Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight gain among men1–3

Pauline Koh-Banerjee, Mary Franz, Laura Sampson, Simin Liu, David R Jacobs Jr, Donna Spiegelman, Walter Willett, and Eric Rimm

ABSTRACT

Background: Epidemiologic studies that directly examine changes in whole-grain consumption in relation to weight gain are sparse, and characterization of this association has been obscured by methodologic inconsistencies in the assessment of whole grains.

Objective: We aimed to ascertain the associations between changes in new quantitative estimates of whole-grain intake and 8-y weight gain among US men.

Design: The study was conducted in a prospective cohort of 27 082 men aged 40–75 y at baseline in 1986. Data on lifestyle factors were obtained periodically by using self-reported questionnaires, and participants measured and reported their body weight in 1986 and 1994.

Results: In multivariate analyses, an increase in whole-grain intake was inversely associated with long-term weight gain (P for trend < 0.0001). A dose-response relation was observed, and for every 40-g/d increment in whole-grain intake from all foods, weight gain was reduced by 0.49 kg. Bran that was added to the diet or obtained from fortified-grain foods further reduced the risk of weight gain (P for trend = 0.01), and, for every 20 g/d increase in intake, weight gain was reduced by 0.36 kg. Changes in cereal and fruit fiber were inversely related to weight gain. No associations were observed between changes in refined-grain or added germ consumption and body weight.

Conclusions: The increased consumption of whole grains was inversely related to weight gain, and the associations persisted after changes in added bran or fiber intakes were accounted for. This suggests that additional components in whole grains may contribute to favorable metabolic alterations that may reduce long-term weight gain.


KEY WORDS Whole grains, cereal fiber, bran, obesity, weight gain

INTRODUCTION

Epidemiologic evidence suggests an inverse relation between the consumption of whole-grain foods and body weight (1–4) and serum biomarkers of obesity, including insulin, C-peptide, and leptin concentrations (1–5). However, investigation of whole grains is relatively nascent, and characterization of the relation between whole-grain consumption and weight has been clouded by several methodologic issues. Currently, there is no uniform definition of a whole-grain food (6, 7), and the term “whole grain” has been equally applied to foods containing the intact grain and to foods that contain the appropriate proportions of all the milled grain constituents (ie, bran, endosperm, and germ) (8). Jacobs et al (3) proposed a definition of whole-grain foods as those with ≥25% whole-grain or bran content by weight. Several studies have adopted this definition and semi-quantitatively assessed the number of servings of whole grain–rich foods. However, as a limitation to this method, the actual whole-grain content may vary substantially per serving of food deemed high in whole grains, which results in potential misclassification and residual bias in the estimation of whole-grain effects. This issue is further compounded by the absence of standard serving sizes in various dietary questionnaires across studies (9).

To provide more standardized nomenclature and to increase consumer awareness of high-whole-grain foods, the FDA approved a whole-grain health claim (10) for foods with ≥51% whole-grain content (by weight) per reference amount customarily consumed (RACC; 11). RACC is a measurement established by the FDA for policy purposes: the amount of foods customarily consumed per eating occasion for each category on the list is based primarily on national food-consumption surveys conducted by the US Department of Agriculture. With regard to whole-grain content, foods must contain all portions of the kernel and provide a minimum of 16 g whole grain/RACC. Compliance with the definition is determined by reference to the fiber content of whole wheat (10). However, data to support these regulatory requirements are lacking, in part because of limitations in existing whole-grain databases. To date, no studies have apportioned foods into their respective whole-grain and non-whole-grain ingredients and calculated the percentage of whole-grain concentration across foods. Further, estimates of whole-grain

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Received March 18, 2004.
Accepted for publication June 21, 2004.
1994 through the use of a semi-quantitative food-frequency questionnaire (FFQ) described previously (14, 15). The FFQ was used to assess typical food intake over the previous year and included questions regarding the consumption of grain foods such as cooked and cold breakfast cereals, white and dark bread, white and brown rice, and pasta. The men were asked to specify the brand and type of cold breakfast cereal usually eaten. For each food, a commonly used unit or portion size was specified, and these portions were converted to gram weights per serving. The participant was asked how often, on average, he had consumed the specified amount during the previous year; 9 responses were possible, ranging from “never” to “26 times/d.” The FFQ included open-ended questions regarding the usual serving size and frequency of consumption of foods not listed on the FFQ.

Using time-specific product labels and US Department of Agriculture national nutrient database information, we partitioned all foods on the FFQ into their whole-grain and non-whole-grain ingredients, consistent with the classification developed by the US Department of Agriculture (16), and we determined the percentage of whole-grain concentration per food serving on a dry weight basis. Complete nutrient and ingredient data were available from breakfast cereal manufacturers for all 3 time periods, which allowed the successful characterization of >250 brand-name breakfast cereals. Manufacturers’ product information was also used to develop whole-grain profiles for commercially prepared foods such as bran muffins, and cookbooks (eg, The Joy of Cooking) were used to create recipes for home-prepared bakery items.

For the survey question on “dark bread,” we used a composite of recipes to represent commercial wheat (not whole-wheat) and wheatberry breads, which were selected on the basis of their proportion of marketplace shelf space during those periods. The nutrient profile was derived from US Department of Agriculture nutrient data and labels from 4 commercial wheat breads, including Home Pride Honey Wheat Berry Bread (Interstate Bakeries Corp, Kansas City, MO), Albertson’s Wheat Bread (Albertson’s Inc, Boise, ID), Pepperidge Farm Light Style Wheat Bread (Pepperidge Farm, Inc, Norwalk, CT), and Country Farms Wheat Berry Bread (Earthgrains Baking Companies, Inc, St Louis). The recipe for “other cooked breakfast cereal” on the FFQ was based on cream of wheat, which was selected on the basis of the proportion of marketplace shelf space for hot cereals from 1986 to 1994.

Whole grains were considered in their intact and pulverized forms, and each whole-grain ingredient was required to satisfy the content of an individual type of grain; ie, whole-grain wheat must have the proper content of bran, endosperm, and germ (C Pratt, personal communication, 2002). The whole-grain designation was assigned to the following items in the database: whole wheat and whole-wheat flour, whole oats and whole-oat flour, whole cornmeal and corn flour, brown rice and brown rice flour, whole barley, whole rye and rye flour, bulgur, buckwheat, popcorn, amaranth, and psyllium. Wheat bran, corn bran, oat bran, rice bran, and wheat germ that were added to foods to increase the fiber content were further considered as added bran and germ, respectively.

The whole-grain percentage for each food was then multiplied by the gram weight per serving to obtain the grams of whole-grain content per RACC. Total whole-grain consumption (in g/d) was then calculated by summing the whole-grain intakes from 1 high-whole-grain foods with ≥51% whole-grain content by

**SUBJECTS AND METHODS**

**Study population**

The Health Professionals Follow-up Study (HPFS) is a prospective investigation of 51,529 male health professionals who were 40–75 y old at baseline in 1986. This cohort includes 29,683 dentists, 10,098 veterinarians, 4,185 pharmacists, 3,745 optometrists, 2,218 osteopathic physicians, and 1,600 podiatrists. In 1986, participants completed a detailed questionnaire regarding medical history, dietary intake, and physical activity. The participants reported their age, current height (in inches), weight (in pounds), current and past smoking history, marital status, and medical history. On a biennial basis thereafter, participants were followed with mailed questionnaires to update information on exposures and to ascertain newly diagnosed disease.

We excluded from the analysis men who died or developed heart disease, stroke, cancer, or diabetes before 1994 (n = 13,169) because the development of these diseases may alter weight measures, dietary intake, and physical activity. Furthermore, we excluded men who failed to report their body weight or dietary data (n = 11,278) for the study period. Our analysis is therefore based on 27,082 healthy men for whom we have a complete set of predictor and outcome information for the study period of 1986 to 1994. The Institutional Review Board of the Harvard School of Public Health approved the protocol for this study.

**Outcome assessment**

The outcome was defined as the difference between the body weights reported by the subjects on the 1986 and 1994 questionnaires. Previously, we evaluated the reproducibility and validity of the self-reported measures of weight by using a subset of the cohort on whom technician-assessed measurements were taken 6 mo apart (12). The validity of self-reported height was not evaluated because that measurement was previously reported as highly valid (13). Self-reported weight and the average of 2 technician measures of weight were highly correlated at 0.97, and there were no significant linear trends in accuracy of reported weight across quartiles of age or body mass index (12).

**Dietary exposures**

Detailed dietary information was obtained in 1986, 1990, and 1994 through the use of a semi-quantitative food-frequency questionnaires. We further examined the associations between changes in whole-grain intakes with long-term weight gain among a cohort of 27,082 men by using new quantitative estimates of grams of consumption from foods that meet various classification criteria. We evaluated the reproducibility and validity of the self-reported measures of weight by using a subset of the cohort on whom technician-assessed measurements were taken 6 mo apart (12). The validity of self-reported height was not evaluated because that measurement was previously reported as highly valid (13). Self-reported weight and the average of 2 technician measures of weight were highly correlated at 0.97, and there were no significant linear trends in accuracy of reported weight across quartiles of age or body mass index (12).
weight in accordance with the FDA whole-grain claim; 2) moderate whole-grain foods with ≥25% whole-grain or bran content by weight according to the classification of Jacobs et al; and 3) all foods consumed. Total bran and germ consumption were calculated in a similar manner and further subdivided into their natural and added components. The natural portion included the amount of bran and germ that would correspond to the amount of whole grain in the food, and any amount exceeding the naturally occurring portion was considered to have been added.

The refined-grain group was calculated in servings per day and included grain foods with <25% whole-grain content by weight, such as cooked and other cold breakfast cereals, dark bread made from wheat flour rather than whole-wheat flour, white bread, English muffins, bagels or rolls, pancakes or waffles, white rice, pasta, cookies, doughnuts, brownies, sweet rolls, coffee cake, and pizza.

The FFQ was validated among a subset of the study participants as reported previously (14, 17). Two FFQs were administered 1 y apart, with two 1-wk diet records administered 6 mo apart during this 1-y period. The performance of the FFQ in assessing the intakes of individual grain products was further evaluated, and the Pearson correlation coefficients between the FFQs and the dietary records ranged from 0.30 for servings of refined-grain foods to 0.86 for those of cold breakfast cereals (17, 18).

Statistical analysis

The differences in mean grain intakes from 1986 to 1994 were compared by using Wilcoxon’s signed-rank tests. We determined the age- and energy-adjusted means for lifestyle and dietary characteristics across increasing quintiles of whole-grain intakes. Tests for linear trend were calculated by assigning the median value for each quintile of intake treated as a continuous variable by using linear (or for continuous outcome variables) or logistic (for dichotomous outcome variables) regression models.

Using multivariate linear regression, we examined how changes in intakes of whole grain, refined grain, and added bran and germ (1986–1994) were associated with the dependent variable, namely the change in weight (in kg) in the same period. We used the robust variance estimate (19) to obtain valid inferences and avoid the necessary assumptions of normality for linear regression. In all analyses, there was one observation per participant. Whole grains were modeled as continuous variables when tests for nonlinearity using spline regression were not statistically significant; otherwise, the exposures were categorized. We calculated the multivariate adjusted least-squares means for changes in body weight across categories of change in whole grains that may potentially mediate the association with weight gain. For these analyses, we further adjusted for intakes of dietary fiber, folate, magnesium, and vitamins E and B-6.

We adjusted for the percentages of energy derived from protein and monounsaturated, polyunsaturated, saturated, and trans unsaturated fatty acids to examine the possibility that dietary patterns associated with diets high in whole grains would explain any apparent inverse associations. We also considered constituents found in whole grains that may potentially mediate the association with weight gain. For these analyses, we further adjusted for intakes of dietary fiber, folate, magnesium, and vitamins E and B-6.

To evaluate the influence of measurement error on the association between changes in whole grains and weight gain, we used a subset of participants from a separate but similar study (15, 20) for whom repeated dietary records and FFQs were available in both 1980 and 1986. Using the regression calibration approach (Appendix A) together with data from our main study, we adjusted the regression coefficients and least-squares means for measurement error. All statistical analyses were conducted by using SAS software (version 8.2; SAS Institute Inc, Cary, NC), and statistical significance was defined as a two-tailed P value < 0.05.

RESULTS

The mean (±SD) whole-grain intakes (in g/d) from foods with various whole-grain concentrations are listed in Table 1. The high-whole-grain foods (≥51% whole-grain content by weight) that contributed most to intake (in g/d) included select cold
breakfast cereals (37.6%), brown rice (25.3%), cooked oatmeal (21.8%), and popcorn (11.6%). Of the participants who reported eating breakfast cereals (76.3% of the cohort), 44.2% reported eating breakfast cereals with ≥51% whole-grain content by weight, 26% reported eating breakfast cereals with 25–50% whole-grain content by weight, and 29.7% reported eating refined-grain cereals (<25% whole-grain content by weight). The foods that fulfilled the ≥25% whole-grain content criterion included specific cold breakfast cereals, crackers, and other grains. On the basis of the composite of commercial wheat bread formulations used, “dark bread” had <25% whole-grain content by weight, and it was therefore classified as a refined grain. Dark bread contributed to the participants’ total whole-grain consumption; each slice provides 2 g whole grain.

Between 1986 and 1994, added bran from all foods increased significantly (P < 0.001), from 2.2 ± 6.0 to 5.3 ± 7.9 g/d, and this increase derived primarily from wheat and oats. The intakes of added germ significantly decreased from baseline to 0.3 ± 1.3 g/d in 1994 (P < 0.001) and were obtained largely from wheat germ (62.7%).

The age and energy-adjusted descriptive characteristics of the study population across quintile categories of whole-grain intake from all foods are shown in Table 2. The median intakes of whole grains ranged from 3.0 g/d in the lowest category of intake to 42.7 g/d in the highest category. Favorable trends in lifestyle and dietary factors across quintile categories of whole-grain intake were significant for all factors (P for trend < 0.001 for all). Compared with participants in the lowest category, those in the highest category of consumption tended to have a lower BMI, were less likely to smoke, and were more physically active. Higher intakes of whole grains were associated with lower intakes of total fat, saturated fat, dietary cholesterol, and alcohol and higher intakes of dietary fiber, magnesium, vitamin E, vitamin B-6, and folate. Glycemic load was higher in those with greater whole-grain intakes.

### Multivariate models

Multivariate-adjusted mean weight gains across quintile categories of whole grains are shown in Table 3. All participants tended to gain weight over the 8-y follow-up period, and the mean weight gain was 1.9 ± 5.2 kg. After adjustment for potential confounding variables and dietary factors associated with diets high in whole grains, increases in consumption of whole grains (g/d) over the 8-y period were inversely related to weight gain (P for trend < 0.01, regardless of the whole-grain concentration of the food sources). For every 40-g/d increment in...
TABLE 3
Multivariate-adjusted mean 8-y weight change (kg) according to quintiles of changes in whole-grain intakes from foods that meet various whole-grain content criteria among US men in the Health Professionals Follow-up Study

<table>
<thead>
<tr>
<th>Quintiles of change in whole-grain intake (g/d)</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA definition²</td>
<td>−17.8</td>
<td>−0.3</td>
<td>15.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>1.64 ± 0.13³</td>
<td>1.62 ± 0.23</td>
<td>1.03 ± 0.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>0.96 ± 0.22</td>
<td>0.96 ± 0.29</td>
<td>0.69 ± 0.21</td>
<td>0.002</td>
</tr>
<tr>
<td>Jacobs et al definition⁴</td>
<td>−11.0</td>
<td>3.3</td>
<td>23.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>1.88 ± 0.12</td>
<td>1.81 ± 0.11</td>
<td>0.98 ± 0.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>1.25 ± 0.22</td>
<td>1.28 ± 0.22</td>
<td>0.73 ± 0.22</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)⁴</td>
<td>1.24 ± 0.23</td>
<td>1.03 ± 0.22</td>
<td>0.75 ± 0.22</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>From all foods</td>
<td>1.24 ± 0.23</td>
<td>1.03 ± 0.22</td>
<td>0.75 ± 0.22</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

¹ n = 27 082. FDA, Food and Drug Administration.
² Whole-grain foods with ≥51% whole-grain content by weight.
³ x ± SE (all such values).
⁴ Multivariate models controlled for age, the respective baseline exposure, smoking (categorized as nonsmokers, habitual smokers, new smokers, and quitters), baseline weight, and baseline values and changes in refined grains, calories, total physical activity, alcohol, protein, and trans, saturated, monounsaturated, and polyunsaturated fats (all as % of total energy).
⁵ Whole-grain foods with ≥25% whole-grain content by weight.

whole grains from all foods (the approximate difference in median intakes between the highest and lowest quintiles), long-term weight gain was reduced by 0.49 kg.

To better understand the relation between whole-grain consumption and weight gain related to nutrients found in whole grains, we adjusted for potential mediating nutrients, including food sources of fiber, magnesium, folate, and vitamins E and B-6. The association between changes in whole-grain intake and weight gain (0.75 and 1.24 kg weight gain for the highest and the lowest quintile category, respectively; P for trend < 0.0001) was mildly attenuated after adjustment for these nutrients (0.93 and 1.33 kg weight gain, respectively; P for trend < 0.01).

Using the results of our validation study, we further corrected for covariate measurement error in the average changes in body weight associated with quintile changes in grain intakes. After correction for measurement error, the 8-y weight gain was 0.39 kg (compared with 0.49 kg, uncorrected).

Dietary fiber was inversely related to weight gain independent of whole grains (P for trend < 0.0001). The men in the lowest quintile of change gained 1.40 kg, whereas the men in the highest quintile of change gained 0.39 kg (Table 4). For every 20-g/d increase in dietary fiber, weight gain was reduced by 1.18 kg. After correction for measurement error, long-term weight gain was reduced by 5.5 kg for each 20-g/d increment in dietary fiber.

Because the physiologic consequences of a high-fiber diet may depend on the type or food source of fiber, we further examined the relations between cereal, fruit, and vegetable fiber and weight change. After simultaneous adjustment for each of the 3 main sources of fiber, significant inverse associations were observed for cereal and fruit fiber, but not vegetable fiber. The dose-response relation was strongest for fruit fiber. For every 20 g/d increment in fruit fiber, weight gain was reduced by 2.51 kg (P for trend < 0.001). Because apples predominantly accounted for the fruit fiber intake (26.7%), we also calculated the mean weight gain for changes in apple consumption. Men who added a single daily apple to their diet gained 0.67 kg less weight over the 8-y period, if all other factors were held constant (P for trend < 0.0001).

Cereal fiber was inversely related to weight gain (P for trend < 0.001). For every 20 g/d increment in cereal fiber, weight gain was reduced by 0.81 kg. Similarly, changes in cold breakfast cereal consumption (servings/d) significantly predicted weight gain. Increases in intake of cereals with ≥51% whole-grain content by weight protected against weight gain (P for trend < 0.001), whereas the association with changes in intake of cereals with 25–50% whole-grain content was only marginally significant (P for trend = 0.05 for trend). In contrast, refined-grain cereals (<25% whole-grain content) were positively related to long-term weight gain (P for trend < 0.001).

Added bran consumption was also inversely associated with weight gain in a dose-response manner, and men in the highest quintile of change gained 15% less weight than did men in the lowest quintile over 8 y (P for trend = 0.01; Table 5). For every 20-g/d increment in added bran intake, weight gain was reduced by 0.36 kg. In contrast, there was no significant trend across categories of refined-grain or added germ intakes.

**DISCUSSION**

In this population of men, an increase in consumption of whole grains protected against long-term weight gain, and the dose-response relation appeared strongest for foods with ≥25% whole-grain or bran content by weight. Changes in added bran consumption also negatively predicted weight gain, whereas no association was observed for changes in servings of refined grains or in grams of added germ intake. To our knowledge, this is the first prospective cohort study to report the independent associations between changes in quantitative estimates of whole grains (in g/d) and weight gain among men.
Whereas whole grains have been inversely associated with body weight and fat distribution (1–4), few experimental studies have been conducted to directly examine this relation. In one randomized crossover trial, body weight was reduced after 6 wk on a whole-grain diet, compared with a refined-grain diet (21). The difference was not significant, but the follow-up period may have been too brief for significant weight loss to occur. Prospective data directly linking changes in consumption of whole grains to weight gain are further lacking, particularly among men (22). In a recent study among female nurses, Liu et al (4) reported that women in the highest quintile of change in whole-grain intake gained 1.07 kg over two 4-y intervals, whereas women in the lowest quintile

### TABLE 4
Multivariate-adjusted mean 8-y weight change (kg) according to quintiles of changes in food sources of fiber among US men in the Health Professionals Follow-up Study.

<table>
<thead>
<tr>
<th>Quintiles of change in fiber intake (g/d)</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fiber</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>−5.2</td>
<td>0.5</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>2.24 ± 0.10²</td>
<td>1.64 ± 0.10</td>
<td>0.68 ± 0.10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.40 ± 0.20</td>
<td>1.04 ± 0.19</td>
<td>0.39 ± 0.20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cereal fiber</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>−2.2</td>
<td>1.0</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>1.84 ± 0.11</td>
<td>1.70 ± 0.10</td>
<td>1.08 ± 0.10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.10 ± 0.20</td>
<td>1.10 ± 0.20</td>
<td>0.76 ± 0.20</td>
<td>0.0002</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.30 ± 0.27</td>
<td>1.15 ± 0.26</td>
<td>0.91 ± 0.26</td>
<td>0.0004</td>
</tr>
<tr>
<td>Fruit fiber</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>−2.2</td>
<td>0.2</td>
<td>3.7</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>2.20 ± 0.11</td>
<td>1.52 ± 0.10</td>
<td>0.79 ± 0.11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.45 ± 0.21</td>
<td>0.91 ± 0.19</td>
<td>0.51 ± 0.20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.59 ± 0.27</td>
<td>0.96 ± 0.26</td>
<td>0.64 ± 0.26</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vegetable fiber</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>−3.2</td>
<td>0.0</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>1.68 ± 0.13</td>
<td>1.63 ± 0.12</td>
<td>1.12 ± 0.12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>0.87 ± 0.22</td>
<td>1.05 ± 0.20</td>
<td>0.83 ± 0.21</td>
<td>0.6</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.08 ± 0.27</td>
<td>1.26 ± 0.26</td>
<td>1.12 ± 0.26</td>
<td>0.8</td>
</tr>
</tbody>
</table>

³ Multivariate models controlled for age, the respective baseline exposure, smoking (categorized as nonsmokers, habitual smokers, new smokers, and quitters), baseline weight, and baseline values and changes in refined grains, calories, total physical activity, alcohol, protein, and trans saturated, monounsaturated, and polyunsaturated fats (all as % of total energy).

³ Multivariate model simultaneously controlled for baseline and changes in other fiber types, folate, magnesium, and vitamin E and vitamin B-6 intakes.

### TABLE 5
Multivariate-adjusted mean 8-y weight change (kg) according to tertiles of changes in added bran and germ intakes among US men in the Health Professionals Follow-up Study.

<table>
<thead>
<tr>
<th>Tertiles of change in bran or germ (g/d)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Added bran from all foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>0.0</td>
<td>0.9</td>
<td>7.3</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>1.70 ± 0.13²</td>
<td>1.68 ± 0.10</td>
<td>1.40 ± 0.08</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.10 ± 0.22</td>
<td>1.05 ± 0.19</td>
<td>0.94 ± 0.19</td>
<td>0.008</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.16 ± 0.23</td>
<td>1.09 ± 0.20</td>
<td>1.00 ± 0.20</td>
<td>0.01</td>
</tr>
<tr>
<td>Added germ from all foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median change in intake (g/d)</td>
<td>−0.4</td>
<td>0.0</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted weight change (kg)</td>
<td>1.53 ± 0.12</td>
<td>1.54 ± 0.08</td>
<td>1.10 ± 0.13</td>
<td>0.3</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.01 ± 0.22</td>
<td>1.02 ± 0.19</td>
<td>0.73 ± 0.22</td>
<td>0.7</td>
</tr>
<tr>
<td>Multivariate-adjusted weight change (kg)</td>
<td>1.01 ± 0.22</td>
<td>1.05 ± 0.19</td>
<td>0.75 ± 0.22</td>
<td>0.9</td>
</tr>
</tbody>
</table>

³ n = 27 082.

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³ Multivariate models controlled for age, the respective baseline exposure, smoking (categorized as nonsmokers, habitual smokers, new smokers, and quitters), baseline weight, and baseline values and changes in refined grains, calories, total physical activity, alcohol, protein, and trans saturated, monounsaturated, and polyunsaturated fats (all as % of total energy).

³ Multivariate model simultaneously controlled for baseline and changes in natural bran.

³ Multivariate model simultaneously controlled for baseline and changes in natural germ.
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The authors' contributions to this publication are as follows: design of the study, analysis of the data, and writing of the manuscript (PK-B, DS, and SL);

We are indebted to Al Wing, Lydia Liu, and Ruiying Li for their technical support.

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REFERENCES


APPENDIX A

Correction of least-squares means for covariate measurement error

This method is a straightforward extension of the methods detailed by Rosner et al (1) and Spiegelman et al (2). An SAS macro (available from DS) performs these calculations (stdls@channing.harvard.edu). Let $Y$ be the dependent variable, $Z$ be a $p_1 \times 1$ vector of covariates measured with error, $X$ be a $p_1 \times 1$ vector of the corresponding perfectly measured covariates, and $U$ be a $p_2 \times 1$ vector of covariates that are always measured without error. To apply this method, a main study must be available with data $(Y_i, Z_i, U_i)$, $i = 1, \ldots, n_1$, and a validation study must be available with data $(X_i, Z_i, U_i)$, $i = 1, \ldots, n_2$. Typically, $n_1 \gg n_2$.

We assume a linear model for $Y$:

$$E(Y \mid X, U) = \beta_0 + \beta_1 (X^T, U^T)^T = \beta^*(I, X^T, U^T)^T \quad (A1)$$

where $\beta^*$ is a $1 \times (I + p)$ vector of regression coefficients, and $p = p_1 + p_2$.

In addition, we assume a linear measurement error model:

$$E(X \mid Z, U) = \Gamma (I, Z^T, U^T)^T \quad (A2)$$

where $\Gamma$ is a $[p_1 \times (I + p)]$ matrix of regression parameters describing the measurement error models for each of the $p_1$ covariates, $X$, measured with error.

As stated by Rosner et al (1) and Spiegelman et al (2), a consistent estimator of $\beta^*, \hat{\beta}^*$, is given by

$$\hat{\beta}^* = \hat{\beta} \hat{\Gamma}^{-1} \quad (A3)$$

where $\hat{\beta}$ is obtained from the regression of $Y$ on $(I, Z^T, U^T)^T$ in the main study, and $\hat{\Gamma}$ is obtained from the regression of $X$ on $(I, Z^T, U^T)^T$ in the validation study.

The variance, $\Sigma_{\beta^*}$, for this estimator is given in references 1 and 2 as a function of the variances of $\hat{\beta}$ and $\hat{\Gamma}$, which are the standard variances from the respective linear regression models.

Then the estimator of the least-squares mean at a specified value of $X = x$ and $U = u$, $\hat{Y} \mid (X = x, U = u)$, is given by

$$\hat{Y} \mid (X = x, U = u) = \hat{\beta}^*(I, x^T, u^T)^T \quad (A4)$$

and

$$\text{Var}[\hat{Y} \mid (X = x, U = u)] = (I, x^T, u^T) \Sigma_{\beta^*}(I, x^T, u^T)^T \quad (A5)$$

REFERENCES
