Is Whole Grain Intake Associated With Reduced Total and Cause-Specific Death Rates in Older Women? The Iowa Women's Health Study

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ABSTRACT

Objectives. This study sought to determine whether nutrient-rich whole grains reduce mortality risk.

Methods. The study included 38 740 Iowa women, aged 55 to 69 years. A food frequency questionnaire was used to obtain data on grain intake.

Results. Median whole grain intake quintiles ranged from a median of 0.2 to more than 3 servings per day. Women with higher intakes had healthier lifestyles and less baseline disease. The total death rate decreased in increasing quintiles, and the pattern repeated for cancer, cardiovascular disease, and other causes combined. Adjusted for lifestyle and baseline disease, the relative hazard rate ratio for total death was about 0.85 in daily consumers of whole grain. Findings persisted in strata of baseline healthy and diseased and were not explained by dietary fiber. Rates of total mortality, but not cardiovascular disease mortality, were higher among frequent consumers of refined grain.

Conclusions. Total mortality risk was inversely associated with whole grain intake and positively associated with refined grain intake. Refined grains contributed more than 20% of energy intake, and whole grains contributed 1%. Substitution of whole for refined grain may reduce chronic disease risk in the United States. (*Am J Public Health.* 1999;89:322–329)

A sizable proportion of energy intake in the United States and elsewhere comes from grains, yet the large majority of grains are eaten in refined form. Whole grains contain a wide variety of nutrients and other constituents that are lost in refining and that may be beneficial for health.[1,2] Intake of whole grain foods is low (S. Gerrior, written communication, January 1997),[3] despite dietary recommendations to the contrary.[4,5]

Reviews of case–control studies have shown a consistently reduced risk of cancer for high vs low intake of whole grain foods and suggested a corresponding increased risk for high vs low intake of refined grains.[6,7] Interpretation is difficult, however, because previous studies have paid little attention to the associations of grain intake with other lifestyle and dietary factors and have not ensured that "high" intake is high in any absolute sense. These deficiencies have occurred in part because many of the reports constituted general surveys of dietary intake and the cancer under study, with no specific hypothesis about grains; in addition, some of the inverse whole grain and direct refined grain associations in the individual studies reviewed did not reach statistical significance. We addressed these deficiencies in a recent analysis of data from the Iowa Women's Health Study,[8] a prospective cohort study of women aged 55 to 69 years and found that whole grain eaters initially free of coronary heart disease (CHD) had a reduced risk of CHD death after careful control for these possibly confounding factors. Refined grain intake was unrelated to risk of CHD death.

Given these findings,[8] the possibility that whole grains may affect other diseases,[6,7] and the wide range of potentially healthful nutrients in whole grain,[1,2] we hypothesized that whole grain intake is associated with reduced risk of total mortality. In this article, we extend our analysis to the associations of whole and refined grain intake with risk of total and cause-specific mortality, both overall and in subgroups reporting prevalent diabetes, cancer, or CHD at baseline.

Methods

This study was approved by the Committee on the Use of Human Subjects in Research of the University of Minnesota.

In the Iowa Women's Health Study, a random sample (n = 99 826) of women 55 to 69 years of age with a valid Iowa driver's license were sent a 16-page mailed survey in January 1986; 41 836 women responded. Women were excluded from analysis if they left 30 or more items blank on the food frequency questionnaire (n = 2782) or reported implausibly high or low energy intakes (<600 or ≥5000 kcal per day) (n = 538). This left 38 740 women for analysis (numbers excluded were not mutually exclusive). Missing covariate data reduced the sample size to 34 333 in multivariate analyses.

Data Collection

The baseline questionnaire included assessment of known or suspected risk factors for CHD and cancer as well as a 127-item food frequency questionnaire similar to that used in the 1984 survey of the Nurses Health Study.[9,10] For each food, a commonly used

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serving size was specified, and participants were asked to report their frequency of consumption from among 9 categories ranging from "never or less than 1 serving per month" to "6+ servings per day." Servings per week were calculated from these categories. Questions were included regarding other regularly consumed foods, current use and dosage of vitamin supplements, and the brand names of multivitamin preparations. Women could specify any number of servings per week for each food item queried, including cold breakfast cereal. Women were asked to name the single breakfast cereal that they usually ate; 152 brands were named. Coding of the cold breakfast cereals for whole/refined grain content has been described elsewhere.[8] About 80% of the participants reported any consumption of a cold breakfast cereal, and approximately 60% of these women reported consuming a whole grain product. The reliability of the questionnaire in this cohort has been described elsewhere.[11]

TABLE 1—Intake of Whole and Refined Grain Among 38 470 Women: Iowa, 1986

	Quintile of Intake				
	1	2	3	4	5
Whole grain, servings per week[a]					
Median	1.5	6.0	8.5	13.0	22.5
Range	0–3.5	4.0–7.0	7.5–10.0	10.5–18.0	18.5–105.0
Refined grain, servings per week[b]					
Median	3.5	8.0	12.0	18.0	30.0
Range	0–5.5	6.0–9.5	10.0–14.0	14.5–22.5	23.0–155.5

[a]Mean ± SE: 10.8 ± 8.3.
[b]Mean ± SE: 15.0 ± 11.6.

Case Ascertainment

Vital status of cohort members was determined through December 31, 1995, via annual linkage with the State Health Registry of Iowa, the National Death Index, and follow-up questionnaires mailed in 1988, 1990, and 1992. In addition to total mortality, several causes of death were studied, including total cancer (as an underlying cause of death; *International Classification of Diseases, 9th Revision* [*ICD-9*], codes 140–239), total cardiovascular disease (*ICD-9* codes 390–459), and noncancer/noncardiovascular disease. More specific causes were also examined: CHD (*ICD-9* codes 410–414, 429.2), stroke (*ICD-9* codes 430–438), and other cardiovascular diseases; respiratory disease (*ICD-9* codes 460–519); accidents and injuries (*ICD-9* codes E800–E999); and other noncancer/noncardiovascular disease. We did not validate cause-of-death coding. Among the 38 740 women included in these analyses, 3320 died (1507 from cancer, 1097 from cardiovascular diseases, and 716 from other causes).

Data Analysis

Length of follow-up was calculated for each individual as the number of days elapsed from completion of the baseline questionnaire until the date of death or December 31, 1995. Analyses examined the associations of whole and refined grain intake with total and cause-specific mortality. The food items composing the total whole and refined grain subgroups have been reported previously.[8]

The association of grains with death was examined primarily by proportional hazards regression analysis. Food group variables were categorized by quintiles, and the mortality rate in each category was compared with that in the lowest intake category. Initial analyses examined associations adjusted for age and total energy intake.

Analyses were also adjusted for other risk factors that were significant predictors of death, including demographic factors (marital status, education) and physiologic or pathologic factors (self-reported history of CHD, self-reported history of cancer, self-reported history of hypertension, self-reported history of diabetes mellitus, self-measured body mass index, waist-to-hip ratio measured by a friend or spouse,[12] and age at first childbirth). Additional covariates represented lifestyle behaviors (cigarette smoking, physical activity, estrogen replacement therapy, alcohol intake, use of vitamin supplements) and aspects of diet other than grains (nutrients: total and saturated fat; food groups: red meat, fish and seafood, and fruits and vegetables, not including juice). To assess possible overadjustment, we ran models for total mortality in which we adjusted for all of the preceding factors except body mass; waist-to-hip ratio; and baseline cancer, CHD, hypertension, or diabetes. Finally, women may have altered their diet if they had prevalent disease; we therefore ran models for total mortality (with the full set of adjusting factors) within 2 subgroups: one with cancer, CHD, or diabetes at baseline and the other with none of these self-reported conditions. In the final analyses, we adjusted for constituents found in whole grain that might mediate the association of whole grains with death: dietary fiber, vitamin E, folate, phytic acid, magnesium, manganese, zinc, and iron, each computed from all dietary sources. Intake from supplements was omitted from nutrient totals in all analyses.

The hazard rate ratio for a given category of intake was estimated by taking the exponent of the proportional hazards regression coefficient for that level of intake. A test for trend was determined across a vector of indicator variables for the grain of interest, with each level of exposure weighted by its median value. The SAS[13] statistical analysis package was used.

We obtained food disappearance data directly from several sources (S. Gerrior, written communication, January 1997).[3] We used a 1919 US Department of Agriculture food disappearance report[14] on stocks of white wheat flour and whole wheat/graham flour to estimate whole wheat consumption in the early 1900s. We multiplied 250 to 275 lb/yr total grain products consumed × 65% to 80% wheat[3] × the proportion (5%) of wheat ground to whole flour in 1918[14] to estimate whole wheat flour consumption. This computation for the early 1900s assumed that the accounting of stocks of wheat flour was fairly complete and that the ratio of stocks of whole wheat to refined wheat flour was equal to the ratio consumed.

Results

The average age of the women was 61.5 years. The mean weekly intake of whole grain foods reported was 11 servings, with dark bread composing 60% of these servings and whole grain breakfast cereals representing the second largest proportion (Tables 1 and 2). The women reported 15 servings per week of intake of refined grain foods, the largest contributors being sweets and desserts and white bread. There was a wide range of intake of whole grain foods, with virtually no consumption in the lowest quintile, 1 to 2 servings per day in quintile 3, and 3 to 4 servings per day in the highest quintile. The quintile distribution was similar for refined grain intake.

As described previously,[8] relative to women who ate whole grains infrequently, those who ate whole grain foods every day were of higher socioeconomic status; were thinner; had less prevalent cancer, CHD, hypertension, and diabetes at baseline; and engaged in a higher number of positive health behaviors (e.g., not smoking, physical

activity, lower alcohol intake, use of hormone replacement therapy, and use of dietary supplements). A higher level of whole grain intake was also associated with less intake of refined grains and red meat and lower total and saturated fat intakes but higher consumption of fruits, vegetables, and fish. Findings were generally reversed in high consumers of refined grains, except for parallel decreases in alcohol and red meat intake and little association with cigarette smoking and saturated fat. Dietary intake of grain constituents from all foods (fiber, vitamin E, folate, zinc, iron, manganese, magnesium, and phytic acid) was steeply and directly correlated with whole grain intake and inversely and shallowly correlated with refined grain intake.

There were striking inverse associations of whole grain intake with risk of death (Table 3). Unadjusted total mortality rates in the lowest to highest quintiles of whole grain intake were 13.4, 10.3, 9.0, 7.9, and 9.2 per 1000 person-years. Age- and energy-adjusted hazard rate ratios for total mortality were reduced by about 40% in daily whole grain consumers (those in the 3 quintiles of highest whole grain intake). Similar reductions in age- and energy-adjusted death rates with increased whole grain intake were seen for major causes of death, except stroke. Reduced mortality with increased whole grain intake among noncancer/noncardiovascular causes was largely attributable to respiratory diseases.

After adjustment for other potential confounding variables, the inverse association with total mortality was attenuated but still present. Hazard ratios of approximately 0.80 to 0.85 for daily or more frequent intake of whole grain were seen for cancer, cardiovascular disease, and noncancer/noncardiovascular disease deaths.

The association of total mortality with whole grain intake was further examined after adjustment for all of the factors listed in Table 3 except body size and self-reported cancer, diabetes, or heart disease, which may be in the causal pathway between whole grain intake and total mortality. In this analysis, hazard rate ratios were 1.00, 0.91 (95% confidence interval [CI] = 0.82, 1.01), 0.81 (95% CI = 0.72, 0.90), 0.73 (95% CI = 0.65, 0.82), and 0.81 (95% CI = 0.72, 0.90) (P for trend < .0001) for increasing whole grain intake quintiles. Another supplemental analysis examined the fully adjusted association between total mortality and whole grain intake according to whether baseline disease was present or not. Hazard rate ratios for increasing quintiles of whole grain intake in the 2 subgroups were comparable. Among those who reported cancer, diabetes, or heart disease at baseline (1354 deaths among 7519 women), rate ratios were 1.00, 0.91 (95% CI = 0.78, 1.05), 0.84 (95% CI = 0.72, 0.99), 0.80 (95% CI = 0.68, 0.94), and 0.86 (95% CI = 0.73, 1.01) (P for trend = .02); among those who were free of these diseases (1538 deaths among 26 814 women), rate ratios were 1.00, 0.98 (95% CI = 0.84, 1.14), 0.89 (95% CI = 0.75, 1.04), 0.81 (95% CI = 0.68, 0.96), and 0.84 (95% CI = 0.71, 1.00) (P for trend = .07).

TABLE 2—Descriptions and Intake of Grain Food Groups Among 38 470 Women: Iowa, 1986

	Portion of Total Servings per Week, %
Whole grain	
Dark bread	60.5
Whole grain breakfast cereal[a]	17.6
Popcorn	13.4
Cooked oatmeal	6.8
Wheat germ	1.5
Brown rice	1.3
Bran	0.6
Other grains (e.g., bulgar, kasha, couscous)	0.3
Refined grain	
Sweets/desserts	45.2
White bread, including pita bread	29.9
Pasta	5.0
English muffins, bagels, or rolls	4.7
Refined grain breakfast cereal[a]	3.9
White rice	3.4
Muffins or biscuits	3.2
Pancakes or waffles	2.6
Pizza	2.5

[a]The one brand name or generic cereal specified was coded for whole grain content; breakfast cereals with a whole grain or bran content of 25% or more by weight were classified as whole grain.

In contrast to the whole grain results, there was evidence of a small positive association between refined grain intake and risk of total mortality (Table 4). A similar pattern was seen for cancer and for noncancer/noncardiovascular disease deaths. Within the latter grouping, there was a statistically significant increased risk associated with nonmalignant respiratory disease. There was no association between refined grain intake and all cardiovascular disease, and there was a tendency toward an inverse association with "other cardiovascular diseases."

The association of whole grain intake with total mortality was independent of intake of refined grain. The reduced risk for increasing whole grain intake was not attenuated by adding refined grain intake to the models, while the increased risk for increasing refined grain intake was attenuated and lost statistical significance when whole grain intake was added to the models (data not shown).

Further analyses were conducted to examine whether the association of whole grain intake with total mortality could be attributed to dietary constituents of grain. After simultaneous adjustment for fiber, vitamin E, folic acid, phytic acid, iron, zinc, magnesium, and manganese intake from all sources (except supplements), the association of whole grains with risk of total death was slightly attenuated, with hazard rate ratios from the lowest to the highest category of intake of 1.00, 0.96 (95% CI = 0.86, 1.07), 0.88 (95% CI = 0.78, 1.00), 0.83 (95% CI = 0.72, 0.95), and 0.89 (95% CI = 0.78, 1.02) (P for trend = .07). The association of refined grain intake with risk of total death was not affected by adjustment for grain constituents.

Discussion

During 9 years of follow-up, the 55- to 69-year-old women in this study who reported eating at least 1 serving per day of whole grain foods at baseline had a substantially lower risk of mortality, including mortality from cancer, cardiovascular disease, and other causes, than did the women who reported eating almost no whole grain products. This finding also held for the subgroup of women who were free of diabetes, cancer, and heart disease at baseline (whose overall 9-year death rate was 5.7%) and for the subgroup who had any of these diseases at baseline (whose overall 9-year death rate was 18.0%). This subgroup analysis is of interest because it reduced the chance that the finding of decreased risk with increased whole grain intake occurred because women with

TABLE 3—Multivariate-Adjusted Hazard Rate Ratios Across Quintiles of Whole Grain Intake for Various Causes of Death in Iowa Women

	Quintile of Whole Grain Intake					
	1	2	3	4	5	*P* for Trend
Person-years	68 262	68 672	64 761	66 329	64 980	...
Total mortality						
Cases	914	705	583	523	595	...
HRR[a]	1.00	0.76	0.65	0.55	0.64	<.0001
95% CI	...	0.69, 0.84	0.58, 0.72	0.49, 0.61	0.57, 0.71	...
Adjusted HRR[b]	1.00	0.95	0.87	0.81	0.86	.005
95% CI	...	0.85, 1.06	0.78, 0.98	0.72, 0.91	0.76, 0.97	...
All cancer						
Cases	405	298	266	256	282	...
HRR[a]	1.00	0.73	0.68	0.63	0.70	.0002
95% CI	...	0.63, 0.85	0.58, 0.79	0.53, 0.73	0.60, 0.82	...
Adjusted HRR[b]	1.00	0.85	0.84	0.83	0.89	.34
95% CI	...	0.72, 1.00	0.71, 0.99	0.70, 0.99	0.75, 1.05	...
All cardiovascular disease						
Cases	304	242	197	164	190	...
HRR[a]	1.00	0.79	0.65	0.51	0.61	<.0001
95% CI	...	0.66, 0.93	0.55, 0.78	0.42, 0.62	0.51, 0.74	...
Adjusted HRR[b]	1.00	1.01	0.85	0.78	0.82	.02
95% CI	...	0.84, 1.21	0.70, 1.04	0.63, 0.97	0.66, 1.01	...
All noncancer/noncardiovascular disease						
Cases	205	165	120	103	123	...
HRR[a]	1.00	0.79	0.58	0.46	0.54	<.0001
95% CI	...	0.64, 0.97	0.46, 0.72	0.36, 0.58	0.43, 0.68	...
Adjusted HRR[b]	1.00	1.07	0.96	0.81	0.86	.09
95% CI	...	0.85, 1.34	0.75, 1.23	0.62, 1.05	0.67, 1.12	...
Coronary heart disease						
Cases	190	163	121	87	121	...
HRR[a]	1.00	0.85	0.64	0.44	0.63	.0001
95% CI	...	0.69, 1.05	0.51, 0.81	0.34, 0.56	0.50, 0.79	...
Adjusted HRR[b]	1.00	1.03	0.86	0.70	0.82	.03
95% CI	...	0.81, 1.30	0.67, 1.11	0.53, 0.93	0.63, 1.06	...
Stroke						
Cases	38	33	36	29	29	...
HRR[a]	1.00	0.85	0.92	0.68	0.68	.09
95% CI	...	0.53, 1.35	0.59, 1.46	0.42, 1.11	0.41, 1.11	...
Adjusted HRR[b]	1.00	1.12	1.08	0.86	0.87	.38
95% CI	...	0.69, 1.82	0.66, 1.79	0.50, 1.47	0.52, 1.48	...
Other cardiovascular disease						
Cases	76	46	40	48	40	...
HRR[a]	1.00	0.60	0.54	0.63	0.55	.03
95% CI	...	0.42, 0.87	0.37, 0.80	0.44, 0.91	0.37, 0.82	...
Adjusted HRR[b]	1.00	0.90	0.71	0.94	0.80	.52
95% CI	...	0.61, 1.32	0.46, 1.10	0.62, 1.43	0.52, 1.24	...
Nonmalignant respiratory disease						
Cases	105	48	46	31	47	...
HRR[a]	1.00	0.44	0.42	0.26	0.37	<.0001
95% CI	...	0.32, 0.62	0.30, 0.60	0.17, 0.38	0.26, 0.52	...
Adjusted HRR[b]	1.00	0.65	0.85	0.59	0.76	.26
95% CI	...	0.44, 0.95	0.58, 1.25	0.38, 0.92	0.51, 1.12	...
Accidents and injuries						
Cases	18	20	13	14	14	...
HRR[a]	1.00	1.09	0.73	0.74	0.73	.29
95% CI	...	0.58, 2.06	0.36, 1.49	0.36, 1.49	0.36, 1.50	...
Adjusted HRR[b]	1.00	1.32	0.87	0.86	0.99	.73
95% CI	...	0.66, 2.62	0.40, 1.89	0.39, 1.90	0.45, 2.14	...
Other noncancer/noncardiovascular disease						
Cases	82	97	61	58	62	...
HRR[a]	1.00	1.17	0.75	0.67	0.74	.01
95% CI	...	0.87, 1.56	0.54, 1.05	0.48, 0.95	0.53, 1.04	...
Adjusted HRR[b]	1.00	1.48	1.14	1.06	1.02	.09
95% CI	...	1.07, 2.06	0.80, 1.64	0.73, 1.55	0.70, 1.50	...

Note. HRR = hazard rate ratio; CI = confidence interval.

[a]Proportional hazards regression model (n = 38 740) adjusted for age (years) and total energy intake (kcal).

[b]Proportional hazards regression model (n = 34 333) adjusted for age, total energy intake, educational attainment, marital status, high blood pressure, diabetes, heart disease, cancer, body mass index, waist-to-hip ratio, age at first childbirth, physical activity, pack-years of cigarette smoking, alcohol intake, use of vitamin supplements, estrogen replacement therapy use, total fat, saturated fat, intake of fruits and vegetables, intake of red meat, and intake of fish and seafood.

TABLE 4—Multivariate-Adjusted Hazard Rate Ratios Across Quintiles of Refined Grain Intake for Various Causes of Death in Iowa Women

	Quintile of Refined Grain Intake					
	1	2	3	4	5	*P* for Trend
Person-years	63 881	68 084	66 058	68 299	66 683	. . .
Total mortality						
Cases	635	665	601	675	744	. . .
HRR[a]	1.00	0.98	0.91	0.98	1.10	.04
95% CI	. . .	0.88, 1.09	0.81, 1.01	0.87, 1.10	0.98, 1.25	. . .
Adjusted HRR[b]	1.00	1.07	1.04	1.09	1.16	.04
95% CI	. . .	0.95, 1.21	0.92, 1.18	0.97, 1.24	1.01, 1.33	. . .
All cancer						
Cases	268	297	292	318	332	. . .
HRR[a]	1.00	1.05	1.07	1.14	1.24	.01
95% CI	. . .	0.89, 1.24	0.90, 1.26	0.96, 1.35	1.03, 1.49	. . .
Adjusted HRR[b]	1.00	1.06	1.08	1.16	1.15	.15
95% CI	. . .	0.89, 1.27	0.90, 1.30	0.96, 1.39	0.94, 1.41	. . .
All cardiovascular disease						
Cases	236	230	197	202	232	. . .
HRR[a]	1.00	0.91	0.79	0.78	0.91	.42
95% CI	. . .	0.76, 1.09	0.65, 0.96	0.64, 0.95	0.74, 1.12	. . .
Adjusted HRR[b]	1.00	1.08	1.03	0.96	1.09	.70
95% CI	. . .	0.88, 1.32	0.83, 1.27	0.77, 1.20	0.86, 1.39	. . .
All noncancer/noncardiovascular disease						
Cases	131	138	112	155	180	. . .
HRR[a]	1.00	0.97	0.79	1.03	1.17	.08
95% CI	. . .	0.76, 1.23	0.61, 1.02	0.81, 1.31	0.91, 1.52	. . .
Adjusted HRR[b]	1.00	1.10	0.96	1.20	1.32	.04
95% CI	. . .	0.84, 1.43	0.72, 1.28	0.91, 1.57	0.98, 1.76	. . .
Coronary heart disease						
Cases	138	136	131	134	143	. . .
HRR[a]	1.00	0.93	0.91	0.91	1.00	.86
95% CI	. . .	0.73, 1.18	0.72, 1.17	0.71, 1.16	0.77, 1.31	. . .
Adjusted HRR[b]	1.00	1.04	1.20	1.12	1.15	.43
95% CI	. . .	0.80, 1.36	0.92, 1.57	0.85, 1.48	0.84, 1.56	. . .
Stroke						
Cases	29	48	24	25	39	. . .
HRR[a]	1.00	1.47	0.71	0.67	0.96	.36
95% CI	. . .	0.92, 2.33	0.41, 1.24	0.39, 1.17	0.56, 1.66	. . .
Adjusted HRR[b]	1.00	1.96	1.02	0.92	1.33	.99
95% CI	. . .	1.19, 3.22	0.57, 1.84	0.50, 1.69	0.73, 2.44	. . .
Other cardiovascular disease						
Cases	69	46	42	43	50	. . .
HRR[a]	1.00	0.63	0.59	0.59	0.71	.33
95% CI	. . .	0.43, 0.91	0.40, 0.87	0.39, 0.88	0.47, 1.08	. . .
Adjusted HRR[b]	1.00	0.76	0.70	0.67	0.90	.88
95% CI	. . .	0.50, 1.14	0.45, 1.09	0.43, 1.06	0.56, 1.45	. . .
Nonmalignant respiratory disease						
Cases	51	39	41	63	83	. . .
HRR[a]	1.00	0.69	0.71	1.00	1.24	.03
95% CI	. . .	0.45, 1.04	0.47, 1.08	0.68-1.48	0.83, 1.85	. . .
Adjusted HRR[b]	1.00	0.72	0.86	1.21	1.28	.05
95% CI	. . .	0.44, 1.17	0.53, 1.39	0.78, 1.88	0.80, 2.03	. . .
Accidents and injuries						
Cases	12	18	16	17	16	. . .
HRR[a]	1.00	1.36	1.22	1.20	1.09	.96
95% CI	. . .	0.65, 2.84	0.57, 2.60	0.56, 2.61	0.47, 2.53	. . .
Adjusted HRR[b]	1.00	1.30	1.20	1.28	1.41	.52
95% CI	. . .	0.61, 2.78	0.53, 2.68	0.56, 2.94	0.57, 3.50	. . .
Other noncancer/noncardiovascular disease						
Cases	68	81	55	75	81	. . .
HRR[a]	1.00	1.12	0.77	1.02	1.13	.49
95% CI	. . .	0.81, 1.55	0.54, 1.11	0.72, 1.44	0.78, 1.63	. . .
Adjusted HRR[b]	1.00	1.33	0.98	1.15	1.31	.34
95% CI	. . .	0.94, 1.88	0.66, 1.45	0.78, 1.69	0.87, 1.99	. . .

Note. HRR = hazard rate ratio; CI = confidence interval.

[a]Proportional hazards regression model (n = 38 740) adjusted for age (years) and total energy intake (kcal).

[b]Proportional hazards regression model (n = 34 333) adjusted for age, total energy intake, educational attainment, marital status, high blood pressure, diabetes, heart disease, cancer, body mass index, waist-to-hip ratio, age at first childbirth, physical activity, pack-years of cigarette smoking, alcohol intake, use of vitamin supplements, estrogen replacement therapy use, total fat, saturated fat, intake of fruits and vegetables, intake of red meat, and intake of fish and seafood.

TABLE 5—Changes in Percentage of Food Energy Contributed From Major Food Groups, According to US Department of Agriculture Food Disappearance Data From Different Time Periods

Food Group	Food Energy, %		
	1909–1919	1972	1990
Meat	13.9	18.8	12.9
Poultry	1.0	2.7	3.8
Fish	0.6	0.8	0.7
Whole milk	5.2	4.8	1.9
Low-fat milk	0.8	1.0	2.1
Cheese	0.6	1.9	3.0
Other dairy	2.1	2.5	2.5
Eggs	1.8	1.9	1.3
Legumes, nuts, and soy	2.4	2.8	2.8
Sugars and sweeteners	12.8	17.7	17.9
Citrus fruit	0.2	1.0	0.8
Noncitrus fruit	2.8	2.0	2.3
White potatoes	4.0	2.6	2.4
Dark green, deep yellow vegetables	0.9	0.4	0.3
Other vegetables	1.7	2.1	1.8
Table spreads	5.1	4.3	3.8
Shortening	3.1	5.8	6.7
Lard and beef tallow	3.8	1.2	0.9
Other fats and oils	0.7	6.2	7.6
Miscellaneous	0.5	1.1	1.2
Grain products (whole or refined)	36.2	18.5	23.3
Whole grain products	. . .[a]	0.5	1.4

Note. All data were derived from Table 41 of Putnam and Allshouse,[3] except those for the whole grain products food group; data for the latter were also derived from S. Gerrior (written communication, January 1997).
[a]Not available.

prevalent disease had altered their diet. The corresponding increase in death rates associated with high intake of refined grains barely achieved statistical significance and was not seen for cardiovascular diseases. This may reflect reduced red meat intake in those who eat more grains, regardless of whether the grains are whole or refined.

The approximately 40% reduced death rates in analyses controlling for age and energy intake were partially explained by adjustment for demographic factors, healthy behaviors, body size, and prevalent disease, with about a 15% reduction remaining in those who ate whole grain foods every day vs those who rarely or never ate whole grain foods. It is plausible that greater whole grain intake may decrease body weight, diabetes, CHD, and cancer, thereby masking the association of whole grain with total mortality. Analyses that adjusted for demographic and other behavioral variables but not for body weight or prevalent disease showed a risk reduction of about 25%.

An important issue is whether increased intake of whole grain in women already regularly consuming whole grain food would be beneficial. On the one hand, benefit is suggested because abundant nutrients are contained in a natural combination in whole grains, and several servings per day do not appear to provide these nutrients in excess. On the other hand, hazard rate ratios were observed to be relatively constant for quintiles 3 to 5 of whole grain intake in this study; we do not know whether this reflects an artifact such as unreliability in the questionnaire or a true threshold effect.

These findings support our a priori hypothesis of reduced total mortality in those who are regular eaters of whole grain foods. Reviews[6,7] of 40 case–control studies of whole grain intake investigating 20 different cancers found consistently reduced risk in high vs low consumers of whole grain foods. The earlier review[6] suggested the opposite for refined grain foods, with consistently increased cancer risks in published case–control studies of individuals with high vs low intakes of refined grain. Most[8,15,16] but not all[17] studies have found reduced risk of CHD in those with high intakes of whole grain. One randomized clinical trial of secondary prevention in survivors of myocardial infarction followed for 2 years produced ambiguous results, in that total mortality was increased in those who were advised to eat more whole grain but reduced in those who were also advised to reduce fat intake and increase fish intake.[18,19] Feeding studies have established that intake of whole oats or corn reduces serum cholesterol[20,21] and that whole grain intake contributes to blood pressure reduction.[22,23]

Plausible mechanisms exist for whole grains to influence health through multiple pathways (e.g., those involving antioxidants, minerals, and phytoestrogens).[1,2,24–34] Conversely, refined grains would be more likely to influence health through effects on insulin metabolism.[35,36] Further investigation of the effect of refined grain on health is needed, particularly studies addressing whether refined grains whose consumption results in a low glycemic response[35,36] have a different effect on health than those that result in a high glycemic response.

A limitation of epidemiologic studies of diet is that dietary measures are highly variable; thus, our hazard rate ratio estimate is probably attenuated. A source of potential misspecification was our assignment of grains into whole and refined categories. The food frequency questionnaire used in this study had limited ability to distinguish between whole and refined grain. Since this study was observational and not randomized, selection bias in responders to an unsolicited survey and residual confounding also cannot be ruled out. Strengths of this study are that it was longitudinal, allowed quantitative estimation of whole and refined grain intake, and included careful adjustment for many potentially confounding factors.

The US scientific community has, in recent years, promulgated a message to reduce saturated fat and cholesterol and increase consumption of fruits and vegetables.[4,5] However, although food disappearance data suggest many positive changes in the US diet since the early 1900s (Table 5), the largest change in terms of contribution to energy intake has been reduced total grain intake, which constituted 36% of energy in 1909 to 1919, declined to 18% in 1972, and increased to 23% in 1990.[3] It appears that the American public has reduced its intake of saturated fat, cholesterol, vegetables, and total grain in favor of food sources rich in unsaturated fats and sugars.

Although data are readily available to estimate total grain intake patterns, the US Department of Agriculture does not routinely collect data on refined vs whole grains. A variety of food disappearance source material was used to piece together the following description of grain intake (S. Gerrior, written communication, January 1997)[3,14,37]: The per capita availability of grains in the United States was estimated to be 291 lb (131 kg) per year in 1909 to 1913, decreasing to 135 lb per year (77% wheat) in 1970 to 1974, and then increasing to 199 lb per year (65% wheat) in 1994.[3] Estimates for whole wheat intake were available only for whole wheat flour: the per capita intake of 2.1 lb per year in 1954 declined steadily to 0.8 lb per year in

1972; since then (particularly from 1983 to the present), it has increased (to 2.3 lb per year) (S. Gerrior, written communication, January 1997). Using a 1919 US Department of Agriculture report,[14] we estimated that about 8 to 10 lb per year of whole wheat flour were consumed in the early 1900s. Estimated annual consumption of oats (based on food disappearance data) from 1962 to 1986 was about 3 to 5 lb, increasing to 9.2 lb in 1994.[3] We could find no information on other whole grains, such as rye. Thus, although records separating intake of whole and refined grain are sparse, it appears that there have been major reductions in whole grain intake, to 1% of energy intake or less in recent years. (The energy intake from whole grains in the Iowa women appeared to be greater than suggested by the food disappearance data. However, the food frequency data are likely to overstate actual whole grain intake, because many breads that may be taken to be whole grain [e.g.,"multigrain"] actually contain a predominance of refined flour.)

Amid substantial attention to the health effects of saturated fat and cholesterol, little public attention has been drawn to the importance of whole vs refined grains. This is not because the scientific community questions the benefit of whole grains. The popular and scientific belief that something of nutritional importance is lost in the refining process is underscored by the fact that refined flour products are enriched with several micronutrients. Nevertheless, whole grain continues to constitute a small proportion of most US diets. Grain fortification illustrates the current scientific emphasis on constituent nutrients rather than whole foods. Yet nutrients may act synergistically, and study of individual food constituents may mask the total health effect of whole grains.[1,2,38]

The US Department of Agriculture dietary guidelines for Americans recommend 6 to 11 daily servings of grain products, including "several servings of whole grain breads and cereals."[4] Although this guideline recognizes the importance of whole grain consumption, it also encourages intake of a substantial amount of refined grain. It would be relatively simple for individuals and the food industry to substitute fairly large quantities of whole grain for refined grain in the diet.

Given the consistency of epidemiologic evidence and plausible biological mechanisms, we calculated risk of total mortality attributable to increased consumption of whole grains. The total mortality rate in 9 years was observed to be about 8% in women who ate at least 1 serving per day of whole grain foods. A 15% risk reduction implies a death rate of 9.4% in the 50% of women who do not consume this much whole grain, an attributable risk of 8% (computed as 50% × (9.4% − 8%)/8%); a 25% risk reduction would imply a 10.6% death rate in the 50% of women who do not eat 1 or more servings per day, an attributable risk of 14%. This calculation suggests that if all women consumed at least 1 serving per day of whole grain foods, total mortality rates might be reduced, through a variety of mechanisms, by 8% or more. A specific clinical trial addressing these issues is desirable.

In support of our a priori hypothesis, daily or more frequent intake of whole grain foods was inversely related to total mortality in our data. However, whole grains represent only 1% of total energy consumed, according to US Department of Agriculture food disappearance data (S. Gerrior, written communication, January 1997).[3] We believe that these findings on whole grain intake have important public health implications; namely, it would be prudent for the general population to increase its whole grain intake. □

Contributors

D. R. Jacobs, Jr, and K. Meyer formulated the hypothesis and analyzed the data. L. H. Kushi and A. R. Folsom collected the data. All 4 authors wrote the report and are guarantors for the integrity of the study.

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