

Carbohydrates, dietary fiber, and incident type 2 diabetes in older women¹⁻³

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ABSTRACT

Background: Dietary carbohydrates may influence the development of type 2 (non-insulin-dependent) diabetes, for example, through effects on blood glucose and insulin concentrations.

Objective: We examined the relations of baseline intake of carbohydrates, dietary fiber, dietary magnesium, and carbohydrate-rich foods and the glycemic index with incidence of diabetes.

Design: This was a prospective cohort study of 35988 older Iowa women initially free of diabetes. During 6 y of follow-up, 1141 incident cases of diabetes were reported.

Results: Total grain, whole-grain, total dietary fiber, cereal fiber, and dietary magnesium intakes showed strong inverse associations with incidence of diabetes after adjustment for potential nondietary confounding variables. Multivariate-adjusted relative risks of diabetes were 1.0, 0.99, 0.98, 0.92, and 0.79 (*P* for trend: 0.0089) across quintiles of whole-grain intake; 1.0, 1.09, 1.00, 0.94, and 0.78 (*P* for trend: 0.005) across quintiles of total dietary fiber intake; and 1.0, 0.81, 0.82, 0.81, and 0.67 (*P* for trend: 0.0003) across quintiles of dietary magnesium intake. Intakes of total carbohydrates, refined grains, fruit and vegetables, and soluble fiber and the glycemic index were unrelated to diabetes risk.

Conclusion: These data support a protective role for grains (particularly whole grains), cereal fiber, and dietary magnesium in the development of diabetes in older women. *Am J Clin Nutr* 2000;71:921-30.

KEY WORDS Type 2 diabetes, non-insulin-dependent diabetes mellitus, diet, nutrition, prospective studies, carbohydrates, dietary fiber, sugar, glycemic index, grains, magnesium, Iowa Women's Health Study, women

INTRODUCTION

Despite the public health significance of type 2 diabetes, relatively little is understood about the role of diet in the development of this disease. Diet is known to influence body weight and thus is recognized as a modifiable risk factor for type 2 diabetes (1). Other effects of diet in the etiology of diabetes are not widely endorsed. This is illustrated by a recent position statement by the American Dietetic Association supporting dietary modification in the management, but not the prevention, of diabetes (2).

Findings from metabolic and epidemiologic studies on the relations between carbohydrates and dietary fiber and diabetes are inconsistent. Evidence from metabolic studies supports bene-

ficial (3), detrimental (4, 5), and neutral (6) effects of a high-carbohydrate diet relative to high-fat diets on glycemic response. The results of ecologic and cross-sectional studies support decreased prevalences of diabetes with high intakes of carbohydrate (7-9), whereas the results of cohort studies do not support an association between diabetes and total dietary carbohydrate (10-13). Dietary fiber is reported to improve the postprandial glycemic response and insulin concentrations, most likely by slowing the digestion and absorption of food and by regulating several metabolic hormones (14, 15). However, results on dietary fiber and diabetes from prospective and case-control studies have been mixed (7, 11, 12, 16). Magnesium is a component of grains and is found in the fibrous component of cereal plants. Dietary magnesium was inversely related to incident type 2 diabetes in some (11, 12), but not all (17), prospective cohort studies.

Clinical work on the glycemic index and the glycemic load supports the notion that the form and content of carbohydrate and fat in foods may be important determinants of the short-term glycemic response (18). The glycemic index and glycemic load were directly related to diabetes risk in 2 large cohort studies (11, 12). In addition, recent attention has been directed to the potential effects of whole compared with refined grains on the glycemic response (19). The long-term effect of whole-grain compared with refined-grain food intake on incident diabetes has not been widely examined in the epidemiologic literature.

We examined the relations between incident diabetes and carbohydrate-related dietary variables in the Iowa Women's Health Study, a large cohort study of older women. Detailed dietary information collected at baseline enabled us to examine the long-term effects on diabetes incidence of several variables, including dietary carbohydrates, dietary fiber, the glycemic index and load, dietary magnesium, and carbohydrate-rich foods such as whole

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grains. These findings contribute to the long-standing discussion of the importance of carbohydrates and dietary fiber in the etiology of diabetes as well as to the relatively recent focus on glycemic index, the glycemic load, and whole-grain intake.

SUBJECTS AND METHODS

Subjects

The Iowa Women's Health Study is a prospective cohort study of postmenopausal Iowa women. In January 1986, a random sample of 99826 women aged 55–69 y who had a valid Iowa driver's license were mailed a 16-page questionnaire and asked to participate in the study. The present study sample is composed of those 41836 women who returned the baseline questionnaire. Compared with nonresponders, responders had a mean body mass index (BMI; in kg/m²) that was smaller by ≈0.4, were 3 mo older, and were more likely to live in rural, less-affluent counties (20).

Women were excluded from these analyses if they reported implausibly high (>20920 kJ) or low (<2510 kJ) energy intakes ($n = 538$), left ≥30 items blank on the food-frequency questionnaire ($n = 2782$), or had diabetes at baseline ($n = 3121$). Women were considered diabetic at baseline if they responded "yes" or "don't know" to the following questions: Have you ever been told by a doctor that you have sugar diabetes (diabetes mellitus)? ($n = 2947$) and Have you ever taken insulin or pills for sugar diabetes (or to lower blood sugar)? ($n = 2747$). A total of 35988 women remained eligible for the study. The study was approved by the Human Subjects Review Committee at the University of Minnesota.

Data collection

The baseline questionnaire included questions on known or suspected risk factors for diabetes, including age, BMI, waist-to-hip ratio (WHR), physical activity, and smoking history. BMI was calculated from weight and height measurements provided by the participants. WHR was calculated as the average of 2 measurements taken by the participant's spouse or a friend using a paper tape measure included with the questionnaire (21). A 3-level physical activity score was created by combining questions on the frequency of moderate and vigorous leisure-time activity. Pack-years of smoking (number of packs of cigarettes smoked daily times the number of years smoked) were calculated from information on the intensity and duration of cigarette smoking.

The principal dietary exposure of interest was intake of carbohydrates, including dietary fiber. This variable was examined by analyzing food sources of carbohydrates, subtypes of carbohydrates, components of carbohydrates, and the glycemic index and load. The food groups analyzed included grains, vegetables, fruit, and legumes. Total grain intake was subdivided into refined and whole grains as outlined previously (22). In addition to total dietary carbohydrates, starch, sucrose, glucose, fructose, maltose, and lactose were analyzed individually. Because the physiologic effects of fiber may relate to subtype (23), soluble and insoluble fiber were analyzed separately. Also, total dietary fiber was divided into mutually exclusive categories representing fiber contributed to the diet by cereals, fruit, vegetables, and legumes.

A 127-item food-frequency questionnaire similar to that used in the 1984 Nurses' Health Study was used to assess typical food

intake over the previous year (24). The validity of the food-frequency questionnaire was evaluated in this cohort by comparing nutrient values determined from the questionnaire with values estimated from the average of five 24-h dietary recall surveys in 44 study participants. Energy-adjusted Pearson's correlation coefficients for total carbohydrates and crude fiber were 0.45 and 0.24, respectively (25).

The glycemic index and glycemic load variables measure the glycemic response and insulin demand that result from specific carbohydrate-containing foods. The glycemic index and load values were available for most foods and were calculated as described by Salmerón et al (11, 12). The average dietary glycemic index for each individual was calculated as follows:

$$\frac{\{[\text{Servings of food per day}] \times (\text{carbohydrate content of food}) \times (\text{glycemic index})\}}{\text{total carbohydrate in diet}} \quad (1)$$

Similarly, a glycemic load score was obtained for each individual as follows:

$$\sum [(\text{Servings of food per day}) \times (\text{carbohydrate content of food}) \times (\text{glycemic index})] \quad (2)$$

Diabetes incidence was determined by an affirmative response to the following question on one of the follow-up surveys: Since (baseline or respective follow-up), were you diagnosed for the first time by a doctor as having sugar diabetes? Over 6 y of follow-up, 1141 women reported having diabetes in the 3 follow-up surveys administered in 1987 ($n = 344$), 1989 ($n = 331$), and 1992 ($n = 466$). Response rates for the 3 follow-up surveys were 91%, 86%, and 79%, respectively.

A validation study of self-reported diabetes was conducted with 85 cohort participants in 1988 after the first follow-up survey (26). Subjects tended to overreport diabetes: of 44 women who reported diabetes at baseline, 28 (64%) were confirmed as being diabetic by their physician. All 41 women who reported not having diabetes at baseline were confirmed as not being diabetic.

Statistical analysis

Person-time of follow-up was calculated for each study participant as follows. For those women who did not report a diagnosis of diabetes, person-time was calculated from baseline to the date of the last completed questionnaire. For women who reported having been diagnosed with diabetes on one of the follow-up surveys, person-time was calculated as the sum of the known disease-free period and half of the period during which the diagnosis was first made. Mortality status was determined annually through linkage with the State Health Registry of Iowa. In addition, nonrespondents to the 3 follow-up surveys and emigrants from Iowa were linked with the National Death Index.

Dietary variables were categorized as appropriate for analysis. Relative risks calculated with proportional hazards regression are comparisons between the upper categories of intake and the lowest category. Trend analyses weighted each category of intake by the median intake for that category. Nutrient intakes were adjusted for total energy by the method described by Willett and Stampfer (27). Initial analyses were adjusted only for age and total energy. Further analyses were also adjusted for potential confounders of the observed diet-diabetes associations, including physical activity, BMI, WHR, smoking, alcohol intake, and education. Addi-



TABLE 1

Distribution of various baseline risk factors for diabetes mellitus across quintiles of whole-grain and energy-adjusted dietary fiber intake in 35 988 Iowa women, 1986–1992¹

Variable	Quintile of intake					<i>P</i> for trend ²
	1	2	3	4	5	
Whole grains						
Range of intake (servings/wk)	<3.0	3.0–5.5	6.0–8.0	8.5–17.5	>17.5	—
Median intake (servings/wk)	1	4	7	10.5	20.5	—
Never drinker (%)	55.1	51.9	51.9	52.5	54.4	0.69
High school graduate (%)	76.7	81.8	83.2	85.4	84.1	<0.001
Vigorous activity (%)	18.6	23.6	24.9	29.7	28.5	<0.001
Current smoker (%)	22.7	16.8	14.6	10.1	12.7	<0.001
Family history of diabetes mellitus (%)	28.5	27.3	27.6	27.2	28.1	0.65
Age (y)	61.4	61.3	61.6	61.7	61.6	<0.0001
BMI (kg/m ²)	26.9	26.8	26.8	26.6	26.8	<0.0001
WHR	0.844	0.835	0.832	0.828	0.830	<0.0001
Total energy (kJ)	6879	6879	7297	7945	8577	<0.0001
Dietary fiber (g/d)	17.0	18.6	19.2	21.1	21.9	<0.0001
Dietary fiber						
Range of intake (g/d)	≤15.3	15.3–17.8	17.9–20.3	20.4–23.6	>23.6	—
Median intake (g/d)	13.27	16.64	19.03	21.82	26.50	—
Never drinker (%)	47.3	52.0	53.9	54.4	58.3	<0.001
High school graduate (%)	78.4	81.8	82.9	84.0	84.2	<0.001
Vigorous activity (%)	15.7	19.8	24.3	29.4	36.5	<0.001
Current smoker (%)	27.9	17.7	13.7	9.5	7.8	<0.001
Family history of diabetes mellitus (%)	28.5	26.9	27.3	28.1	27.9	0.96
Age (y)	60.9	61.2	61.6	61.8	62.0	<0.0001
BMI (kg/m ²)	26.8	27.0	26.9	26.7	26.4	<0.0001
WHR	0.846	0.838	0.832	0.827	0.825	<0.0001
Total energy (kJ)	8368	7075	7046	7226	8021	<0.0001
Whole grains (servings/wk)	6.2	7.8	8.9	10.7	13.7	<0.0001

¹Dietary fiber intake adjusted for total energy intake according to the method of Willett and Stampfer (27). WHR, waist-to-hip ratio.

²For covariate proportions, chi-square tests for trends were calculated across quintiles of dietary intake. For covariate means, *t* tests were calculated from a linear regression of dietary intake on the covariate of interest; both dietary intakes and covariates were modeled as 5-level ordinal variables, with the covariate variable taking on the mean covariate value within each quintile of dietary intake.

tional analyses excluded women who reported having cancer ($n = 3202$) or heart disease ($n = 3110$) at baseline (because these women may have recently modified their diets) and controlled for reported family history of diabetes in a first-degree relative (mother, father, brother, or sister), which was asked only in the third follow-up. The SAS package was used (28).

RESULTS

Age-adjusted relative risks (RRs) of diabetes were 1.0, 0.67, and 0.55 (P for trend: 0.0001) for low, medium, and high physical activity, respectively. RRs were also notable for ever versus never drinking alcohol (RR: 0.62; 95% CI: 0.55, 0.70) and a family history of diabetes in a first-degree relative versus no family history (RR: 2.60; 95% CI: 2.31, 2.93). As shown previously, BMI and WHR strongly predicted diabetes in this cohort (26). Age-adjusted RRs were 1.0, 1.92, 3.38, 5.70, and 10.86 (P for trend: 0.0001) across quintiles of WHR and 1.0, 2.39, 2.98, 6.50, and 14.59 (P for trend: 0.0001) across quintiles of BMI.

The distribution of these risk factors across quintiles of whole-grain and energy-adjusted dietary fiber intake are shown in **Table 1**. Trends in most covariates across quintiles of dietary intakes were statistically significant. However, this was assuredly due to the large sample size, and the trends of

only some covariates can be presumed to be clinically relevant. For example, women who reported higher intakes of whole grains and dietary fiber at baseline were appreciably more likely to have engaged in vigorous physical activity, have graduated from high school, have been nonsmokers, and have had low WHRs. In addition, the prevalence of abstinence from alcohol was 11% higher for women in the highest category of dietary fiber intake than for women in the lowest category of intake.

The multivariate-adjusted analyses for intakes of total carbohydrate, starch, and sugars are shown in **Table 2**. After adjustment for potential confounding variables, total carbohydrates, starch, lactose, and maltose were unrelated to incidence of diabetes. RRs across total carbohydrate quintiles were 1.0, 1.05, 0.98, 0.90, 0.93 (P for trend: 0.22). Sucrose was inversely associated with incidence of diabetes. Women in the highest quintile of sucrose intake had an RR of 0.81 compared with women in the lowest quintile. Glucose and fructose intakes were positively associated with diabetes risk. The RRs comparing the highest quintile of intake with the lowest were 1.30 and 1.27 for glucose and fructose, respectively. Age- and energy-adjusted risk estimates were similar to the multivariate-adjusted findings, except that total carbohydrate intake showed a stronger inverse relation to type 2 diabetes in the age- and energy-adjusted model. The RR estimates in the age- and

TABLE 2Multivariate-adjusted relative risks of incident type 2 diabetes across quintiles of energy-adjusted carbohydrate intake among 35 988 Iowa women, 1986–1992¹

Variable	Quintile of intake					P for trend
	1	2	3	4	5	
Total carbohydrates						
Range of intake (g/d)	<192.1	192.1–210.6	210.7–225.6	225.7–243.8	>243.8	—
Median (g/d)	176	202	218	234	259	—
Cases (<i>n</i>)	239	255	227	206	214	—
Person-years	40 123	40 624	40 397	40 999	40 512	—
Relative risk (95% CI)	1.00	1.05 (0.87, 1.26)	0.98 (0.81, 1.19)	0.90 (0.74, 1.09)	0.93 (0.76, 1.13)	0.22
Starch						
Range of intake (g/d)	<50.5	50.5–59.3	59.4–67.0	67.1–76.8	>76.8	—
Median (g/d)	43.4	55.3	63.2	71.4	85.3	—
Cases (<i>n</i>)	254	204	234	220	229	—
Person-years	40 162	40 865	40 822	40 471	40 334	—
Relative risk (95% CI)	1.00	0.79 (0.65, 0.96)	0.86 (0.71, 1.03)	0.82 (0.68, 1.00)	0.83 (0.69, 1.00)	0.12
Glucose						
Range of intake (g/d)	<13.9	13.9–17.6	17.7–21.1	21.2–25.8	>25.8	—
Median (g/d)	11.1	15.9	19.3	23.2	30.0	—
Cases (<i>n</i>)	213	201	226	231	270	—
Person-years	39 958	40 798	41 022	40 627	40 248	—
Relative risk (95% CI)	1.00	0.95 (0.78, 1.17)	1.11 (0.91, 1.35)	1.18 (0.97, 1.44)	1.30 (1.08, 1.57)	0.0007
Sucrose						
Range of intake (g/d)	<31.2	31.2–38.0	38.1–43.6	43.7–51.0	>51.0	—
Median (g/d)	25.8	34.9	40.9	46.9	57.7	—
Cases (<i>n</i>)	245	236	230	220	210	—
Person-years	40 082	40 650	40 824	40 710	40 387	—
Relative risk (95% CI)	1.00	0.98 (0.82, 1.19)	0.96 (0.79, 1.16)	0.93 (0.76, 1.13)	0.81 (0.67, 0.99)	0.027
Fructose						
Range of intake (g/d)	<15.9	15.9–20.3	20.4–24.5	24.6–30.0	>30.0	—
Median (g/d)	12.5	18.3	22.4	26.9	35.5	—
Cases (<i>n</i>)	216	200	230	232	263	—
Person-years	39 897	40 929	40 865	40 641	40 322	—
Relative risk (95% CI)	1.00	0.95 (0.77, 1.16)	1.17 (0.96, 1.42)	1.18 (0.97, 1.43)	1.27 (1.06, 1.54)	0.0015
Lactose						
Range of intake (g/d)	<11.9	11.9–16.7	16.8–29.5	29.6–101.8	>101.8	—
Median (g/d)	4.7	9.7	14.3	19.7	33.8	—
Cases (<i>n</i>)	230	246	221	232	212	—
Person-years	40 209	40 431	40 741	40 295	40 978	—
Relative risk (95% CI)	1.00	1.16 (0.96, 1.41)	1.02 (0.84, 1.24)	1.09 (0.90, 1.32)	0.94 (0.77, 1.14)	0.24
Maltose						
Range of intake (g/d)	<0.92	0.92–1.19	1.20–1.45	1.46–1.85	>1.85	—
Median (g/d)	0.71	1.06	1.32	1.63	2.28	—
Cases (<i>n</i>)	239	201	250	234	217	—
Person-years	40 452	40 675	40 638	40 727	40 161	—
Relative risk (95% CI)	1.00	0.86 (0.71, 1.05)	1.11 (0.92, 1.34)	1.07 (0.88, 1.30)	0.98 (0.81, 1.19)	0.60

¹Proportional hazards regression models were adjusted for the following: age, total energy intake, BMI (quintiles), waist-to-hip ratio (quintiles), education (no high school diploma, high school diploma, some college or vocational school, or college degree), pack-years of smoking (none, 1–19, 20–39, or ≥40), alcohol intake (none, <4 g/d, 4–9.9 g/d, or ≥10 g/d), and physical activity (low, medium, or high). Person-years were calculated as described in Methods.

energy-adjusted model were 1.00, 1.06, 0.96, 0.84, and 0.86 (*P* for trend: 0.018) across quintiles of intake.

The glycemic index and glycemic load were not associated with diabetes in these data (**Table 3**). The pattern of risk across quintiles of glycemic index was inconsistent; RRs first rose to 1.22 in quintile 3 and then dropped to 0.84 in quintile 5. Glycemic load was nonsignificantly inversely related to diabetes. These findings did not appear to have been due to confounding or effect modification by dietary fiber intake. Relative risk estimates were similar in age- and energy-adjusted analyses.

The multivariate-adjusted RRs of diabetes across quintiles of total dietary fiber, insoluble fiber, and soluble fiber intake and fiber obtained from cereal, fruit, vegetable, and legume sources

are shown in **Table 4**. In the multivariate analysis, total dietary fiber was inversely associated with diabetes risk (RR = 0.78 comparing the fifth with the first quintile of intake; *P* for trend: 0.005). Intake of insoluble fiber was inversely associated with diabetes risk, whereas intake of soluble fiber did not appear to be strongly related to diabetes risk. Women in the highest quintile of intake had RRs of 0.89 and 0.75 for soluble and insoluble fiber, respectively, compared with women in the first quintile of intake. Fiber derived from cereals was also inversely associated with diabetes (RR = 0.64 for the highest versus the lowest quintile). Fiber derived from fruit, vegetables, or legumes was unrelated to diabetes risk. Also shown in Table 4 are the multivariate-adjusted RRs of diabetes across quintiles of intake of dietary



TABLE 3Multivariate-adjusted relative risks of incident type 2 diabetes across categories of glycemic index and glycemic load among 35988 Iowa women, 1986–1992¹

Variable	Category of intake					P for trend
	1	2	3	4	5	
Glycemic index						
Range	<58	59–65	66–71	72–80	>80.0	—
Median	53	62	69	75	89	—
Cases (<i>n</i>)	230	257	260	200	194	—
Person-years	39960	40663	40405	40822	40804	—
Relative risk ² (95% CI)	1.00	1.17 (0.97, 1.40)	1.22 (1.02, 1.47)	0.91 (0.75, 1.11)	0.84 (0.69, 1.03)	0.0079
Relative risk ³ (95% CI)	1.00	1.19 (0.98, 1.43)	1.26 (1.05, 1.53)	0.96 (0.78, 1.17)	0.89 (0.72, 1.10)	0.0507
Relative risk ⁴						
Lowest tertile of fiber (95% CI)	1.00	1.06 (0.84, 1.34)	0.95 (0.74, 1.22)	—	—	—
Middle tertile of fiber (95% CI)	1.07 (0.86, 1.34)	1.11 (0.90, 1.37)	0.84 (0.66, 1.08)	—	—	—
Highest tertile of fiber (95% CI)	0.92 (0.69, 1.24)	0.97 (0.77, 1.22)	0.71 (0.56, 0.89)	—	—	—
Glycemic load						
Range	<103	104–114	115–124	125–136	>136	—
Median	94	110	120	129	145	—
Cases (<i>n</i>)	247	236	220	214	224	—
Person-years	40160	40740	40574	40629	40550	—
Relative risk ² (95% CI)	1.00	0.95 (0.79, 1.15)	0.85 (0.70, 1.03)	0.88 (0.73, 1.07)	0.89 (0.73, 1.08)	0.17
Relative risk ³ (95% CI)	1.00	0.96 (0.79, 1.15)	0.86 (0.71, 1.05)	0.92 (0.75, 1.12)	0.95 (0.78, 1.16)	0.53
Relative risk ⁴						
Lowest tertile of fiber (95% CI)	1.00	0.96 (0.76, 1.21)	0.97 (0.75, 1.26)	—	—	—
Middle tertile of fiber (95% CI)	1.09 (0.87, 1.37)	0.98 (0.79, 1.22)	0.91 (0.72, 1.15)	—	—	—
Highest tertile of fiber (95% CI)	0.81 (0.60, 1.10)	0.77 (0.60, 0.99)	0.85 (0.69, 1.05)	—	—	—

¹Person-years were calculated as described in Methods.²Proportional hazards regression models were adjusted for the same covariates listed in Table 2.³Additional adjustment for total dietary fiber.⁴Models were adjusted for the same covariates listed in Table 2. Relative risks are across tertiles of glycemic index or glycemic load within tertiles of total dietary fiber intake.

magnesium, which is found in the fibrous component of cereal plants. There was an inverse relation between dietary magnesium and type 2 diabetes.

Results from the multivariate-adjusted analyses shown in Table 4 and the age- and energy-adjusted analyses did not differ appreciably. Exceptions to this were an inverse relation between diabetes and soluble fiber and the lack of an association between diabetes and fiber from fruit in the age- and energy-adjusted analyses. Relative risks in the age- and energy-adjusted analysis were 1.00, 0.91, 0.94, 0.86, and 0.77 (*P* for trend: 0.0046) across quintiles of soluble fiber intake and 1.00, 0.96, 1.12, 0.97, and 1.05 (*P* for trend: 0.63) across quintiles of fiber intake from fruit.

Associations between diabetes and food groups that contribute carbohydrates and fiber to the diet were also examined (Table 5). Consistent with the finding for cereal fiber, total grain intake was inversely related to incident diabetes. The multivariate-adjusted RR comparing the fifth and first quintiles of total grain intake was 0.68 (95% CI: 0.54, 0.87). Whole grains were more strongly inversely associated with risk of diabetes than were refined grains. Women in the highest quintile of whole grain intake had an adjusted RR of 0.79 (95% CI: 0.65, 0.96) compared with women in the lowest quintile (*P* for trend: 0.0089). Intakes of fruit, vegetables, and legumes were not strongly related to diabetes risk. These findings from the multivariate analysis differed only slightly from the age- and energy-adjusted estimates and the interpretation of findings did not change with adjustment for potential confounding factors. For

example, age- and energy-adjusted RRs for whole grain intake were 1.00, 0.86, 0.92, 0.83, and 0.70 (*P* for trend: 0.0029) across quintiles of intake.

Inclusion of family history of diabetes as a covariate did not substantially alter the risk estimates presented in Tables 2–5. To control for recent dietary changes, multivariate models were also run that excluded women who reported cancer or heart disease at baseline. Relative risk estimates were not appreciably changed by these exclusions.

Results from multivariate regression models that included more than one of the dietary components under study are shown in Table 6. Dietary intakes of foods and nutrients are highly correlated and these models were intended to help distinguish the effects of dietary variables that appeared related to type 2 diabetes in these data. Each of the 4 models was adjusted for the covariates listed in the footnote as well as for the dietary components listed below the model headings. Because our findings were strongest for grain intake, these analyses focused on the effects of adjusting grains for cereal fiber and dietary magnesium, 2 components of grains that were strongly related to type 2 diabetes in these data. Results for total grains and whole grains were attenuated after the models were adjusted for cereal fiber. For example, RRs were 1.00, 1.01, 1.02, 1.01, and 0.93 (*P* for trend: 0.46) across quintiles of whole-grain intake. However, both cereal fiber and dietary magnesium remained significantly and inversely related to type 2 diabetes. Simultaneous adjustment for grains, cereal grains, and dietary magnesium attenuated the findings for cereal fiber and dietary magnesium, but inverse dose-response relations were still apparent for these 2 grain

TABLE 4

Multivariate-adjusted relative risks of incident type 2 diabetes across quintiles of energy-adjusted dietary fiber and magnesium intakes among 35 988 Iowa women, 1986–1992¹

Variable	Quintile of intake					P for trend
	1	2	3	4	5	
Total dietary fiber						
Range (g/d)	<15.3	15.3–17.8	17.9–20.3	20.4–23.6	>23.6	—
Median (g/d)	13.27	16.64	19.03	21.82	26.50	—
Cases (n)	253	265	234	212	177	—
Person-years	39 587	40 016	40 534	41 396	41 120	—
Relative risk (95% CI)	1.00	1.09 (0.91, 1.31)	1.00 (0.83, 1.21)	0.94 (0.78, 1.15)	0.78 (0.64, 0.96)	0.005
Total soluble fiber						
Range (g/d)	<4.8	4.8–5.5	5.6–6.2	6.3–7.2	>7.2	—
Median (g/d)	4.19	5.19	5.88	6.64	8.01	—
Cases (n)	250	231	237	221	202	—
Person-years	39 576	40 572	40 637	40 988	40 880	—
Relative risk (95% CI)	1.00	1.00 (0.83, 1.21)	1.02 (0.84, 1.23)	0.99 (0.82, 1.20)	0.89 (0.73, 1.08)	0.23
Total insoluble fiber						
Range (g/d)	<11.4	11.4–13.4	13.5–15.2	15.3–17.7	>17.7	—
Median (g/d)	9.93	12.48	14.31	16.34	19.84	—
Cases (n)	268	255	232	204	182	—
Person-years	39 737	40 159	40 680	41 080	40 996	—
Relative risk (95% CI)	1.00	0.96 (0.80, 1.15)	0.92 (0.77, 1.11)	0.81 (0.67, 0.99)	0.75 (0.61, 0.91)	0.0012
Fiber from cereals						
Range (g/d)	<3.4	3.4–4.3	4.4–5.5	5.6–7.5	>7.5	—
Median (g/d)	2.66	3.87	4.91	6.40	9.43	—
Cases (n)	281	265	241	198	156	—
Person-years	39 637	40 218	40 621	40 956	41 222	—
Relative risk (95% CI)	1.00	0.93 (0.78, 1.11)	0.88 (0.73, 1.05)	0.77 (0.63, 0.93)	0.64 (0.53, 0.79)	0.0001
Fiber from fruit						
Range (g/d)	<2.55	2.55–3.85	3.86–5.19	5.20–7.02	>7.02	—
Median (g/d)	1.71	3.22	4.51	6.00	8.72	—
Cases (n)	221	212	251	218	239	—
Person-years	39 471	40 491	40 698	41 083	40 911	—
Relative risk (95% CI)	1.00	0.98 (0.81, 1.20)	1.14 (0.94, 1.38)	1.06 (0.87, 1.29)	1.17 (0.96, 1.42)	0.081
Fiber from vegetables						
Range (g/d)	<5.75	5.75–7.11	7.12–8.38	8.39–10.14	>10.14	—
Median (g/d)	4.71	6.48	7.72	9.15	11.74	—
Cases (n)	228	227	237	228	221	—
Person-years	39 877	40 657	40 721	40 797	40 601	—
Relative risk (95% CI)	1.00	1.07 (0.88, 1.30)	1.12 (0.92, 1.35)	1.12 (0.92, 1.36)	0.97 (0.80, 1.18)	0.77
Fiber from legumes						
Range (g/d)	<0.31	0.31–0.56	0.57–0.83	0.84–1.21	>1.21	—
Median (g/d)	0.095	0.45	0.70	0.98	1.74	—
Cases (n)	250	227	216	219	229	—
Person-years	40 183	40 603	40 582	40 593	40 692	—
Relative risk (95% CI)	1.00	0.97 (0.80, 1.18)	0.95 (0.78, 1.16)	1.04 (0.85, 1.27)	1.10 (0.91, 1.33)	0.17
Dietary magnesium						
Range (mg/d)	<242	242–270	271–297	298–332	>332	—
Median (mg/d)	220	257	284	312	362	—
Cases (n)	309	235	220	216	161	—
Person-years	39 866	40 085	40 670	40 909	41 123	—
Relative risk (95% CI)	1.0	0.81 (0.68, 0.96)	0.82 (0.68, 0.98)	0.81 (0.67, 0.97)	0.67 (0.55, 0.82)	0.0003

¹Proportional hazards regression models were adjusted for the same covariates listed in Table 2. Person-years were calculated as described in Methods.

components. For example, RRs from model 4 were 1.00, 0.93, 0.90, 0.80, and 0.71 (*P* for trend: 0.0017) across quintiles of cereal fiber intake and 1.00, 0.82, 0.86, 0.88, and 0.76 (*P* for trend: 0.048) across quintiles of dietary magnesium intake. Overall, these findings suggest that the inverse relation between whole-grain intake and type 2 diabetes may be due to fiber and components of whole grains that are highly correlated with fiber.

DISCUSSION

This prospective study of older women indicates that dietary carbohydrates may influence the risk of type 2 diabetes. After multivariate adjustment for several risk factors for diabetes, the data suggested strong inverse associations between incidence of diabetes and intakes of total grains, whole grains, dietary fiber, cereal fiber, and dietary magnesium.



TABLE 5

Multivariate-adjusted relative risks of incident type 2 diabetes across quintiles of carbohydrate-rich food groups among 35 988 Iowa women, 1986–1992¹

Food group	Quintile of food group intake					P for trend
	1	2	3	4	5	
Total grains						
Range of intake (servings/wk)	<13.0	13–18.5	19–24.5	25–33	>33	—
Median (servings/wk)	9.5	15.5	21.5	28.5	41.5	—
Cases (<i>n</i>)	235	218	237	234	217	—
Person-years	40 107	40 670	39 674	41 013	41 190	—
Relative risk (95% CI)	1.00	0.89 (0.74, 1.08)	0.94 (0.77, 1.14)	0.81 (0.66, 0.99)	0.68 (0.54, 0.87)	0.0011
Whole grains						
Range of intake (servings/wk)	<3.0	3.0–5.5	6.0–8.0	8.5–17.5	>17.5	—
Median (servings/wk)	1.0	4.0	7.0	10.5	20.5	—
Cases (<i>n</i>)	250	234	234	216	207	—
Person-years	38 577	39 622	40 548	41 899	42 007	—
Relative risk (95% CI)	1.00	0.99 (0.82, 1.18)	0.98 (0.81, 1.18)	0.92 (0.76, 1.11)	0.79 (0.65, 0.96)	0.0089
Refined grains						
Range of intake (servings/wk)	<6.0	6.0–9.5	10–13.5	14–22	>22	—
Median (servings/wk)	3.5	7.5	11.5	17.5	29.5	—
Cases (<i>n</i>)	228	235	175	253	250	—
Person-years	40 402	43 117	36 757	42 196	40 182	—
Relative risk (95% CI)	1.00	0.96 (0.79, 1.16)	0.81 (0.66, 0.99)	0.98 (0.81, 1.19)	0.87 (0.70, 1.08)	0.36
Total fruit and vegetable						
Range of intake (servings/wk)	<23	23–30	31–39	40–51	>51	—
Median (servings/wk)	18.0	27.0	35.0	44.0	62.0	—
Cases (<i>n</i>)	213	215	244	240	229	—
Person-years	39 047	39 813	42 850	39 927	41 016	—
Relative risk (95% CI)	1.00	1.00 (0.82, 1.22)	1.12 (0.92, 1.36)	1.21 (0.99, 1.49)	1.05 (0.84, 1.31)	0.41
Total fruit						
Range of intake (servings/wk)	<6.25	6.5–10	10.1–13.5	13.6–19	>19	—
Median (servings/wk)	4.0	8.5	12.0	16.0	23.5	—
Cases (<i>n</i>)	218	246	206	227	244	—
Person-years	39 451	43 325	38 352	39 911	41 614	—
Relative risk (95% CI)	1.00	1.05 (0.87, 1.26)	1.00 (0.82, 1.22)	1.08 (0.88, 1.32)	1.14 (0.93, 1.39)	0.20
Total vegetable						
Range of intake (servings/wk)	<14	14–19.4	19.5–25	25.1–33.5	>33.5	—
Median (servings/wk)	11.0	17.0	22.0	28.5	41.5	—
Cases (<i>n</i>)	230	217	227	229	238	—
Person-years	40 243	38 628	43 378	39 374	41 029	—
Relative risk (95% CI)	1.00	1.03 (0.85, 1.24)	0.99 (0.82, 1.21)	1.09 (0.90, 1.34)	1.07 (0.86, 1.32)	0.45
Mature beans						
Range of intake (servings/wk)	<1.5	1.5–2	2.25–3	3.5–4.5	>4.5	—
Median (servings/wk)	1.0	2.0	2.5	4.0	6.5	—
Cases (<i>n</i>)	151	328	208	244	210	—
Person-years	29 059	61 571	37 269	38 530	36 224	—
Relative risk (95% CI)	1.00	1.01 (0.82, 1.23)	1.06 (0.85, 1.31)	1.10 (0.89, 1.36)	0.96 (0.76, 1.20)	0.85

¹Proportional hazards regression models were adjusted for the same covariates listed in Table 2. Person-years were calculated as described in Methods.

The relation between dietary fiber and diabetes has received much attention (11, 12, 14–16, 29–36). Fiber, particularly soluble fiber, has repeatedly been shown to decrease postprandial glucose and insulin concentrations both in persons with diabetes and in those without (36). In addition, several cross-sectional epidemiologic studies reported inverse associations of serum insulin with fiber intake (30–34).

In the present study, women in the highest quintile of dietary fiber intake had a 22% lower risk of developing diabetes than did women in the lowest quintile. These data corroborate a report from the Nurses' Health Study in which a similar magnitude of diabetes risk was associated with dietary fiber intake (11). In contrast, in a cohort of male health professionals, no association was found between diabetes risk and total dietary fiber intake (12).

Similarly, no association was seen in a case-control study of 702 men and women (16). The 20-y follow-up of the Finnish and Dutch cohorts of the Seven Countries Study yielded no association of dietary fiber with impaired glucose tolerance or diagnosed diabetes (35).

The plasma glucose-lowering effects of fiber are attributed primarily to soluble fiber, which slows the absorption of food by creating a gel-like substance in the stomach (14, 36). For this reason, a stronger inverse association between soluble fiber and diabetes risk than between insoluble fiber and diabetes risk was expected. Insoluble fiber may also slow the absorption of food (36). The finding that insoluble fiber, but not soluble fiber, was inversely associated with diabetes risk is consistent with previous reports from other cohort studies. The Nurses' Health Study



TABLE 6

Diet and multivariate-adjusted relative risks of incident type 2 diabetes across quintiles of grain, dietary fiber, and dietary magnesium intake among 35 988 Iowa women, 1986–1992¹

Variable	Quintile of intake					P for trend
	1	2	3	4	5	
Model 1						
Total grains						
Relative risk (95% CI)	1.00	0.92 (0.76, 1.12)	0.99 (0.81, 1.21)	0.88 (0.71, 1.09)	0.80 (0.62, 1.04)	0.090
Cereal fiber						
Relative risk (95% CI)	1.00	0.96 (0.80, 1.15)	0.92 (0.76, 1.12)	0.82 (0.67, 1.00)	0.69 (0.55, 0.86)	0.0002
Model 2						
Total grains						
Relative risk (95% CI)	1.00	0.90 (0.74, 1.10)	0.96 (0.79, 1.17)	0.84 (0.67, 1.04)	0.73 (0.56, 0.96)	0.022
Cereal fiber						
Relative risk (95% CI)	1.00	0.98 (0.82, 1.18)	0.97 (0.80, 1.18)	0.88 (0.71, 1.09)	0.78 (0.62, 0.99)	0.025
Dietary magnesium						
Relative risk (95% CI)	1.00	0.81 (0.68, 0.97)	0.84 (0.70, 1.01)	0.85 (0.70, 1.03)	0.72 (0.58, 0.90)	0.013
Model 3						
Whole grains						
Relative risk (95% CI)	1.00	1.01 (0.84, 1.21)	1.02 (0.85, 1.23)	1.01 (0.83, 1.24)	0.93 (0.75, 1.16)	0.46
Cereal fiber						
Relative risk (95% CI)	1.00	0.93 (0.78, 1.11)	0.89 (0.74, 1.08)	0.78 (0.64, 0.96)	0.66 (0.53, 0.83)	0.0001
Model 4						
Whole grains						
Relative risk (95% CI)	1.00	1.03 (0.86, 1.24)	1.05 (0.87, 1.27)	0.97 (0.86, 1.29)	0.82 (0.78, 1.21)	0.69
Cereal fiber						
Relative risk (95% CI)	1.00	0.93 (0.78, 1.12)	0.90 (0.74, 1.09)	0.80 (0.65, 0.99)	0.71 (0.56, 0.89)	0.0017
Dietary magnesium						
Relative risk (95% CI)	1.00	0.82 (0.69, 0.99)	0.86 (0.71, 1.03)	0.88 (0.73, 1.06)	0.76 (0.62, 0.95)	0.048

¹Proportional hazards regression models were simultaneously adjusted for the same covariates listed in Table 2 and for the dietary factors listed under each model heading.

reported that of the associations of diabetes with different sources of dietary fiber, only the inverse association between cereal fiber and diabetes remained statistically significant after multivariate adjustment (11). In the Health Professionals' Follow-up Study, cereal fiber was inversely associated with diabetes risk, whereas fiber from fruit and vegetables was unrelated to diabetes risk (12). The findings from these prospective cohort studies, all of which used a similar questionnaire, support a stronger association of insoluble fiber than of soluble fiber with diabetes risk.

Our findings indicate a strong inverse relation between dietary magnesium intake—a component of grains—and risk of type 2 diabetes. This finding remained after adjustment for cereal fiber and grain intakes. In clinical studies, low plasma magnesium concentrations were associated with insulin resistance (37), and magnesium supplementation was shown to improve glucose handling (38). Findings from 2 large prospective studies suggested strong inverse relations between magnesium intake and incident type 2 diabetes (11, 12) and fasting insulin concentrations (39). For example, Salmerón et al (11, 12) reported a 38% decreased risk of diabetes for persons in the highest quintile of magnesium intake compared with the lowest quintile of intake. Investigators with the Atherosclerosis Risk in Communities Study reported that incident diabetes was inversely associated with serum magnesium but not with dietary magnesium intake (17).

The associations of insoluble fiber and cereal fiber intakes with diabetes risk were consistent with the analysis of food groups (Table 5), suggesting that whole-grain cereals were more strongly inversely related to disease risk than were

refined cereals. Whole and refined grains contain similar amounts of carbohydrate, but whole grains contain substantially more dietary fiber and magnesium (40). It is important to note that what was included as whole grains herein may have consisted largely of whole meal. It has been shown that particle size may be important in the glycemic response (19) and thus the beneficial effects of whole grain reported here may have been more striking in a population that consumed grains primarily in an intact form.

The glycemic index was devised to measure the effect of various foods on postprandial glycaemic responses. Energy sources that are slowly absorbed have low glycaemic indexes and have been shown to result in better short-term glycaemic control in clinical studies than energy sources with high glycaemic indexes (18). Two prospective studies showed positive relations between the glycaemic index and diabetes risk (11, 12). However, the present analyses do not support a consistent, dose-response relation between glycaemic index and risk of type 2 diabetes. The RR estimates increased through the third quintile of intake and then dropped in the fourth and fifth quintiles. The findings of positive relations between both fructose and glucose and diabetes similarly do not support the hypothesis of a positive relation between the glycaemic index and diabetes risk. Fructose has a glycaemic index of 26 and glucose has a glycaemic index of 138 when white bread is used as the reference (18). However, in this study, both the high correlation ($r = 0.94$) between fructose and glucose intake—which makes it difficult to differentiate their associations with diabetes—and the typically poor measurement of sugars hinders clear interpretation of these data.



There is a long-standing debate regarding the effect of sugar intake, particularly sucrose, on diabetes risk. Clinical studies have generally reported an effect of sucrose on postprandial glycemic response similar to that of potatoes or white bread (18, 41). In non-diabetic subjects, increased fructose consumption did not alter fasting or postprandial glucose concentrations in one study (42) and improved glycemic response in others (43). Among diabetic subjects, improved glycemic response has generally been associated with increased consumption of fructose (43, 44).


Results of the few epidemiologic studies of the relation between sugars and diabetes risk are inconsistent. Cross-sectional studies showed both similar intakes of fructose and sucrose in subjects with and without diabetes (9) and decreased intakes of refined carbohydrates in those with compared with those without diabetes (8). A cross-sectional study of persons of Japanese descent living in Hawaii or Japan reported a positive association between intake of sugars and prevalent diabetes (7). Colditz et al (10) reported no association of sucrose with diabetes incidence in either lean or obese women. The present analysis suggests that, despite its high glycemic index, sucrose does not increase the risk of diabetes.

We found no evidence for an effect of total carbohydrate intake on diabetes risk, consistent with the results of previous cohort studies. Over separate follow-up periods, investigators with the Nurses' Health Study twice reported no association between intake of total carbohydrate and risk of diabetes (11, 12). Similarly, a study of 1462 Swedish women found no significant differences between intakes of carbohydrates in those who developed diabetes and those who did not over 12 y of follow-up (13). Overall, these findings argue against an independent effect of total carbohydrate intake in the etiology of diabetes.

Errors in the measurement of dietary intake, diabetes incidences, and the covariates in this study may have limited our ability to obtain accurate RR estimates. The food-frequency questionnaire was completed only once by study participants and no effort was made to examine potential dietary changes over the course of follow-up. Also, the baseline dietary survey was assumed to represent the participants' predisease diet. Although data were not available to examine the effects of inaccurate dietary assessment, random measurement error in dietary exposures most frequently attenuates risk estimates (45). There remains the potential for residual confounding by poorly measured covariates or by unmeasured differential changes in covariates over the course of follow-up.

It was not feasible to measure glucose concentrations in the study participants; incident cases of diabetes were ascertained by self-report. However, a validation study in this cohort showed low accuracy in the self-report of diabetes (26), consistent with findings from one study in which 29 of 44 (66%) positive reports of diabetes were validated with medical records (46). Several studies have provided evidence that nonvalidated positive reports may nevertheless reflect some level of diabetes. One study found that of 6 persons with nonvalidated positive reports of diabetes, 3 persons had renal glycosuria and 2 had been diagnosed with glycosuria at some point in the past, but no longer had glycosuria (47). This suggests that nondiabetic concentrations of blood glucose may not be entirely benign and that women who falsely reported a diagnosis of diabetes may still have had some level of underlying disease, such as impaired glucose tolerance, which had been mentioned to them in the past. This possibility is underscored by a recent change in the

diagnostic criteria for diabetes to include lower concentrations of fasting glucose (48). Assuming that the error in diabetes ascertainment was independent and nondifferential, the present findings would only be strengthened by more accurate ascertainment of disease.

Data from this prospective study of older women support inverse associations between total and whole-grain intake and risk of incident diabetes. These findings are consistent with those of several other published studies of the health effects of whole grains. Inverse associations were also observed for dietary fiber, cereal fiber, and dietary magnesium intake. These findings suggest a role for diet in the development of diabetes that is independent of diet's effect on body weight. 

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