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Whole-grain and fiber intake and the incidence of type 2 diabetes[1,2]

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ABSTRACT

Background: Epidemiologic evidence of a preventive effect of whole grain against type 2 diabetes is mainly based on data from women. Information specific to men and women is needed.

Objective: The objective was to study the relation between the intake of whole grain and fiber and the subsequent incidence of type 2 diabetes.

Design: The design was a cohort study of 2286 men and 2030 women aged 40–69 y and initially free of diabetes. Food consumption data were collected from 1966 through 1972 with the use of a dietary history interview covering the habitual diet during the previous year. During a 10-y follow-up, incident type 2 diabetes cases were identified in 54 men and 102 women from a nationwide register.

Results: Whole-grain consumption was associated with a reduced risk of type 2 diabetes. The relative risk (adjusted for age, sex, geographic area, smoking status, body mass index, energy intake, and intakes of vegetables, fruit, and berries) between the highest and lowest quartiles of whole-grain consumption was 0.65 (95% CI: 0.36, 1.18; P for trend = 0.02). Cereal fiber intake was also associated with a reduced risk of type 2 diabetes. The relative risk between the extreme quartiles of cereal fiber intake was 0.39 (95% CI: 0.20, 0.77; P = 0.01).

Conclusions: An inverse association between whole-grain intake and the risk of type 2 diabetes was found. The similar result for cereal fiber intake suggests that the whole-grain association is due to cereal fiber or another factor related to cereal fiber intake. *Am J Clin Nutr* 2003;77:622–9.

KEY WORDS Diet, grain, whole grains, fiber, diabetes, epidemiology

INTRODUCTION

Obesity and a low level of physical activity are the most potent risk factors for type 2 diabetes. Lowered overall intake of dietary energy can reduce the incidence of type 2 diabetes, as shown in a recent primary prevention study (1), but the effect of specific dietary components on the incidence is still largely unknown. Dietary fiber is one nutrient that may provide protection against the disease. The beneficial effect of soluble fiber may be mediated through the slow absorption and digestion of carbohydrates that lead to a reduced demand for insulin (2). Insoluble fiber shortens intestinal transit, which therefore allows less time for carbohydrates to be absorbed (3). In line with this hypothesis, some of the few published epidemiologic studies have found an inverse association between fiber intake and the occurrence of type 2 diabetes (4–7). Whole-grain products are a rich source of fiber. Accordingly, studies on the consumption of whole grains have also reported a reduced risk of type 2 diabetes with higher intakes of whole grains (6, 8). The epidemiologic evidence on the role of dietary fiber and whole grains in the prevention of type 2 diabetes is, however, still scarce and contradictory.

The Finnish population has a high intake of whole grains, especially rye, and therefore of cereal fiber. The aim of the present Finnish prospective study was to investigate whether dietary intake of whole-grain total fiber and various fiber components predicts the incidence of type 2 diabetes in men and women.

SUBJECTS AND METHODS

The Finnish Mobile Clinic Health Examination Survey carried out health examinations in various regions of Finland from the beginning of 1966 through 1972 (9). The survey included a dietary history interview of 10 054 citizens. Participants who did not satisfy the criterion of age 40–69 y, who reported a daily energy intake < 800 or > 6000 kcal, or who had a history of diabetes or heart disease were excluded. The final study population consisted of 4316 men and women, who were fully informed about the study and the intended use of the data.

All participants completed a self-administered questionnaire that was reviewed at the baseline examination. The questionnaire yielded information on previous and current illnesses, medication use, and health behaviors such as smoking. Subjects were classified according to smoking status as never smokers, exsmokers, smokers of pipes or cigars only, smokers of < 15 cigarettes/d, and smokers of ≥ 15 cigarettes/d (10). Body weight and height were measured, and body mass index (BMI; in kg/m^2) was calculated. Casual blood pressure was measured by the auscultatory method. Four hypertension categories were formed on the basis of systolic (SBP) and diastolic (DBP) blood pressure and the use of antihypertensive medication (11). Persons with an SBP ≥ 170 mm Hg and a DPB ≥ 100 mm Hg and persons using antihypertensive medication were considered definitely hypertensive. Persons with an SBP ≥ 160 mm Hg and a DBP ≥ 95 mm Hg but not defined as hypertensive were considered to have mild hypertension, and

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those with an SBP < 140 mm Hg and a DBP < 90 mm Hg were considered normotensive. All persons with intermediate values were considered to have borderline hypertension. Serum cholesterol concentration was determined by using an autoanalyzer modification (Auto-Analyzer Methodology N-24a and N-77; Technicon, Tarrytown, NY) of the Liebermann-Burchard reaction (12, 13). Participants with a history of diabetes diagnosed by the physician at baseline were identified by information that the participants themselves gave. An oral-glucose-tolerance test was carried out for every subject who was not already diagnosed with diabetes (14). The oral glucose load was graded according to body surface area. For practical reasons, only 3 doses of glucose (60, 75, and 90 g) were used. A blood sample was taken 1 h after the glucose load, and plasma glucose concentrations were determined with the use of an autoanalyzer. New diabetes cases were diagnosed at baseline with the use of diagnostic criteria of the World Health Organization (15), and the persons in whom that diagnosis was made were also excluded from the study population.

Total habitual food consumption during the previous year was estimated by use of a dietary history interview (16). The interviewers were nutrition professionals employing a questionnaire that listed over 100 food items to facilitate the interview. Several questions were open-ended, which allowed respondents to be more specific in their answers. The respondents indicated the amounts of food consumed per day, week, month, or year. Reported amounts of food were converted to grams per day. Food models were used to help participants remember portion sizes. Mixed foods were evaluated in terms of their component ingredients with the use of a recipe file. Finally, the intakes of separate food items were combined and calculated per day (16).

For classifying whole-grain and refined-grain variables, we used a modification of the procedure developed by Jacobs et al (17). In contrast with previous studies, the whole-grain and refined-grain groups in the present study included only grains, mainly different breads and flour derived from mixed dishes. More specifically, the whole-grain food group contained rye bread, rye crisp bread, and all whole-grain flours and other products (rye, whole wheat, wheat germ, rolled oats, barley, millet, and buckwheat) derived from different grain foods [eg, porridge, gruel, and Karelian pie (a national food of rice pudding baked in rye pastry and greased by butter)]. In addition, breads prepared from mixtures of whole grains and refined grains were classified into the whole-grain group. The proportion of whole-grain flours in these mixtures was 25–50%, as determined from the available cookbook information. The refined-grain group contained white bread, wheat rusk, cream crackers, refined breakfast cereals, polished rice, and pasta. White wheat flour in sweet wheat buns and wheat flour and starches in cookies, cakes, and other foods (eg, porridge, gruel, sauce, pudding, and pancakes) were included in the refined-grain category.

The vitamin B-6, folic acid, and magnesium contents of food items were estimated with the use of Finnish food-composition tables (18). Data on fiber constituents (19), fatty acids (20, 21), vitamin E (22), and β-carotene (23) contents were estimated with the use of analyzed values for Finnish foods. The intake of flavonoids was estimated from Dutch food-composition values (24, 25). For berries not included in the Dutch analyses and commonly used in Finland, the flavonoids were estimated with recently analyzed values for berries in Finland (26).

Grain products, especially whole grains, represented a major source of dietary fiber. On average, whole grains provided 71% and 56% of the total fiber in the diet of men and women, respectively. Whole grains contributed greatly to the intake of insoluble noncellulose polysaccharides (86% in men and 70% in women). The contribution to the intakes of lignin (72% in men and 57% in women) and cellulose (46% in men and 36% in women) was somewhat lower. In total, cereal fiber made up four-fifths (82%) of the total fiber intake in men and two-thirds (67%) of that in women.

Repeatability of the dietary history method was estimated after 4–8 mo (93 subjects) and 4–7 y (1844 subjects) by a second interview. The intraclass correlation coefficient for the short-term repeatability of total grain intake was 0.62 (27). The corresponding coefficient for long-term repeatability (4–7 y) was 0.39. For whole-grain and refined-grain intakes, the short-term intraclass correlation coefficients were 0.57 and 0.49. In 4–7 y, the corresponding values had decreased to 0.35 and 0.36, respectively. The coefficient for total fiber intake of short-term repeatability was 0.65 and that of long-term repeatability was 0.39.

In Finland, all diabetic persons needing drug therapy are entitled to reimbursement of drug costs. A detailed medical certificate from the attending physician is required for reimbursement, and a central register of all patients receiving drug reimbursement is kept by the Social Insurance Institution. Participants in the present study were linked to this register through the individual social security code that is assigned to each Finnish citizen. During a 10-y follow-up, incident type 2 diabetes cases occurred in 54 male and 102 female participants. All medical certificates of the cases were checked, and all met the World Health Organization diagnostic criteria (15) for type 2 diabetes (14).

Relative risks of type 2 diabetes, with 95% CIs between quartiles of different food items and nutrients, were calculated with the use of Cox's life table regression model (28). Potential confounding factors including age, geographic area, smoking, body mass index, energy intake, and intakes of fruit and berries and vegetables were adjusted for in different multivariate models. Models for men and women separately and for men and women combined were used. When the data were analyzed for men and women combined, sex was added to the model. Tests of potential linear trends across quartiles of the dietary variables were carried out on the basis of a likelihood ratio test by including the variables in the model as continuous variables.

In addition, we examined whether alternative hypotheses might explain the associations by including in the model intakes of saturated fat, vitamins E and C, β-carotene, vitamin B-6, folic acid, flavonoids, and magnesium. Finally, a model including serum cholesterol and hypertension and a model including cereal fiber and lignin were used. Potential effect-modifying factors were studied by including interaction terms in the model.

RESULTS

Type 2 diabetes risk was positively associated with age (**Table 1**). In addition, sex, higher BMI, and hypertension were significantly associated with the disease. At baseline, the mean consumption of whole grains was higher in men than in women. The average whole-grain intake was 218 ± 116.4 g/d for men and 150 ± 87.6 g/d for women. Nondietary risk factors showed no strong associations with whole-grain (**Table 2**) or fiber (**Table 3**) intake. A significant trend (*P* for trend < 0.01) was observed

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TABLE 1
Relative risk by category of potential risk factors for type 2 diabetes[1]

Variable	Cases/persons at risk	Relative risk[2]
Age (y)[3]		
<50	24/1919	1
50–59	65/1475	3.73 (2.33, 5.95)
60–69	67/922	6.81 (4.27, 10.86)
P for trend		<0.001
Sex[4]		
Male	54/2286	1
Female	102/2030	1.81 (1.30, 2.53)
P value		<0.001
BMI (kg/m^2)		
<27	33/2535	1
≥27	123/1781	4.57 (3.11, 6.72)
P value		<0.001
Smoking		
No	124/2915	1
Currently	32/1401	0.69 (0.47, 1.03)
P value		0.06
Hypertension[5]		
No	84/3596	1
Yes[5]	72/720	3.47 (2.52, 4.77)
P value		<0.001
Serum cholesterol (mmol/L)		
<6.7	68/1914	1
≥6.7	88/2402	0.97 (0.71, 1.33)
P value		0.86

[1] Adjusted for age and sex unless indicated otherwise.
[2] 95% CIs in parentheses.
[3] Adjusted for sex only.
[4] Adjusted for age only.
[5] Persons with mild or definite hypertension combined.

between whole-grain and fiber consumption and the dietary variables considered, except for the intakes of whole grains and vegetables (Table 2) and of fiber, protein, and polyunsaturated fat (Table 3). Grain consumption and fiber intake were positively associated with whole-grain intake, whereas the intakes of fruit and berries and of fat were inversely associated. The distribution of dietary variables by quartile of total fiber intake was quite similar to that by whole-grain intake (Table 3). Grain consumption and the intake of different fiber components were positively associated with total fiber intake.

During a 10-y follow-up, an inverse association between the intakes of total grain and whole grains and the incidence of type 2 diabetes was observed (**Table 4**). When the highest and lowest quartiles of total grain consumption were compared, the relative risk of type 2 diabetes, adjusted for age, sex, geographic area, and energy intake, was 0.39 (95% CI: 0.20, 0.76; *P* for trend = 0.001). The corresponding value for whole-grain intake was 0.64 (95% CI: 0.36, 1.15; *P* = 0.02). Further adjustment for smoking, BMI, and consumption of fruit and berries and vegetables did not notably alter the associations (Table 4), nor did inclusion in the model of the potential intermediate factors serum cholesterol and hypertension (data not shown). The inverse relation between high whole-grain intake and diabetes was similar but nonsignificant after further adjustments for intake of saturated fat, vitamins E and C, β-carotene, vitamin B-6, folic acid, flavonoids, and magnesium. The relative risk in the final model including all considered confounders was 0.67 (95% CI: 0.32, 1.38; *P* = 0.09). Exclusion of the first 2 y of follow-up had no notable effect on the results (data not shown). We also included cereal fiber and lignin individually in the final model. After the inclusion of cereal fiber, the relative risk was 1.14 (95% CI: 0.49, 2.66; *P* = 0.63), and after that of lignin, it was 0.62 (95% CI: 0.29, 1.33; *P* = 0.95).

A higher intake of refined grains was related to a reduced incidence of disease (Table 4). The relative risk, adjusted for age, sex, geographic area, and energy intake, between the highest and lowest quartiles of refined-grain intake was 0.61 (95% CI: 0.36, 1.05; *P* = 0.05). Inclusion in the model of intermediate or potential confounding nutritional factors had no essential effect on the results. The relative risk in the final model including age, sex, geographic area, smoking, BMI, energy intake, consumption of fruit and berries and vegetables, and intakes of saturated fat, vitamins E and C, β-carotene, vitamin B-6, folic acid, flavonoids, and magnesium was 0.58 (95% CI: 0.32, 1.05; *P* = 0.04).

Higher fiber intake was associated with a reduced risk of type 2 diabetes (**Table 5**). For total fiber intake, the relative risk, adjusted for age, sex, geographic area, and energy intake, was 0.57 (95% CI: 0.30, 1.08; *P* = 0.07) between the highest and lowest quartiles. The corresponding value for insoluble noncellulose polysaccharides was 0.48 (95% CI: 0.25, 0.91; *P* = 0.02). Of fiber provided by different food groups, fiber from cereal, but not that from vegetables or fruit, was significantly associated with the risk of type 2 diabetes. The relative risk for cereal fiber was 0.36 (95% CI: 0.18, 0.70; *P* = 0.005). All associations remained significant in analyses including age, sex, geographic area, smoking, BMI, energy intake, and intakes of fruit and berries and vegetables in the models (Table 5). Further adjustment for intakes of saturated fat, vitamins E and C, β-carotene, vitamin B-6, folic acid, flavonoids, and magnesium did not notably attenuate the associations. The relative risk between the highest and lowest quartiles of total fiber intake was 0.53 (95% CI: 0.23, 1.22; *P* = 0.16) and that for cereal fiber intake was 0.37 (95% CI: 0.16, 0.82; *P* = 0.04). The corresponding values for insoluble noncellulose polysaccharides and lignin were 0.46 (95% CI: 0.21, 1.03; *P* = 0.06) and 0.77 (95% CI: 0.35, 1.71; *P* = 0.45), respectively.

Factors potentially modifying the association between whole-grain intake and type 2 diabetes incidence were also studied. No significant interaction was found for sex or any of the other variables considered (**Table 6**).

DISCUSSION

In the present study, an inverse association between whole-grain consumption and type 2 diabetes was observed. The association persisted after adjustment for potential confounding factors related to lifestyle, and the association was independent of the consumption of fruit and vegetables. Therefore, it appears conceivable that the beneficial association of whole-grain intake and the development of type 2 diabetes could be ascribed to factors specifically related to whole grains.

Whole-grain products are a good source of several vitamins (including vitamins E and B), minerals, and fiber. In epidemiologic studies, higher serum concentrations of α-tocopherol were related to a reduced risk of type 2 diabetes (14, 29). Vitamin B-6 and folic acid have a potential effect of reducing the development of diseases linked to metabolic syndrome and type 2 diabetes through a lower concentration of serum homocysteine (30). An inverse relation between magnesium intake and the risk of type 2

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TABLE 2
Characteristics and several dietary variables in quartiles of whole-grain intake of subjects at baseline[1]

	Quartile of whole-grain intake[2]			
	1 (lowest) (n = 1070)	2 (n = 1078)	3 (n = 1084)	4 (highest) (n = 1084)
Quartile median (g/d)	79	136	198	302
Characteristics				
Age (y)	53 ± 8.2[3]	52 ± 8.0	52 ± 8.0	51 ± 7.6
Sex (%)[4]	44	52	57	59
BMI (kg/m^2)	26.7 ± 4.3	26.5 ± 4.0	26.3 ± 3.8	26.4 ± 3.7
Smoking (%)[5]	36	36	31	28
Hypertension (%)[6]	18	16	14	18
Serum cholesterol (mmol/L)	7.1 ± 1.4	7.1 ± 1.4	7.0 ± 1.4	6.9 ± 1.4
Intakes (g/d)				
Vegetables	326 ± 122	322 ± 134	332 ± 140	325 ± 164
Fruit and berries	183 ± 140	154 ± 126	145 ± 122	123 ± 116
Total grain	185 ± 58	228 ± 49	283 ± 56	391 ± 121
Rye	66 ± 32	102 ± 44	137 ± 65	212 ± 131
Other whole grains	21 ± 27	39 ± 43	59 ± 63	105 ± 118
Refined grains	95 ± 53	84 ± 46	84 ± 50	71 ± 59
Refined grain from wheat	71 ± 38	69 ± 41	69 ± 45	61 ± 52
Energy[7]	2014 ± 611	2308 ± 677	2546 ± 700	3093 ± 816
Carbohydrate	265 ± 70	274 ± 72	290 ± 74	315 ± 98
Protein	93 ± 26	91 ± 28	90 ± 29	89 ± 35
Total fat	121 ± 37	117 ± 43	110 ± 44	99 ± 47
Saturated fat	68 ± 22	66 ± 25	62 ± 26	56 ± 27
Monounsaturated fat	36 ± 12	35 ± 14	33 ± 14	29 ± 15
Polyunsaturated fat	8.7 ± 3.6	8.4 ± 4.3	8.0 ± 3.9	7.4 ± 4.5
Total fiber	20 ± 5.2	24 ± 5.3	28 ± 5.8	37 ± 12.2
Cereal fiber	12 ± 3.4	16 ± 3.4	20 ± 4.4	29 ± 11
Magnesium[8]	336 ± 76	363 ± 81	393 ± 89	456 ± 137

[1] Adjusted for age, sex, and energy intake, except for age, which was adjusted for sex and energy intake; energy intake, which was adjusted for age and sex; and sex, which was adjusted for age and energy intake.
[2] Whole-grain intake was significantly (P for trend < 0.01) associated with all dietary variables except vegetables. n = number of observations.
[3] $\bar{x}$ ± SD.
[4] Proportion of men.
[5] Proportion of current smokers.
[6] Proportion of persons with systolic blood pressure ≥ 160 mm Hg and diastolic blood pressure ≥ 95 mm Hg, or who were taking antihypertensive medication.
[7] kcal/d.
[8] mg/d.

diabetes was shown in several prospective studies (4–6). An abundant intake of saturated fat has also been related to an increased incidence of diabetes (31). In the present study, the protective effect of whole-grain consumption was apparently not completely due to a higher intake of antioxidant vitamins, vitamin B-6, folic acid, or magnesium or to a lower intake of saturated fatty acids, because adjustment for these nutrients did not alter the results in men.

Whole grains, particularly rye, are a major source of dietary fiber for Finns. Accordingly, we found an inverse relation between the intake of total fiber, especially cereal fiber, and the risk of type 2 diabetes, whereas fiber derived from fruit or vegetables did not have an effect on diabetes risk. Adjustment for cereal fiber considerably weakened the association between whole-grain consumption and type 2 diabetes risk, which suggests that the relation of whole grain may be due to cereal fiber or to factors related to cereal fiber intake. These findings give further support to previous studies from the United States, which reported a reduced risk of type 2 diabetes with greater whole-grain (6, 8) or cereal-fiber (4–7) intake.

In the present study, whole-grain consumption consisted mainly of rye bread, whereas in earlier studies, in the United States, whole-grain consumption was mainly whole wheat or other grains (6, 8). There is evidence, based mainly on studies of diabetic subjects, that rye bread consumption also results in a lower glucose response than does white bread consumption (32).

Cereal fiber consists of several components that apparently have different effects on glucose metabolism. Soluble fiber has been associated with reduced glucose and insulin responses, apparently because of the retarding effect of soluble fiber on gastric emptying and absorption (2). On the other hand, a closer association between the intake of insoluble noncellulose polysaccharides, rather than of soluble fiber, and the risk of type 2 diabetes has been reported (6). It is suggested that the quicker intestinal transit allows less time for carbohydrates to be absorbed in the upper jejunum, thus relieving insulin demand (33).

In the present study, whole-grain consumption was considerably lower in women than in men. Despite this difference, significant sex-specific interaction was not found, possibly because of the small number of subjects.

Certain methodologic limitations in our study may have influenced the results. The dietary history method used has limitations that may have caused some misclassification of subjects, and that

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TABLE 3
Characteristics and several dietary variables in quartiles of total fiber intake of subjects at baseline[1]

	Quartile of total fiber intake[2]			
	1 (lowest) (n = 1079)	2 (n = 1079)	3 (n = 1079)	4 (highest) (n = 1079)
Quartile median (g/d)	16	22	29	40
Characteristics				
Age (y)	53 ± 8.3[3]	53 ± 7.8	51 ± 7.9	51 ± 7.6
Sex (%)[4]	50	53	56	53
BMI (kg/m²)	26.5 ± 4.4	26.5 ± 4.0	26.4 ± 3.9	26.5 ± 3.6
Smoking (%)[5]	39	36	31	23
Hypertension (%)[6]	16	17	16	19
Serum cholesterol (mmol/L)	7.1 ± 1.5	7.1 ± 1.4	7.0 ± 1.4	6.9 ± 1.4
Intakes (g/d)				
Vegetables	269 ± 96	311 ± 111	340 ± 124	385 ± 171
Fruit and berries	111 ± 98	145 ± 114	165 ± 135	183 ± 148
Total grain	193 ± 53	238 ± 59	280 ± 71	377 ± 128
Whole grain	112 ± 45	151 ± 50	191 ± 60	288 ± 116
Rye	48 ± 36	90 ± 46	137 ± 59	242 ± 111
Other whole grains	64 ± 56	61 ± 70	54 ± 82	46 ± 98
Refined grains	78 ± 35	84 ± 44	85 ± 53	86 ± 61
Refined grain from wheat	62 ± 30	68 ± 38	69 ± 45	70 ± 53
Energy[7]	1915 ± 563	2262 ± 576	2592 ± 651	3200 ± 804
Carbohydrate	254 ± 55	275 ± 60	292 ± 68	324 ± 94
Protein	92 ± 26	90 ± 24	90 ± 27	91 ± 34
Fat	126 ± 38	117 ± 38	110 ± 44	95 ± 48
Saturated fat	72 ± 23	66 ± 23	62 ± 26	52 ± 28
Monounsaturated fat	38 ± 12	35 ± 12	32 ± 14	28 ± 15
Polyunsaturated fat	8.3 ± 3.6	8.2 ± 3.1	8.0 ± 4.2	7.9 ± 4.6
Soluble fiber	4.1 ± 0.84	5.4 ± 0.69	6.4 ± 0.80	8.6 ± 2.1
Insoluble NCP[8]	7.9 ± 1.6	11 ± 1.4	14 ± 1.9	21 ± 6.2
Cellulose	3.1 ± 0.66	4.0 ± 0.64	4.7 ± 0.75	6.1 ± 1.5
Lignin	2.1 ± 0.42	2.9 ± 0.32	3.5 ± 0.41	5.0 ± 1.4
Cereal fiber	11 ± 2.9	16 ± 3.0	20 ± 3.7	31 ± 10
Fruit fiber	1.7 ± 1.5	2.4 ± 1.9	2.8 ± 2.3	3.3 ± 2.9
Vegetable fiber	4.5 ± 1.6	5.2 ± 1.9	5.7 ± 2.1	6.5 ± 2.9
Magnesium[9]	327 ± 70	359 ± 66	392 ± 73	471 ± 127

[1] Adjusted for age, sex, and energy intake, except for age, which was adjusted for sex and energy intake; energy intake, which was adjusted for age and sex; and sex, which was adjusted for age and energy intake.
[2] P for trend < 0.01 in all dietary variables except protein and polyunsaturated fat. n = number of observations.
[3] $\bar{x}$ ± SD.
[4] Proportion of men.
[5] Proportion of current smokers.
[6] Proportion of persons with systolic blood pressure ≥ 160 mm Hg and diastolic blood pressure ≥ 95 mm Hg, or who were taking antihypertensive medication.
[7] kcal/d.
[8] Noncellulose polysaccharides.
[9] mg/d.

could tend to diminish the associations observed between exposure and outcome (34). The result of the dietary history interview is always a subjective assessment of the respondent's own dietary habits. A period of 1 y is a lengthy time to recall. Food models were used to diminish errors in recall, and open-ended questions enabled respondents to be more specific in their answers. To minimize possible bias, trained nutrition professionals employed structured questionnaires.

In the present study, the whole-grain and refined-grain groups were more specifically composed than in previous studies, because these categories included only grain, mainly different breads and flour in mixed dishes. Nevertheless, besides whole-grain bread, our whole-grain category included breads prepared from a mixture of whole-grain and refined-grain flours. The proportion of whole-grain flours in these mixed breads was not known, but, according to common recipes, it was estimated that whole-grain flours provided between one-quarter and one-half of the total amount of flour in these breads. When we excluded these mixed breads from the analysis, the suggested association of whole grains was not substantially changed (data not shown).

The short-term repeatability of the dietary history method was fairly good (27). Long-term repeatability was poorer, which can be partly explained by changes in Finnish dietary habits. For this reason, the present study's follow-up was limited to 10 y. Because results did not change notably after the exclusion of incident cases during the first 2 y, it can be concluded that no preclinical disease phase biased our results.

We were unable to take into account some potential confounding factors. Physical activity could not be controlled for, but might have been partly considered indirectly by adjustment for BMI and

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TABLE 4
Relative risk of type 2 diabetes in quartiles of grain intake

	Quartile of grain intake[1]				
	1 (lowest)	2	3	4 (highest)	*P* for trend
Total grain (g/d)	10–181	182–248	249–339	340–1535	
Adjustment A[2]	1	0.78 (0.52, 1.15)	0.49 (0.29, 0.82)	0.39 (0.20, 0.76)	0.001
Adjustment B[3]	1	0.80 (0.54, 1.20)	0.48 (0.28, 0.81)	0.38 (0.19, 0.77)	0.001
Whole grain (g/d)	0–109	110–162	163–237	238–1321	
Adjustment A	1	0.99 (0.68, 1.45)	0.49 (0.29, 0.82)	0.64 (0.36, 1.15)	0.02
Adjustment B	1	1.05 (0.71, 1.55)	0.52 (0.31, 0.88)	0.65 (0.36, 1.18)	0.02
Rye (g/d)	0–58	59–112	113–181	182–1026	
Adjustment A	1	0.89 (0.59, 1.33)	0.93 (0.60, 1.44)	0.60 (0.34, 1.08)	0.17
Adjustment B	1	0.99 (0.66, 1.48)	1.00 (0.65, 1.54)	0.65 (0.36, 1.18)	0.30
Other whole grain (g/d)	0–5	6–23	24–75	76–632	
Adjustment A	1	1.11 (0.71, 1.73)	1.08 (0.68, 1.72)	1.06 (0.65, 1.74)	0.84
Adjustment B	1	1.20 (0.77, 1.88)	1.12 (0.71, 1.79)	1.14 (0.69, 1.87)	0.69
Refined grain (g/d)	0–45	46–73	74–110	111–567	
Adjustment A	1	0.67 (0.44, 1.01)	0.66 (0.42, 1.03)	0.61 (0.36, 1.05)	0.05
Adjustment B	1	0.70 (0.47, 1.07)	0.68 (0.43, 1.06)	0.62 (0.36, 1.06)	0.05
Refined grain from wheat (g/d)	0–33	34–58	59–90	91–389	
Adjustment A	1	0.77 (0.51, 1.17)	0.71 (0.45, 1.11)	0.70 (0.41, 1.19)	0.13
Adjustment B	1	0.81 (0.53, 1.22)	0.70 (0.45, 1.10)	0.69 (0.41, 1.17)	0.11

[1] Relative risk; 95% CIs in parentheses.
[2] Adjusted for age, sex, geographic area, and energy intake.
[3] Adjusted for age, sex, geographic area, smoking, BMI, and intakes of energy, fruit and berries, and vegetables.

energy intake. The use of vitamin supplements was another potential confounder that could not be controlled for. However, the influence of supplements was apparently negligible because, at the time of the baseline interviews, their use in Finland was rare (35).

It has been suggested that a family history of diabetes could predict the development of type 2 diabetes. The fact that we could not control for a family history of diabetes may have altered the observed associations. The lack of significant interaction with

TABLE 5
Relative risk of type 2 diabetes in quartiles of fiber intake

	Quartile of fiber intake[1]				
Nutrient	1 (lowest)	2	3	4 (highest)	*P* for trend
Total fiber (g/d)	2.6–19.2	19.3–25.3	25.4–33.1	33.2–118	
Adjustment A[2]	1	0.72 (0.48, 1.09)	0.70 (0.43, 1.14)	0.57 (0.30, 1.08)	0.07
Adjustment B[3]	1	0.70 (0.46, 1.07)	0.67 (0.40, 1.11)	0.51 (0.26, 1.00)	0.04
Soluble fiber (g/d)	0.53–4.5	4.6–5.8	5.9–7.3	7.4–22.7	
Adjustment A	1	0.62 (0.40, 0.97)	0.90 (0.57, 1.43)	0.80 (0.44, 1.45)	0.57
Adjustment B	1	0.50 (0.31, 0.81)	0.74 (0.44, 1.25)	0.57 (0.29, 1.12)	0.21
Insoluble NCP[4] (g/d)	1.1–8.7	8.8–12.0	12.1–16.5	16.6–69.3	
Adjustment A	1	0.76 (0.51, 1.13)	0.71 (0.44, 1.13)	0.48 (0.25, 0.91)	0.02
Adjustment B	1	0.75 (0.50, 1.12)	0.72 (0.45, 1.17)	0.47 (0.25, 0.91)	0.03
Cellulose (g/d)	0.48–3.2	3.3–4.2	4.3–5.3	5.4–15.2	
Adjustment A	1	0.63 (0.40, 0.99)	0.86 (0.54, 1.37)	0.84 (0.47, 1.50)	0.60
Adjustment B	1	0.53 (0.32, 0.85)	0.67 (0.39, 1.14)	0.60 (0.29, 1.21)	0.19
Lignin (g/d)	0.48–2.3	2.4–3.1	3.2–4.1	4.2–14.5	
Adjustment A	1	0.80 (0.53, 1.20)	0.70 (0.43, 1.15)	0.68 (0.36, 1.28)	0.15
Adjustment B	1	0.79 (0.52, 1.20)	0.69 (0.42, 1.15)	0.68 (0.36, 1.30)	0.16
Cereal fiber (g/d)	0.47–12.0	12.1–17.3	17.4–24.4	24.5–111	
Adjustment A	1	0.76 (0.51, 1.13)	0.72 (0.45, 1.14)	0.36 (0.18, 0.70)	0.005
Adjustment B	1	0.81 (0.54, 1.21)	0.74 (0.46, 1.18)	0.39 (0.20, 0.77)	0.01
Fruit fiber (g/d)	0–0.99	1.0–2.0	2.1–3.3	3.4–36.8	
Adjustment A	1	0.63 (0.39, 1.01)	0.87 (0.56, 1.36)	0.98 (0.63, 1.53)	0.78
Adjustment B	1	0.68 (0.39, 1.20)	0.79 (0.39, 1.60)	0.92 (0.40, 2.13)	0.87
Vegetable fiber (g/d)	0.11–3.7	3.8–5.0	5.1–6.7	6.8–26.5	
Adjustment A	1	1.02 (0.67, 1.55)	0.91 (0.57, 1.45)	1.33 (0.81, 2.18)	0.44
Adjustment B	1	1.02 (0.58, 1.79)	0.89 (0.43, 1.85)	1.19 (0.46, 3.04)	0.86

[1] Relative risk; 95% CIs in parentheses.
[2] Adjusted for age, sex, geographic area, and energy intake.
[3] Adjusted for age, sex, geographic area, smoking, BMI, and intakes of energy, fruit and berries, and vegetables.
[4] Noncellulose polysaccharides.

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TABLE 6
Relative risk of type 2 diabetes between highest and lowest quartiles of whole-grain and fiber intakes in strata of potential effect-modifying factors[1]

	Whole grain	Fiber
Age (y)		
<50 (*n* = 1919)[2]	0.52 (0.13, 2.09)	0.35 (0.09, 1.41)
50–69 (*n* = 2395)	0.74 (0.40, 1.38)	0.52 (0.26, 1.03)
Sex		
Males (*n* = 2286)	0.43 (0.18, 1.00)	0.43 (0.18, 1.02)
Females (*n* = 2028)	0.91 (0.44, 1.86)	0.61 (0.27, 1.39)
BMI (kg/m^2)		
<27 (*n* = 2533)	0.93 (0.36, 2.41)	1.07 (0.38, 2.99)
≥27 (*n* = 1781)	0.57 (0.28, 1.14)	0.37 (0.17, 0.80)
Smokers		
Nonsmokers (*n* = 2915)	0.76 (0.40, 1.42)	0.56 (0.27, 1.14)
Current smokers (*n* = 1401)	0.41 (0.12, 1.41)	0.39 (0.12, 1.24)
Hypertension		
No (*n* = 3594)	0.90 (0.44, 1.85)	0.65 (0.30, 1.43)
Yes[3] (*n* = 720)	0.35 (0.13, 0.94)	0.39 (0.15, 1.02)
Serum cholesterol (mmol/L)		
<6.7 (*n* = 1912)	0.52 (0.24, 1.13)	0.44 (0.19, 1.02)
≥6.7 (*n* = 2402)	0.81 (0.37, 1.74)	0.59 (0.26, 1.33)
Refined grain consumption[4]		
Lower tertiles (*n* = 2880)	0.60 (0.30, 1.19)	0.52 (0.24, 1.12)
Highest tertile (*n* = 1434)	0.73 (0.27, 1.97)	0.52 (0.18, 1.51)

[1] Relative risk; 95% CIs in parentheses. Adjusted for age, sex, geographic area, smoking status, BMI, energy intake, and intakes of vegetables and fruit and berries except when included in the interaction term. There were no significant interactions for any variable and risk of type 2 diabetes.
[2] *n* = number of observations.
[3] Persons with either mild or definite hypertension combined.
[4] The extreme tertile of refined grain intake was >96 g/d.

potential effect-modifying factors may be due to the relatively small number of cases.

During the 10-y follow-up, information on cases of diagnosed type 2 diabetes was received from a nationwide registry of drug reimbursements. Patients treated by nutritional therapy only are not included in this registry. These "missing cases" may have led to a loss of statistical power.

In summary, we found a reduced risk of type 2 diabetes in persons with high whole-grain intake. This reduced risk was apparently due to cereal fiber intake. Alternatively, the reduction may be due to other bioactive compounds found in whole-grain products, such as lignans, tocotrienols, phytic acids, and other antinutrients.

REFERENCES

1. Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343–50.
2. Slavin JL, Martini MC, Jacobs DR Jr, Marquart L. Plausible mechanisms for the protectiveness of whole grains. Am J Clin Nutr 1999; 70(suppl):459S–63S.
3. Anderson JW, Bryant CA. Dietary fiber: diabetes and obesity. Am J Gastroenterol 1986;81:898–906.
4. Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545–50.
5. Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulin-dependent diabetes mellitus in women. JAMA 1997;277:472–7.
6. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921–30.
7. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med 2001;345:790–7.
8. Liu S, Manson JE, Stampfer MJ, et al. A prospective study of whole-grain intake and risk of type 2 diabetes mellitus in US women. Am J Public Health 2000;90:1409–15.
9. Aromaa A. Epidemiology and public health impact of high blood pressure in Finland. Series AL, no. 17. Helsinki, Finland: Social Insurance Institution, 1981 (in Finnish with an English summary).
10. Knekt P, Aromaa A, Maatela J, et al. Serum vitamin E and risk of cancer among Finnish men during a 10-year follow-up. Am J Epidemiol 1988;127:28–41.
11. Knekt P. Serum alpha-tocopherol and the risk of cancer. Series ML, no. 83. Helsinki: Social Insurance Institution, 1988.
12. Reunanen A, Aromaa A, Pyörälä K, Punsar S, Maatela J, Knekt P. The Social Insurance Institution's coronary heart disease study. Baseline data and 5-year mortality experience. Acta Med Scand Suppl 1983; 673:1–120.
13. Huang TC, Chen CP, Wefler V, Raftery A. A stable reagent for the Lieberman-Burchard reaction. Application to rapid serum cholesterol determination. Anal Chem 1961;33:1405–7.
14. Reunanen A, Knekt P, Aaran RK, Aromaa A. Serum antioxidants and risk of non-insulin dependent diabetes mellitus. Eur J Clin Nutr 1998; 52:89–93.
15. Diabetes mellitus: Report of a WHO study group. Geneva: World Health Organization, 1985.
16. Järvinen R. Epidemiological follow-up study on dietary antioxidant vitamins. Studies in social security and health 11. Helsinki: The Social Insurance Institution, 1996.
17. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. Am J Clin Nutr 1998;68: 248–57.
18. Rastas M, Seppänen R, Knuts L-R, Karvetti R-L, Varo P. Nutrient composition of foods. Helsinki: Social Insurance Institution, 1989.
19. Varo P, Laine R, Veijalainen K, Pero K, Koivistoinen P. Dietary fibre and available carbohydrates in Finnish cereal products. J Agric Sci Finland 1984;56:39–48.
20. Hyvönen L, Lampi A-M, Varo P, Koivistoinen P. Fatty acid analysis, TAG equivalents as net fat values, and nutritional attributes of commercial fats and oils. J Food Comp Anal 1993;6:24–40.
21. Hyvönen L, Koivistoinen P. Fatty acid analysis, TAG equivalents as net fat value, and nutritional attributes of fish products. J Food Comp Anal 1994;7:44–58.
22. Piironen V. Tocopherols and tocotrienols in foods and in average Finnish diet. PhD dissertation. University of Helsinki, Finland, 1986 (in Finnish with an English summary).
23. Heinonen M. Carotenoids and retinoids in Finnish foods and the average diet. PhD dissertation. University of Helsinki, Finland, 1990.
24. Hertog MG, Hollman PC, Katan MB, Kromhout D. Intake of potentially anticarcinogenic flavonoids and their determinants in adults in The Netherlands. Nutr Cancer 1993;20:21–9.
25. Hertog M. Flavonols and flavones in foods and their relation with cancer and coronary heart disease risk. Hague: CIP-data Koninklijke Bibliotheek, 1994.
26. Häkkinen SH, Kärenlampi S, Heinonen M, Mykkänen HM, Törrönen AR. Content of flavonoids quercetin, myricetin, and kaempferol in 25 edible berries. J Agric Food Chem 1999;47:2274–9.
27. Järvinen R, Seppanen R, Knekt P. Short-term and long-term reproducibility of dietary history interview data. Int J Epidemiol 1993; 22:520–7.
28. Cox D. Regression models and life tables. J R Stat Soc B 1972;34:187–220.

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29. Salonen JT, Nyyssönen K, Tuomainen TP, et al. Increased risk of non-insulin dependent diabetes mellitus at low plasma vitamin E concentrations: a four year follow up study in men. BMJ 1995;311:1124–7.
30. Boushey CJ, Beresford SA, Omenn GS, Motulsky AG. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. JAMA 1995;274:1049–57.
31. Virtanen SM, Aro A. Dietary factors in the aetiology of diabetes. Ann Med 1994;26:469–78.
32. Foster-Powell K, Miller JB. International tables of glycemic index. Am J Clin Nutr 1995;62(suppl):871S–90S.
33. Cummings JH, Englyst HN. Fermentation in the human large intestine and the available substrates. Am J Clin Nutr 1987;45:1243–55.
34. Willet W. Nutritional epidemiology. New York: Oxford University Press, 1998.
35. Klaukka T, Martikainen J, Kalimo E. Drug utilization in Finland 1967–1987. Helsinki, Finland: Social Insurance Institution, 1990.

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