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Dietary glycemic index, dietary glycemic load, and cardiovascular disease in middle-aged and older Swedish men1–,3

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Abstract

Background—In women, dietary glycemic index (GI) and dietary glycemic load (GL) have been associated with cardiovascular disease; in men, however, the evidence for an association is weaker.

Objective—We tested the hypothesis that men consuming diets high in GI or GL have a greater risk of cardiovascular disease.

Design—At baseline, we assessed dietary GI and dietary GL by using food-frequency questionnaires in 36 246 Swedish men aged 45–79 y without diabetes or prior cardiovascular disease. Participants were followed through inpatient, cause-of-death, and death registries from 1 January 1998 until 31 December 2003 for myocardial infarction, ischemic stroke, hemorrhagic stroke, and cardiovascular mortality and until 31 December 2005 for all-cause mortality. We used Cox models with age as the time scale to estimate relative risks adjusted for cigarette smoking, body mass index, physical activity, demographic characteristics, and nutritional factors.

Results—Dietary GI and dietary GL were not associated with myocardial infarction (n = 1324), ischemic stroke (n = 692), cardiovascular mortality (n = 785), or all-cause mortality (n = 2959). Dietary GL was associated with hemorrhagic stroke [n = 165; relative risk = 1.44 comparing extreme quartiles (95% CI: 0.91, 2.27); P for trend = 0.047].

Conclusions—Dietary GI and dietary GL were not associated with ischemic cardiovascular disease or mortality, but dietary GL was associated with a greater risk of hemorrhagic stroke.

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The authors' responsibilities were as follows—EBL, MAM, and AW: designed the study; EBL and NH: analyzed the data; NH and AW: collected the data; AW: obtained funding; and EBL: wrote the first draft of the manuscript, which all authors revised and approved.

None of the authors had a conflict of interest.

Discrepancies between these findings and those of previous studies may be due to variations in the associations by sex or to differences in dietary contributions to GI and GL.

Keywords

Carbohydrate; glycemic index; glycemic load; myocardial infarction; stroke

INTRODUCTION

Elevated postprandial blood glucose may increase the risk of cardiovascular disease even in nondiabetic persons (1). Glycemic index (GI) and glycemic load (GL) have been used to quantify the glycemic burden of carbohydrate from foods. GI is a functional measure of the blood glucose response to a standard amount of carbohydrate from a food compared with a reference, which is generally glucose or white bread (2). GL reflects both GI and the amount of carbohydrate in a food and is defined as the product of GI and the carbohydrate content (3). Dietary GI, the average GI of foods in the diet, and dietary GL, the product of carbohydrate consumed and dietary GI, estimate the overall potential of the diet to increase blood glucose (4). The associations of dietary GI and dietary GL with cardiovascular disease have been evaluated in several populations. Both dietary GI and dietary GL were associated with coronary artery disease among women in the United States (5, 6). The association with dietary GL was particularly strong in women with a body mass index ≥ 23 (in kg/m^2), possibly because of underlying insulin resistance in heavier women (5). In the same cohort, dietary GL, but not dietary GI, was associated with total stroke among women with a body mass index ≥ 25 (7). Neither measure was associated with coronary artery disease in elderly men in the Netherlands (8), and dietary GI, but not dietary GL, was associated with hospitalization for myocardial infarction among overweight (body mass index ≥ 25) or older (≥60 y) male and female participants in a case-control study in Italy (9). Because the results have been somewhat inconsistent, particularly among men, we examined the associations of dietary GI and dietary GL with myocardial infarction, ischemic stroke, hemorrhagic stroke, cardiovascular mortality, and all-cause mortality among middle-aged and older Swedish men. We tested whether the associations varied by body mass index and waist-to-hip ratio.

SUBJECTS AND METHODS

Participants

The Cohort of Swedish Men, a prospective study of men living in Västmanland and Örebro Counties in central Sweden, was established in 1997 and 1998. The Swedish population register was used to identify all men aged 45–79 y living in the 2 counties. The men were mailed a 4-page questionnaire; 48 850 (49%) responded. The study design and the questionnaire were described previously (10, 11). Men who provided incorrect national identification numbers or who did not provide national identification numbers (n = 260), who returned blank questionnaires (n = 92), or who had a previous diagnosis of cancer (except nonmelanoma skin cancer) (n = 2592) were excluded. Participants with a history of cardiovascular disease before 1 January 1998 determined from record linkage to the Swedish inpatient register or a history of diabetes (n = 5069) determined from record linkage and self-report were excluded, as were participants who did not report their height

and weight or who reported implausible energy intakes (>3 SDs from the natural logarithm–transformed mean; n = 4591). This left 36 246 participants. The ethics committees for the Karolinska Institutet, Uppsala University Hospital, and the Örebro region approved the Cohort of Swedish Men.

Assessment of diet and other covariates

The baseline questionnaire contained questions regarding sociodemographic factors, anthropometric data, and physical activity and a 96-item food-frequency questionnaire (FFQ). We calculated body mass index and waist-to-hip ratio from self-reported anthropometric data. Participants reported their time spent walking, cycling, and exercising; using these questions, we estimated minutes per day of activity. The self-administered FFQ asked participants to report their usual frequency of consumption of foods and beverages over the previous year. There were 8 possible responses ranging from never to 3 or more times per day. Total consumption of each of the foods and beverages was calculated by multiplying the frequency of consumption by age-specific portion sizes. The portion sizes were determined from a validation study of the questionnaire that included two 1-wk weighted diet records completed by 152 men. Nutrient values were calculated by using food-composition data from the Swedish National Food Administration (12).A database of GI and GL values with white bread as the reference food was created on the basis of primarily the international GI and GL tables (3). Food items and mixed meals with no reported GI value were assigned the value for a comparable food. We calculated average dietary GI from the FFQs by using the following formula:

$$\text{DietaryGI}=\sum_{foods} F \times C \times \text{GI}/\sum_{foods} F \times C \quad (1)$$

where F represents the frequency of consumption, C represents the available carbohydrate content of an age-specific portion of food, and GI represents the glycemic index of a specific food (4). Dietary GL was calculated as the product of the dietary GI and carbohydrate intake divided by 100 (4). The correlation between the FFQ and two 1-wk diet records was 0.62 for dietary GI and 0.77 for dietary GL among men in the validation study of the FFQ (13). With the use of the residuals method, nutrient values and dietary GL were adjusted to 2200 kcal/d, the mean energy intake from the validation study diet records (14).

Outcome assessment

We followed the participants from 1 January 1998 until 31 December 2003 for incidence of myocardial infarction, ischemic stroke, hemorrhagic stroke, and cardiovascular disease mortality. Cases were ascertained through computer linkage to the Swedish hospital discharge and cause-of-death registries. All-cause mortality was ascertained through the Swedish death registry with follow-up through 31 December 2005. These registries are considered >99% complete (15, 16).

Statistical analysis

We calculated means and SDs or percentages of cigarette smoking, body mass index, physical activity, demographic characteristics, and nutritional factors by quartile of dietary GI and dietary GL. We tested for trends across quartiles by using the median in each quartile

as a predictor in linear models for continuous variables and in logistic models for categorical variables. We used Cox proportional hazard models with age as the time scale to estimate the relative risk (RR) of myocardial infarction, ischemic stroke, hemorrhagic stroke, cardiovascular mortality, and total mortality by quartile of dietary GI and dietary GL (17). We chose variables to control for on the basis of their associations with dietary GI and dietary GL and a priori knowledge of risk factors for cardiovascular disease. The RRs of all outcomes except hemorrhagic stroke were adjusted for body mass index (<20, 20–24.9, 25–29.9, and ≥30), cigarette smoking (current, past, never), self-reported history of hypertension (yes, no), physical activity (approximate tertiles), family history of myocardial infarction before 60 y of age (yes, no), use of aspirin (yes, no), marital status (single, married, divorce, widowed), education (less than high school, high school, university), and quartiles of intake of total energy, carbohydrate (dietary GI models only), saturated fat, polyunsaturated fat, protein, alcohol, and cereal fiber. Because of the small number of cases of hemorrhagic stroke, RRs were estimated by using a more parsimonious model adjusted for body mass index (<20, 20–24.9, 25–29.9, and ≥30), cigarette smoking (current, past, never), self-reported history of hypertension (yes, no), physical activity (approximate tertiles), and quartiles of intake of total energy and cereal fiber. Tests of linear trend were performed by entering the median of each quartile as a predictor into the models. We tested for deviations from the proportional hazards assumption by entering interaction terms between dietary GI, dietary GL, and the natural logarithm of time in the models.

One mechanism by which dietary GI and GL may influence the risk of cardiovascular disease is through effects on body weight regulation (1). In a sensitivity analysis, we calculated RRs that were adjusted for the dietary and lifestyle factors listed above but not for body mass index. In this population, some foods, such as crisp bread and whole-grain bread, that make large contributions to the dietary GL and that have a relatively high GI are also high in fiber (13). The common food sources may cause difficulty in separating out the effects of dietary GI and dietary GL from those of cereal fiber. We therefore constructed additional sensitivity models without adjustment for cereal fiber.

Because high dietary GI and dietary GL may be more detrimental in heavier persons (5, 7, 9), we conducted a stratified analysis and tests for interaction by body mass index (<25 or ≥25 and <30 or ≥30) and waist-to-hip ratio (<0.9 or ≥0.9). The analysis stratified by waist-to-hip ratio was limited to the 29 151 men who reported both waist and hip circumferences. Post hoc, we tested for interaction by cereal fiber intake (lowest 25% or remaining 75%), physical activity (≤30 or >30 min/d), being overweight and having low physical activity, and being overweight, having low physical activity, and having a low intake of cereal fiber. We performed a secondary analysis classifying dietary GI and dietary GL into deciles to better describe the associations with extreme values of dietary GI and dietary GL. Analyses were conducted by using SAS version 9.1 (SAS Institute Inc, Cary, NC). A two-sided *P* value of 0.05 was considered statistically significant.

RESULTS

During 6 y of follow-up of 36 246 men who were apparently healthy at baseline, we recorded 1324 myocardial infarctions, 692 ischemic strokes, 165 hemorrhagic strokes, and

785 cardiovascular deaths. After 8 y, 2959 men had died of all causes combined. Men in the top quartile of dietary GI tended to be somewhat less physically active and less likely to have completed high school or university than men in the lower quartiles (data not shown). They consumed more carbohydrates and less protein and alcohol. Men with a higher dietary GL tended to be somewhat more physically active and less likely to be current smokers than men with lower dietary GL (Table 1). They also consumed less fat, protein, and alcohol and more carbohydrate. Both dietary GI and dietary GL were positively correlated with cereal fiber (r = 0.19 for dietary GI and 0.37 for dietary GL).

In unadjusted models with age as the time scale, high dietary GI was associated with an elevated risk of cardiovascular and all-cause mortality and a suggestion of elevated risk of myocardial infarction (Table 2). However, after adjustment for other covariates, we did not observe any significant associations of dietary GI with cardiovascular disease or all-cause mortality. Dietary GL was not associated with cardiovascular disease in unadjusted models, but in the multivariate-adjusted models, high dietary GL was associated with an increased risk of hemorrhagic stroke [RR comparing top with bottom quartile = 1.44 (95% CI: 0.91, 2.27); P for linear trend = 0.047; Table 3]. Dietary GL appeared to be protective for all-cause mortality in unadjusted models (P for trend = 0.02), but no association was evident after control for other covariates. The results were unchanged in the models that were not adjusted for body mass index, but in the models without adjustment for cereal fiber, there was no longer a statistically significant association between dietary GL and hemorrhagic stroke [RR comparing top with bottom quartile = 1.28 (95% CI: 0.83, 1.98); P for linear trend = 0.11]. Additional adjustment for self-reported history of high cholesterol (yes, no), multivitamin use (regular, occasional, never), and quartiles of intake of magnesium, vitamin E, folate, and coffee did not substantially change the results. We did not find evidence of deviations from the proportional hazards assumption.

The relations did not vary by overweight (body mass index ≥ 25), obesity (body mass index ≥ 30), high waist-to-hip ratio (≥0.9), low physical activity (≤30 min/d), or combinations of overweight, low physical activity, and low fiber consumption (<12.8 g/d). There was a significant interaction between dietary GL and cereal fiber intake on all-cause mortality (P = 0.02). In men with cereal fiber intake in the lowest 25% (<12.8 g/d), the risk of mortality was slightly higher in the top quartile of dietary GL than in the bottom quartile, but the association was not significant [RR comparing top with bottom quartile = 1.12 (95% CI: 0.82, 1.51); P for linear trend = 0.59]. In men with cereal fiber intake ≥ 12.8 g/d, dietary GL appeared to be associated with a reduced risk of mortality [RR comparing top with bottom quartile = 0.85 (95% CI: 0.70, 1.04], although the test for linear trend was not significant (P = 0.24). Dietary GI and dietary GL were not associated with cardiovascular diseases or mortality when we compared extreme deciles.

DISCUSSION

In this population of middle-aged and older Swedish men, dietary GI and dietary GL were not significantly associated with myocardial infarction, ischemic stroke, cardiovascular disease mortality, or all-cause mortality after adjustment for potential confounders. There was a statistically significant association of dietary GL with risk of hemorrhagic stroke. The

association was not evident in the model that was not adjusted for cereal fiber. The associations did not vary by body mass index, waist-to-hip ratio, or physical activity. The association of dietary GL with all-cause mortality appeared to vary by cereal fiber intake. Among men with cereal fiber intake ≥12.8 g/d, there was an inverse association between dietary GL and all-cause mortality, and among men with lower cereal fiber intake, higher dietary GL was associated with an elevated risk. However, in stratified analyses, the trends were not statistically significant, and the finding must be interpreted in the context of the large number of interactions tested and the post hoc nature of the test.

Our results are in contrast with those seen in the Nurses' Health Study, in which higher dietary GL and dietary GI were associated with increased risk of coronary artery disease, and higher dietary GL was associated with increased risk of total stroke, but not specifically hemorrhagic stroke, in overweight women (5–7). Our results are also in contrast with a case-control study in Italy in which dietary GI was associated with myocardial infarction in overweight and older men and women (9). In the Zutphen Elderly Study, however, the investigators also found no association of dietary GI or dietary GL with cardiovascular disease or cardiovascular disease risk factors (8).

The Nurses' Health Study, which supplies the strongest epidemiologic evidence for a link between dietary GI, dietary GL, and cardiovascular disease, differs from the Cohort of Swedish Men in several important ways. First, the current study was restricted to men, whereas the Nurses' Health Study is restricted to women. Elevated triacylglycerol concentrations, a mechanism by which diets high in GI and GL could increase the risk of cardiovascular disease, may be a stronger risk factor for women than for men (18). Additionally, diet trials have suggested that the adverse changes in HDL cholesterol and triacylglycerol concentrations with increased carbohydrate consumption may be greater in women than in men (19). In a case-control study with both male and female participants, the odds ratios for myocardial infarction comparing the top with the bottom tertile of dietary GL were 0.85 for men and 1.73 for women (9). Although those investigators did not find a significant association in either group, the study included many fewer women than men.

A second major difference between the present study and previous studies is the difference in diet patterns and dietary contributors to the GL. White bread and potatoes are major contributors to the dietary GL in both the United States and Sweden: white bread contributes 5.2% to total dietary GL in the United Stated and 14.1% in Sweden; potatoes contribute 7.7% to total dietary GL in the United States and 10.5% in Sweden (13, 20). In Sweden, however, foods with a high fiber content such as crisp bread and whole-grain bread are also major contributors to GL: crisp bread, 7.0%; whole-grain bread, 6.8% (13). Cereal fiber intake in the Swedish men was substantially higher than in the Nurses' Health Study: 6.2 g of cereal fiber per 1000 kcal in the Swedish men compared with ≈2–3 g of cereal fiber per 1000 kcal in the Nurses' Health Study (5). We did not find strong evidence for an adverse effect of dietary GL or dietary GI in men with cereal fiber intake in the lowest 25%, but even these men had high intakes compared with other populations. The men in the present study spent approximately twice as much time engaged in physical activity as did the participants of the Nurses' Health Study. Physical activity increases insulin sensitivity (21) and may reduce the harmful effects of diets with high a GL or GI, although we saw no

variation in the associations by physical activity. The Cohort of Swedish Men relies on a single assessment of diet at baseline, whereas the Nurses' Health Study features repeated dietary assessment. Misclassification of exposure to dietary GI and dietary GL in this study due to errors in completing the FFQ or changes in diet habits may have obscured associations, although the follow-up in this study was relatively short. Finally, the men in this study ranged from 45 to 79 y of age at the beginning of follow-up, and many of the cardiovascular events occurred in the older participants. It is possible that men who were susceptible to ill effects of foods with a high propensity to increase blood glucose did not survive to join this study, which would leave men who were relatively immune, or that dietary GI and dietary GL do not have adverse effects in older participants.

Changes in cardiovascular disease risk factors such as reduced total cholesterol (22, 23), LDL cholesterol (23, 24), triacylglycerol (25, 26), plasminogen activator inhibitor 1 (26), insulin resistance (25), and C-reactive protein (25) concentrations seen in trials of low GL or GI diets support a causal association between the glycemic burden of diet and cardiovascular disease. However, the observed effects of the diets have been relatively modest and have not been observed consistently across trials.

A strength of the present study is the large number of cases of myocardial infarction, ischemic stroke, and cardiovascular mortality and the use of the Swedish inpatient registry, cause-of-death registry, and death registry, which are nearly 100% complete (15, 16), to identify cases. There were many fewer cases of hemorrhagic stroke, resulting in wide CIs around the RRs for this outcome. The difference in dietary GL and dietary GI between the top and the bottom quartile was not large (70 units of dietary GL and 9.9 units of dietary GI), which reduced the likelihood of observing an association, but no association was evident when we examined extreme deciles (103 units of dietary GL and 14.5 units of dietary GI). Men with high dietary GL were less likely to be smokers, engaged in more physical activity, and consumed less saturated fat and more cereal fiber then did men with low dietary GL. We cannot rule out residual or unmeasured confounding by these or other cardiovascular protective factors that could mask an association.

In summary, dietary GI and dietary GL were not associated with ischemic cardiovascular disease or mortality in this population, but dietary GL was associated with and increased risk of hemorrhagic stroke. Discrepancies between these findings and previous studies may be due to variations in the associations by sex or differences in dietary contribution to GI and GL.

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TABLE 1

Characteristics of 36 246 men by quartile of dietary glycemic load[1]

Characteristic	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* for trend[2]
Age (y)	58.7 ± 9.1[3]	58.7 ± 9.3	59.0 ± 9.5	59.4 ± 9.7	< 0.001
BMI (kg/m^2)	25.8 ± 3.3	25.6 ± 3.2	25.5 ± 3.2	25.6 ± 3.3	< 0.001
Physical activity (min/d)	53.9 ± 42.7	56.7 ± 43.2	57.6 ± 43.2	58.6 ± 45.3	< 0.001
History of hypertension (%)	20.0	19.3	19.2	21.6	0.005
Family history of MI at < 60 y (%)	11.4	11.7	11.1	11.7	0.76
Aspirin use (%)	31.8	30.4	31.2	30.5	0.13
Cigarette smoking (%)					
Never	31.4	37.7	40.1	40.0	< 0.001
Past	39.2	38.0	37.7	37.0	< 0.001
Current	29.4	24.4	22.2	23.1	< 0.001
Marital status (%)					
Single	5.8	5.6	5.8	9.1	< 0.001
Married	82.8	84.7	85.6	80.7	< 0.001
Divorced	8.0	6.3	6.0	7.0	0.02
Widowed	3.5	3.4	2.7	3.2	0.07
Education (%)					
Less than high school	63.1	63.5	67.3	73.8	< 0.001
High school	16.0	16.1	15.0	12.7	< 0.001
University	20.9	20.5	17.7	13.5	< 0.001
Dietary intake					
Total energy (kcal/d)	2703 ± 864	2728 ± 808	2710 ± 800	2705 ± 845	0.84
Saturated fat (g/d)[4]	40.5 ± 7.3	35.5 ± 5.6	32.3 ± 5.3	27.4 ± 5.7	< 0.001
Monounsaturated fat (g/d)[4]	28.5 ± 3.8	26.4 ± 3.2	24.8 ± 3.2	22.0 ± 3.7	< 0.001
Polyunsaturated fat (g/d)[4]	10.4 ± 2.4	10.3 ± 2.1	9.9 ± 1.8	9.3 ± 1.8	< 0.001
Carbohydrate (g/d)[4]	237 ± 21	265 ± 13	284 ± 13	314 ± 22	< 0.001
Protein (g/d)[4]	94.7 ± 13.0	88.5 ± 10.3	84.9 ± 9.7	78.3 ± 10.6	< 0.001
Alcohol (g/d)	14.8 ± 13.2	11.5 ± 9.6	9.5 ± 8.7	7.1 ± 7.4	< 0.001

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Characteristic	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P* for trend[2]
Cereal fiber (g/d)[4]	13.7 ± 4.7	16.4 ± 4.8	17.7 ± 5.4	19.0 ± 7.1	< 0.001
Dietary glycemic index[5]	74.4 ± 4.6	77.1 ± 3.5	78.7 ± 3.3	81.3 ± 3.5	< 0.001

[1] MI, myocardial infarction.

[2] Obtained from linear regression for continuous variables and logistic regression for categorical variables by using the median dietary glycemic load in each quartile as a predictor.

[3] $\bar{x} \pm$ SD (all such values).

[4] Energy-adjusted by the residuals method.

[5] White bread was used as the reference food.

TABLE 2

Relative risks (RRs) of cardiovascular disease and mortality by quartile of dietary glycemic index in 36 246 Swedish men[1]

	Quartile 1 (median: 73.0)	Quartile 2 (median: 76.6)	Quartile 3 (median: 79.3)	Quartile 4 (median: 82.9)	*P* for trend
Myocardial infarction (*n* = 1324)					
RR (95% CI)[2]	1	0.92 (0.78, 1.07)	1.00 (0.86, 1.17)	1.12 (0.97, 1.30)	0.08
RR (95% CI)[3]	1	0.91 (0.77, 1.07)	0.96 (0.82, 1.13)	0.99 (0.84, 1.17)	0.93
Ischemic stroke (*n* = 692)					
RR (95% CI)[2]	1	1.19 (0.96, 1.48)	1.11 (0.89, 1.37)	1.12 (0.90, 1.39)	0.44
RR (95% CI)[3]	1	1.21 (0.97, 1.50)	1.12 (0.89, 1.41)	1.09 (0.85, 1.38)	0.67
Hemorrhagic stroke (*n* = 165)					
RR (95% CI)[2]	1	1.04 (0.67, 1.61)	0.97 (0.62, 1.51)	1.17 (0.77, 1.79)	0.52
RR (95% CI)[4]	1	1.11 (0.71, 1.72)	1.04 (0.66, 1.63)	1.19 (0.77, 1.83)	0.49
Cardiovascular mortality (*n* = 785)					
RR (95% CI)[2]	1	0.93 (0.76, 1.14)	0.90 (0.73, 1.11)	1.23 (1.02, 1.48)	0.04
RR (95% CI)[3]	1	0.98 (0.80, 1.21)	0.93 (0.74, 1.15)	1.09 (0.88, 1.36)	0.46
All-cause mortality (*n* = 2959)					
RR (95% CI)[2]	1	0.96 (0.87, 1.07)	0.91 (0.82, 1.01)	1.12 (1.02, 1.24)	0.04
RR (95% CI)[3]	1	1.02 (0.92, 1.14)	0.96 (0.86, 1.07)	1.06 (0.95, 1.19)	0.41

[1] White bread was used as the reference food for determining dietary glycemic index.

[2] From Cox proportional hazards models with age as the time scale.

[3] From Cox proportional hazards models with age as the time scale and adjusted for BMI (in kg/m^2: <20, 20–24.9, 25–29.9, or ≥30), physical activity (approximate tertiles), self-reported history of hypertension (yes or no), family history of myocardial infarction before 60 y of age (yes or no), use of aspirin (yes or no), cigarette smoking (current, past, or never), marital status (single, married, divorced, or widowed), education (less than high school, high school, or university), and quartiles of intake of total energy, carbohydrate, saturated fat, polyunsaturated fat, alcohol, and cereal fiber.

[4] From Cox proportional hazards models with age as the time scale and adjusted for BMI (in kg/m^2: <20, 20–24.9, 25–29.9, or ≥30), physical activity (approximate tertiles), self-reported history of hypertension (yes or no), cigarette smoking (current, past, or never), and quartiles of intake of total energy and cereal fiber.

TABLE 3

Relative risks (RRs) of cardiovascular disease and mortality by quartile of dietary glycemic load in 36 246 Swedish men[1]

	Quartile 1 (median: 180)	Quartile 2 (median: 204)	Quartile 3 (median: 223)	Quartile 4 (median: 250)	*P* for trend
Myocardial infarction (*n* = 1324)					
RR (95% CI)[2]	1	0.88 (0.75, 1.03)	0.97 (0.83, 1.13)	1.03 (0.89, 1.19)	0.45
RR (95% CI)[3]	1	0.91 (0.77, 1.08)	1.02 (0.83, 1.25)	1.04 (0.80, 1.34)	0.65
Ischemic stroke (*n* = 692)					
RR (95% CI)[2]	1	0.94 (0.75, 1.16)	0.93 (0.75, 1.15)	1.05 (0.85, 1.29)	0.60
RR (95% CI)[3]	1	0.94 (0.74, 1.19)	0.95 (0.72, 1.26)	1.05 (0.74, 1.49)	0.76
Hemorrhagic stroke (*n* = 165)					
RR (95% CI)[2]	1	0.85 (0.53, 1.38)	1.31 (0.85, 2.01)	1.23 (0.80, 1.90)	0.16
RR (95% CI)[4]	1	0.98 (0.60, 1.59)	1.57 (1.01, 2.44)	1.44 (0.91, 2.27)	0.047
Cardiovascular mortality (*n* = 785)					
RR (95% CI)[2]	1	0.81 (0.66, 1.00)	0.88 (0.72, 1.08)	1.05 (0.87, 1.27)	0.38
RR (95% CI)[3]	1	0.93 (0.74, 1.17)	1.06 (0.81, 1.37)	1.13 (0.81, 1.56)	0.39
All-cause mortality (*n* = 2959)					
RR (95% CI)[2]	1	0.80 (0.73, 0.89)	0.82 (0.74, 0.91)	0.87 (0.79, 0.97)	0.02
RR (95% CI)[3]	1	0.90 (0.80, 1.00)	0.95 (0.83, 1.08)	0.94 (0.79, 1.11)	0.54

[1] White bread was used as the reference food for determining dietary glycemic load.

[2] From Cox proportional hazard models with age as the time scale.

[3] From Cox proportional hazard models with age as the time scale and adjusted for BMI (in kg/m^2: <20, 20–24.9, 25–29.9, or ≥30), physical activity (approximate tertiles), self-reported history of hypertension (yes or no), family history of myocardial infarction before 60 y of age (yes or no), use of aspirin (yes or no), cigarette smoking (current, past, or never), marital status (single, married, divorced, or widowed), education (less than high school, high school, or university), and quartiles of intake of total energy, saturated fat, polyunsaturated fat, protein, alcohol, and cereal fiber.

[4] From Cox proportional hazard models with age as the time scale and adjusted for BMI (in kg/m^2: <20, 20–24.9, 25–29.9, or ≥30), physical activity (approximate tertiles), self-reported history of hypertension (yes or no), cigarette smoking (current, past, or never), and quartiles of intake of total energy and cereal fiber.