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Prospective Study of Dietary Fiber, Whole Grain Foods, and Small Intestinal Cancer

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Abstract

Background & Aims—Although a number of epidemiologic studies have found dietary fiber and whole grains to be inversely associated with colorectal cancer incidence, studies of dietary and other risk factors for small intestinal cancer have been sparse and all of a case-control design. We conducted a prospective cohort study to determine the relationship between intake of dietary fiber/whole grains and the incidence of small intestinal cancer.

Methods—We analyzed dietary data collected in 1995 and 1996 from 293,703 men and 198,618 women in the NIH-AARP Diet and Health Study. We used multivariate Cox proportional hazards models to estimate relative risk (RR) and two-sided 95% confidence intervals (CIs) for quintiles of dietary fiber and whole grain intake.

Results—165 individuals developed small intestinal cancers through 2003. Dietary fiber/whole grain intake was generally associated with a lower risk of small intestinal cancer. The multivariate RR (95% CIs; 5th vs. 1st. intake quintile) were 0.79 (0.43–1.44) (p-trend, 0.41) for total dietary fiber, 0.51 (0.29–0.89) (p-trend, 0.01) for fiber from grains, and 0.59 (0.33–1.05) (p-trend=0.06) for whole-grain foods.

Conclusions—Intake of fiber from grains and whole-grain foods was inversely associated with small intestinal cancer incidence; the RR values were consistent with those of the same dietary factors for large bowel cancer in this cohort. In conjunction with the anatomic and physiologic commonalities of the large and small bowel, as well as the mutually increased risks for second cancer for both organs, grain fiber and whole grain foods appear to protect against lower gastrointestinal cancers.

Keywords

dietary fiber; whole grain; small intestinal cancer; cohort study

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Cancer of the small intestine remains rare, incidence rates in the U.S. among men and women, respectively, are 2.2 and 1.5 per 100,000[1]. In contrast, the comparable figures for colorectal cancer are 61 and 45 per 100,000. This enormous incidence disparity occurs in spite of the fact that the small intestine comprises 75% of the human alimentary tract and 90% of its mucosal area.[2]

A number of epidemiologic studies have found dietary fiber, and more recently whole grains, to be inversely associated with colorectal cancer, though the evidence is inconsistent.[3–6] Studies of dietary and other risk factors for small intestinal cancer are sparse and all have been of the case-control design.[7–10] None of these previous studies has focused on fiber and whole grain intake. Prospective cohort studies of the role of dietary factors in small intestinal cancer are desirable—the possibility of recall bias is largely precluded[11]--but need to be large given the relative rarity of the disease.

Methods

The NIH-AARP Diet and Health Study has been described previously.[12, 13] Of the 567,169 men and women AARP members who were 50 to 71 years old and returned satisfactorily completed questionnaires in 1995–1996, we excluded individuals who provided duplicate questionnaires (n=179), indicated they were proxies for the intended respondents (n=15,760), requested to be withdrawn (n=6), had moved out of the study area or died at baseline (n=617), had prevalent cancer except non-melanoma skin cancer at baseline (n=51,193), reported end stage renal disease at baseline (n=997), or had extreme intakes of fiber or total energy (values greater than two times the interquartile range of sex-specific Box-Cox log-transformed intake of total energy or fiber, n=6096). Our analytic cohort comprised 293,703 men and 198,618 women.

Dietary Assessment

At baseline, we assessed diet with a self-administered 124-item food-frequency questionnaire (FFQ) and also collected information on lifestyle and medical history. Participants were asked to report their usual frequency of intake and portion size over the last 12 months, using 10 predefined frequency categories ranging from `never' to `6+ times per day' for beverages, from `never' to `2+ times per day' for solid foods and 3 categories of portion size. The food items, portion sizes and nutrient database were based on Subar et al's method[14] using the United States Department of Agriculture's 1994–96 Continuing Survey of Food Intake by Individuals (CSFII).[15] The nutrient database for dietary fiber was informed by the Association of Official Analytical Chemist (AOAC) method.[16] In addition, food groups and their serving sizes were defined by the Pyramid Servings Database corresponding to the 1994–1996 CSFII, which utilizes a recipe file to disaggregate food mixtures into their component ingredients and assigns them to food groups. One serving of whole grain was defined based on standard portion sizes developed by USDA such as; one slice of whole grain bread, one cup of ready-to-eat whole grain cereal, or ½ cup of cooked whole grains[17].

The FFQ used in the study was validated using two non-consecutive 24-hour dietary recalls in 1,953 participants (personal communication. Thompson FE). The energy-adjusted correlation coefficients for dietary fiber intake assessed by FFQ and two 24-hour recalls was 0.72 in men and 0.66 in women.[18]

Case Ascertainment

We identified cancer cases through probabilistic linkage with 11 state cancer registry databases through December 31, 2003.[19] Small intestinal cancer was defined as a first

primary malignancy with International Classification of Diseases for Oncology, 3rd ed. (ICD-O) code C170-C179. Information on small intestinal cancer tumor site and histology was also obtained through linkage with state cancer registries. We ascertained vital status through annual linkage of the cohort to the Social Security Administration Death Master File (SSA DMF) of deaths in the U.S., follow-up searches of the National Death Index Plus (NDI +) for participants who matched to the SSA DMF, cancer registry linkage, questionnaire responses, and responses to other mailings.

Statistical Analysis

We used multivariate Cox proportional hazards models, after verifying that the proportional hazards assumption was met, to estimate relative risks (RRs) and two-sided 95% confidence intervals (CIs) for quintiles of dietary fiber and whole grain intakes; age was the underlying time metric.[20] We calculated person-years of follow-up time from the date of the baseline questionnaire until the date of cancer diagnosis, death, moving out of the registry areas, or end of follow-up, whichever occurred first. Dietary fiber intake was energy-adjusted using a residual method[21] and whole grain intake was expressed as servings per 1,000 kcal of total energy.

The study was approved by the National Cancer Institute Special Studies Institutional Review Board.

Results

During the average of 7 years of follow-up, we identified 165 small intestinal cancers (51 in duodenum, 70 in jejunum, or ileum, and 44 in other sites; 60 adenocarcinoma, 80 carcinoids, and 25 others). The 10th and 90th percentile values were 12 and 28 g/day for dietary fiber and 0.2 and 1.3 servings/1,000 kcal for whole grains. The correlation between intakes of dietary fiber and whole grains was 0.6. The participants who consumed more fiber or whole grains were more likely to be educated, slightly less overweight, a nonsmoker, more physically active, consumer of less red meat and total fat (Table 1).

Total dietary fiber was significantly associated with a lower risk of small intestinal cancer in the age and sex adjusted model (RR for the highest vs. the lowest quintile ($RR_{Q5\ vs.\ Q1}$) = 0.57, 95% CI: 0.34–0.97, p-trend 0.02, Table 2). After adjustment for other risk factors, however, the association was attenuated and no longer statistically significant (multivariate $RR_{Q5\ vs.\ Q1}$ = 0.79, 95% CI: 0.43–1.44, p-trend 0.41). Fiber from grains was significantly inversely associated with small intestinal cancer (multivariate $RR_{Q5\ vs.\ Q1}$= 0.51, 95% CI: 0.29–0.89, p-trend=0.01). The associations of fiber from grains did not differ by sex. For a 5 g/day increment of fiber from grains, the multivariate RR was 0.76 (95% CI: 0.56–1.05) in men (111 cases) and 0.60 (95% CI: 0.32–1.12) in women (54 cases). The association for fiber from beans was similar to that for fiber from grains, although the trend was not statistically significant. Neither fruit nor vegetable fiber was associated with the malignancy. Intake of whole grains was marginally inversely related to small intestinal cancer (multivariate $RR_{Q5\ vs.\ Q1}$= 0.59, 95% CI: 0.33–1.05, p-trend=0.06). After exclusion of small intestinal cancer cases diagnosed during the first 2 years of follow-up, the results were essentially unchanged. The observed associations with small intestinal cancer did not differ by cigarette smoking status (never vs. former vs. current): p for interactions were 0.54, 0.74, and 0.59, respectively for total dietary fiber, fiber from grains, and intake of whole grains.

Associations for total dietary fiber, fiber from specific sources, and whole grain foods were not statistically significantly different among small intestinal subsites (Table 3). The inverse associations for fiber from grains, fiber from beans, and whole grain foods did not differ significantly between adenocarcinomas and carcinoid tumors. The associations for fiber

from fruits (p=0.03) and fiber from vegetables (p=0.02) did differ according to histotype. The numbers of anatomic subsite- and histology-specific cases were small.

Discussion

Intakes of fiber from grains and whole grain foods were inversely associated with small as well as large intestinal cancers[13] in this cohort. No other prospective study has examined these dietary factors in relation to small intestinal cancer. Our previous analysis of fiber and whole grains in relation to colorectal cancer in this cohort yielded similar results: inverse associations for intakes of fiber from grains and whole grain foods.[13]

Grain fiber and whole grain foods could affect pathophysiologic processes common to carcinogenesis within both the small and large intestines. Investigators have proposed several mechanisms by which dietary fiber can protect against colorectal cancer. These include a) stool bulking; b) decreased transit time (both a and b result in less contact between potential carcinogens and mucosal surface); c) bile acid and carcinogen binding; d) short chain fatty acid, especially butyrate, production via fermentation (butyrate has anti-carcinogenic properties.[22] Moreover, whole grain components other than fiber-- vitamins (including B-vitamins), minerals, phenols, and phyto-estrogens—could affect intestinal (both small and large) carcinogenesis.[13] Some of these mechanisms, however—stool bulking and fermentation, for example--are not likely relevant to carcinogenesis in the small intestine. It is also conceivable that grain fiber and whole grains protect against cancer in the small intestine via processes not operative in the large bowel.

We found no statistically significant difference in the relations between grain fiber/whole grain foods and small intestinal cancer according to histology. We recognize, however, that the limited number of cases within each histologic category makes it difficult to rule out such differences. If the inverse relation and its constancy across histotypes is confirmed, that would suggest that the cancer-protective processes engendered by dietary grain fiber and whole grain foods operate similarly for columnar and enteroendocrine cells in the small intestinal epithelium.

The prospective nature of this study is a strength, but even in a cohort of this size the relatively small number of cases through up to eight years of follow-up remains a limitation. This is particularly true for anatomic subsite- and histology-specific analyses. It would be desirable to confirm our findings in other large cohorts, pooling projects, or consortial efforts, especially those studies attempting to reduce measurement error by incorporating more intensive dietary assessment instruments such as multiple recalls or records. Excluding the first two years of follow-up did not alter the inverse grain fiber and whole grain associations, which provides some evidence that these findings were not due to reverse causation, that is, the effect of preclinical disease on diet. As with any observational study, even our careful adjustment for behavioral and socioeconomic covariates cannot entirely rule out confounding factors associated with grain fiber or whole grain foods as well as small intestinal cancer.

The small and large intestines have substantial anatomic and physiologic commonalities. Moreover, persons with a cancer at one of these two sites have an increased risk of malignancy at the other.[23] The similar protective associations in our cohort for grain fiber and whole grain foods vis-à-vis small as well as large intestinal cancer supports a causal role for these dietary factors in both organs. The discovery of common causes for small and large intestinal cancers, coupled with greater insight into the factors conferring relative resistance to malignant change in the small bowel[24], can help clarify the nature of—and suggest preventive strategies for--lower gastrointestinal carcinogenesis.

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Abbreviations

CI	confidence interval
FFQ	food frequency questionnaire
RR	relative risk

References

1. Ries, LAG.; Melbert, D.; Krapcho, M.; Mariotto, A.; Miller, BA.; Feuer, EJ.; Clegg, L.; Horner, MJ.; Howlader, N.; Eisner, MP.; Reichman, M.; Edwards, BKe. SEER Cancer Statistics Review, 1975–2004. National Cancer Institute; Bethesda, MD: 2007. http://seer.cancer.gov/csr/1975_2004/, based on November 2006 SEER data submission, posted to the SEER web site
2. Beebe-Dimmer, JL.; Schottenfeld, D. Cancers of the small intestine. In: Schottenfeld, D.; Fraumeni, FJ., Jr., editors. Cancer epidemiology and prevention. Oxford University Press; New York: 2006. p. 801-808.
3. Bingham SA, Day NE, Luben R, Ferrari P, Slimani N, Norat T, Clavel-Chapelon F, Kesse E, Nieters A, Boeing H, Tjonneland A, Overvad K, Martinez C, Dorronsoro M, Gonzalez CA, Key TJ, Trichopoulou A, Naska A, Vineis P, Tumino R, Krogh V, Bueno-de-Mesquita HB, Peeters PH, Berglund G, Hallmans G, Lund E, Skeie G, Kaaks R, Riboli E. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. Lancet. 2003; 361:1496–501. [PubMed: 12737858]
4. Park Y, Hunter DJ, Spiegelman D, Bergkvist L, Berrino F, van den Brandt PA, Buring JE, Colditz GA, Freudenheim JL, Fuchs CS, Giovannucci E, Goldbohm RA, Graham S, Harnack L, Hartman AM, Jacobs DR Jr. Kato I, Krogh V, Leitzmann MF, McCullough ML, Miller AB, Pietinen P, Rohan TE, Schatzkin A, Willett WC, Wolk A, Zeleniuch-Jacquotte A, Zhang SM, Smith-Warner SA. Dietary fiber intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies. Jama. 2005; 294:2849–57. [PubMed: 16352792]
5. Jacobs DR, Marquart L, Slavin J, Kushi LH. Whole-grain intake and cancer: an expanded review and meta-analysis. Nutrition and Cancer. 1998; 30:85–96. [PubMed: 9589426]
6. Larsson SC, Giovannucci E, Bergkvist L, Wolk A. Whole grain consumption and risk of colorectal cancer: a population-based cohort of 60,000 women. Br J Cancer. 2005; 92:1803–7. [PubMed: 15827552]
7. Negri E, Bosetti C, La Vecchia C, Fioretti F, Conti E, Franceschi S. Risk factors for adenocarcinoma of the small intestine. Int J Cancer. 1999; 82:171–4. [PubMed: 10389747]
8. Chow WH, Linet MS, McLaughlin JK, Hsing AW, Chien HT, Blot WJ. Risk factors for small intestine cancer. Cancer Causes Control. 1993; 4:163–9. [PubMed: 8481495]
9. Wu AH, Yu MC, Mack TM. Smoking, alcohol use, dietary factors and risk of small intestinal adenocarcinoma. Int J Cancer. 1997; 70:512–7. [PubMed: 9052748]
10. Chen CC, Neugut AI, Rotterdam H. Risk factors for adenocarcinomas and malignant carcinoids of the small intestine: preliminary findings. Cancer Epidemiol Biomarkers Prev. 1994; 3:205–7. [PubMed: 8019367]
11. Willett, W. Nutritional Epidemiology. Oxford University Press; 1998.
12. Schatzkin A, Subar AF, Thompson FE, Harlan LC, Tangrea J, Hollenbeck AR, Hurwitz PE, Coyle L, Schussler N, Michaud DS, Freedman LS, Brown CC, Midthune D, Kipnis V. Design and serendipity in establishing a large cohort with wide dietary intake distributions : the National Institutes of Health-American Association of Retired Persons Diet and Health Study. Am J Epidemiol. 2001; 154:1119–25. [PubMed: 11744517]

13. Schatzkin A, Mouw T, Park Y, Subar AF, Kipnis V, Hollenbeck A, Leitzmann MF, Thompson FE. Dietary fiber and whole-grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study. Am J Clin Nutr. 2007; 85:1353–60. [PubMed: 17490973]

14. Subar AF, Midthune D, Kulldorff M, Brown CC, Thompson FE, Kipnis V, Schatzkin A. Evaluation of alternative approaches to assign nutrient values to food groups in food frequency questionnaires. Am J Epidemiol. 2000; 152:279–86. [PubMed: 10933275]

15. Tippett, KS.; Cypel, YS. Continuing survey of food intakes by individuals, nationwide food surveys. US Department of Agriculture, Agricultural Research Service; 1997. Design and operation: the continuing survey of food intakes by individuals and diet and health knowledge survey, 1994–96.

16. Prosky L, Asp NG, Furda I, DeVries JW, Schweizer TF, Harland BF. Determination of total dietary fiber in foods and food products: collaborative study. J Assoc Off Anal Chem. 1985; 68:677–9. [PubMed: 2993226]

17. U.S. Department of Agriculture. Home and Garden Bulletin No. 252. GPO; Washington, DC: 1992. The food guide pyramid; p. 30

18. Thompson FE, Kipnis V, Midthune D, Freedman LS, Carroll RJ, Subar AF, Brown CC, Butcher MS, Mouw T, Leitzmann M, Schatzkin A. Performance of a food-frequency questionnaire in the US NIH-AARP (National Institutes of Health-American Association of Retired Persons) Diet and Health Study. Public Health Nutr. 2008; 11:183–95. [PubMed: 17610761]

19. Michaud DS, Midthune D, Hermansen S, Leitzmann M, Harlan L, Kipnis V, Schatzkin A. Comparison of cancer registry case ascertainment with SEER estimates and self-reporting in a subset of the NIH-AARP Diet and Health Study. Journal of registry management. 2005; 32:70–75.

20. Cox DR. Regression models and life-tables [with discussion]. J Royal Stat Soc (B). 1972; 34:187–220.

21. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. American Journal of Epidemiology. 1986; 124:17–27. [PubMed: 3521261]

22. Young GP, Hu Y, Le Leu RK, Nyskohus L. Dietary fibre and colorectal cancer: a model for environment--gene interactions. Mol Nutr Food Res. 2005; 49:571–84. [PubMed: 15864783]

23. Curtis, RE.; Freedman, DM.; Ron, E.; Ries, LAG.; Hacker, DG.; Edwards, BK.; Tucker, MA.; Fraumeni, JF, Jr.. New malignancies among cancer survivors: SEER cancer registries, 1973–2000. National Cancer Institute; Bethesda, MD: 2006. NIH Publ. No. 05-5302

24. Neugut AI, Jacobson JS, Suh S, Mukherjee R, Arber N. The epidemiology of cancer of the small bowel. Cancer Epidemiol Biomarkers Prev. 1998; 7:243–51. [PubMed: 9521441]

Table 1

Selected characteristics of study participants by quintiles of dietary fiber and whole grain intakes

	Total population	Quintiles of dietary fiber intake					Quintiles of whole grain intake				
		Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
Participants (n)	49,2321	98,464	98,464	98,465	98,464	98,464	98,464	98,465	98,464	98,464	98,464
Dietary fiber (g/day)[1]	19.5	11	16	19	22	30	15	17	19	21	24
Whole grain (servings/1,000kcal)[1]	0.7	0.4	0.5	0.7	0.8	1.0	0.2	0.4	0.6	0.8	1.4
Age (years)	62	61	62	62	62	63	62	62	62	62	63
Men (%)	60	45	54	60	66	73	63	59	58	59	60
College/post college (%)	62	54	60	62	65	68	56	61	63	65	65
Body mass index (kg/m^2)	27.1	27.3	27.3	27.3	27.0	26.5	27.3	27.4	27.2	27.0	26.6
Current smoking (%)	12	24	14	10	7	5	20	13	11	8	7
Physical activity, ≥3 times/week (%)	46	31	39	46	52	62	37	43	47	50	53
Current menopausal hormone therapy (%)	44	41	45	45	46	45	39	43	45	47	47
Family history of cancer (yes, %)	49	48	49	49	49	48	47	48	49	49	49
Red meat (g/1000 kcal)[1]	35	42	39	36	32	24	41	38	35	32	27
Total fat (% energy/day)[1]	30	33	32	31	29	26	32	32	31	30	28
Energy (kcal/day)[1]	1831	1758	1822	1861	1871	1844	1970	1906	1853	1774	1654

[1]Mean values

Table 2

Relative risks and 95% confidence intervals of small intestinal cancer by quintiles of fiber and whole grain intakes

	Quintile					p-trend‡
	1	2	3	4	5	
Total fiber (g/day) *	<14	14–<17	17–<20	20–<24.5	≥24.5	
Cases/person years	35/673845	37/676599	35/676113	33/676016	25/677395	
Age, sex-adjusted	1.00	0.98 (0.61–1.55)	0.88 (0.55–1.41)	0.79 (0.49–1.28)	0.57 (0.34–0.97)	0.02
Multivariate †	1.00	0.99 (0.62–1.60)	0.95 (0.57–1.56)	0.92 (0.54–1.56)	0.79 (0.43–1.44)	0.41
Fiber from grains (g/day)	<3.7	3.7–<5	5–<6.4	6.4–<8.4	≥8.4	
Cases/person years	34/675077	41/677599	32/676861	37/675221	21/675209	
Age, sex-adjusted	1.00	1.13 (0.72–1.78)	0.83 (0.51–1.36)	0.92 (0.52–1.48)	0.49 (0.28–0.85)	0.01
Multivariate †	1.00	1.10 (0.70–1.74)	0.81 (0.50–1.33)	0.91 (0.56–1.47)	0.51 (0.29–0.89)	0.01
Fiber from fruits (g/day)	<1.6	1.6–<2.9	2.9–<4.2	4.2–<6.3	≥6.3	
Cases/person years	30/662136	39/675448	35/675979	31/678319	30/678085	
Age, sex-adjusted	1.00	1.23 (0.76–1.97)	1.07 (0.66–1.74)	0.93 (0.56–1.53)	0.88 (0.53–1.46)	0.29
Multivariate †	1.00	1.21 (0.75–1.95)	1.08 (0.65–1.78)	0.97 (0.57–1.64)	1.03 (0.60–1.78)	0.76
Fiber from vegetables (g/day)	<6.5	6.5–<8.7	8.7–<11	11–<14.2	≥14.2	
Cases/person years	33/662247	46/675012	25/677415	29/677288	32/678005	
Age, sex-adjusted	1.00	1.35 (0.86–2.11)	0.71 (0.42–1.20)	0.81 (0.49–1.34)	0.88 (0.54–1.44)	0.21
Multivariate †	1.00	1.31 (0.83–2.05)	0.70 (0.41–1.18)	0.82 (0.49–1.37)	0.99 (0.60–1.66)	0.50
Fiber from beans (g/day)	<0.7	0.7–<1.3	1.3–<1.9	1.9–<3.0	≥3.0	
Cases/person years	45/676908	27/677760	25/675727	42/664660	26/674912	
Age, sex-adjusted	1.00	0.59 (0.36–0.93)	0.52 (0.32–0.85)	0.84 (0.55–1.29)	0.51 (0.31–0.84)	0.09
Multivariate †	1.00	0.54 (0.34–0.88)	0.48 (0.29–0.78)	0.77 (0.50–1.19)	0.49 (0.30–0.81)	0.08
Whole grain (servings/1,000 kcal)	<0.3	0.3–<0.5	0.5–<0.7	0.7–<1.0	≥1.0	
Cases/person years	39/670289	34/675902	41/677448	29/677897	22/678431	
Age, sex-adjusted	1.00	0.86 (0.54–1.36)	1.01 (0.65–1.57)	0.70 (0.43–1.13)	0.52 (0.31–0.88)	0.01
Multivariate †	1.00	0.86 (0.54–1.37)	1.03 (0.65–1.63)	0.73 (0.44–1.22)	0.59 (0.33–1.05)	0.06

* Median intake

[†]Adjusted for age, sex, education (less than high school, high school graduate, and college graduate/postgraduate), family history of cancer (no, yes), smoking (never, past, current), body mass index (continuous), physical activity (never/rarely, ≤3 times/month, 1–2, and ≥3 time/week), hormone replacement therapy use in women (never, past, and current), and intakes of red meat (quintiles), total fat (quintiles), and total energy (continuous). In analyses of total fiber and whole grains, these variables were mutually adjusted one for the other.

[≠]Linear trends were tested by including in regression models variables constructed from the medians of the intake quintiles.

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Table 3

Multivariate relative risks* and 95% confidence intervals of subtypes of small intestinal cancer by sites and histology

		Sub-site†§		Histologic type‡§	
	Total	**Duodenum (n=51)**	**Jejunum/ileum (n=70)**	**Adenocarcinomas (n=60)**	**Carcinoids (n=80)**
Total fiber	0.91 (0.68–1.23)	0.68 (0.39–1.19)	0.81 (0.49–1.33)	0.65 (0.38–1.12)	1.19 (0.79–1.79)
Fiber from grains	0.73 (0.55–0.97)	0.78 (0.31–1.42)	0.74 (0.47–1.16)	0.78 (0.49–1.10)	0.62 (0.40–0.96)
Fiber from fruits	1.01 (0.76–1.34)	0.75 (0.43–1.30)	0.99 (0.63–1.56)	0.62 (0.35–1.10)	1.34 (0.94–1.91)**
Fiber from vegetables	1.02 (0.87–1.21)	0.87 (0.64–1.20)	0.92 (0.69–1.22)	0.78 (0.56–1.07)	1.25 (1.01–1.55)**
Fiber from beans	0.81 (0.66–0.99)	0.72 (0.48–1.08)	0.86 (0.64–1.17)	0.81 (0.58–1.13)	0.76 (0.56–1.03)
Whole grains	0.67 (0.43–1.03)	1.04 (0.52–2.09)	0.54 (0.27–1.10)	0.77 (0.38–1.57)	0.53 (0.28–1.01)

*The relative risk is for an increment of 10g/day of total fiber, 5g/day of fiber from grains, fruits, and vegetables, 2g/day of fiber from beans and 1 serving/1,000 kcal of whole grains. The models adjusted for age, sex, education, family history of cancer, smoking, body mass index, physical activity, hormone replacement therapy use in women, and intakes of red meat, total fat and total energy. Total fiber and whole grains were mutually adjusted. Results were essentially unchanged when the jejunum was combined with the duodenum rather than the ileum.

†Tumor sub-sites were defined by International Classification of Diseases for Oncology, 3rd ed. (ICD-O-3) codes: Duodenum (C170, n=51) and jejunum (C171, n=21) and ileum (C172, n=49).

‡Adenocarcimomas were tumors with histologic codes 8140, 8144, 8145, 8210, 8260, 8261, 8263, 8480, 8481, and 8490 and carcinoids were tumors with histologic codes 8240, 8241, 8246, and 8249.

§Differences in results among tumor sites and histologic types were evaluated with the Wald test.

**P<0.05