Whole-grain intake and insulin sensitivity: the Insulin Resistance Atherosclerosis Study[1–3]

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ABSTRACT

Background: Increased intake of whole-grain foods has been related to a reduced risk of developing diabetes and heart disease. One underlying pathway for this relation may be increased insulin sensitivity.

Objective: We assessed the relation between dietary intake of whole grain–containing foods and insulin sensitivity (S_I).

Design: We evaluated data from the Insulin Resistance Atherosclerosis Study (IRAS Exam I, 1992–1994). Usual dietary intakes in 978 middle-aged adults with normal (67%) or impaired (33%) glucose tolerance were ascertained by using an interviewer-administered, validated food-frequency questionnaire. Whole-grain intake (servings per day) was derived from dark breads and high-fiber and cooked cereals. S_I was assessed by minimal model analyses of the frequently sampled intravenous-glucose-tolerance test. Fasting insulin was measured by using a radioimmunoassay. We modeled the relation of whole-grain intake to $\log(S_I + 1)$ and to log(insulin) by using multivariable linear regression.

Results: On average, IRAS participants consumed 0.8 servings of whole grains/d. Whole-grain intake was significantly associated with S_I ($\beta = 0.082$, $P = 0.0005$) and insulin ($\beta = -0.0646$, $P = 0.019$) after adjustment for demographics, total energy intake and expenditure, smoking, and family history of diabetes. The addition of body mass index and waist circumference attenuated but did not explain the association with S_I. The addition of fiber and magnesium resulted in a nonsignificant association that is consistent with the hypothesis that these constituents account for some of the effect of whole grains on S_I.

Conclusion: Higher intakes of whole grains were associated with increases in insulin sensitivity. *Am J Clin Nutr* 2003;78:965–71.

KEY WORDS Whole grain, diet, nutrition, insulin sensitivity, fasting insulin

INTRODUCTION

The 2000 *Dietary Guidelines for Americans* recommends that consumers choose a variety of grains daily, especially whole grains, as part of their recommended 6–11 servings of the bread, cereal, rice, and pasta food group/d (1). On average, Americans consume only 0.9–1.1 servings of whole grains/d (2). Compared with refined-grain foods, whole-grain foods contain larger amounts of particular micronutrients that may convey significant health advantages. Whole-grain–containing foods have been studied in relation to the development of diabetes, heart disease, stroke, and cancer and to death (3–10). Most studies have reported a beneficial, protective effect of higher intakes of whole grains. Two epidemiologic studies showed an inverse relation of whole-grain intake to fasting insulin, which is a surrogate measure of insulin sensitivity (11, 12). To our knowledge, no population-based data exist on the effect of whole grains on a direct measure of insulin sensitivity. Various beneficial constituents of whole grains, such as fiber, magnesium, zinc, and vitamin E, have been identified (13); however, the underlying mechanisms linking diet to some of the observed health advantages remain unclear.

The purpose of our study was to evaluate the relation of the usual dietary intake of whole grain–containing foods to a direct measure of insulin sensitivity. Insulin resistance is increasingly recognized as one important step in the pathophysiologic pathways leading to the 4 abovementioned diseases. Insulin sensitivity was assessed with the use of the frequently sampled intravenous-glucose-tolerance test in a large cohort of middle-aged adults.

SUBJECTS AND METHODS

Subject selection

The design of the Insulin Resistance and Atherosclerosis Study (IRAS) was described in detail elsewhere (14). More than 1600 participants were recruited at 4 clinical centers between 1992 and 1994 for the IRAS baseline examination. The goal was to obtain nearly equal representation of participants across categories of glucose tolerance status (ie, normal, impaired, and noninsulin-taking type 2 diabetes); ethnicity (African American, Hispanic, and non-Hispanic white); sex; and age (40–49, 50–59, and 60–69 y). Ethnicity was estab-

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lished by self-report. Two of the clinical centers (Los Angeles and Oakland, CA) recruited African American and non-Hispanic white participants, and the other 2 (San Luis Valley, CO, and San Antonio, TX) recruited Hispanic and non-Hispanic white participants. The final sample comprised 1625 subjects, of whom 38% were non-Hispanic white, 34% were Hispanic, and 29% were African American; 44.2% ($n = 718$) had normal glucose tolerance, 22.7% ($n = 369$) had impaired glucose tolerance, and 33.1% ($n = 537$) had type 2 diabetes. All participants provided written informed consent. The study was approved by the institutional review board of each center.

Data collection

IRAS required a 2-visit protocol; the purpose of the first visit was to determine glucose tolerance status, and that of the second visit was to measure insulin sensitivity. Participants were asked to fast for 12 h before each of the 2 visits, to abstain from heavy exercise and alcohol for 24 h before the visit, and to refrain from smoking the morning of each visit. A 2-h, 75-g oral-glucose-tolerance test (Orange-dex; Custom Laboratories, Baltimore) was performed during the first visit, and World Health Organization criteria (15) were used to assign glucose tolerance status. Persons currently taking oral hypoglycemic medications were classified as having type 2 diabetes regardless of their oral-glucose-tolerance test results.

Insulin sensitivity (S_I) was assessed by using the frequently sampled intravenous-glucose-tolerance test (16, 17) with minimal model analysis (18). Two modifications of the protocol were used: injection of insulin rather than of tolbutamide (19) and a reduced number of plasma samples ($n = 12$ rather than 30) (20). Glucose, in the form of a 50% solution (0.3 g/kg body wt), and regular human insulin (0.03 U/kg) were injected at 0 and 20 min, respectively. Blood specimens were collected over a 3-h period (at −5, 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 min). S_I was calculated with the use of mathematical modeling methods; the time course of plasma glucose was fitted by using nonlinear least-squares methods with the plasma insulin values as a known input to the system, according to the method known as MINMOD that was developed by Bergman in 1986 (21). Fasting plasma insulin was measured with the use of a radioimmunoassay (22).

The usual intakes of foods and nutrients were assessed by interview with the use of a 1-y, semiquantitative 114-item food-frequency questionnaire (FFQ) modified from the National Cancer Institute Health History and Habits Questionnaire to include regional and ethnic food choices appropriate to the 4 clinical centers (23). Participants were asked to recall their usual intakes of foods and beverages over the previous year. For foods, 9 categories of possible responses ranged from "never or <1 time/mo" to "≥ 2 times/d." For beverages, responses ranged from "never or <1 time/mo" to "≥ 6 times/d." Serving size was ascertained simply as "small, medium, or large compared with other men or women about your age."

The whole-grain variable used for the analysis was compiled from 3 FFQ lines worded as follows: *1*) "dark bread (including whole wheat, rye, pumpernickel, other high-fiber bread)"; *2*) "high-fiber bran or granola cereals, shredded wheat"; and *3*) "cooked cereal (including oatmeal, cream of wheat, and grits)." Whole grain was calculated in servings per day by weighting the intake frequency with a factor based on the serving size (small: 0.5; medium: 1.0; large: 1.5). Although the questionnaire ascertained the intake of other grain-based foods, only these 3 lines were included in the whole-grain analyses because their respective underlying recipes specifically included whole grains for at least one of the items.

The validity and reproducibility of the IRAS FFQ in measuring nutrient intake was shown in a subset of the IRAS population (23). Participants were also queried as to special diets they currently followed, the use of dietary supplements, and food preparation methods. Interviewers were centrally trained and certified, and audiotapes of interviews were reviewed quarterly. The nutrient database (HHHQ-DIETSYS analytic software, version 3.0; NCI, Bethesda, MD) was expanded to include several additional nutrients. Alcohol intake was evaluated by using the FFQ with additional questions about recent use and average lifetime use.

Physical activity assessment was based on an interviewer-administered instrument, 1-y activity recall, that incorporated activities current among IRAS participants (24). Estimated energy expenditure was measured from the frequency and duration of activities, and it was expressed as metabolic equivalent tasks. Anthropometric measures were taken while the participant was wearing lightweight clothing and not wearing shoes. Height and weight were measured in duplicate and recorded to the nearest 0.5 cm and 0.1 kg, respectively. Body mass index (BMI; in kg/m^2) was calculated. Minimum waist circumference was measured twice by using a flexible-steel tape measure at the natural indentation or, if no natural indentation was present, at a level midway between the iliac crest and the lower edge of the rib cage. Waist circumference was recorded to the nearest 0.5 cm. The mean of 2 measures ≤ 1 cm apart was used, unless the measures twice differed by >1 cm, in which case the measurement was taken a third time.

Statistical analysis

We limited our analyses to 1087 persons with normal (67%) or impaired (33%) glucose tolerance, excluding those with previously or recently diagnosed diabetes at baseline, because that disease might have altered their dietary behavior. We subsequently excluded 84 participants who were missing data on insulin sensitivity, 4 who were missing anthropometric data, 2 who were missing alcohol consumption data, 17 who had dietary data found to have severe errors, and 2 who were missing fasting insulin data. This left 978 participants with complete data for analysis.

Because the distribution of S_I is skewed right and 58 participants had an S_I value of 0 and the log of 0 cannot be taken, we calculated the natural log after adding a constant 1 to assess all values. With this transformation, the distributions of the resulting residual values approached normality. Fasting insulin was log transformed for all analyses. For descriptive purposes, sample means, SDs, and frequencies were calculated for all characteristics of interest, and data were plotted to elucidate distributions and simple bivariate relations. Pearson correlation coefficients were estimated between whole-grain intake, S_I, fasting insulin, and other relevant mediators or confounders. After initially stratifying the sample with regard to impaired glucose tolerance, we combined the data because no substantial differences were observed, and the tests for interaction were negative.

Because the goal of the analysis was to assess the relation of whole grains to S_I and to evaluate the effect of potentially

confounding or mediating variables, a statistical modeling approach was used. Linear regression analysis was used to examine the association, given that descriptive analyses had shown no evidence of a threshold effect of whole-grain intake on S_I. We evaluated the effect of potential effect modifiers, including ethnicity, sex, and family history, by conducting stratified analyses and comparing the size and direction of the effect estimates. Interactions were examined and not found to be significant. The relation of whole grains to S_I was first estimated after adjustment for demographic factors (age, sex, race, and clinic) only. Additional potential confounders determined from previous work, such as total energy intake, dietary fat, alcohol intake, estimated energy expenditure, smoking, BMI, and waist circumference, were assessed in a stepwise manner. The influence of potential biological mediators—which in fact are constituents of whole grains, such as fiber, magnesium, zinc, and vitamin E—was explored separately. Finally, we partitioned the whole-grain food group into its 3 questionnaire line components (dark breads, high-fiber cereals, and cooked cereals) to evaluate the relation of the individual foods to S_I. The modeling strategy described above was applied in parallel to the relation of whole grains to fasting insulin. All analyses were performed with the use of SAS software (version 8.2; SAS Institute, Cary, NC).

RESULTS

Characteristics of the study sample used for these analyses are shown in **Table 1**. On average, IRAS participants consumed 0.8 servings/d of whole grain–containing foods, mostly as dark breads. The mean intake of whole grain did not differ significantly by ethnic group, sex, or glucose tolerance status (data not shown). The average S_I was 2.16 $\text{min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1} \cdot 10^{-4}$, and fasting insulin was 113.8 pmol/L (15.9 μU/mL). A higher S_I value indicates increased insulin sensitivity, and a greater fasting insulin concentration is associated with increased insulin resistance.

The crude correlations of whole-grain intake, S_I, fasting insulin, and various dietary and other correlates are shown in **Table 2**. Whole-grain intake was positively correlated with S_I but not with fasting insulin in this unadjusted analysis. In addition, strong correlations between whole grains and some of the constituents, including fiber, magnesium, zinc, and vitamin E, were observed.

Increased intake of whole grains continued to be significantly associated with higher S_I values, after adjustment for age, sex, ethnicity, clinic, and total energy intake (**Table 3**). Of the characteristics previously shown to be predictors of S_I that we considered potential confounders, only estimated energy expenditure, smoking, and family history of diabetes were informative enough to be retained in a final, most parsimonious model on which all further analyses were based (model 2).

Furthermore, our results indicate that adjustment for BMI and waist circumference—2 important correlates of S_I that we conceptualized as part of the mediating pathway —attenuated the effect of whole grains, but did not explain it entirely. To explore the question of whether the constituents of whole grains accounted for the observed effect, we evaluated the contribution of dietary magnesium, zinc, vitamin E, and fiber relative to that of whole grains by adding those 4 constituents first individually and then jointly to model 2. Only fiber and magnesium explained a significant amount of the association, as shown in model 4. Both of these constituents were in and of themselves associated with S_I ($\beta_{\text{magnesium(mg/d)}} = 0.00013$, $P = 0.0469$; $\beta_{\text{fiber(g/d)}} = 0.011$, $P = 0.0151$). Excluding dietary vitamin or mineral supplement users did not affect the association of whole grain and S_I.

TABLE 1
Characteristics of study participants with normal or impaired glucose tolerance in the Insulin Resistance Atherosclerosis Study, 1992-1994[1]

Characteristics	Value
Age (y)	54.8 ± 8.5[2]
Sex (%)	
M	45
F	55
Race or ethnicity (%)	
Non-Hispanic white	39.9
Hispanic	34.0
African American	26.1
Diabetes status (%)	
Normal	67.4
Impaired glucose tolerance	32.6
Insulin sensitivity ($\text{min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1} \cdot 10^{-4}$)	2.16 ± 1.96
Fasting insulin (pmol/L)	113.8 ± 107.8
Family history of diabetes, 1st-degree relative (%)	39.6
Whole grain (servings/d)	0.8 ± 0.7
Dark bread	0.6 ± 0.6
High-fiber cereal	0.2 ± 0.3
Hot cereal	0.1 ± 0.2
Total energy intake (kcal/d)	1887 ± 813
Dietary fiber (g/d)	14 ± 6
Dietary magnesium (mg/d)	398 ± 290
Dietary zinc (mg/d)	11 ± 6
Total energy expenditure ($\text{kcal} \cdot \text{kg}^{-1} \cdot \text{y}^{-1}$)	14 839 ± 2755
BMI (kg/m^2)	28.4 ± 5.7
Waist circumference (cm)	90.6 ± 12.8
Current smoking (%)	16.2

[1] $n = 978$.
[2] $\bar{x}$ ± SD.

Table 3 also shows that increased intake of whole grain was significantly associated with lower fasting insulin concentrations once age, sex, ethnicity, clinic, and total energy intake were taken into account. Unlike their effect on S_I, however, whole grains were not associated with fasting insulin concentrations independently of BMI and waist circumference.

We estimated the difference in S_I and fasting insulin for a one-serving increase in whole-grain intake for a hypothetical person with approximately average characteristics consuming 0.8 servings whole grains/d. An intake of whole grains one serving higher was associated with 0.23 $\text{min}^{-1} \cdot \mu\text{U}^{-1} \cdot \text{mL}^{-1} \cdot 10^{-4}$ (13.5%) higher S_I and a 5.7 pmol/L (0.8 μU/mL; 6.3%) lower fasting insulin concentration.

In a final set of analyses (**Table 4**), we explored the relation of whole grains to S_I and to fasting insulin at the levels of the individual foods by partitioning the whole-grain food group into the individual food lines. Dark breads (including whole wheat, rye, pumpernickel, and other high-fiber bread) and, even more strongly, high-fiber cereals (including high-fiber bran or granola cereals and shredded wheat) were associated positively with increased S_I and negatively with fasting insulin,

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TABLE 2
Correlations of whole grains, insulin sensitivity (S_I), fasting insulin, and related characteristics[1]

	Log(S_I + 1)	Log insulin	Whole grain	Total energy intake	Dietary fiber	Dietary magnesium	Dietary zinc	Dietary vitamin E	Total energy expenditure	BMI	Waist circumference
Log(S_I + 1)	—	—	—	—	—	—	—	—	—	—	—
Log insulin	−0.620 (< 0.001)	—	—	—	—	—	—	—	—	—	—
Whole grains	−0.076 (0.017)	−0.038 (0.233)	—	—	—	—	—	—	—	—	—
Total energy intake	−0.089 (0.005)	0.148 (< 0.001)	0.203 (< 0.001)	—	—	—	—	—	—	—	—
Dietary fiber	−0.009 (0.786)	0.074 (0.020)	(0.444) (< 0.001)	0.744 (< 0.001)	—	—	—	—	—	—	—
Dietary magnesium	0.057 (0.073)	−0.053 (0.099)	0.331 (< 0.001)	0.338 (< 0.001)	0.407 (< 0.001)	—	—	—	—	—	—
Dietary zinc	−0.035 (0.273)	0.091 (0.004)	0.228 (< 0.001)	0.861 (< 0.001)	0.695 (< 0.001)	0.429 (< 0.001)	—	—	—	—	—
Dietary vitamin E	−0.032 (0.315)	0.087 (0.007)	0.182 (< 0.001)	0.709 (< 0.001)	0.621 (< 0.001)	0.336 (< 0.001)	0.801 (< 0.001)	—	—	—	—
Total energy expenditure	0.085 (0.008)	−0.027 (0.396)	0.007 (0.817)	0.265 (< 0.001)	0.183 (< 0.001)	0.070 (0.030)	0.252 (< 0.001)	0.150 (< 0.001)	—	—	—
BMI	−0.502 (< 0.001)	0.493 (< 0.001)	−0.035 (0.274)	0.111 (0.001)	0.032 (0.323)	−0.008 (0.806)	0.082 (0.010)	0.061 (0.055)	−0.080 (0.013)	—	—
Waist circumference	−0.538 (< 0.001)	0.497 (< 0.001)	−0.026 (0.416)	0.228 (< 0.001)	0.116 (< 0.001)	0.037 (0.254)	0.190 (< 0.001)	0.113 (< 0.001)	0.001 (0.967)	0.805 (< 0.001)	—

[1] Pearson correlation coefficient; *P* value in parentheses.

but no associations were observed for cooked cereals (including oatmeal, cream of wheat, and grits).

DISCUSSION

The effect of whole grains on carbohydrate metabolism and pathophysiology is currently being investigated from a number of scientific angles, including controlled experiments. It has been suggested that the intact botanical structure of cereal may have a critical effect on the metabolism of insulin and glucose. An intake of whole-kernel rye bread, $\beta-$glucan rye bread, or wholemeal pasta seems to result in a significant decrease in insulin response compared with the intake of white bread (25), and this difference could not be explained by fiber content, type of cereal, or rate of gastric emptying. A randomized intervention study including overweight and hyperinsulinemic adults who consumed an experimentally controlled whole-grain diet for 6 wk focused directly on the effects on insulin sensitivity as measured with the use of a euglycemic hyperinsulinemic clamp (26). The whole-grain diet resulted in higher concentrations of insulin sensitivity and lower concentrations of fasting insulin than did a refined-grain diet. Similarly, patients with coronary artery disease benefited from a 16-wk isocaloric intervention diet administered in a randomized controlled trial, which substantially increased their intake of whole grain (administered via a whole-grain and legume powder; 27). Significantly reduced fasting glucose concentrations and a reduced demand for insulin as evidenced by lower glucose and insulin response areas were observed in the intervention group. Additional benefits included a reduced diastolic blood pressure and increased HDL-cholesterol and serum tocopherol concentrations.

The analysis of the IRAS population presents evidence from an epidemiologic perspective based on a large, observational cohort of free-living, middle-aged individuals. Our results indicate that the usual dietary intake of whole grains is associated with greater insulin sensitivity, as assessed by a state-of-the art measurement method, the frequently sampled intravenous-glucose-tolerance test. Given that insulin sensitivity is one of the main predictors of diabetes, our findings support previous reports on the protective effects of whole grains on the risk of developing diabetes in men (4) and women (3) by substantiating one of the underlying mechanisms. To our knowledge, only 2 previous epidemiologic studies have focused on the relation of whole-grain intake to fasting insulin (11, 12). Among a population of young white and African American adults, Pereira et al (11) estimated that replacing 2 servings of white bread each day with whole-grain foods could result in a 15% reduction in fasting insulin, a finding of an order of magnitude similar to our results of a 6.3% lower fasting insulin concentration associated with a one-serving increase in the intake of whole grains. Similarly, McKeown et al (12) reported an inverse relation between whole-grain intake and fasting insulin concentrations.

Whole-grain intakes have differed somewhat across populations but essentially hovered around the US national average of 0.9–1.1 servings/d (2). Our average intake of 0.8 servings/d reflected the dietary behaviors of our tri-ethnic, middle-aged IRAS population in 1992–1994, whereas the exclusively white Framingham Offspring population surveyed in 1991–1995 consumed 1.2 servings/d (12). In the Coronary Artery Risk De-

TABLE 3
Association of whole-grain intake with insulin sensitivity and fasting insulin[1]

	Insulin sensitivity			Fasting insulin		
	β	SE	P	β	SE	P
Model 1, whole grain (servings/d)[2]	0.075	0.024	0.001	−0.055	0.028	0.048
Model 2, whole grain (servings/d)[3]	0.082	0.023	0.001	−0.065	0.028	0.020
Model 3, whole grain (servings/d)[4]	0.043	0.020	0.030	−0.024	0.024	0.319
Model 4, whole grain (servings/d)[5]	0.041	0.026	0.117	−0.031	0.031	0.322

[1] Separate regression models for insulin sensitivity and fasting insulin.
[2] Adjusted for age, sex, ethnicity, clinic, and total energy intake (kcal).
[3] Adjusted for age, sex, ethnicity, clinic, total energy intake (kcal), total energy expenditure, smoking, and family history of diabetes.
[4] Adjusted for age, sex, ethnicity, clinic, total energy intake (kcal), total energy expenditure, smoking, family history of diabetes, BMI, and waist circumference.
[5] Adjusted for age, sex, ethnicity, clinic, total energy intake (kcal), total energy expenditure, smoking, family history of diabetes, dietary fiber, and dietary magnesium.

velopment in Young Adults Study (CARDIA; 11), whole-grain intake declined from 1.3 times/wk in 1985 and 1986 to 0.9 times/wk in 1992 and 1993.

Whole grains contain a number of important constituents, including minerals and trace elements (eg, magnesium, zinc, and manganese), vitamins (eg, vitamin E), fermentable carbohydrates (eg, dietary fiber, resistant starch, and oligosaccharides), and other compounds (eg, phytoestrogens) and antinutrients. Because of the particularly high concentration of these substances in the outer layers of the grain, the nutrient content of grains is reduced when the bran and germ layers are removed during the refining process. Several mechanisms have been proposed for the effect of whole grains and their constituents on physiology (13). Short-chain fatty acids produced by the fermentation of undigested carbohydrates may lead to enhanced glucose oxidation and insulin clearance. Undigested carbohydrates also decrease intestinal transit time. High viscosity of soluble fiber sources (oats, barley, and rye) delays gastric emptying and intestinal absorption and may result in lower glucose and insulin responses. Starch structure also affects glucose and insulin responses. In particular, low magnesium concentrations have been related to the development of diabetes (28–30). Antioxidants may improve insulin action by reducing lipid peroxidation in muscle cell membranes, which would enhance the ability of insulin to bind to its receptor (31). A recent analysis of IRAS data found that a protective effect of vitamin E on diabetes incidence may exist within the range of intakes available from food (32). In addition to the constituents of whole grains, food structure has been found to be highly influential in determining the glucose and insulin responses to foods; any disruption of the physical or botanical structure increases the response (13). To allow comparison with previous studies, we also presented results taking into account some of the nutritional constituents of whole grain—ie, fiber and magnesium. As expected, dietary fiber and magnesium explained most of the association of whole grains with insulin sensitivity, which is similar to the results of other studies focusing on insulin concentrations or diabetes (4, 11, 28). A more informative analysis, however, might involve separating the intake of fiber from whole grain from the intake of fiber from other foods, because it has been shown that whole-grain fiber is much more beneficial (5).

Given that nutrition recommendations are most easily applied when expressed in terms of foods, the focus of our analyses was clearly on foods and food groups, not on nutrients. In an exploratory analysis, we partitioned the whole-grain food group into the 3 food lines of the interview. Higher intakes of dark breads and high-fiber cereals were positively associated with greater S_I, whereas those of cooked cereals were not, which may be consistent with the glycemic index values (33). Liu et al (3) reported that a more frequent intake of dark breads, whole-grain breakfast cereals, and brown rice was associated with a decreased likelihood of developing diabetes, a finding similar to that of Jacobs et al (10) of an association of dark bread and whole-grain breakfast cereals with ischemic heart disease mortality in women. One limitation of the IRAS FFQ is that other potentially whole grain–containing foods, such as whole-grain pasta or brown rice, were not measured separately, which did not allow us to distinguish between whole-grain and refined-grain products. It has been suggested (10), however, that only those whole grain–containing foods

TABLE 4
Association of individual food group lines with insulin sensitivity and fasting insulin[1]

	Insulin sensitivity			Fasting insulin		
Whole-grain food group lines	β	SE	P	β	SE	P
Model 1, dark bread (servings/d)	0.067	0.028	0.018	−0.048	0.033	0.147
Model 2, high-fiber cereal (servings/d)	0.226	0.058	<0.001	−0.195	0.068	0.004
Model 3, cooked cereal (servings/d)	−0.019	0.076	0.806	0.007	0.090	0.934

[1] Separate regression models for insulin sensitivity and fasting insulin. All models were adjusted for age, sex, ethnicity, clinic, total energy intake (kcal), total energy expenditure, smoking, and family history of diabetes.

that are consumed more frequently or that can be considered staple foods could be identifiable.

The interest the whole grains have received is partially due to the more recent shift toward a food-based approach in nutritional epidemiology, with attention focusing on dietary patterns, food groups, and foods rather than on individual dietary constituents or nutrients. A variety of sophisticated statistical techniques have been used to identify dietary patterns. For example, a "Western" dietary pattern, determined by factor analysis and characterized by higher intakes of red meats, high-fat dairy products, and refined grains, was associated with higher insulin concentrations in healthy men, whereas a "prudent" dietary pattern characterized by higher intakes of fruit, vegetables, whole grains, and poultry was associated with lower insulin concentrations (34). Similarly, food patterns characterized by high-fiber bread intake identified through cluster analysis were favorably related to many components of the metabolic syndrome, including hyperinsulinemia (35).

In conclusion, our findings indicate that dietary behaviors characterized by higher intakes of whole grains may be associated with increased insulin sensitivity. Greater insulin sensitivity, or lower insulin resistance, may be one underlying factor leading to the previously reported health benefits associated with whole-grain intake, including a reduced risk of developing diabetes.

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ADL conceptualized the paper, designed the analytic approach, provided oversight for data management and analyses, interpreted the data, and drafted and revised the manuscript. AKR identified and synthesized relevant literature, implemented the statistical analyses, and contributed to the revision of the manuscript. KCS was responsible for management of dietary data and contributed to the revision of the manuscript. LM provided particular nutritional expertise for the interpretation of the data and the revision of the manuscript. RBD'A Jr provided statistical expertise and contributed significantly to the revision of the manuscript and the interpretation of the data. EJM-D was involved in the conception of the paper, the interpretation of the data, and critical revisions of the manuscript. LM was employed by the General Mills Corporation at the inception of this project. None of the other authors had any conflict of interest.

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