hypertension, through the compensatory hyperinsulinaemia which can develop with insulin resistance.[9] In addition, water-soluble fiber aids regulation of blood cholesterol levels by slowing the absorption of cholesterol from the small intestine through the formation of viscous gels.[10, 11]

Many epidemiological studies have examined stroke risk in relation to dietary fiber intake,[12-19] with some suggesting a protective association[7, 15, 16, 19] but others not[13, 14, 17]. Yet, to date, there are no published meta-data. Consequently, the aim of this work was to collate and meta-analyse data relating total dietary fiber intake or fiber from key food sources and primary stroke events.

Methods

Search strategy

Literature searches for articles published between 1st January 1990 to November 2009 and reporting an association between carbohydrate intake in any form with cardiometabolic health outcomes were conducted using six electronic databases:

The Cochrane Library, MEDLINE, MEDLINE in-process, Embase, CAB Abstracts, ISI Web of Science and BIOSIS. To extend this search from 2009 to 30th May 2012, MEDLINE, MEDLINE in-process and Embase were re-searched, as these databases were the main source of included articles in the initial search. The top-up search was just carried out for articles reporting dietary fiber and incident stroke but the same key terms were included. Key terms used, among others, included 'fiber', 'fibre', 'cellulose', 'lignin', non starch polysaccharide and other fiber sub-fractions, 'stroke' and 'transient ischemic accident/incident'. Bibliographies of relevant articles were also screened and hand-searching of selected journals was carried out.

Study selection

Initial screening of titles and abstracts was undertaken by members of the review team to remove those it was immediately apparent were not relevant such as editorials, single case-study reports and therapeutic approach articles. Pre-specified guidelines were in place to ensure consistency between separate reviewers. [From the articles identified with the full carbohydrate and cardiometabolic health search terms, a 10% sample of those articles deemed not potentially relevant were double-checked by another review team member to ensure an acceptable level of agreement. Of the 2,214 re-screened, 17 were re-marked as potentially relevant. Five of these 17 were ultimately included in the review, however hand-

searching had identified 4 of the 5 articles ultimately included in the review, leaving 1 RCT publication which was mis-identified as not being relevant in the checking sample.] Full-text copies of potentially relevant articles were read independently by two review team members and disagreements were settled by a third reviewer. A structured flow chart and detailed guidelines were used to determine eligibility for inclusion.

Eligible articles reported original research from prospective observational studies (with ≥3-year follow-up), published in English language since 1990 and reporting incident first stroke events in relation to dietary fiber intake.

Prevention of primary stroke was the main focus for this work (not secondary prevention) and therefore, only studies with generally healthy participants were included, i.e. cohort participants were not recruited specifically because of their ill health or personal history of disease.

Data Extraction

Data were extracted into a Microsoft Access database, with pre-defined fields which captured aspects of study design and quality as well as individual results (relative risks and confidence intervals), including cohort design, exposure type and quantity, case numbers, definition of outcome and adjustments used within analyses. This method of data extraction was based on the approach used for the WCRF Second Expert Report.[20] Methodological quality of studies was not evaluated using a formal scoring approach but aspects of study quality, such as follow-up duration, case ascertainment and adjustment for various important confounders was investigated through meta-regression.

Statistical Methods

Because different studies use different definitions for their exposure categories, we derived an estimated dose-response trend for each study, using the method recommended by Greenland and Longnecker.[21] These dose-response trends were then combined using random effects meta-analysis. The method therefore computes study-specific slopes (with 95% confidence intervals), based on the results presented for each category of fiber intake. To derive a study's dose-response curve, the distribution of cases and person-years, or cases and non-cases, with relative risks and estimates of uncertainty (e.g. confidence interval) for at least three categories of quantified fiber intake must be presented in the reviewed publication. Where the total number of cases or person-years was presented, but not the distribution, we estimated this based on definitions of the quantiles. We then assigned the median or mean level of fiber intake to the corresponding relative risk for each study. Where medians and means were not presented, we used the category midpoint. Where the highest or lower category was unbounded, we assumed the width of the category to be the same as the next adjacent category, so that we could assign a midpoint. Where studies already reported a linear dose-response trend, with confidence interval or standard error, this was used directly.

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Nonlinear dose-response curves were plotted using restricted cubic splines for each study, using knots fixed at percentiles 10%, 50% and 90% through the distribution.[22] These were combined using multivariate meta-analysis.[23] All analyses were performed in Stata 12.1.[24]

In order to include results from one study in meta-analyses,[17] the method of Hamling and colleagues was used to first combine data for stroke sub-types in a random effect meta-analysis.[25] Where results were only presented separately for men and women, separate dose-

response curves were derived, and these were then combined into a single estimate for the study using a fixed effects meta-analysis, before combining with the other studies using a random effects meta-analysis. This maintained the correct degrees of freedom for tests of heterogeneity.

Pooled estimates are only presented when heterogeneity (I^2) did not exceed our pre-specified cut point of 75% and when studies had included appropriate adjustments. For comparability, fiber increments presented in the dose-response figures were chosen to be approximately one standard deviation, based on European population intakes, from multiple sources[17, 26-28] and are equivalent to Association of Official Analytical Chemist (AOAC) fiber values.

Heterogeneity between studies was tested using Cochran's Q statistic, alongside the more useful proportion of total variation in study estimates that is due to heterogeneity (I^2)[29]. Meta-regression of pre-defined study characteristics was also undertaken and the following were explored: fiber intake assessment method (AOAC/non-AOAC), inclusion of non-fatal events, follow-up length (<10years/≥10years), geographic location (Americas/EU/Other) and whether the results were adjusted for the following: age, alcohol, anthropometry, energy intake, physical activity or gender.

The potential for small-study effects such as publication bias were explored using funnel plots with Egger's test of asymmetry where were sufficient studies to allow the test.

Results

Eight cohort studies were identified[12-19] (Supplemental figure 1), three from the US,[12, 13, 18] two were Japanese,[14, 16] two were from northern Europe[17, 19] and one from Australia.[15] Study follow-up ranged from 8 to 19 years (see Table 1) and case numbers ranged from 95 fatal strokes[15] to 2781 incident events.[17] Only fatal events were reported in two studies[14, 15] and another reported only ischaemic stroke risk,[19] but five publications reported stroke incidence

data.[12, 13, 16-18] Fiber intakes were estimated using AOAC values, or equivalent, in all but the two northern European studies.[17, 19]

Total fiber intake and stroke risk

Seven studies reported total dietary fiber intake in relation to stroke risk, all of which were included in the dose-response meta-analysis (Figure 1).[12-14, 16-19] The pooled relative risk (RR) per 7g/day increase was 0.93 (95% confidence intervals (CI) 0.88 to 0.98). There was some evidence of heterogeneity between studies I^2=59% (95% CI: 7 to 82%). The dose-response curve for total fiber intake and stroke (Figure 2) suggests that risk steadily reduces with increasing total fiber intake. Data points become especially sparse above intakes of 25g/day and so extrapolation of risk at higher intakes should be undertaken with caution. There was evidence of a small-study effect (p=0.002).

Haemorrhagic or Ischaemic stroke

Four studies reported ischaemic stroke risk. A protective association for total dietary fiber was reported in both Japanese women RR 0.73 (95%CI: 0.55 to 0.97)[16] and Swedish men RR 0.69 (95%CI: 0.49 to 0.96) (Supplemental table 1).[19] In the Nurses' Health Study (NHS), the risk estimate was less than one, but the confidence intervals were wide, RR 0.78 (95%CI: 0.56 to 1.09) [18] reflecting greater uncertainty about the role of fiber in this cohort In a cohort of male smokers, no association was apparent.[17]

Haemorrhagic stroke, was reported in three studies and evidence of a protective association was only seen for intracerebral haemorrhagic stroke in women of a Japanese study[16] and not in the two other cohorts.[17, 18]

Soluble fiber intake and stroke risk

Four studies presented stroke risk in relation to water-soluble fiber intake[13, 14, 16, 17] and all but one, which did not present an estimate of soluble fiber intake,[16] were included in the meta-analysis (Figure 3). For each 4g/day increase in soluble fiber, risk was reduced by 6%: RR 0.94 (95% CI: 0.88 to 1.01). Evidence of relatively low heterogeneity between studies was seen, I^2=21% (95% CI: 0 to 92%) but since the pooled estimate was based on only three studies, it should be interpreted with care. In the study which was not included in the meta-analysis, there was an indication of a protective association for total stroke with greater soluble fiber intake, (p-trend=0.031). However, the comparison of high to low consumers did not show strong evidence of an association RR 0.78 (95%CI: 0.58 to 1.06) and the results for male participants were omitted from the paper.[16] There were too few studies to investigate any small-study effects.

Insoluble fiber and stroke risk

Three cohorts reported an association between stroke risk and insoluble fiber intake,[14, 16, 17] but a meta-analysis could not be conducted as one paper did not provide an estimate for insoluble fiber intake in the sample.[16] A protective association for total stroke RR 0.62 (95%CI: 0.45 to 0.85) and cerebral infarction RR 0.62 (95%CI: 0.40 to 0.98) was reported in Japanese women in one study (results for men were not presented in the paper)[16] but associations were not observed in another Japanese cohort[14] or in the Finnish Alpha-Tocopherol Beta-Carotene Study (ATBC) of male smokers.[17]

Cereal fiber intake and stroke risk

Three cohorts reported stroke risk in relation to cereal fiber intake (including fiber from breads, crackers, grains and pasta etc.).[15, 17, 18] When pooled, there was evidence of very high

heterogeneity between studies I^2=90% (95%CI: 73 to 96%) and a pooled estimate is therefore not presented because this would be unreliable. The NHS reported evidence of an association when the highest cereal fiber consumers were compared to lowest (5.7 vs. 1.4g/day) for total stroke RR 0.66 (95%CI: 0.52 to 0.83) and haemorrhagic stroke RR 0.51 (95%CI: 0.33 to 0.78) but this was not apparent for ischaemic stroke, RR 0.80 (95%CI: 0.57 to 1.12).[18] Another study also saw a significant association with risk of total stroke when the lowest consumers were compared to highest (3 vs. 11g/day) RR 2.13 (95%CI: 1.19 to 3.80)[15] but in the ATBC study, there was no evidence to support a significant association.[17]

Fruit and vegetable fiber and stroke risk

Two cohorts reported stroke risk and fruit or vegetable fiber intake. In the NHS, there was no strong evidence of an association for stroke and fruit fiber, RR 0.87 (95%CI: 0.70 to 1.09) and for vegetable fiber RR 0.92 (95%CI: 0.74 to 1.14) for highest compared to lowest consumers.[18] In the ATBC study, no strong evidence of an association existed for fruit fiber, but vegetable fiber intake was significantly inversely associated with risk of ischaemic stroke, RR 0.86 (95%CI: 0.76 to 0.99).[17]

Meta-regression

When study subgroups were pooled, the results largely offered similar estimates (Supplemental table 2), however it should be recognised that due to small numbers of included studies, analyses may have a limited capacity to fully explain potential sources of heterogeniety. Different results were observed when data from the two European studies, which did not assess fiber intake using AOAC methods, were pooled RR 0.94 (95%CI: 0.81 to 1.08, I^2=82%).[17, 19] A non-significant association was also reported in one study which

presented only fatal stroke data and total fiber intake RR 0.89 (95%CI: 0.73 to 1.10).[14] Studies were also grouped on the basis of included adjustments but as all seven studies adjusted for each of the variables listed in the method section, no additional pooled values are presented.

Discussion

The results of this meta-analysis indicate that greater total dietary fiber intake is associated with a significantly reduced risk of primary stroke occurrence. Our findings support recommendations to increase fiber content of the diet. Notably, an increase of 7g/day of total dietary fiber, equivalent to the standard deviation of European population level fiber intakes, was associated with a significant 7% reduction in stroke risk. To place this in context, increasing dietary fiber intake (AOAC) by 7g/day is achievable and it is equivalent to fiber within a portion of wholemeal pasta (70g), a piece of fruit (apple/pear/orange) plus a serving of tomatoes each day.[10]

Average fiber intakes in the US are estimated to be around 13g/day in women and 17g/day in men.[30] These values are estimated to be around 5g lower than actual consumption as inulin and oligosaccharides were not included in values.[30] Increasing fibre by 7g/day would bring intakes close to current recommended levels in the US of around 21-25g/day for women of different ages and 30-38g/day for men.[30]

Biologically plausible mechanisms exist for fiber and key risk factors for stroke, such as overweight and high cholesterol levels. Soluble types of fiber form gels in the stomach and small intestine, slowing the rate of nutrient absorption and slowing gastric emptying which increases satiety and influences the overall amount of food eaten, resulting in lower levels of overweight.[10, 11] Bacterial fermentation of resistant starch and soluble fibers in the large intestine produces short-chain fatty-acids which inhibit cholesterol synthesis by the liver,

consequently lowering serum levels.[10] Bile acid reabsorption is also slowed through physically binding to insoluble fiber molecules and the presence of soluble fiber gels. Bile acids contain cholesterol and when absorption is slowed, blood cholesterol is shunted into bile acid production, thus lowering circulating levels.[10, 11]

Physiological effects of high-fiber diets may depend on the food sources and types of fiber consumed[31] and so examining risk associations with different foods is potentially important. As studies focusing on cereal, fruit or vegetable sources of fiber were too few or too heterogeneous to pool, conclusions cannot be made and future studies should explore risk with food sources of fiber and also with fractions (soluble/insoluble), to fill this research gap.

Although no previous reviews were identified which examined fiber and stroke risk, one review on wholegrains found a similar lack of published data relating to stroke risk.[32] The review presented mixed findings in the few studies identified, but concluded there was a strong suggestion of a protective effect of whole grain on stroke risk.[32] Our findings are aligned with this observation for wholegrain diets, but whole grains contain many other potentially protective components aside from having a high fiber content.[33] Other protective components of whole grains include plant stannols and sterols, found in oilseeds, grains, nuts and legumes, which are associated with reducing both biliary and dietary cholesterol absorption and also unsaturated fatty-acids, found in wholegrain wheat and oats which additionally contribute towards lowering cholesterol levels.[34]

Differing results seen in the studies using AOAC methods to estimate fiber intake, or not, could indicate that the resistant starch or lignin components are protective since the non-AOAC fiber values do not include these elements.[35] However, there was strong evidence of between study heterogeneity and the associations reported in the Finnish study of male smokers pull the pooled result for the two European studies towards the null. The different

observations from this study suggest beneficial effects of fiber on stroke risk differ from non-smoking populations.[17]

The contrasting results for the studies reporting incident events and the one study reporting mortality data suggest that protective associations may be best explained with the inclusion of non-fatal events. This is unsurprising since the addition of cases will increase statistical power and reduce misclassification of the non-fatal events, which are not identified and are combined with non-cases in analyses.

A potential source of heterogeneity in the total fibre meta-analysis was small-study effects, with some evidence of asymmetry in the funnel plots. This could be because of publication bias, or possibly better dietary assessment in the smaller studies.

A key strength of this work is the inclusion of large cohort studies with long follow-up durations and therefore many case observations. The prospective nature of the included studies also substantially reduces recall bias. A limitation in observational cohort studies is the inherent problem of unadjusted confounding, which remains when data are pooled and means that fiber may be acting as a surrogate for another healthy lifestyle factor. Greater intakes of fibre are associated with other healthy behaviours such as lower smoking rates and increased physical activity[14, 16], both of which may independently influence stroke occurrence, so it is particularly important that these factors are taken into account. It is difficult to estimate the extent to which other behaviours are accurately controlled for when used as adjustments in models and therefore we cannot ascribe causality to the associations from observational studies. These weaknesses of observational studies therefore apply equally to meta-analysis of such studies. All of the pooled studies did, however, include adjustment for potentially important confounding variables such as age, BMI, blood pressure or history of hypertension, smoking status, alcohol intake, physical activity and gender (where applicable) and also a variety of other health and lifestyle variables (see Table 1).

Conclusion

Findings for this meta-analysis confirm that dietary fiber significantly protects against the risk of stroke. Our study supports current guidelines to increase fiber consumption. The identification of potentially protective food sources of fiber may help tailor recommendations for at-risk populations. To achieve this, further work is needed to explore the relationship between the various fiber types and stroke types.

Summary

Higher total dietary fiber intake is significantly associated with lower risk of first stroke. Overall, findings support dietary recommendations to increase intake of total dietary fiber. However, a paucity of data on fiber from different foods precludes conclusions regarding the association between fiber type and stroke. There is a need for future studies to focus on fiber type and to examine risk for ischaemic and haemorrhagic strokes separately.

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Figure 1. Relative risk (RR) plus 95% confidence intervals (CI) for stroke and each 7g/day increase in total dietary fiber. Heterogeniety (I^2) for the pooled estimate was 59% (95% CI 7%, 82%)

Figure 2. Restricted cubic spine displaying relative risk (RR) for stroke with increasing total dietary fiber intake levels

Figure 3. Relative risk (RR) plus 95% confidence intervals (CI) for stroke risk with each 4g/day increase in soluble dietary fiber. Heterogeniety (I^2) for the pooled estimate was 21% (95% CI 0%, 92%)

Table 1. Details of cohorts studies reporting stroke risk and dietary fiber intake

Authors Cohort name	Country/ Sex of participants	Age at recruitment (years)	Follow-up duration (years)	Initial cohort size (eligible after exclusions)	Fiber estimation method	Outcomes examined	Case numbers	Relative Risk (95% Confidence intervals)	P trend	Model adjustments
[12] Ascherio et al., 1998 Health-professionals Follow-up Study	United States Male	40-75	8	51529 (43738)	AOAC High vs. low consumers	Total stroke incidence	328	TF: 0.70 (0.48, 1.00)	0.028	Age, total energy intake, smoking, alcohol, history of hypertension or hypercholesterolemia, parental MI before 65y, profession, BMI, physical activity
[13] Bazzano et al., 2003 National Health and Nutrition Examination Survey I	United States Male/ Female	25-74 (mean 49)	19	14407 (9776)	Method not reported, likely AOAC. High vs. low consumers for all exposures	Total stroke incidence	928	TF: 0.95 (0.78, 1.16) SF:0.88 (0.73, 1.06)	0.44 0.14	Age, sex, race, education, SBP, serum total cholesterol, DM, physical activity, alcohol, smoking, BMI, saturated fat intake

*[14] Eshak et al., 2010
Japan Collaborative Cohort Study
	Japan
	Male/ Female
		40-79	14.3	110792
				(58730)
					Assessment similar to AOAC
					High vs. low consumers for all exposures
						Total stroke mortality	983	TF(M):1.09 (0.75, 1.58)
								TF(F):1.05 (0.73, 1.51)
								SF(M): 0.90 (0.61, 1.31)
								SF(F): 1.02 (0.73, 1.42)
								IF(M):0.96 (0.64, 1.45)
								IF(F): 0.90 (0.63, 1.28)
									0.555
									0.775
									0.790
									0.643
									0.715
									0.128
										Age, BMI, history of hypertension or DM, alcohol, smoking, education, physical activity, mental stress, sleep, fish intake, saturated fat, n-3 fatty acids, sodium, folate, Vitamin E

[15] Kaushik et al., 2009 Blue Mountains Eye Study	Australia Male/ Female	Median 65	13	3654 (2897)	AOAC CF (energy adjusted) low vs. high consumers	Total stroke mortality	95	CF: 0.94 (0.73, 1.22)	0.65	Age, gender, SBP, DBP, antihypertensive medication, BMI, smoking, education, self-rated health, history of MI, stroke or DM
*[16] Kokubo et al., 2011 Japan Public Health Centre-based cohort	Japan Male/ Female	40-69	10.4	133323 (86387)	Assessment similar to AOAC High vs. low consumers for all exposures	Total stroke incidence	2553	TF(M):1.00(0.76, 1.32) TF(F):0.64 (0.46, 0.88) SF(F):0.78 (0.58, 1.06) IF(F):0.62 (0.45, 0.85)	0.976 0.005 0.031 0.001	Age, sex, smoking, alcohol, BMI, history DM, medication for hypertension or hypercholesterolemia, physical activity, fruit intake, vegetables, fish, sodium, isoflavone, energy intake, health centre
						Cerebral infarction incidence	265	TF(M):0.94 (0.66, 1.34) TF(F):0.73 (0.55, 0.97) SF(F):0.73 (0.47, 1.14) IF(F):0.62 (0.40, 0.98)	0.540 0.029 0.051 0.006	
						Intracerebral haemorrhage incidence	163	TF(M):1.08 (0.66, 1.78) TF(F): 0.53 (0.28, 0.97) SF(F):0.71 (0.40, 1.26) IF(F):0.55 (0.30, 1.00)	0.588 0.100 0.183 0.070	
						Subarachnoid haemorrhage	83	TF(M):1.02 (0.45, 2.54) TF(F):0.72 (0.37, 1.43)	0.672 0.419	

Authors Cohort name	Country/ Sex of participants	Age at recruitment (years)	Follow-up duration (years)	Initial cohort size (eligible after exclusions)	Fiber estimation method	Outcomes examined	Case numbers	Relative Risk (95% Confidence intervals)	P trend	Model adjustments
[17] Larsson et al., 2009 Alpha-tocopherol beta-carotene study	Finland Male	50-69	13.6	29133 (26556)	Assessed using Englyst method High vs. low consumers for all exposures	Subarachnoid haemorrhage incidence	196	TF:1.09 (0.69, 1.71) SF:0.95 (0.51, 1.79) IF:1.10 (0.70, 1.75) CF:1.02 (0.66, 1.57) FF:1.23 (0.80, 1.91) VF:0.74 (0.48, 1.14)	0.87 0.66 0.80 0.84 0.15 0.12	Age, supplementation group, smoking, BMI, SBP, DBP, serum total cholesterol, serum HDL, history of DM or CHD, physical activity, alcohol, energy intake
						intracerebral haemorrhage incidence	383	TF: 0.94 (0.66, 1.35) SF:0.99 (0.69, 1.42) IF:0.89 (0.63, 1.26) CF:0.93 (0.66, 1.30) FF:0.82 (0.58, 1.15) VF:0.81 (0.57, 1.14)	0.37 0.35 0.29 0.55 0.21 0.62	
						Cerebral infarction incidence	2702	TF:0.86 (0.76, 0.98) SF:0.79 (0.69, 0.89) IF:0.88 (0.76, 0.99) CF:0.92 (0.82, 1.04) FF:0.86 (0.76, 0.97) VF:0.82 (0.73, 0.93)	0.03 0.001 0.06 0.36 0.05 <0.001	
[18] Oh et al., 2005 Nurses' Health Study	United States Female	30-55	18	121700 (78779)	AOAC High vs. low consumers for all exposures	Total stroke incidence	1020	TF:0.83 (0.66, 1.04) CF:0.66 (0.52, 0.83) FF:0.87 (0.70, 1.09) VF:0.92 (0.74, 1.14)	0.07 0.001 0.28 0.14	Age, BMI, smoking, alcohol, parental MI, history of hypertension, hypercholesterolemia or DM, menopausal status and postmenopausal hormone use, aspirin use, multivitamin use, vitamin E, physical activity, energy intake and carbohydrate intake
						Ischaemic stroke incidence	515	TF:0.78 (0.56, 1.09) CF:0.80 (0.57, 1.12) FF:0.87 (0.63, 1.21) VF:1.01 (0.74, 1.38)	0.09 0.23 0.22 0.48	
						Haemorrhagic stroke incidence	279	TF:0.84 (0.54,1.30) CF:0.51 (0.33, 0.78) FF:0.86 (0.57, 1.29) VF:0.76 (0.51, 1.13)	0.34 0.01 0.64 0.18	
*[19] Wallstrom et al., 2012 Malmo Diet and Cancer Cohort	Sweden Male/ Female	Age: 58 years	13	28098 (20674)	Non starch polysaccharide high vs. low consumers	Ischaemic stroke incidence	743	TF(M):0.69 (0.49, 0.96) TF(F):0.73 (0.52, 1.04)	0.050 0.18	Age, total energy intake, season, BMI, smoking, education, alcohol, SBP, antihypertensive treatment, physical activity

Abbreviations: AOAC Association of Official Analytical Chemists, BMI body mass index, CF cereal fiber, CHD coronary heart disease, DBP diastolic blood pressure, DM diabetes mellitus, F female, FF fruit fiber, HDL high density lipoprotein, IF water-insoluble fiber, M male, MI myocardial infarction, SBP systolic blood pressure, SF water-soluble fiber, TF total fiber, VF vegetable fiber