Dietary Fiber Intake and Risk of Cardiovascular Disease in the Japanese Population: The Japan Public Health Center-Based (JPHC) Study Cohort

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Abstract

Background/Objectives: There has been no study on the association between dietary fibers and the incidence of stroke and coronary heart disease (CHD) in Asia. We investigated the association between dietary fiber and the risk of cardiovascular disease (CVD), which we defined as stroke or CHD, in a Japanese population.

Subjects/Methods: We studied 86,387 Japanese subjects (age 45-65 years, without CVD or cancer in 1995 as Cohort I and in 1998 as Cohort II) and used a self-administered questionnaire to follow-up the participants until the end of 2004. Dietary fiber intake was estimated from food-frequency questionnaires comprising 138 food items.

Results: After 899,141 person-years of follow-up, we documented the incidence of 2,553 strokes and 684 cases of CHD. Multivariable-adjusted hazard ratios (95%CIs) of CVD for the third to fifth quintiles of total fiber were 0.79 (0.63-0.99), 0.70 (0.54-0.89), and 0.65 (0.48-0.87) in women, respectively, compared with the lowest quintile. Total fiber intake was inversely associated with the incidence of stroke, either cerebral infarction or intracerebral hemorrhage in women. The results for insoluble fiber in women were similar to those for total fiber, while those for soluble fiber were weak. An inverse association of total fiber with CVD was observed primarily in non-smokers (P for trend=0.045 and 0.001) and not in smokers (Probability values for interaction between total fiber and smoking were 0.06 and 0.01 in men and women, respectively).

Conclusions: Higher total dietary fiber was associated with reduced risk of CVD in Japanese non-smokers.

(243 words: word limitation 250 words)

Keywords: dietary fiber, stroke, ischemic heart disease, smoking, cohort study

Introduction

Prospective studies have revealed dietary fiber to be inversely associated with the risks of coronary heart disease (CHD) (Bazzano et al 2003, Mente et al 2009, Pietinen et al 1996, Rimm et al 1996, Wolk et al 1999) and of stroke (Oh et al 2005). Total fiber may provide the benefits of both water-soluble and -insoluble fiber. Water-soluble fiber may exert a cholesterol-lowering effect (Brown et al 1999), especially on low-density lipoprotein cholesterol, without affecting the concentration of high-density lipoprotein cholesterol. Insoluble fiber may reduce the risk of CHD by slowing intestinal absorption of foods and by reducing clotting factors (Marckmann et al 1990). However, most of these cohort studies were conducted in Western populations and targeted for CHD. The evidence for an inverse association between dietary fiber and stroke has been limited (Oh et al 2005), especially in Asia. No study has comprehensively evaluated the effects of soluble and insoluble fiber on the incidence of stroke and CHD in Asia. In this study, we examined the effect of the dietary intake of total fiber and its components on the incidences of cardiovascular disease in the Japanese population.

Subjects and Methods

Study Design and Samples

The Japan Public Health Center-Based Prospective (JPHC) Study is an ongoing cohort study focusing on cardiovascular disease and cancer (Baba et al 2006, Kokubo et al 2007, Mannami et al 2004, Otani et al 2006). The study participants were residents of 27 cities and towns served by nine Public Health Centers, located in Akita, Iwate, Nagano, Ibaraki, Niigata, Kochi, Nagasaki, and Okinawa Prefectures. The age distributions at the time of entry were 40 to 59 for Cohort I and 40 to 69 for Cohort II, started in 1990 and 1993, respectively. Participants were identified using the population registry in each city or town without overlap (65,803 men and 67,520 women).

Baseline Data Collection

We assessed the dietary habits of participants using a food-frequency questionnaire in 1995 and 1998 for Cohorts I and II, respectively. The questionnaires were returned by 47,400 men (72%) and 53,538 women (79%). We estimated the dietary intake of each individual based on 138-food-item questionnaire, which was previously validated for estimating various nutrients and food groups (Ishihara J et al 2006). The questionnaire also collected data on demographics, lifestyle factors, occupation, height, weight, smoking, alcohol consumption, physical activity, working hours, and mental stress. Cohort members were excluded from the

analyses if they reported CHD, stroke, or cancer in the questionnaires, moved out of the area before the baseline survey, or incompletely answered the food-frequency questionnaire. After applying these exclusions, 40,046 men and 46,341 women in total were included in the analyses. This study was approved by the institutional review board of the National Cancer Center, Tokyo, and the University of Tsukuba, Ibaraki, Japan. Each participant provided informed consent upon completion of the baseline questionnaire, which described the study purposes and follow-up. The study design was described in detail elsewhere (Watanabe et al 2001).

The frequency response choices were as follows: "never", "1-3 times/month", "1-2 times/week", "3-4 times/week", "5-6 times/week", "once/day", "2-3 times/day", "4-6 times/day", and "≥7 times/day". A standard portion was shown for each food item, e.g., 30g per cabbage intake. The relative portion sizes were as follows: small (~50% smaller than the standard size), medium (approximately the same as the standard), and large (~50% larger than the standard size). Questions on white rice intake asked the relative sizes of rice-bowls and the frequency of intake, and provided nine choices ranging from "<1 bowl/day" to "10 bowls/day" (Sasaki et al 2003). The frequency for miso soup intake provided six choices: "almost never", "1-3 times/month", "1-2 times/week", "3-4 times/week", "5-6 times/week", or "daily".

We computed daily food intakes by multiplying the frequency by the relative portion of each food item from the food-frequency questionnaire. Daily intakes of individual nutrients was calculated using the food composition table developed for each questionnaire based on the fifth revised edition of the Standard Tables of Food Composition in Japan (2000). Using this table, the dietary fiber content of each food can be estimated by employing the method of Prosky (Prosky L et al 1985).

The rank correlations between dietary fiber estimates from dietary records and those from the food-frequency questionnaire were 0.41 and 0.57 in Cohort I and II for men; and 0.41 and 0.53 in Cohorts I and II for women, respectively, all of which were assessed in our validation study (Tsubono et al 1996). For both men and women, the major sources of dietary fiber consisted of natto (fermented soybeans; 7.9% and 7.3%), rice (7.4% and 5.1%), miso (fermented soybean paste; 6.2% and 4.4%), bread (4.4% and 4.9%), carrots (3.9% and 4.4%), shiitake (oriental black mushroom; 3.4% and 3.8%), and radish (2.9% and 2.9%), respectively (Otani et al 2006).

Confirmation of Stroke and Ischemic Heart Disease

In total, 54 hospitals in the nine Public Health Center (PHC) areas were capable of computer tomographic scanning and/or magnetic resonance imaging (Kokubo et al 2007). All were major hospitals that admitted acute stroke and CHD cases. Medical records were reviewed by registered hospital workers, PHC physicians, or research physicians who were

blinded to the baseline data. Incidences of stroke and CHD were registered during the follow-up period. To complete surveillance for fatal stroke and CHD, we also conducted a systematic search for death certificates. We obtained information on the underlying cause of death by checking against death certificate files with permission to confirm mortality from cardiovascular diseases according to the International Classification of Death, 10th Revision: I00 to I99. All fatal strokes and CHD based on death certificates only have been registered as death certificates only cases, medical records in the registered hospitals were also reviewed to determine whether these cases were defined as stroke or CHD.

Strokes were confirmed according to the National Survey of Stroke criteria. These criteria require the rapid onset of a constellation of neurological deficits lasting at least 24 hours (or until death). For each stroke subtype, i.e., ischemic stroke (thrombotic or embolic stroke), intracerebral hemorrhage, and subarachnoid hemorrhage, a definite diagnosis was established based on the examination of computer tomographic scans, magnetic resonance images, or autopsy findings (Iso et al 2000). CHD indicated in the medical records was confirmed according to the criteria of the MONICA project, which requires chest pain, electrocardiographic evidence, cardiac enzyme abnormalities, and/or autopsy findings (Tunstall-Pedoe et al 1994). In this study, cardiovascular disease was defined as stroke or CHD.

For each subject, we calculated person-days of follow-up from the baseline to whichever of the following came first: the first endpoint, death, emigration, or December 31, 2004. Changes in residential status were identified through the residential registry in each area. Subjects who moved from their original residence (2% of the total participants) were censored at that time.

Statistical Analysis

The Cox proportional-hazards ratios (HRs) were fitted to the categorized consumption (the reference group is the first quartile of dietary fiber) after adjusting for age, sex, and other potential confounding factors, i.e., smoking status (never, ex-smoker, or current smoker of 1 to 19 or $\geq$20 cigarettes per day); alcohol intake (non-drinkers [<1 day/month], occasional drinkers [1-3 days/month], weekly ethanol intake of 1-149 g/week, 150-299 g/week, 300-449 g/week, or ≥450 g/week); body mass index (in quintiles); history of diabetes (yes or no); medication use for hypertension or hypercholesterolemia (yes or no); quintiles of energy-adjusted dietary intakes of fruits, vegetables, fish, sodium, and isoflavone; leisure time spent engaged in exercise (<1 day/month, 1 to 3 days/month, or $\geq$1 day/week); and proximity to the nearest public health center. The Cox proportional HRs were fitted to the combination of categorized consumption and current smoking (yes or no) after adjusting for age, sex, and other potential confounding factors, including interactive terms for the categorized dietary fiber intake and current smoking. We conducted tests for trends in confounding variables and

hazard ratios across increasing quintiles of dietary fiber intake by assigning a median value of each quintile. All statistical analyses were conducted using the SAS statistical package (version 8.2, SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the cardiovascular risk factors and intake of selected foods according to quintiles of dietary total fiber. In the food frequency questionnaire, both men and women in the higher quintiles of total dietary fiber intake were older, had lower prevalence of current smoking and drinking, had higher prevalence of engaging in exercise during leisure time (≥1 time/ week) and of taking anti-hypertensive and/or anti-hyperlipidemic drugs, and had higher rates of diabetes . As for the daily intake of nutrients, both men and women, in the higher quintiles of dietary total fiber intake had a higher intake of vegetables, fruits, fish, sodium, and isoflavones. The findings were similar for water-soluble and -insoluble fibers (not shown in table).

During a follow-up period that averaged 10.4 years, we documented 2,553 strokes (1,499 in men and 1,054 in women) and 684 CHD events (485 in men and 199 in women). The strokes included 1,428 cerebral infarctions (910 in men and 518 in women), 766 intracerebral hemorrhages (456 in men and 310 in women), and 359 subarachnoid hemorrhages (133 in men and 226 in women). Of the CHD events, 383 were confirmed clinically or by autopsy and 14 were sudden cardiac deaths. In total, 3,237 cardiovascular disease events (1,984 in men and 1,253 in women) were documented.

Multivariable-adjusted hazard ratios (95% confidence intervals) of cardiovascular disease for the second to fifth quintiles of total fiber were 0.88 (0.78 to 0.99), 0.93 (0.81 to 1.07), and 0.77 (0.65 to 0.92) in men and women combined, respectively, compared with the

lowest quintile (P for trend=0.02; data not shown). In the age-adjusted analysis, total fiber intake was inversely associated with cardiovascular diseases (stroke and CHD combined) in both men (P for trend<0.001) and women (P for trend=0.004) (Table 2). After further adjustment for confounding factors, these relationships in women persisted. Likewise, there were inverse associations in women, though no statistically significant association in men. between total fiber and the incidences of cardiovascular diseases, stroke, and either cerebral infarction or intracerebral hemorrhage, but not CHD

We observed inverse associations between insoluble fiber and the incidences of cardiovascular disease, total stroke, cerebral infarction, and intracerebral hemorrhage in women, whereas the inverse associations for soluble fiber in women were weak (Table 3). In men, these relationships were not statistically significant for either soluble or insoluble fiber (not shown in table).

The inverse associations of total dietary fiber intake with incidence of cardiovascular diseases were statistically significant for both men and women who had never smoked (trend P=0.045 and 0.001, respectively), but not in smokers of either gender (Table 4). Interactions between total, water-soluble, and water-insoluble dietary fiber intake and smoking with regard to cardiovascular diseases were highly significant in women (P=0.01, 0.01, and 0.002, respectively); and weakly significant in men (P=0.06, 0.79, and 0.04).

Discussion

In this study of middle-aged Japanese individuals, dietary intake of total fiber was found to be inversely associated with cardiovascular diseases in men and women who had never smoked. However, the association was not statistically significant in smokers of either gender. To the best of our knowledge, this is the first study on the association between dietary fiber intakes and the incidences of CHD and stroke in Asia.

A higher intake of dietary fiber, particularly water-soluble fiber, was associated with reduced risk of CHD in the NHANES I Study (Bazzano et al 2003). In men, stronger inverse associations have been observed between cereal fiber and the risk of CHD than between vegetable or fruit fiber (mainly insoluble fiber) and the risk of CHD (Pietinen et al 1996, Rimm et al 1996). However, the evidence of stroke has been limited. In women, dietary fiber, especially cereal fiber, has been also inversely associated with the risk of stroke, particularly hemorrhagic stroke, but not with cerebral infarction (Oh et al 2005). In Asia, recently, dietary intake of total fiber has been inversely associated with the risk of mortality from CHD (Eshak et al 2010). In the present study, dietary intake of total and insoluble fiber was inversely associated in Japanese women with the incidence of cardiovascular diseases particularly cerebral infarction and intracerebral hemorrhage.

Insoluble fiber affects intestinal absorption of foods, reducing clotting factors (Anderson 2000, Marckmann et al 1990), fibrinolysis (Pereira and Pins 2000), and coagulation (Jenkins et al 2000). It also reduces the levels of inflammatory markers, such as

C-reactive protein (Ajani et al 2004, Ma et al 2006). On the other hand, dietary water-soluble fiber reduces cholesterol levels (Brown et al 1999, Pereira and Pins 2000), improves glycemic control, and lowers triglyceride levels (Anderson and Tietyen-Clark 1986). However, based on a meta-analysis of 20 studies in which oat bran was added to the diet, the effects of water-soluble fiber on serum cholesterol appeared relatively modest (Ripsin et al 1992) and could not account for the substantial effect of fiber on CHD incidence. A meta-analysis of 45 prospective cohort studies showed no association between blood cholesterol levels and stroke except in those under 45 years of age when screened (1995). Although water-soluble fiber moderately reduces cholesterol levels, it may not contribute to the reduction of incident stroke~~, because hyperlipidemia was not a risk factor for stroke in the Japanese population (Okamura et al 2009)~~.

A meta-analysis of randomized placebo-controlled trials has shown that dietary and supplemental fiber intakes (average dose, 11.5 g/d) lowers systolic and diastolic blood pressure by approximately -1 mm Hg, especially in older and hypertensive populations (Streppel et al 2005). In prospective studies, dietary fiber was significantly and inversely associated with blood pressure (Ascherio et al 1996) and the incidence of hypertension (Ascherio et al 1992). Since hypertension is the strongest risk factor for stroke (Kokubo et al 2008), dietary fiber may moderately reduce the risk of stroke through a blood pressure-lowering effect.

In both men and women, there were inverse associations of total fiber with cardiovascular diseases only for those who had never smoked. The incidence of smoking is an established risk factor for stroke (Mannami et al 2004) and coronary heart disease (Baba et al 2006, Higashiyama et al 2009) and seems to diminish the benefit of dietary fiber as was also shown previously (Liu et al 2002). In women, the persistent inverse association between dietary fiber and cardiovascular diseases after the adjustment for cardiovascular risk factors was probably due to the very low prevalence of women smokers (5% of women versus 45% of men). The increased requirement for antioxidants among smokers may offset the protective effect of dietary fiber against cardiovascular disease (Jimenez et al 2008). Habitual smoking may lead to other lifestyle changes, especially in dietary patterns; smokers consumed more calories, fat, alcohol, and caffeine than did non-smokers (Liu et al 2002). These dietary patterns may also diminish the benefit of dietary fiber. However, the mechanisms by which these factors interact to offset these benefits remains to be determined.

The present study has certain methodological strengths compared to previous investigations. First, we evaluated a large prospective cohort (n=86,387) enrolled from the Japanese general population. A prospective study has little recall bias, and results obtained from the general population are more relevant than data obtained from an occupational, hospital-based cohort, and/or volunteers. Second, incidence is a more direct measure of strokes risk than death because treatment influences stroke death. Third, we estimated dietary

fiber intakes using a validated questionnaire. Our participants came from different areas of Japan and these populations consumed a sufficient variety of fiber types.

Our study has several limitations. First, data regarding present illnesses were self-reported, raising the problem of potential misclassification. However, our self-reported data may be reasonably accurate because nationwide annual health screenings, conducted since 1992 in Japan, produced similar results (Kawada and Suzuki 2005). Second, measurement errors concerning nutrient intake are inevitable when using the food frequency questionnaire. However, the reproducibility of fiber intake measurements in the questionnaire was good, as previously documented (Tsubono et al 1996). In the current study, the reproducibility of fiber intake estimates suggests that any over- or under-estimates are likely to cancel each other out and result in an accurate overall estimate. Third, since we studied dietary fiber intake, our results are not relevant to the association between fiber supplements and stroke risk.

In conclusion, our community-based prospective study showed higher dietary intakes of total and insoluble fibers to be associated with reduced risk of total strokes, cerebral infarction, and intracerebral hemorrhage in women. The inverse associations between dietary total fiber intake and cardiovascular diseases were statistically significant only for non-smokers. Our results suggest that dietary fiber may be beneficial for the prevention of cardiovascular diseases in non-smokers.

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Conflict of interest: None declared

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Supplementary contents

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TABLE 1. Distributions of Cardiovascular Risk Factors and Selected Dietary Variables in Men and Women According to Quintiles of Energy-adjusted Dietary Intake of Total Fiber: JPHC Cohorts I and II

	Men					Women				
	Q1 (Lowest)	Q2	Q3	Q4	Q5 (Highest)	Q1 (Lowest)	Q2	Q3	Q4	Q5 (Highest)
Dietary total fiber intake, g/day	6.0	9.8	11.7	14.0	19.9	7.8	11.8	13.7	15.9	21.6
Number of subjects	8,009	8,009	8,009	8,009	8,010	9,268	9,268	9,268	9,268	9,269
Age at baseline, y	51.6	53.0	54.0	55.0	56.0	52.9	54.0	54.8	55.2	55.6
Mean body mass index, kg/m^2	23.7	23.6	23.6	23.5	23.6	23.7	23.5	23.5	23.6	23.7
Current smoker, %	57	49	42	40	35	8	5	4	4	3
Current drinker, %	90	79	71	68	64	23	18	16	16	14
Exercise in leisure time $1\geq$ time/week, %	17	19	21	23	26	17	18	20	21	25
Medication for hypertension, %	15	17	19	19	21	17	20	21	22	22
Medication for hyperlipidemia, %	2	3	3	4	4	4	5	7	8	9
Present history of diabetes, %	5	5	7	8	9	2	3	4	4	5
Mean daily intake										
Vegetables, g/day	132	138	165	222	392	166	163	198	255	447
Fruits, g/day	119	124	148	203	355	194	178	214	277	457
Fish, g/day	111	85	85	95	119	110	81	83	89	105
sodium, g/day	3.5	4.7	5.1	5.5	6.3	3.9	4.7	4.7	5.1	5.9
Isoflavone, mg/day	26	37	43	49	64	29	38	43	48	61

TABLE 2. Sex-specific, Age-, and Multivariable-adjusted Hazard Ratios (HRs) and 95% Confidence Intervals for Cardiovascular Disease, Stroke, and Coronary Heart Disease According to Dietary Total Fiber Intake: JPHC Cohorts I and II

	Quintiles of energy-adjusted dietary total fiber intake					
	Q1 (Lowest)	Q2	Q3	Q4	Q5 (Highest)	Trend P
Men						
Person-years	82,828	82,274	81,907	82,191	81,702	
Cardiovascular diseases						
Number of cases	396	387	376	401	424	
Age-adjusted HR	1	0.84 (0.73-1.00)	0.79 (0.68-0.91)	0.78 (0.68-0.90)	0.79 (0.69-0.91)	<0.001
Multivariable-adjusted HR	1	0.93 (0.78-1.10)	0.86 (0.71-1.04)	0.89 (0.72-1.09)	0.94 (0.74-1.20)	0.649
All strokes						
Number of cases	303	286	279	303	328	
Age-adjusted HR	1	0.84 (0.71-0.98)	0.76 (0.65-0.90)	0.77 (0.65-0.90)	0.79 (0.67-0.93)	0.004
Multivariable-adjusted HR	1	0.94 (0.78-1.14)	0.89 (0.71-1.11)	0.92 (0.73-1.17)	1.00 (0.76-1.32)	0.976
Cerebral infarction						
Number of cases	173	186	163	180	208	
Age-adjusted HR	1	0.92 (0.75-1.13)	0.74 (0.60-0.92)	0.74 (0.60-0.92)	0.81 (0.66-0.99)	0.012
Multivariable-adjusted HR	1	0.98 (0.77-1.26)	0.79 (0.59-1.05)	0.83 (0.61-1.14)	0.94 (0.66-1.34)	0.540
Intracerebral hemorrhage						
Number of cases	96	76	99	92	93	
Age-adjusted HR	1	0.73 (0.54-0.99)	0.90 (0.68-1.20)	0.81 (0.60-1.08)	0.78 (0.58-1.05)	0.240
Multivariable-adjusted HR	1	0.84 (0.59-1.20)	1.10 (0.74-1.61)	0.99 (0.64-1.52)	1.08 (0.66-1.78)	0.588
Subarachnoid hemorrhage						
Number of cases	34	24	17	31	27	
Age-adjusted HR	1	0.66 (0.39-1.12)	0.45 (0.25-0.82)	0.77 (0.47-1.27)	0.67 (0.40-1.13)	0.279

Multivariable-adjusted HR	1	0.95 (0.51-1.76)	0.74 (0.35-1.57)	1.32 (0.63-2.78)	1.02 (0.45-2.54)	0.672
Coronary heart disease						
Number of cases	93	101	97	98	96	
Age-adjusted HR	1	0.97 (0.73-1.28)	0.87 (0.65-1.15)	0.82 (0.62-1.10)	0.71 (0.53-0.95)	0.036
Multivariable-adjusted HR	1	0.85 (0.61-1.19)	0.77 (0.53-1.13)	0.78 (0.51-1.20)	0.76 (0.47-1.25)	0.327
Women						
Person-years	97,578	98,089	97,930	97,669	96,973	
Cardiovascular diseases						
Number of cases	246	260	269	244	234	
Age-adjusted HR	1	0.95 (0.80-1.14)	0.91 (0.77-1.09)	0.82 (0.69-0.98)	0.80 (0.67-0.96)	0.004
Multivariable-adjusted HR	1	0.89 (0.73-1.09)	0.79 (0.63-0.99)	0.70 (0.54-0.89)	0.65 (0.48-0.87)	0.002
All strokes						
Number of cases	208	211	235	208	192	
Age-adjusted HR	1	0.92 (0.76-1.12)	0.95 (0.79-1.15)	0.83 (0.69-1.01)	0.78 (0.64-0.95)	0.008
Multivariable-adjusted HR	1	0.89 (0.71-1.11)	0.85 (0.67-1.08)	0.73 (0.55-0.95)	0.64 (0.46-0.88)	0.005
Cerebral infarction						
Number of cases	92	106	120	97	103	
Age-adjusted HR	1	1.01 (0.76-1.33)	1.06 (0.81-1.40)	0.84 (0.63-1.12)	0.89 (0.67-1.19)	0.208
Multivariable-adjusted HR	1	0.95 (0.78-1.17)	0.86 (0.611-1.22)	0.75 (0.58-0.96)	0.73 (0.55-0.97)	0.029
Intracerebral hemorrhage						
Number of cases	67	60	73	65	45	
Age-adjusted HR	1	0.82 (0.58-1.17)	0.95 (0.68-1.32)	0.83 (0.59-1.17)	0.57 (0.39-0.84)	0.012
Multivariable-adjusted HR	1	0.88 (0.58-1.32)	0.95 (0.61-1.47)	0.83 (0.50-1.36)	0.53 (0.28-0.97)	0.100
Subarachnoid hemorrhage						

Number of cases	49	45	42	46	44	
Age-adjusted HR	1	0.88 (0.58-1.32)	0.77 (0.51-1.17)	0.83 (0.56-1.25)	0.81 (0.54-1.23)	0.337
Multivariable-adjusted HR	1	0.84 (0.52-1.37)	0.74 (0.44-1.27)	0.81 (0.45-1.44)	0.72 (0.37-1.43)	0.419
Coronary heart disease						
Number of cases	38	49	34	36	42	
Age-adjusted HR	1	1.11 (0.73-1.70)	0.72 (0.45-1.15)	0.77 (0.48-1.21)	0.90 (0.58-1.40)	0.242
Multivariable-adjusted HR	1	0.86 (0.52-1.41)	0.51 (0.28-0.93)	0.54 (0.28-1.03)	0.68 (0.32-1.42)	0.149

Multivariable HRs were adjusted for age, sex, smoking, alcohol, body mass index, history of diabetes, medications for hypertension and hypercholesterolemia, exercise, dietary intakes of fruits, vegetables, fish, sodium, isoflavone, and energy, and public health center.

Cardiovascular disease was defined as stroke or coronary heart disease

TABLE 3. Multivariable-adjusted Hazard Ratios (HRs) and 95% Confidence Intervals for Cardiovascular Diseases, Strokes, and Coronary Heart Diseases According to Dietary Soluble and Insoluble Fiber Intake in Women: JPHC Cohorts I and II

	Dietary soluble and insoluble fiber intake					
	Q1 (Lowest)	Q2	Q3	Q4	Q5 (Highest)	trend P
Soluble Fiber						
Person-years	97,433	98,176	97,524	97,838	97,268	
Cardiovascular diseases						
Number of cases	241	268	264	244	236	
Multivariable-adjusted HR	1	0.94 (0.77-1.16)	0.82 (0.65-1.03)	0.74 (0.58-0.95)	0.74 (0.56-0.97)	0.012
All strokes						
Number of cases	199	224	235	197	199	
Multivariable-adjusted HR	1	1.00 (0.80-1.25)	0.95 (0.75-1.21)	0.76 (0.58-1.00)	0.78 (0.58-1.06)	0.031
Cerebral infarction						
Number of cases	90	113	119	92	104	
Multivariable-adjusted HR	1	0.97 (0.70-1.34)	0.92 (0.65-1.31)	0.65 (0.44-0.97)	0.73 (0.47-1.14)	0.051
Intracerebral hemorrhage						
Number of cases	66	62	72	59	51	
Multivariable-adjusted HR	1	0.98 (0.65-1.47)	1.00 (0.64-1.55)	0.76 (0.46-1.26)	0.71 (0.40-1.26)	0.183
Coronary heart disease						
No of cases	42	44	29	47	37	
Multivariable-adjusted HR	1	0.67 (0.41-1.10)	0.34 (0.18-0.63)	0.66 (0.36-1.21)	0.60 (0.29-1.21)	0.252
Insoluble Fiber						
Person-years	97,789	98,099	98,050	97,414	96,886	
Cardiovascular diseases						
Number of cases	236	273	268	253	223	
Multivariable-adjusted HR	1	1.08 (0.82-1.23)	0.82 (0.66-1.03)	0.77 (0.60-0.98)	0.64 (0.47-0.85)	<0.001
All strokes						
Number of cases	201	232	218	218	185	
Multivariable-adjusted HR	1	1.02 (0.82-1.27)	0.81 (0.63-1.03)	0.79 (0.60-1.03)	0.62 (0.45-0.85)	0.001

Cerebral infarction						
Number of cases	90	117	113	99	99	
Multivariable-adjusted HR	1	1.06 (0.78-1.46)	0.82 (0.57-1.17)	0.65 (0.44-0.97)	0.62 (0.40-0.98)	0.006
Intracerebral hemorrhage						
Number of cases	66	68	65	65	46	
Multivariable-adjusted HR	1	1.01 (0.68-1.50)	0.80 (0.51-1.26)	0.84 (0.51-1.37)	0.55 (0.30-1.00)	0.070
Coronary heart disease						
Number of cases	35	41	50	35	38	
Multivariable-adjusted HR	1	0.86 (0.61-1.20)	0.75 (0.51-1.10)	0.82 (0.54-1.25)	0.78 (0.48-1.27)	0.396

Multivariable HRs were adjusted for age, sex, smoking, alcohol, body mass index, histories of diabetes, hypertensive and hypercholesterolemic drug use, exercise, dietary intakes of fruits, vegetables, fish, sodium, isoflavone, and energy, and public health center.

Cardiovascular disease was defined as stroke or coronary heart disease

TABLE 4. Sex-specific, Age-, and Multivariable-adjusted Hazard Ratios (HRs) and 95% Confidence Intervals for Cardiovascular Disease According to Dietary Intake of Total Fiber in Smokers and Non-smokers: JPHC Cohorts I and II

	Total fiber intake					
	Q1 (Lowest)	Q2	Q3	Q4	Q5 (Highest)	trend P
Men						
Non-smokers						
Person-years	25,882	30,246	34,038	36,513	38,299	
Number of cases	122	123	140	155	172	
Age-adjusted HR	1	0.76 (0.59-0.98)	0.73 (0.57-0.94)	0.71 (0.56-0.90)	0.73 (0.58-0.93)	0.023
Multivariable-adjusted HR	1	0.68 (0.50-0.93)	0.57 (0.40-0.81)	0.60 (0.41-0.87)	0.59 (0.38-0.90)	0.045
Smokers						
Person-years	61,647	57,207	52,860	50,936	48,892	
Number of cases	303	291	272	269	289	
Age-adjusted HR	1	0.92 (0.78-1.08)	0.85 (0.72-1.01)	0.81 (0.68-0.96)	0.84 (0.71-0.99)	0.014
Multivariable-adjusted HR	1	1.01 (0.83-1.23)	0.95 (0.76-1.19)	0.98 (0.77-1.25)	1.05 (0.79-1.40)	0.862
Women						
Non-smokers						
Person-years	88,922	92,203	93,155	93,521	93,430	
Number of cases	218	235	252	230	217	
Age-adjusted HR	1	0.95 (0.79-1.14)	0.95 (0.79-1.14)	0.85 (0.70-1.02)	0.80 (0.66-0.96)	0.009
Multivariable-adjusted HR	1	0.88 (0.71-1.01)	0.80 (0.63-1.01)	0.69 (0.53-0.90)	0.61 (0.45-0.83)	0.001
Smokers						
Person-years	15,989	14,434	12,564	11,863	10,391	
Number of cases	47	46	49	36	40	
Age-adjusted HR	1	0.88 (0.58-1.32)	0.98 (0.65-1.48)	0.75 (0.48-1.17)	0.96 (0.62-1.47)	0.633
Multivariable-adjusted HR	1	0.85 (0.48-1.51)	0.68 (0.35-1.30)	0.60 (0.29-1.25)	0.58 (0.24-1.39)	0.158

Multivariable HRs were adjusted for age, sex, alcohol, body mass index, histories of hypertension and diabetes, hypercholesterolemic drug use, exercise, dietary intakes of fruits, vegetables, fish, sodium, isoflavone, and energy, and public health center.

Cardiovascular disease was defined as stroke or coronary heart disease.