Whole grains and incident hypertension in men[1–3]

Alan J Flint, Frank B Hu, Robert J Glynn, Majken K Jensen, Mary Franz, Laura Sampson, and Eric B Rimm

ABSTRACT

Background: Prospective data on the relation between whole grain intake and incident hypertension in men are limited, and no previous studies have quantitatively estimated total grams of whole grains in relation to risk of hypertension.

Objective: The purpose of this study was to estimate the association of whole-grain intake (g/d) and risk of incident hypertension in a large prospective cohort of men.

Design: The Health Professionals Follow-Up Study is a prospective cohort consisting of 51,529 male health professionals ranging in age from 40 to 75 y at enrollment in 1986. Baseline and updated measurement of whole-grain intake as well as important covariates were measured, and 31,684 participants without known hypertension, cancer, stroke, or coronary heart disease were followed prospectively for 18 y through 2004 for onset of hypertension.

Results: A total of 9227 cases of incident hypertension were reported over the 18 y of follow-up. In multivariate-adjusted analyses, whole-grain intake was inversely associated with risk of hypertension, with a relative risk (RR) of 0.81 (95% CI: 0.75–0.87) in the highest compared with the lowest quintile (*P* for trend < 0.0001). In the multivariate model, total bran was inversely associated with hypertension, with a relative risk (RR) of 0.85 (95% CI: 0.78, 0.92) in the highest compared with the lowest quintile (*P* for trend: 0.002).

Conclusions: In summary, we found an independent inverse association between intake of whole grains and incident hypertension in men. Bran may play an important role in this association. These findings have implications for future dietary guidelines and prevention of hypertension. *Am J Clin Nutr* 2009;90:493–8.

INTRODUCTION

Hypertension remains a major cause of morbidity among men and is particularly important as a contributing factor in the development of coronary heart disease, stroke, and renal failure (1–5). Recent studies have suggested an inverse relation between daily servings of whole-grain foods and incident hypertension among women (6). Prospective data on the relation between whole-grain intake and incident hypertension among men are limited, and, to our knowledge, no previous studies have quantitatively estimated total grams of whole grains in relation to risk of hypertension.

In contrast with refined grains, in which only the starchy endosperm is retained, whole grains contain the bran and germ components, thus providing a wider range of nutrients with potential health benefits, including potassium, magnesium, folate, carbohydrates, cereal fiber and other compounds in smaller quantities.

The most recent (2005) *Dietary Guidelines for Americans* (7) recommend the consumption of ≥3 oz equivalents (85 g) of whole-grain products per day and that ≥50% of grains be consumed as whole grains. Increasingly, food manufacturers' product labels have listed the whole-grain content for relevant foods. It is now both advisable and feasible to make dietary assessments of whole-grain intake in epidemiologic studies on a gram weight basis. In previous analyses of prospective cohorts, measurement of whole-grain intake has been limited to summing servings of specific foods, selected for their relatively high whole-grain content. We developed a new food-composition database, allowing estimation of whole-grain intake in g/d from all foods.

SUBJECTS AND METHODS

Study population

The Health Professionals Follow-up Study (HPFS) is a prospective cohort of 51,529 male health professionals ranging in age from 40 to 75 y at enrollment in 1986. The cohort of 29,683 dentists, 3745 optometrists, 2218 osteopaths, 4185 pharmacists, 1600 podiatrists, and 10,098 veterinarians completed a baseline mailed survey of detailed information about medical history, dietary intake, lifestyle, and demographic information in 1986. Every 2 y subsequently, follow-up questionnaires were completed that contained information on interim medical history and updated lifestyle characteristics. Detailed dietary intake, assessed with a semiquantitative food-frequency questionnaire (FFQ) (8, 9) was collected at baseline in 1986 and every 4 y subsequently. For these analyses we excluded participants with *1*) prevalent cancer, stroke, or coronary heart disease at baseline; *2*) a diagnosis of hypertension at baseline; and *3*) missing diet information. After these exclusions, 31,684 men were eligible. The procedures followed

[1] From the Departments of Epidemiology (AJF, FBH, and EBR), Nutrition (AJF, FBH, MKJ, MF, LS, and EBR), and Biostatistics (RJG), Harvard School of Public Health, Boston, MA, and Channing Laboratory (FBH and EBR) and the Division of Preventive Medicine (RJG), Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

[2] Supported by National Institutes of Health grants CA 55075 and HL35464.

[3] Address correspondence to AJ Flint, Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115. E-mail: aflint@hsph.harvard.edu.

Received January 3, 2009. Accepted for publication June 3, 2009.

First published online July 1, 2009; doi: 10.3945/ajcn.2009.27460.

were in accordance with the ethical standards of the Institutional Review Board of the Harvard School of Public Health.

Exposure measurement

Information on whole-grain intake and other dietary measures was collected with a validated semiquantitative FFQ (8, 9). Briefly, the FFQ was designed to assess average food intakes over the previous year and included questions regarding the consumption of grain foods such as white and dark bread, cooked white and brown rice, and cold breakfast cereals and pasta. The nutrient composition database was updated with each FFQ cycle to reflect the foods sold in that time period, thus capturing secular trends in food availability and composition. The new food-composition database, which allowed estimation of whole-grain intake in g/d, is described in detail elsewhere (10, 11). In brief, intakes of whole grains, bran, and germ were calculated by determining the whole-grain content of each grain food according to the dry weight of its whole-grain ingredients. Nutrient profiles of the various grain foods were derived by using composite recipes, US Department of Agriculture nutrient data, and product labels, whereas cookbooks were used to estimate contents of home-prepared bakery items. Whole grains were considered by definition to contain the expected proportion of bran, endosperm, and germ for the specific grain type. *Natural*, as applied here to bran and germ, refers to that quantity of each typically naturally occurring in each grain type. *Added* bran or germ is that quantity of each contained in the food, as assessed by manufacturer label or other information sources, in excess of that naturally occurring. *Added* also includes that amount from specific responses on the FFQ, where men reported average intake of bran or wheat germ that they added to other foods. Total bran and total germ are the sum of naturally occurring and added components. Intakes were categorized into quintiles by using the cumulative average update (average of all past measures) method (9, 12–14). Simple update intakes were defined as those reported on the most recent FFQ.

Outcome measurement

Incident hypertension was self reported, based on each biennial questionnaire. Each participant was asked to report if he has “had any of the following professionally diagnosed illnesses,” with the first response item being “high blood pressure.” The calendar year of diagnosis was recorded and used to estimate a time to event month assignment for the purposes of survival analysis, based on the month of questionnaire return. Self report of hypertension was previously validated in this cohort (15, 16).

Covariates

Information on potential confounding factors, including medical history, food, and nutrient intake, and lifestyle behaviors that could influence the relation between whole-grain intake and hypertension were gathered from the 1986 baseline and updated on subsequent follow-up surveys by using validated measures (16). Family history of coronary heart disease was reported on the 1986 questionnaire and was considered positive for myocardial infarction occurring in either parent before age 60 y. Family history of hypertension in a sibling or parent was also recorded. Cigarette smoking status was based on the baseline survey and subsequent updates and was categorized as current, former, or never. In the multivariate models, the current smokers were further classified according to 3 categories of daily cigarette dose.

Information on dietary intake of total energy, fruit, vegetables, alcohol, potassium, magnesium, total fiber, folate, and cereal fiber were derived from a semiquantitative FFQ (8) completed at baseline (1986) and at 4-y intervals (1990, 1994, 1998, and 2002) during follow-up.

Height and weight were self-reported at baseline, and weight was updated from follow-up questionnaire responses. Body mass index (BMI) was calculated as weight (kg)/height^2 (m). In studies of validity of self-report by men and women in the HPFS and other samples, the correlations between self-reported height and weight and direct measurements have been high ($r > 0.9$) (17). BMI (in kg/m^2) was divided into categories of 18.5–22.9, 23.0–24.9, 25.0–29.9, and $\geq$30. Participants reported their physical activity level on each questionnaire by indicating the number of hours per week spent in specific activities in the preceding year, a measure that was previously validated (18). Total hours per week spent in moderate-to-vigorous activity was calculated and categorized in quintiles.

Statistical analysis

Cox proportional hazard regression was used to model the relation between time-varying whole-grain intake and incident hypertension (19). All analyses were adjusted for age and total energy intake. Potential confounding factors were considered a priori on the basis of known risk factors for hypertension.

In addition to multivariate models, exploratory models were run separately with the use of additional terms for whole-grain constituents, specifically naturally occurring and added bran and naturally occurring and added germ, potassium, magnesium, total fiber, folate, and cereal fiber.

The assumption of proportional hazards was tested formally by introducing an interaction term for time by exposure and assessing the contribution of this interaction to each final model with a likelihood ratio test. All analyses were conducted by using SAS 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

A total of 9227 cases of incident hypertension among the 31,684 men were reported over the 18 y of follow-up. The participants’ baseline characteristics and mean energy-adjusted intakes by quintile of whole-grain intake are shown in **Table 1**.

We used the cumulative average update method to assign participants to quintiles of whole-grain intake during follow-up and calculated the relative risks (RRs) and 95% CIs for incident hypertension (**Table 2**). Results derived by using the simple update method were not substantially different (data not shown). In the age- and energy-adjusted analyses, the RR decreased by quintile of whole grains to a minimum of 0.72 (95% CI: 0.67, 0.77) in the highest compared with the lowest quintile of intake. The inverse association persisted, although moderately attenuated (RR: 0.81; 95% CI: 0.75, 0.87), after multivariate adjustment for potential confounding factors (*see* Table 2 footnote). The test for inverse linear trend was still strongly significant.

BMI was not included in the main multivariate model because weight was presumed to play a role in the causal pathway by

TABLE 1

Baseline characteristics and mean energy-adjusted intakes by quintile of whole-grain intake in 31,684 men: Health Professionals Follow-Up Study, 1986[1]

	Quintile of whole-grain intake				
	1	2	3	4	5
Median intake (g/d)[2]	3.3	9.8	17.1	26.9	46.0
	(0–6.5)	(6.6–13.2)	(13.3–21.4)	(21.5–34.2)	(34.3–326.4)
Age (y)	52.5 ± 9.3[3]	51.9 ± 9.2	52.4 ± 9.2	53.0 ± 9.4	53.7 ± 9.7
Current smoking (%)	16.0	11.3	7.6	5.3	3.7
BMI (kg/m^2)	25.5 ± 3.0	25.5 ± 3.1	25.4 ± 3.1	25.1 ± 2.9	24.6 ± 2.8
Family history of hypertension (%)	24.2	25.7	25.3	24.8	27.0
Family history of myocardial infarction (%)	11.6	11.8	11.6	11.1	11.4
Nutrient intake					
Total energy (kcal/d)	1996 ± 648	2050 ± 646	2075 ± 643	2031 ± 595	1876 ± 554
Whole grains (g/d)	3.2 ± 2.0	9.8 ± 1.9	17.1 ± 2.4	27.2 ± 3.7	52.4 ± 21.5
Naturally occurring bran (g/d)	0.37 ± 0.33	1.13 ± 0.56	2.06 ± 1.00	3.41 ± 1.62	6.64 ± 4.26
Naturally occurring germ (g/d)	0.15 ± 0.13	0.39 ± 0.21	0.62 ± 0.30	0.92 ± 0.44	1.80 ± 1.40
Added bran (g/d)	0.13 ± 0.48	0.62 ± 1.61	1.81 ± 3.43	3.11 ± 4.99	5.12 ± 11.32
Added germ (g/d)	0.07 ± 0.28	0.15 ± 0.56	0.25 ± 0.80	0.44 ± 1.51	0.97 ± 3.13
Cereal fiber (g/d)	3.0 ± 1.2	3.9 ± 1.3	5.3 ± 1.7	7.0 ± 2.3	10.5 ± 5.9
Total fiber (g/d)	16.3 ± 4.9	18.2 ± 4.9	20.1 ± 5.2	22.5 ± 5.6	27.2 ± 8.2
Folate (μg/d)	395 ± 230	430 ± 247	472 ± 259	516 ± 273	575 ± 316
Total carbohydrate (g/d)	218 ± 43	224 ± 38	231 ± 36	241 ± 36	262 ± 41
Total sugar (g/d)	105 ± 39	105 ± 34	107 ± 32	109 ± 31	109 ± 32
Saturated fat (g/d)	27.4 ± 6.4	26.4 ± 5.6	25.2 ± 5.4	23.8 ± 5.2	20.9 ± 5.7
Polyunsaturated fat (g/d)	13.1 ± 3.7	13.4 ± 3.4	13.4 ± 3.4	13.2 ± 3.3	13.0 ± 3.5
trans Fat (g/d)	3.19 ± 1.22	3.06 ± 1.08	2.94 ± 1.06	2.75 ± 1.03	2.33 ± 1.06
Glycemic load per day	115 ± 49	122 ± 48	127 ± 48	130 ± 46	132 ± 48
Sodium (mg/d)	3322 ± 1217	3353 ± 1154	3290 ± 1064	3283 ± 1049	3177 ± 1077
Potassium (mg/d)	3106 ± 626	3222 ± 601	3341 ± 600	3464 ± 599	3631 ± 659
Magnesium (mg/d)	295 ± 59	313 ± 53.9	335 ± 55.3	357 ± 56.7	406 ± 79.8
Vitamin E (mg/d)	36.9 ± 78.1	40.9 ± 82.1	47.0 ± 87.5	52.1 ± 90.3	67.3 ± 107.6
Food intake					
Fruit (servings/d)	2.0 ± 1.6	2.2 ± 1.6	2.4 ± 1.6	2.6 ± 1.6	2.8 ± 1.8
Vegetables (servings/d)	2.8 ± 1.6	3.2 ± 1.6	3.3 ± 1.7	3.4 ± 1.8	3.5 ± 2.0

[1] For all continuous variables, P for trend < 0.0001.

[2] Ranges in parentheses.

[3] Mean ± SD (all such values).

which whole-grain intake might affect risk of hypertension. In exploratory models, the addition of updated BMI resulted in moderate attenuation of the inverse association (RR: 0.87; 95% CI: 0.81, 0.93) for the highest quintile of whole grains.

In further exploratory analyses, constituents of whole grains—specifically naturally occurring bran, added bran, naturally occurring germ, added germ, potassium, magnesium, total fiber, folate, and cereal fiber—were introduced individually to the

TABLE 2

Relative risks (RRs) and 95% CIs of incident hypertension in 31,684 men by quintile of whole-grain intake: Health Professionals Follow-Up Study, 1986–2004[1]

	Quintile of whole-grain intake					
	1	2	3	4	5	*P* for trend
Median intake (g/d)[2]	3.3	9.8	17.1	26.9	46.0	—
	(0–6.5)	(6.6–13.2)	(13.3–21.4)	(21.5–34.2)	(34.3–326.4)	
No. of cases	1826	1917	1922	1914	1648	—
Person-years	61,137	68,966	72,196	73,184	69,877	—
Age- and energy-adjusted RR[3]	1.00	0.90	0.83	0.81	0.72	<0.0001
		(0.84, 0.96)	(0.78, 0.89)	(0.76, 0.87)	(0.67, 0.77)	
Multivariate-adjusted RR[3,4]	1.00	0.94	0.89	0.89	0.81	<0.0001
		(0.88, 1.01)	(0.83, 0.95)	(0.84, 0.96)	(0.75, 0.87)	

[1] RRs derived from proportional hazards models.

[2] Ranges in parentheses.

[3] 95% CIs in parentheses.

[4] Adjusted for age, energy, family history of coronary heart disease, family history of hypertension, smoking, alcohol, marital status, profession, height, fruit and vegetable intakes, sodium intake, physical activity, multivitamin use, and cholesterol screening.

TABLE 3
Relative risks (RRs) and 95% CIs of incident hypertension in 31,684 men by quintile of total bran intake: Health Professionals Follow-Up Study, 1986–2004[1]

	Quintile of bran intake					
	1	2	3	4	5	*P* for trend
Median intake (g/d)[2]	0.3 (0–0.7)	1.3 (0.8–1.9)	2.8 (2.0–3.8)	5.5 (3.9–7.8)	12.0 (7.9–236.8)	—
No. of cases	1839	1988	1869	1845	1686	—
Person-years	62,258	71,499	72,080	71,933	67,590	—
Age- and energy-adjusted RR[3]	1.00	0.91 (0.85, 0.97)	0.81 (0.76, 0.87)	0.78 (0.73, 0.84)	0.76 (0.71, 0.81)	$<$0.0001
Multivariate-adjusted RR[3,4]	1.00	0.95 (0.88, 1.02)	0.88 (0.81, 0.94)	0.87 (0.80, 0.94)	0.85 (0.78, 0.92)	0.002

[1] RRs derived from proportional hazards models.
[2] Ranges in parentheses.
[3] 95% CIs in parentheses.
[4] Adjusted for age, energy, family history of coronary heart disease, family history of hypertension, smoking, alcohol, marital status, profession, height, fruit and vegetable intakes, sodium intake, physical activity, multivitamin use, and cholesterol screening.

multivariate model. Only cereal fiber substantially attenuated the whole grain–hypertension effect. Adding cereal fiber to the model resulted in an RR of 0.94 (95% CI: 0.84, 1.05) for the highest quintile of whole grains (*P* for trend of 0.23). Total fiber (sum of fiber from cereal, fruit, and vegetable sources) had a lesser attenuating effect, with the whole-grain RR and trend test remaining significant. Of note, ≈64% of dietary intake of cereal fiber was in the form of whole-grain foods on the baseline 1986 FFQ. The addition of naturally occurring bran to the multivariate model resulted in an RR of 0.88 (95% CI: 0.77, 1.00; *P* for trend: 0.04) for the highest quintile of whole grains, whereas total bran (sum of naturally occurring and added bran) modestly attenuated the RR to 0.88 (95% CI: 0.79, 0.99). More than 99% of total bran intake was from whole-grain foods. Neither germ nor any of the other remaining constituents (folate, magnesium, and potassium) introduced into the multivariate model substantially attenuated the whole-grain effect.

Because bran and germ may be important constituents of whole grains, we also estimated the RRs of incident hypertension associated with intake of total bran and total germ in models without whole grains (**Tables 3** and **4**). Total bran intake was inversely associated with hypertension, with a multivariate-adjusted RR for the highest quintile of intake compared with the lowest quintile of 0.85 (95% CI: 0.78, 0.92), and the test for trend was significant. Although total germ intake appeared to be inversely associated with hypertension in the age- and energy-adjusted model, it was not significant after adjustment for potential confounders in the multivariate model.

DISCUSSION

In these analyses of whole-grain intake from a large ongoing prospective cohort study of men with >9000 incident cases of hypertension, whole grains and total bran were inversely associated with new onset of hypertension. The new measure of whole grains in grams per day allows a better quantitative understanding of these relations.

Ascherio et al (20) reported the results of a 4-y follow-up of women in the Nurses' Health Study. They found an inverse association between intake of both dark bread and dietary fiber

TABLE 4
Relative risks (RRs) and 95% CIs of incident hypertension in 31,684 men by quintile of total germ intake: Health Professionals Follow-Up Study, 1986–2004[1]

	Quintile of germ intake					
	1	2	3	4	5	*P* for trend
Median intake (g/d)[2]	0.1 (0–0.2)	0.4 (0.3–0.5)	0.7 (0.6–0.8)	1.1 (0.9–1.5)	2.4 (1.6–58.6)	—
No. of cases	1772	1965	1875	1912	1703	—
Person-years	60,986	71,150	68,236	74,442	70,546	—
Age- and energy-adjusted RR[3]	1.00	0.93 (0.87, 1.00)	0.89 (0.83, 0.95)	0.84 (0.79, 0.90)	0.78 (0.73, 0.84)	$<$0.0001
Multivariate-adjusted RR[3,4]	1.00	1.02 (0.95, 1.09)	1.02 (0.93, 1.08)	1.00 (0.93, 1.08)	0.96 (0.88, 1.04)	0.11

[1] RRs derived from proportional hazards models.
[2] Ranges in parentheses.
[3] 95% CIs in parentheses.
[4] Adjusted for age, energy, family history of coronary heart disease, family history of hypertension, smoking, alcohol, marital status, profession, height, fruit and vegetable intakes, sodium intake, physical activity, multivitamin use, and cholesterol screening.

and incident hypertension, with 2526 cases reported. Steffen et al (21) reported findings based on a cohort of 4304 men and women over a 15-y follow-up in the CARDIA (Coronary Artery Risk Development in Young Adults) Study. Using a dietary-history measure of servings of whole grains per day, the authors reported a suggestion of an inverse association with incident hypertension (997 cases reported), with a multivariate-adjusted RR of 0.83 (95% CI: 0.67, 1.03) in the highest quintile compared with the lowest quintile. The top quintile in that study had whole-grain intakes of ≥1.9 serving/d. Most recently, Wang et al (6) reported on the 10-y follow-up of 28,926 women in the Women's Health Study, 8722 of whom developed incident hypertension. The authors found a multivariate-adjusted RR of 0.89 (95% CI: 0.82, 0.97) in the highest quintile of whole-grain intake quantified as servings per day compared with the lowest quintile of intake.

With the use of a more precise method to derive whole-grain intake on a grams per day basis, >9000 cases of incident hypertension in a large cohort of men, and 18 y of updated measures and follow-up, the current study is in a unique position to add to and expand the existing knowledge base on the relation between intake of whole grains and risk of incident hypertension. The true magnitude of the inverse association may be stronger than we estimated because of attenuation as a consequence of measurement error.

There is a growing body of evidence from both observational epidemiologic studies and randomized clinical trials that diet influences blood pressure, particularly intakes of potassium and fiber, both of which are constituent components of whole grains (15, 22). Dietary patterns such as the Dietary Approaches to Stop Hypertension (DASH) diet, which promotes greater intakes of whole grains, also have been found to lower blood pressure (23, 24). A meta-analysis restricted to trials increasing dietary fiber alone found a significant reduction in blood pressure (25). A few randomized trials have been reported that are directly relevant to whole-grains intake and the effect on blood pressure, each with between 18 and 88 human subjects and a 4–8-wk duration of dietary modification (oats or oat cereal) (26–30). Results have been mixed; some have shown a decrease in blood pressure (28–30) and others have shown no significant differences (26, 27).

We found that the inverse association between whole-grain intake and incident hypertension was independent of sodium intake as well as that of alcohol, fruit, and vegetables. The relation persisted after adjustment for physical activity, multivitamin use, and cholesterol screening, which suggests that the association was independent of these markers of a healthy lifestyle behavior pattern.

Lower weight gain over time may be a mechanism by which whole-grain intake is related to hypertension. There is a large body of evidence from both clinical trails and observational studies linking lower weight and weight loss to lower blood pressure and reduced risk of hypertension (22, 31–34). Also, we previously found in an 8-y follow-up of men in this cohort that for each 40-g/d difference in whole-grain intake, there was a relative decrease in 0.49 kg body weight (35). Thus, excess weight may play an important role in a causal pathway by which whole-grain intake influences risk of hypertension.

Several mechanisms have been suggested by which whole grains can reduce the risk of blood pressure. (36–42) These mechanisms include whole-grain effects of increased insulin sensitivity (36, 37) and improved endothelial function (38). The cereal fiber of whole grains is predominantly insoluble fiber and can act through satiety reflex mechanisms to reduce energy intake, which leads to a more favorable weight pattern over time (39, 40). Increased whole-grain intake has been found to be associated with lower postprandial blood glucose concentrations and thus a reduced risk of development of insulin resistance (41, 42). Intake of oat and wheat may diminish the vascular reactivity impairment associated with a high-fat meal (38). In individuals with hypertension, consumption of whole-grain wheat cereal has been found to be associated with improved blood pressure control and decreased doses of antihypertensive medications (30).

Our finding of an inverse association between total bran and hypertension, independent of potential confounding factors, is consistent with the reduced risk of hypertension observed with higher whole-grain intakes. However, the quantitative estimates of intake suggest that added bran is a relatively small component compared with total whole-grain and cereal fiber intakes.

In summary, we found an independent inverse association between intake of whole grains and incident hypertension during 18 y of follow-up of >33,000 men. These findings have implications for future dietary guidelines and the prevention of hypertension.

The authors' responsibilities were as follows—EBR: funding support; AJF and EBR: study concept and design; AJF, FBH, MF, LS, and EBR: data collection; AJF, RJG, and MKJ: data analysis; and RJG: statistical support. All authors contributed to the writing and editing of the manuscript. No conflicts of interest were reported.

REFERENCES

1. Vasan RS, Larson MG, Leip EP, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med 2001;345:1291–7.
2. ALLHAT Officers and Coordinators. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981–97.
3. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988 –2000. JAMA 2003;290:199–206.
4. Fields LE, Burt VL, Cutler JA, Hughes J, Roccella EJ, Sorlie P. The burden of adult hypertension in the United States 1999 to 2000: a rising tide. Hypertension 2004;44:398–404.
5. Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among US adults according to the new joint national committee guidelines: new challenges of the old problem. Arch Intern Med 2004;164:2126–34.
6. Wang L, Gaziano JM, Liu S, Manson JE, Buring JE, Sesso HD. Whole- and refined-grain intakes and the risk of hypertension in women. Am J Clin Nutr 2007;86:472–9.
7. US Department of Health and Human Services, US Department of Agriculture. Dietary guidelines for Americans, 2005. 6th ed. Washington, DC: US Government Printing Office, 2005.
8. Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992;135:1114–26.
9. Willett WC. Food frequency methods. In: Willett W, ed. Nutritional epidemiology. 2nd ed. New York, NY: Oxford University Press, 1998:74–100.
10. Jensen MK, Koh-Banerjee P, Hu FB, et al. Intakes of whole grains, bran, and germ and the risk of coronary heart disease in men. Am J Clin Nutr 2004;80:1492–9.
11. Franz M, Sampson L. Challenges in developing a whole grain database. Definitions, methods, and quantification. J Food Comp Anal 2006;19:S38–44.

12. Hu F, Stampfer M, Manson J, et al. Dietary fat intake and the risk of coronary heart disease in women. N Engl J Med 1997;337:1491–9.
13. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol 1986;124:17–27.
14. Willett W, Stampfer MJ. Implications for total energy intake for epidemiologic analyses. In: Willett W, ed. Nutritional epidemiology. 2nd ed. New York, NY: Oxford University Press, 1998:273–301.
15. Ascherio A, Rimm EB, Giovannucci EL, et al. A prospective study of nutritional factors and hypertension among US men. Circulation 1992; 86:1475–84.
16. Colditz GA, Martin P, Stampfer M. Validation of questionnaire information on risk factors and disease outcomes in a prospective study of women. Am J Epidemiol 1986;123:894–900.
17. Rimm EB, Stampfer MJ, Colditz GA. Validity of self-reported waist and hip circumferences in men and women. Epidemiology 1990;1:466–73.
18. Chasan-Taber S, Rimm EB, Stampfer MJ, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. Epidemiology 1996;7:81–6.
19. Hosmer D, Lemeshow S. Applied survival analysis. New York, NY: John Wiley & Sons, Inc, 1999.
20. Ascherio A, Hennekens C, Willett WC, et al. Prospective study of nutritional factors, blood pressure, and hypertension among US women. Hypertension 1996;27:1065–72.
21. Steffen LM, Kroenke CH, Yu X, et al. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Am J Clin Nutr 2005;82: 1169–77.
22. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM. Dietary approaches to prevent and treat hypertension: a scientific statement from the American Heart Association. Hypertension 2006;47: 296–308.
23. Sacks FM, Svetkey LP, Vollmer WM, et al., for the DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet: DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3–10.
24. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med 1997;336:1117–24.
25. He J, Whelton PK. Effect of dietary fiber and protein intake on blood pressure: a review of epidemiologic evidence. Clin Exp Hypertens 1999; 21:785–96.
26. Swain JF, Rouse IL, Curley CB, Sacks FM. Comparison of the effects of oat bran and low-fiber wheat on serum lipoprotein levels and blood pressure. N Engl J Med 1990;322:147–52.
27. Kestin M, Moss R, Clifton PM, Nestel PJ. Comparative effects of three cereal brans on plasma lipids, blood pressure, and glucose metabolism in mildly hypercholesterolemic men. Am J Clin Nutr 1990;52:661–6.
28. Saltzman E, Das SK, Lichtenstein AH, et al. An oat-containing hypocaloric diet reduces systolic blood pressure and improves lipid profile beyond effects of weight loss in men and women. J Nutr 2001;131:1465–70.
29. Keenan JM, Pins JJ, Frazel C, Moran A, Turnquist L. Oat ingestion reduces systolic and diastolic blood pressure in patients with mild or borderline hypertension: a pilot trial. J Fam Pract 2002;51:369.
30. Pins JJ, Geleva D, Leemam K, Frazer C, O'Connor PJ, Cherney LM. Do whole-grain oat cereals reduce the need for antihypertensive medications and improve blood pressure control? J Fam Pract 2002; 51:353–9.
31. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. Ann Intern Med 1998;128:81–8.
32. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. Am J Clin Nutr 2003;78:920–7.
33. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension 2003;42:878–84.
34. Whelton SP, Hyre AD, Pedersen B, Yi Y, Whelton PK, He J. Effect of dietary fiber intake on blood pressure: a meta-analysis of randomized, controlled clinical trials. J Hypertens 2005;23:475–81.
35. Koh-Banerjee P, Franz M, Sampson L, et al. Changes in whole grain, bran, and cereal fiber consumption in relation to 8-year weight gain among men. Am J Clin Nutr 2004;80:1237–45.
36. Fukagawa NK, Anderson JW, Hageman G, Young VR, Minaker KL. High-carbohydrate, high-fiber diets increase peripheral insulin sensitivity in healthy young and old adults. Am J Clin Nutr 1990;52:524–8.
37. Steffen LM, Jacobs DR, Murtaugh MA, et al. Whole grain intake is associated with lower body mass and greater insulin sensitivity among adolescents. Am J Epidemiol 2003;158:243–50.
38. Katz DL, Nawaz H, Boukhalil J, et al. Effects of oat and wheat cereals on endothelial responses. Prev Med 2001;33:476–84.
39. Porikos K, Hagamen S. Is fiber satiating? Effects of a high fiber preload on subsequent food intake of normal-weight and obese young men. Appetite 1986;7:153–62.
40. Howarth NC, Saltzman E, Roberts SB. Dietary fiber and weight regulation. Nutr Rev 2001;59:129–39.
41. Hallfrisch J, Behall KM. Mechanisms of the effects of grains on insulin and glucose responses. J Am Coll Nutr 2000;19:320S–5S.
42. Liese AD, Roach AK, Sparks KC, Marquart L, D'Agostino RB Jr, Mayer-Davis EJ. Whole-grain intake and insulin sensitivity: the Insulin Resistance Atherosclerosis Study. Am J Clin Nutr 2003;78:965–71.