Whole-grain intake and the risk of type 2 diabetes: a prospective study in men[1–3]

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ABSTRACT

Background: Certain dietary components may play a role in the prevention of type 2 diabetes.

Objective: We examined prospectively the associations between whole- and refined-grain intake and the risk of type 2 diabetes in a large cohort of men.

Design: Men from the Health Professionals Follow-up Study without a history of diabetes or cardiovascular disease in 1986 ($n = 42\,898$) were followed for ≤ 12 y. Intakes of whole and refined grains, measured every 4 y by use of food-frequency questionnaires, were used to predict subsequent type 2 diabetes risk through multivariate analysis.

Results: We ascertained 1197 cases of incident type 2 diabetes. After adjustment for age; physical activity; cigarette smoking; alcohol consumption; family history of diabetes; and fruit, vegetable, and energy intakes, the relative risk of type 2 diabetes was 0.58 (95% CI: 0.47, 0.70; P for trend < 0.0001) comparing the highest with the lowest quintile of whole-grain intake. The association was moderately attenuated when additionally adjusted for body mass index (relative risk: 0.70; 95% CI: 0.57, 0.85; P for trend = 0.0006). Intake of refined grains was not significantly associated with risk of type 2 diabetes. After further adjustment for magnesium intake, cereal fiber intake, and glycemic load, the association between whole grains and type 2 diabetes was attenuated and the trend no longer significant.

Conclusions: In men, a diet high in whole grains is associated with a reduced risk of type 2 diabetes in men that may be mediated by cereal fiber. Efforts should be made to replace refined-grain with whole-grain foods. *Am J Clin Nutr* 2002;76:535–40.

KEY WORDS Type 2 diabetes, whole grains, refined grains, men

INTRODUCTION

Dietary modification has long been thought to play an important role in the prevention of type 2 diabetes. Recently, 2 prospective studies showed an inverse association between whole-grain intake and type 2 diabetes in women (1, 2). Other epidemiologic studies, which focused on specific foods or nutrient components, showed an inverse association between dietary fiber and type 2 diabetes and a positive association with glycemic load (1, 3, 4). In addition to the influence of fiber and glycemic load on postprandial glucose and insulin response, whole grains may also reduce the risk of type 2 diabetes through the action of nutrients such as vitamin E and magnesium (5–7). These may influence diabetes risk by affecting postprandial glucose and insulin response (8). Although the current *Dietary Guidelines for Americans* encourage whole-grain intake as part of overall carbohydrate intake (9), actual intake is far from the recommended level (10). Because the 2 previous studies were limited to women (1, 2), the purpose of the present analysis was to examine the association between the intake of whole grains and the risk of type 2 diabetes in a cohort of men, the ongoing Health Professionals Follow-up Study. We also examined whether the association was consistent in subgroups defined by obesity, family history of diabetes, and other risk factors for diabetes.

SUBJECTS AND METHODS

Study population

In 1986, 51 529 male health professionals aged 40–75 y were recruited for a prospective study of diet, lifestyle, and chronic diseases, the Health Professionals Follow-up Study. The cohort comprises dentists, veterinarians, pharmacists, optometrists, osteopathic physicians, and podiatrists. Since the inception of the study, questionnaires on health and lifestyle have been mailed to participants every 2 y to update this information. Response to the questionnaire has been ≈94% at each cycle.

Members of the Health Professionals Follow-up Study cohort were included in this analysis if they completed the 1986 food-frequency questionnaire with fewer than 70 missing items and reported a total daily energy intake between 3347 and 17 573 kJ/d (800 and 4200 kcal/d). Men with a prior history of cardiovascular disease, diabetes, or cancer were excluded because of possible changes in diet. This left 42 898 men for the present analysis. The Health Professionals Follow-up Study was approved by the Institutional Review Board of the Harvard School of Public Health.

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Assessment of nutrient intake

Dietary information was collected with a validated semiquantitative food-frequency questionnaire (11). The questionnaire was designed to assess average food intake over the previous year, and standard portion sizes were given for each food item. Cohort members were asked to choose from 9 possible frequency responses, ranging from "never" to "more than 6 times a day" for each food. Macro- and micronutrient intakes were computed for the frequency and portion size of each food, and contributions from all foods were summed. Information on supplemental vitamin and mineral intakes was also collected. Nutrient values were adjusted for total energy by the residual method and categorized into quintiles (12). Dietary questionnaires were first administered in 1986 and updated in 1990 and 1994.

Whole-grain foods were classified by the methods of Jacobs et al (13) and Liu et al (14). Whole-grain items included brown rice, dark breads, whole-grain ready-to-eat cereals, cooked cereal, popcorn, wheat germ, bran, and other grains. Refined-grain foods included white bread, white rice, English muffins, pancakes, waffles, cakes, sweet rolls, refined-grain ready-to-eat cereals, muffins and biscuits, and pizza. Classification of whole-grain ready-to-eat cereals was based on having ≥25% whole-grain content by weight. This was evaluated by food package label or by information supplied by General Mills, Inc (Minneapolis). Previous validation studies among members of this cohort indicated good correlations between foods and nutrients assessed by the dietary questionnaires and multiple weeks of food records completed over the previous year (11, 15). The correlation coefficients between intake assessed by dietary questionnaires and diet records were 0.75 for ready-to-eat cereals, 0.71 for white bread, and 0.77 for dark breads (16). The glycemic index in the diet was calculated by using glycemic index values for individual foods (17–19). The glycemic load of each food was calculated by multiplying the grams of carbohydrate in each serving by its glycemic index value. The glycemic load for each food was then multiplied by the number of servings consumed per day and summed over all the foods consumed to give the overall dietary glycemic load. The glycemic index is the glycemic load divided by total carbohydrate intake, which represents the average glycemic index value of the diet.

Case ascertainment

Type 2 diabetes diagnoses were first identified by self-report on the biennial questionnaires and then confirmed by a supplementary questionnaire that assessed symptoms, diagnostic tests, and treatment. Diabetes was confirmed if the participant fulfilled one or more of the following criteria: *1*) manifestation of classic symptoms (excessive thirst, polyuria, weight loss, hunger) plus an elevated fasting glucose concentration (>140 mg/dL, or 7.8 mmol/L) or elevated nonfasting concentration (>200 mg/dL, or 11.1 mmol/L), *2*) asymptomatic but plasma glucose concentration was elevated on ≥2 different occasions or abnormal oral glucose tolerance test (>200 mg/dL 2 h after glucose load), *3*) undergoing any treatment for diabetes. These criteria for diabetes classification were consistent with those of the National Diabetes Data Group during our follow-up period (20). The validity of self-reporting in the cohort was assessed by a review of a sample of 71 medical records by a physician blinded to the information on the supplementary questionnaire. Of these 71 men, 12 were excluded because of incomplete medical records. Type 2 diabetes was confirmed in 57 (97%) of the remaining 59 men; one person denied the diagnosis, and the diagnosis of another was rejected based on the medical records. In a parallel cohort of women, confirmation of physician-diagnosed diabetes by the same procedure was also found to be highly accurate (98% confirmed) as compared with medical records review (21).

Assessment of other variables

Cigarette smoking and body weight were assessed biennially. Body mass index (BMI), a measurement of obesity, was calculated for each 2-y cycle as weight (kg)/height (m)^2. Leisure-time physical activity was assessed every 2 y starting from 1986 through a series of questions on the specific type of activity and the average total time per week spent on the activity over the past year. Questions about the number of hours per week spent in walking or hiking outdoors, jogging, running, bicycling, lap swimming, playing tennis, playing squash or racketball, doing calisthenics, or rowing were included in the 1986 questionnaire. We added heavy outdoor work in 1988 and weightlifting in 1992. Walking pace, categorized as casual (≤3.2 km/h, or 2 mph), normal (3.2–4.6 km/h, or 2–2.9 mph), brisk (4.7–6.2 km/h, or 3–3.9 mph), or striding (≥6.2 km/h, or 4 mph), was also assessed. We calculated total weekly energy expenditure from leisure-time physical activities for each individual, expressed as metabolic equivalents (22). Among a subsample (n = 238) of the Health Professionals Follow-up Study cohort, we assessed the validity and reproducibility of this method by comparing physical activity assessed by the questionnaire with the average of four 1-wk activity diaries in 1991 that covered all seasons (23). The deattenuated correlation between reported overall activity in the diaries and the 1992 questionnaire was 0.41. The deattenuated correlation between the vigorous activities recorded in the diaries and the 1992 questionnaire was 0.58. Family history of diabetes included parents and siblings and was assessed in 1987.

Statistical analysis

Person-time for each participant was calculated from the date of return of the 1986 questionnaire to the date of confirmation of type 2 diabetes, death, or 1 January 1998, whichever came first. We excluded from analysis those with a history of diabetes, those with a history of cardiovascular disease, and those with missing diagnosis date. Incidence rates were obtained by dividing the number of cases by person-years in each category of whole- or refined-grain intake. We used pooled logistic regression to assess the association between whole- and refined-grain intake and the risk of type 2 diabetes (24, 25). This method, which pooled each 2-y period in the follow-up as an independent block, is asymptomatically equivalent to the Cox proportional hazard model. To reduce random within-person variation and best represent long-term dietary intake, we calculated cumulative averages of food and nutrient intakes from our repeated dietary measurements (26). For example, dietary intake in 1986 was used to predict diabetes occurrence from 1986 to 1990, and the average of 1986 and 1990 intake was used to model disease risk in 1990–1994, and so on. The regression models were adjusted for age (7 categories), physical activity (quintiles), alcohol intake (0, 0.1–4.9, 5.0–14.9, 15.0–29.9, and ≥30 g/d), fruit and vegetable intake (quintiles), family history of diabetes, smoking (never, past, current smokers ≤24 cigarettes/d, current smokers >24 cigarettes/d, and current smokers but unknown quantity), and energy intake (quintiles).

To explore the mechanism for any observed association between intake of whole grains and the risk of diabetes, we addi-

TABLE 1
Age-standardized baseline characteristics and nutrient intakes of subjects by quintile (Q) of grain intake[1]

	Whole grains			Refined grains		
	Q1	Q3	Q5	Q1	Q3	Q5
Median intake (serving/d)	0.2 (0.0–0.4)[2]	1.1 (1.0–1.4	3.4 (2.9–28.1)	0.6 (0.0–0.9)	1.7 (1.4–2.0)	4.3 (3.2–21.5)
BMI (kg/m^2)	25.7[3]	25.6	24.9	25.4	25.5	25.4
Physical activity (MET-h/wk)	17	20	24	22	21	19
Smokers (%)	16	8	7	10	9	11
Family history of diabetes (%)	14	13	13	13	13	14
Hypertension (%)	24	21	19	22	21	19
Hypercholesterolemia (%)	11	12	13	13	12	12
Nutrient intakes[4]						
Total energy (kJ/d)	7501 ± 25[5]	8190 ± 29	9563 ± 25	6695 ± 25	8093 ± 25	10 454 ± 25
Total fiber (g/d)	17 ± 0.1	21 ± 0.1	25 ± 0.1	23 ± 0.1	21 ± 0.1	19 ± 0.1
Cereal fiber (g/d)	3.1 ± 0.04	5.9 ± 0.04	8.6 ± 0.04	6.0 ± 0.04	5.7 ± 0.04	5.9 ± 0.04
Carbohydrates (g/d)	220 ± 0.4	235 ± 0.5	250 ± 0.4	230 ± 0.4	236 ± 0.4	241 ± 0.4
Alcohol (g/d)	13 ± 0.2	11 ± 0.2	10 ± 0.2	13 ± 0.2	11 ± 0.2	10 ± 0.2
Daily glycemic load[6]	115 ± 0.4	124 ± 0.4	134 ± 0.4	118 ± 0.4	124 ± 0.4	130 ± 0.4
Daily glycemic index[7]	75 ± 0.05	76 ± 0.06	77 ± 0.06	74 ± 0.06	76 ± 0.05	77 ± 0.05
Protein (g)	90 ± 0.2	92 ± 0.2	93 ± 0.2	96 ± 0.2	92 ± 0.2	87 ± 0.2
Fat (g/d)						
Total	76 ± 0.1	72 ± 0.2	68 ± 0.1	70 ± 0.2	71 ± 0.1	73 ± 0.1
Saturated	27 ± 0.1	25 ± 0.1	22 ± 0.1	24 ± 0.1	25 ± 0.1	25 ± 0.1
trans	3.1 ± 0.01	2.8 ± 0.01	2.7 ± 0.01	2.4 ± 0.01	2.8 ± 0.01	3.4 ± 0.01
Polyunsaturated	12.9 ± 0.04	13.1 ± 0.04	13.5 ± 0.04	13.1 ± 0.04	13.1 ± 0.04	13.4 ± 0.04
Food intake (servings/d)						
Vegetables	2.4 ± 0.02	2.9 ± 0.02	3.3 ± 0.02	2.8 ± 0.02	2.9 ± 0.02	2.9 ± 0.02
Fruit	1.8 ± 0.02	2.3 ± 0.02	2.9 ± 0.02	2.3 ± 0.02	2.4 ± 0.02	2.4 ± 0.02
Whole-grain cereals	0.03 ± 0.004	0.37 ± 0.005	0.52 ± 0.005	0.35 ± 0.005	0.33 ± 0.005	0.29 ± 0.005
Dark breads	0.1 ± 0.007	0.5 ± 0.007	2.3 ± 0.007	0.8 ± 0.01	0.7 ± 0.01	0.7 ± 0.01
Brown rice	0.02 ± 0.001	0.06 ± 0.002	0.10 ± 0.002	0.08 ± 0.002	0.06 ± 0.002	0.05 ± 0.002
Bran	0.01 ± 0.005	0.04 ± 0.005	0.4 ± 0.005	0.14 ± 0.005	0.11 ± 0.005	0.09 ± 0.005
White bread	0.8 ± 0.01	0.5 ± 0.01	0.3 ± 0.01	0.1 ± 0.01	0.3 ± 0.01	1.6 ± 0.01
Pasta	0.1 ± 0.002	0.1 ± 0.002	0.2 ± 0.002	0.1 ± 0.002	0.2 ± 0.002	0.2 ± 0.002
White rice	0.14 ± 0.002	0.13 ± 0.003	0.12 ± 0.002	0.06 ± 0.002	0.13 ± 0.002	0.18 ± 0.002
Doughnuts	0.09 ± 0.002	0.08 ± 0.002	0.07 ± 0.002	0.02 ± 0.002	0.07 ± 0.002	0.17 ± 0.002
Muffins and biscuits	0.08 ± 0.002	0.09 ± 0.002	0.12 ± 0.002	0.03 ± 0.002	0.09 ± 0.002	0.17 ± 0.002

[1] n = 42 540. MET, metabolic equivalents. P for trend < 0.0001 for all.
[2] Range in parentheses.
[3] $\bar{x}$.
[4] Adjusted for energy.
[5] $\bar{x}$ ± SE.
[6] Sum of (glycemic index for individual foods × carbohydrate content of the food item) for each food.
[7] Average daily dietary glycemic index = glycemic load/total carbohydrate in the diet.

tionally adjusted for BMI (< 21, 21–22.9, 23–24.9, 25–26.9, 27–28.9, 29–30.9, and ≥ 31), fiber intake (quintiles), magnesium intake (quintiles), and glycemic load (quintiles). Furthermore, we conducted stratified analyses according to risk factors for diabetes, including BMI, smoking status, alcohol intake, family history of diabetes, and physical activity. All analyses were done with SAS (version 6.12; SAS Institute Inc, Cary, NC).

RESULTS

Between 1986 and 1998, we accumulated 441 171 person-years of follow-up and 1197 cases of incident type 2 diabetes. As shown in **Table 1**, those with higher whole-grain intakes tended to be leaner and more physically active, to consume less fat, and to be less likely to smoke or have a history of hypertension. In contrast, those with higher refined-grain intakes tended to exercise less and have lower intakes of fiber. In the top quintile of whole-grain intake, cereal fiber contributed approximately one-third of the total fiber intake. The median intake of whole grains was 0.4 servings/d at the lowest quintile and 3.2 servings/d at the highest quintile (**Table 2**). Median refined-grain intake was 0.8 servings/d at the lowest quintile and 4.1 servings/d at the highest.

After adjusting for age, we observed a significant inverse association between whole-grain intake and the risk of type 2 diabetes [relative risk (RR) comparing the top intake quintile with that of the bottom quintile: 0.57; 95% CI: 0.48, 0.69; Table 2]. After adjusting for potential confounders and risk factors for diabetes other than BMI, we found that those in the top quintile of whole-grain intake had an RR of 0.58 (95% CI: 0.47, 0.70) when compared with the bottom quintile (P for trend: < 0.0001). Additional adjustment for BMI moderately attenuated the association (RR of the top compared with the bottom quintile: 0.70; P for trend: 0.0006), but it remained significant. We obtained similar results when we restricted the analysis to the 734 symptomatic cases only (data not shown). We then addi-

TABLE 2
Relative risks (and 95% CIs) of cumulative average whole- and refined-grain intakes on the risk of type 2 diabetes in men by quintile (Q) of grain intake (1986–1998)

Food (servings/d)	Q1	Q2	Q3	Q4	Q5	*P* for trend
Whole grains						
Median intake (servings/d)	0.4	0.8	1.3	1.9	3.2	
Number of cases	290	289	221	218	179	
Person-years	88 233	91 035	85 680	88 569	87 654	
Age-adjusted model	1	0.89 (0.76, 1.05)	0.74 (0.62, 0.88)	0.72 (0.60, 0.85)	0.57 (0.48, 0.69)	<0.0001
Multivariate model[1]	1	0.90 (0.76, 1.06)	0.75 (0.63, 0.90)	0.73 (0.60, 0.87)	0.58 (0.47, 0.70)	<0.0001
Multivariate model + BMI[2]	1	0.88 (0.74, 1.04)	0.77 (0.65, 0.92)	0.79 (0.66, 0.95)	0.70 (0.57, 0.85)	0.0006
Refined grains						
Median intake (servings/d)	0.8	1.3	1.9	2.6	4.1	
Number of cases	227	245	246	231	248	
Person-years	84 226	88 442	89 061	90 118	89 324	
Age-adjusted model	1	1.09 (0.91, 1.31)	1.11 (0.92, 1.33)	1.04 (0.86, 1.25)	1.12 (0.93, 1.34)	0.43
Multivariate model[1]	1	1.07 (0.89, 1.29)	1.07 (0.88, 1.29)	0.98 (0.80, 1.19)	1.01 (0.82, 1.25)	0.78
Multivariate model + BMI[2]	1	1.07 (0.89, 1.29)	1.08 (0.90, 1.30)	1.00 (0.82, 1.22)	1.08 (0.87, 1.33)	0.69

[1] Adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, 65–69, and ≥70), period, physical activity (quintiles), energy intake (quintiles), missing food-frequency questionnaire, smoking (never, past, current ≤24 cigarettes/d, current >24 cigarettes/d, and current but unknown quantities), family history of diabetes, alcohol intake (0, 01.–4.9, 5.0–14.9, 15.0–29.9, and ≥30 g/d), fruit intake (quintiles), and vegetable intake (quintiles).

[2] Additionally adjusted for BMI (<21, 21–22.9, 23–24.9, 25–26.9, 27–28.9, 29–30.9, and ≥31).

tionally adjusted for cereal fiber, magnesium, and glycemic load in the diet and found that the inverse association was largely explained by cereal fiber and a significant association was no longer observed between whole-grain intake and the risk of type 2 diabetes (RR comparing extreme quintiles: 0.98; 95% CI: 0.76, 1.26; *P* for trend: 0.98).

Intake of refined grains was not appreciably associated with the risk of type 2 diabetes. The multivariate RR comparing the top with the bottom quintile was 1.01; additional adjustment for BMI did not alter the association.

Joint classification analysis showed that those with a higher BMI (≥30) or with a family history of diabetes were consistently at elevated risk of diabetes (**Table 3**). There was a suggestion of an inverse association between whole-grain intake and risk of diabetes in each subgroup. BMI is an especially powerful predictor for type 2 diabetes, and we found the association between whole-grain intake and diabetes was significantly modified by BMI. Among obese men (BMI ≥30), whole-grain consumption was only weakly associated with diabetes risk, whereas among men with a BMI <30, those in the highest quintile of whole-grain consumption had a risk that was ≈50% lower than that of those with the lowest intake. In addition, stratification by tertiles of saturated fat intake did not substantially alter the associations.

TABLE 3
Multivariate relative risks (and 95% CIs) for joint classification of quintile (Q) whole-grain intake and risk factors for diabetes[1]

	Whole grains					*P* for main effect		
	Q1	Q2	Q3	Q4	Q5	*P* for interaction	Whole-grain intake	Joint classification variable
Median intake (servings/d)	0.4	0.8	1.3	1.9	3.2			
BMI ≥ 30 (*n* = 3234)	1 (reference)	0.91 (0.69, 1.20)	0.76 (0.56, 1.04)	0.94 (0.70, 1.26)	0.83 (0.60, 1.14)	0.01	<0.0001	<0.0001
BMI < 30 (*n* = 39 306)	0.23 (0.18, 0.29)	0.20 (0.16, 0.26)	0.18 (0.14, 0.23)	0.16 (0.12, 0.20)	0.13 (0.10, 0.17)			
Current smokers (*n* = 4106)	1 (reference)	1.07 (0.70, 1.63)	0.87 (0.54, 1.41)	0.87 (0.50, 1.50)	0.73 (0.42, 1.26)	0.50	0.0007	<0.0001
Nonsmokers (*n* = 38 434)	1.07 (0.78, 1.47)	0.90 (0.65, 1.23)	0.79 (0.57, 1.10)	0.81 (0.58, 1.12)	0.73 (0.52, 1.01)			
Abstainers (*n* = 32 795)	1.13 (0.87, 1.48)	1.05 (0.79, 1.40)	0.92 (0.67, 1.25)	1.02 (0.76, 1.37)	0.81 (0.59, 1.10)	0.62	0.0005	<0.0001
Drinkers (*n* = 9745)	1 (reference)	0.87 (0.72, 1.05)	0.77 (0.63, 0.94)	0.77 (0.62, 0.95)	0.71 (0.56, 0.89)			
Family history of diabetes (*n* = 5550)	1 (reference)	0.84 (0.59, 1.19)	0.87 (0.61, 1.24)	0.81 (0.56, 1.16)	0.84 (0.58, 1.22)	0.27	0.0006	<0.0001
No family history of diabetes (*n* = 36 990)	0.54 (0.41, 0.71)	0.48 (0.36, 0.63)	0.40 (0.30, 0.54)	0.43 (0.32, 0.57)	0.35 (0.26, 0.48)			
Exercise below median (*n* = 21 164)	1 (reference)	0.90 (0.72, 1.13)	0.70 (0.54, 0.91)	0.88 (0.68, 1.13)	0.75 (0.57, 0.98)	0.42	0.0006	<0.0001
Exercise above median (*n* = 21 085)	0.86 (0.67, 1.00)	0.69 (0.52, 0.91)	0.71 (0.53, 0.93)	0.51 (0.38, 0.69)	0.48 (0.35, 0.66)			

[1] The multivariate model was adjusted for age (<45, 45–49, 50–54, 55–59, 60–64, 65–69, and ≥70), period, physical activity (quintiles), energy intake (quintiles), missing food-frequency questionnaire, smoking (never, past, current ≤24 cigarettes/d, current >24 cigarettes/d, and current but unknown quantities), family history of diabetes, alcohol intake (0, 0.1–4.9, 5.0–14.9, 15.0–29.9, and ≥30 g/d), fruit intake (quintiles), vegetable intake (quintiles), and BMI (<21, 21–22.9, 23–24.9, 25–26.9, 27–28.9, 29–30.9, and ≥31), except for the variable of stratification.

DISCUSSION

We observed an inverse association between long-term average whole-grain intake and the incidence of type 2 diabetes in men during follow-up of ≤ 12 y. The decrease in risk was 42% when comparing the extreme quintiles of whole-grain intake, and this was reduced to 30% after additional adjustment for BMI, which may be one mechanism through which whole-grain intake reduces the risk of type 2 diabetes. Refined-grain intake, however, did not appear to be associated with type 2 diabetes risk. The magnitude of the observed association is similar to 2 previous epidemiologic studies in women (1, 2). The consistency among these 3 epidemiologic studies supports the theory of a protective effect of whole grains on diabetes risk. Our findings on refined grains also agree with the other 2 studies.

Although the substantial reduction in diabetes risk we observed was among nonobese persons with high whole-grain intakes, there may be a small reduction of risk in obese persons with a higher intake of whole-grain foods. Men who had a combination of a lower BMI and a high whole-grain intake had an 87% lower risk of type 2 diabetes than did obese men with the lowest quintile of whole-grain intake. Similarly, a favorable profile of high whole-grain intakes and higher levels of physical activity was associated with a 52% lower risk of diabetes when compared with the opposite profile.

When compared with consumption of refined-grain foods, consumption of whole grains may result in lower insulinemic and glycemic responses (27, 28), and this may contribute to the reduction in the risk of developing type 2 diabetes. The major difference between whole and refined grains is the preservation of the bran and germ in whole grains (8). Fiber is particularly concentrated in the bran fraction. If consumed in substantial amounts, viscous fiber, such as the β-glucan found in oat bran, delays gastric emptying and hence leads to a slower release of glucose into the circulation (29, 30). Foods higher in fiber can reduce postprandial insulin response (31), and a diet higher in fiber may improve insulin sensitivity and lower insulin secretion as assessed by insulin clamp (32), minimal model (33), glucose tolerance test (34, 35), and fasting insulin (34, 36).

Magnesium content is higher in whole grains than in refined grains; this may also contribute to the inverse association between whole-grain intake and type 2 diabetes. In a small sample of nondiabetic subjects, those with lower plasma magnesium concentration had higher plasma glucose and insulin concentrations after an oral glucose challenge (37). In addition, daily supplementation of 4.5 g Mg for 4 wk in a small sample of elderly subjects improved glucose and insulin responses in a euglycemic glucose clamp test (6). In 2 large epidemiologic studies, higher magnesium intake was associated with a reduced risk of type 2 diabetes (3, 4). Pereira et al (36) found that magnesium intake explained part of the inverse association between whole-grain intake and fasting insulin in a cohort study of young adults. In our primary analysis, we did not adjust for cereal fiber, glycemic load, and magnesium intake because these are potential intermediate factors. To elucidate whether the relation of whole-grain intake to diabetes risk is explained by these components, we additionally adjusted for their intake. Cereal fiber greatly attenuated the inverse association, suggesting that the effect of whole grains is caused by these or other, related components.

Because information on whole-grain consumption was obtained with a self-administered questionnaire, misclassification could be an issue. We compared the reports of whole-grain intake from the food-frequency questionnaire with those from the diet records and found that the former had reasonable reliability. In addition, we used repeated measurements that better represent average long-term intake. Nevertheless, the limited number of whole-grain foods listed on the food-frequency questionnaire and the subjects' perception of what constitutes whole grains probably resulted in some degree of measurement error. This error should not be related to diabetes because of the prospective nature of our analysis but could weaken any association between whole grains and diabetes, rendering our estimates conservative. Underdiagnosis of diabetes should be relatively low in this cohort compared with the general population because our participants were all health professionals. Any such underdiagnosis would reduce statistical power but would not materially alter the relative risk estimates.

The *Dietary Guidelines for Americans* 2000 specifically recommend choosing several servings of whole grains per day from the recommended 6–11 servings of grains (9). Similarly, *Healthy People 2010* also established an objective for whole-grain intake: "Increase the proportion of persons aged 2 years and older who consume at least six daily servings of grain products, with at least three being whole grain" (38). However, whole-grain intake among Americans is far from the recommended level. In a sample of 2000 households surveyed by Market Research Corporation of America (39), whole-grain intake among adults between 1990 and 1992 was only one-half of a serving per day. Results from the 1994–1996 Continuing Survey of Food Intakes by Individuals suggested a slight improvement, with an average intake of 1 serving whole grains/d in adults (10). Approximately 15% of grain intake was in the form of whole-grain products, with breakfast cereals and yeast breads as the major contributors.

The benefits of whole grains do not appear to be limited to diabetes risk. Epidemiologic studies have found inverse associations between whole-grain intake and ischemic stroke and coronary artery disease risk and deaths (13, 14, 40, 41). In the study by Jacobs et al (13), 3.2 servings (median for the highest quintile) whole grains/d was associated with a 30% reduction of coronary artery disease risk when compared with an intake of 0.2 servings (median for the lowest quintile). Similarly, in the Nurses' Health Study, a median of 2.7 servings of whole grains (median for the highest quintile) was associated with a risk reduction of 25% for coronary artery disease and 31% for ischemic stroke when compared with an average of 0.13 servings (median for the lowest quintile; 14, 40). These findings, together with our present findings, suggest that consumption of ≈3 servings whole grains/d is an achievable dietary goal and will probably be accompanied by important health benefits.

In conclusion, we found that a higher whole-grain intake was associated with a lower risk of type 2 diabetes in men, especially in nonobese men. Given the current overall low intake of whole grains, efforts should be made to decrease the cost and increase the availability and consumption of whole-grain products. This has the potential to reduce substantially the incidence of type 2 diabetes and possibly other chronic diseases when sustained over time.

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