Dietary Fiber Intake and Risk of Colorectal Cancer
A Pooled Analysis of Prospective Cohort Studies

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Context  Inconsistent findings from observational studies have continued the controversy over the effects of dietary fiber on colorectal cancer.

Objective  To evaluate the association between dietary fiber intake and risk of colorectal cancer.

Design, Setting, and Participants  From 13 prospective cohort studies included in the Pooling Project of Prospective Studies of Diet and Cancer, 725,628 men and women were followed up for 6 to 20 years across studies. Study- and sex-specific relative risks (RRs) were estimated with the Cox proportional hazards model and were subsequently pooled using a random-effects model.

Main Outcome Measure  Incident colorectal cancer.

Results  During 6 to 20 years of follow-up across studies, 8,081 colorectal cancer cases were identified. For comparison of the highest vs lowest study- and sex-specific quintile of dietary fiber intake, a significant inverse association was found in the age-adjusted model (pooled RR=0.84; 95% confidence interval [CI], 0.77-0.92). However, the association was attenuated and no longer statistically significant after adjusting for other risk factors (pooled multivariate RR=0.94; 95% CI, 0.86-1.03). In categorical analyses compared with dietary fiber intake of 10 to <15 g/d, the pooled multivariate RR was 1.18 (95% CI, 1.05-1.31) for less than 10 g/d (11% of the overall study population); and RR, 1.00 (95% CI, 0.85-1.17) for 30 or more g/d. Fiber intake from cereals, fruits, and vegetables was not associated with risk of colorectal cancer. The pooled multivariate RRs comparing the highest vs lowest study- and sex-specific quintile of dietary fiber intake were 1.00 (95% CI, 0.90-1.11) for colon cancer and 0.85 (95% CI, 0.72-1.01) for rectal cancer (P for common effects by tumor site=.07).

Conclusions  In this large pooled analysis, dietary fiber intake was inversely associated with risk of colorectal cancer in age-adjusted analyses. However, after accounting for other dietary risk factors, high dietary fiber intake was not associated with a reduced risk of colorectal cancer.

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For editorial comment see p 2904.
the other hand, most prospective cohort studies have found no association between dietary fiber intake and risk of colorectal cancer or adenomas (precursors of colorectal cancer), and randomized clinical trials of dietary fiber supplementation have failed to show reductions in the recurrence of colorectal adenomas. Recently, the European Prospective Investigation into Cancer and Nutrition (EPIC) study and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial observed a statistically significant 25% lower risk of colorectal cancer or adenomas, respectively, in the highest quintile of dietary fiber intake compared with the lowest. Because of these discordant results, the debate continues on whether dietary fiber consumption decreases colorectal cancer risk. In this study, we evaluated the association between dietary fiber intake and risk of colorectal cancer by reanalyzing the primary data from 13 prospective cohort studies.

**METHODS**

**Study Population**

The Pooling Project of Prospective Studies of Diet and Cancer (Pooling Project) was established to summarize the association between dietary factors and risk of cancers, and the details of the Pooling Project have been described previously. For the colorectal cancer analyses, we identified 13 prospective cohort studies that met the following inclusion criteria: (1) at least 50 incident colorectal cancer cases; (2) assessment of usual dietary intake; (3) completion of a validation study of the dietary assessment method or a closely related instrument; and (4) assessment of dietary fiber intake. Studies including men and women were separated into sex-specific cohorts.

**Dietary and Nondietary Assessment**

Each study provided baseline intake data of foods and nutrients that were assessed by a study-specific food frequency questionnaire. We calculated energy-adjusted intakes using the residual method, in which log-transformed intake of each nutrient (excluding energy) was regressed against log-transformed energy intake and then standardized to energy intakes of 2100 kcal/d for men and 1600 kcal/d for women. Pearson correlation coefficients between dietary fiber intake from the food frequency questionnaire and the reference method in the validation studies were higher than 0.50 in all studies. Grain foods were categorized as either whole grain foods (>50% whole grain content) or refined grain foods (≤50% whole grain content). We also received information on nondietary risk factors, which was collected by self-administered questionnaires at baseline in each study.

**Case Ascertainment**

Incident colorectal cancer cases were identified by each cohort through self-administered questionnaires with subsequent medical record review, linkage with a cancer registry, or both. Some studies also had an additional linkage with a death registry. The follow-up rate of these studies was generally over 90%.

**Statistical Analysis**

In addition to applying the exclusionary criteria used by each study, we also excluded individuals from the analyses who had a history of cancer other than nonmelanoma skin cancer at baseline and who reported implausible energy intakes (beyond 3 SDs from the study-specific log-transformed mean energy intake).

Data analyses comprised study- and sex-specific analyses and subsequent pooled analyses of the study-specific results. Study- and sex-specific relative risks (RRs) and 2-sided 95% confidence intervals (CIs) were estimated with the Cox proportional hazards model. SAS statistical software (version 8, SAS Institute Inc, Cary, NC) was used for all studies except the Canadian National Breast Screening Study and the Netherlands Cohort Study, which were analyzed as case-cohort studies using Epicure software (version 2.11, HiroSoft International Corp, Seattle, Wash). Age at baseline (in years) and the year when the baseline questionnaire was returned were used as stratification variables, thereby creating a time metric that simultaneously accounted for age, calendar time, and time after entry into the study. Person-years of follow-up time were calculated from the date of the baseline questionnaire until the date of colorectal cancer diagnosis, death, or end of follow-up, whichever came first. The person-time experienced during the follow-up of the Nurses’ Health Study was divided into 2 asymptotically uncorrelated segments to take advantage of the more detailed dietary assessment in 1986. The RRs of colorectal cancer were estimated according to study-specific quintiles, as well as to categories defined by absolute intake cut points that were identical across studies. We performed study- and sex-specific age-adjusted and multivariate analyses. The proportion of missing values for each covariate measured in a study was generally less than 5%; an indicator variable for missing responses was created for each covariate in a study if needed. The test for trend across categories of intake was performed by assigning participants the median value of their category and entering those values as a continuous term in a regression model.

The pooled estimates and 95% CIs were calculated using a random-effects model that weighted individual study-specific log RRs by the inverse of the sum of their variance. Between-studies heterogeneity was tested by the Q statistic. Differences in results among tumor sites were tested by the Wald test statistic. A meta-regression model was used to test for variation in RRs by sex, geographical location of the study, and follow-up time.

In addition, we evaluated whether dietary fiber intake was log-linearly associated with risk of colorectal cancer by comparing the nonparametric regression curve obtained using restricted cubic splines with the linear model using the likelihood ratio test and by visual in-
spection of the restricted cubic spline graphs. 

For this analysis, all studies were combined into a single data set stratified by study, and the number and location of the knots were identified through a stepwise selection process. 

The effect of misclassification of dietary fiber intake was evaluated by the method developed by Zucker and Spiegelman. 

**RESULTS**

During follow-up times of 6 to 20 years in 13 cohort studies, 7,328,414 person-years were accumulated and 8,081 incident colorectal cancer cases were identified (2,776 men and 5305 women; 5726 colon cancer and 2,188 rectal cancer cases plus 167 site unspecified). Among the studies, median energy-adjusted dietary fiber intake ranged from 14 to 28 g/d in men and from 13 to 24 g/d in women. The major source of dietary fiber varied across studies with cereals as a major contributor to dietary fiber intake in the European studies, and fruits and vegetables as the main sources in the North American studies (Table 1).

In the age-adjusted model, dietary fiber intake was significantly associated with a 16% lower risk of colorectal cancer in the highest quintile compared with the lowest (pooled age-adjusted RR=0.84; 95% CI, 0.77-0.92) (Table 2). This association was attenuated slightly but still remained statistically significant after adjusting for nondietary risk factors, multivitamin use, and total energy intake (multivariate model I). Additional adjustment for dietary folate intake further weakened the association (multivariate model II). In the final model, which further adjusted for red meat, total milk, and alcohol intake, only a nonsignificant weak inverse association was found (pooled RR=0.94; 95% CI, 0.86-1.03; P for trend=.75; multivariate model III). There was no statistically significant heterogeneity between studies for the highest quintile indicating that the differences in the study-specific results were compatible with random variation (Figure 1). When we combined the studies into a single data set and analyzed associations using across-study sex-specific quintiles and adjusted for the same covariates in multivariate model III, the results were similar: compared with the lowest quintile (mean intake=11 g/d in men and 10 g/d in women), for quintile 2 (multivariate RR, 0.91; 95% CI, 0.84-0.99); for quintile 3 (multivariate RR, 0.98; 95% CI, 0.89-1.07); for quintile 4 (multivariate RR, 0.95; 95% CI, 0.86-1.04); and for quintile 5 (multivariate RR, 0.95; 95% CI, 0.86-1.06), mean intake=31 g/d in men and 25 g/d

### Table 1. Description of Studies in the Analyses of Dietary Fiber and Colorectal Cancer in the Pooling Project

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up Time</th>
<th>Baseline Cohort, No.</th>
<th>Colorectal Cancer Cases, No.</th>
<th>Dietary Fiber Intake, g/d*</th>
<th>Median (10th–90th Percentile) Fiber Intake From, g/d</th>
<th>Cereals</th>
<th>Fruits</th>
<th>Vegetables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Alpha-Tocopherol Beta-Carotene Cancer Prevention Study (ATBC)</td>
<td>1985-1999</td>
<td>26,987</td>
<td>321</td>
<td>19 (13-27)</td>
<td>12 (7-20) 2 (1-4) 4 (2-6)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cancer Prevention Study II Nutrition Cohort (CPSII)</td>
<td>1992-2000</td>
<td>66,090</td>
<td>720</td>
<td>14 (9-22)</td>
<td>5 (3-9) 3 (1-6) 5 (3-9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Professionals Follow-Up Study (HPFS)</td>
<td>1986-2000</td>
<td>47,766</td>
<td>597</td>
<td>21 (14-31)</td>
<td>5 (3-11) 4 (1-9) 7 (4-12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands Cohort Study (NLCS)</td>
<td>1986-1993</td>
<td>58,279</td>
<td>646</td>
<td>27 (20-38)</td>
<td>11 (6-19) 3 (1-6) 4 (2-7)</td>
<td></td>
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</tr>
<tr>
<td>New York State Cohort (NYSC)</td>
<td>1980-1987</td>
<td>30,363</td>
<td>492</td>
<td>28 (20-39)</td>
<td>6 (5-7) 6 (2-12) 14 (9-22)</td>
<td></td>
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</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Breast Cancer Detection Demonstration Project Follow-up Study (BCDDP)</td>
<td>1987-1998</td>
<td>41,987</td>
<td>436</td>
<td>13 (8-21)</td>
<td>5 (2-9) 3 (1-7) 3 (2-6)</td>
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</tr>
<tr>
<td>Canadian National Breast Screening Study (CNBSS)</td>
<td>1980-2000</td>
<td>49,613</td>
<td>612</td>
<td>16 (10-24)</td>
<td>3 (2-5) 6 (4-11) 3 (1-7)</td>
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<td></td>
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<tr>
<td>Cancer Prevention Study II Nutrition Cohort (CPSII)</td>
<td>1992-1999</td>
<td>74,053</td>
<td>479</td>
<td>13 (8-19)</td>
<td>4 (2-8) 3 (1-6) 4 (2-8)</td>
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<td></td>
</tr>
<tr>
<td>Iowa Women’s Health Study (IWHS)</td>
<td>1986-2001</td>
<td>34,588</td>
<td>1010</td>
<td>18 (12-26)</td>
<td>4 (2-8) 4 (2-8) 7 (4-11)</td>
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<tr>
<td>Netherlands Cohort Study (NLCS)</td>
<td>1986-1993</td>
<td>62,573</td>
<td>501</td>
<td>24 (18-32)</td>
<td>9 (5-15) 4 (2-7) 4 (2-7)</td>
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<tr>
<td>New York State Cohort (NYSC)</td>
<td>1980-1987</td>
<td>22,550</td>
<td>206</td>
<td>24 (17-33)</td>
<td>5 (4-6) 5 (2-10) 11 (7-18)</td>
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<tr>
<td>New York University Women’s Health Study (NYUWHS)</td>
<td>1985-1998</td>
<td>13,258</td>
<td>127</td>
<td>14 (8-22)</td>
<td>3 (2-7) 4 (1-8) 5 (2-10)</td>
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<td></td>
<td></td>
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<tr>
<td>Nurses’ Health Study (a) (NHSa)</td>
<td>1980-1986</td>
<td>88,651</td>
<td>220</td>
<td>13 (8-20)</td>
<td>2 (1-4) 4 (1-8) 4 (2-8)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nurses’ Health Study (b) (NHSb)</td>
<td>1986-2000</td>
<td>68,502</td>
<td>648</td>
<td>17 (12-24)</td>
<td>4 (2-7) 4 (1-8) 6 (3-10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prospective Study on Hormones, Diet, and Breast Cancer (CPSII)</td>
<td>1989-2001</td>
<td>9027</td>
<td>61</td>
<td>18 (13-23)</td>
<td>8 (5-11) 5 (2-9) 3 (2-6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swedish Mammography Cohort (SMC)</td>
<td>1987-2003</td>
<td>61,459</td>
<td>714</td>
<td>20 (14-27)</td>
<td>13 (7-19) 3 (1-7) 1 (1-3)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Women’s Health Study (WHS)</td>
<td>1993-2002</td>
<td>38,384</td>
<td>201</td>
<td>17 (12-25)</td>
<td>4 (2-6) 3 (1-7) 6 (3-10)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Median and 10th-90th percentile intake.
†The NHSb is a subset of the NHSa and is not included in the total baseline cohort.
### Table 2. Pooled Relative Risks of Colorectal Cancer for Quintiles of Dietary Fiber Intake

<table>
<thead>
<tr>
<th>Quintile*</th>
<th>RR (95% Confidence Interval)</th>
<th>P Value for Between-Studies Heterogeneity†</th>
<th>P Value for Between-Studies Heterogeneity Due to Sex‡</th>
<th>P Value for Common Effects by Tumor Site§</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age-adjusted</td>
<td>1.00 (0.90-1.01)</td>
<td>0.06</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>Multivariate I‡</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate II§</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>2</td>
<td>Age-adjusted</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate I‡</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate II§</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>3</td>
<td>Age-adjusted</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate I‡</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate II§</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>4</td>
<td>Age-adjusted</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate I‡</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate II§</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td>5</td>
<td>Age-adjusted</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate I‡</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Multivariate II§</td>
<td>0.91 (0.85-0.97)</td>
<td>0.86</td>
<td>0.92</td>
</tr>
</tbody>
</table>

*The quintiles were defined within each individual study using the subcohort for the 2 case-cohort studies (the Canadian National Breast Screening Study and the Netherlands Cohort Study) and the baseline cohort for the remaining studies.

†For quintile 5.

‡Adjusted for age, body mass index (calculated as weight in kilograms divided by the square of height in meters), smoking (men: <1.70, 1.70-1.75, 1.75-1.80, 1.80-1.85, ≥1.85 m; women: <1.60, 1.60-1.65, 1.65-1.70, 1.70-1.75, ≥1.75 m); education (<high school graduate, high school graduate, >high school graduate); physical activity (low, medium, high); family history of colorectal cancer (no, yes); use of postmenopausal hormone therapy (premenopausal, never, ever); oral contraceptive use (never, ever); use of nonsteroidal anti-inflammatory drugs (no, yes); multivitamin use (no, yes); alcohol consumption (0, 1-24, 25-49, ≥50 g/d); total energy (continuous).

§Multivariate I = intake of dietary folate (quintiles).

¶Multivariate II = intake of red meat (quintiles), total milk (quartiles), and alcohol (0, 1-24, 25-49, ≥50 g/d).

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**Figure 1. Study-Specific and Pooled Multivariate Relative Risks (RRs) of Colorectal Cancer Comparing the Highest vs the Lowest Quintile of Dietary Fiber Intake**

The squares and horizontal lines correspond with the multivariate study-specific relative risks (RRs) and 95% confidence intervals (CIs), for the highest quintile of dietary fiber intake compared with the lowest. The relative risks were adjusted for the covariates listed in multivariate model III in Table 2. The size of a square reflects the study-specific weight (inverse of the variance), and the diamond represents the pooled relative risk and 95% confidence interval. The vertical dashed line represents the pooled relative risk. The abbreviations of the studies are listed in Table 1.

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To examine whether the association between dietary fiber intake and risk of colorectal cancer was modified by length of follow-up, we performed separate analyses for cases diagnosed within the first 5 years of follow-up and for cases diagnosed at least 5 years after their baseline assessment. When follow-up time was limited to only the first 5 years, there was a suggestion of an inverse association (pooled multivariate RR = 0.87; 95% CI, 0.76-1.00 in the highest quintile vs the lowest; 3257 cases). However, after a 5-year latency period between the baseline diet assessment and outcome ascertainment, no association was observed (pooled multivariate RR = 1.00; 95% CI, 0.89-1.12 in the highest quintile vs the lowest; 4824 cases).

In categorical analyses using identical absolute intake cut points across studies, the pooled age-adjusted RR was 0.90 (95% CI, 0.75-1.08) and the pooled multivariate RR was 1.00 (95% CI, 0.85-1.17) (Table 3) for comparisons of dietary fiber intake of 30 or more g/d vs 10 to less than 15 g/d. However, the pooled multivariate RR was significantly elevated (RR = 1.18; 95% CI, 1.05-1.31) among individuals with dietary fiber intake less than 10 g/d (11% of the overall study population) compared with 10 to less than 15 g/d. Because the association between dietary fiber intake and risk of colorectal cancer was nonlinear, we calculated measurement error corrected RRs for comparisons of less than 10 g/d vs 10 or more g/d. For this comparison, the strongest confounder was smoking status. Among the studies that had colorectal cancer cases with dietary fiber intake of less than 10 g/d, measured smoking status, and had a sufficient range of dietary fiber intake in their validation study to perform the misclassification analysis, correction for misclassification of dietary fiber intake strengthened the association: the pooled age and smoking adjusted RR comparing less than 10 g/d vs 10 or more g/d of dietary fiber intake changed from 1.22 (95% CI, 1.10-1.35) to 2.16 (95% CI, 1.12-4.16) after correction for measurement error.

The nonparametric regression curve obtained after combining all studies into a single data set showed a pattern similar to the categorical analyses in which study-specific RRs were pooled (Figure 2): the multivariate RR declined with increasing dietary fiber intake up to about 15 g/d, but then flattened out (P for nonlinearity = .05).

There was a suggestion that the association with dietary fiber intake differed by tumor site (P for common effects by tumor site for the highest quintile = .07) (Table 2). Comparing the highest vs lowest quintile of intake, a

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Table 3. Pooled Relative Risks of Colorectal Cancer for Categories of Dietary Fiber Intake

<table>
<thead>
<tr>
<th>Dietary Fiber Intake, g/d</th>
<th>P Value for Trend</th>
<th>P Value for Between-Studies Heterogeneity*</th>
<th>P Value for Between-Studies Heterogeneity Due to Sexa</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>10--15</td>
<td>15--20</td>
<td>20--25</td>
</tr>
<tr>
<td>Colorectal cancer†</td>
<td>No. of cases</td>
<td>609</td>
<td>1681</td>
</tr>
<tr>
<td>Person-years</td>
<td>513,317</td>
<td>1,591,320</td>
<td>1,870,758</td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.27 (1.15-1.40)</td>
<td>1.00</td>
<td>0.99 (0.93-1.06)</td>
</tr>
<tr>
<td>Multivariate‡</td>
<td>1.18 (1.05-1.31)</td>
<td>1.00</td>
<td>1.02 (0.95-1.10)</td>
</tr>
<tr>
<td>Colon cancer†</td>
<td>No. of cases</td>
<td>430</td>
<td>1,203</td>
</tr>
<tr>
<td>Person-years</td>
<td>5,133,117</td>
<td>1,591,290</td>
<td>1,870,713</td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.24 (1.11-1.40)</td>
<td>1.00</td>
<td>1.00 (0.92-1.08)</td>
</tr>
<tr>
<td>Multivariate‡</td>
<td>1.17 (1.03-1.34)</td>
<td>1.00</td>
<td>1.04 (0.95-1.13)</td>
</tr>
<tr>
<td>Rectal cancer‡</td>
<td>No. of cases</td>
<td>159</td>
<td>427</td>
</tr>
<tr>
<td>Person-years</td>
<td>505,039</td>
<td>1,589,654</td>
<td>1,853,445</td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.35 (1.11-1.64)</td>
<td>1.00</td>
<td>0.98 (0.84-1.14)</td>
</tr>
<tr>
<td>Multivariate‡</td>
<td>1.18 (0.82-1.68)</td>
<td>1.00</td>
<td>1.00 (0.86-1.17)</td>
</tr>
</tbody>
</table>

*For the highest category.
†For the colorectal and colon cancer analyses, the Netherlands Cohort Study and the New York State Cohort were excluded from the &lt;10 g/d category because these studies did not have any cases in that category; ORDET was excluded from the 30 g/d category because this study did not have any cases in that category; and the male cohort of the New York State Cohort was excluded from the rectal cancer analyses because this study had no cases in the reference group.
null association was found for colon cancer (pooled multivariate RR=1.00; 95% CI, 0.90-1.11), whereas a borderline-significant, weak inverse association was found for rectal cancer (pooled multivariate RR=0.85; 95% CI, 0.72-1.01). Further analyses of proximal colon cancer (pooled multivariate RR=1.05; 95% CI, 0.91-1.21) and distal colon cancer separately (pooled multivariate RR=0.96; 95% CI, 0.80-1.14) showed no statistically significant association (P for common effects by tumor site for the highest quintile = .24).

In analyses of the sources of dietary fiber, fiber intakes from cereals and fruits were each associated with approximately a 10% reduction in risk of colorectal cancer in the age-adjusted model comparing the highest quintile with the lowest (Table 4). However, after adjustment for potential colorectal cancer risk factors, the associations were attenuated and not statistically significant (pooled multivariate RR=1.00; 95% CI, 0.93-1.08 for fiber from cereals; pooled multivariate RR=0.96; 95% CI, 0.89-1.04 for fiber from fruits in the highest quintile vs the lowest). Dietary fiber from vegetables was not associated with risk of colorectal cancer in both the age-adjusted and multivariate models. When associations with specific sources of dietary fiber were examined by tumor site, we found that the associations with fiber intake from cereals were significantly different between colon and rectal cancer (P for common effect by tumor site for the highest quintile = .05), even though neither association was statistically significant. Comparing the highest vs the lowest quintile for fiber intake from cereals, the pooled multivariate RR was 0.91 (95% CI, 0.78-1.06, P for trend = .20) for rectal cancer, and 1.03 (95% CI, 0.94-1.13, P for trend = .90) for colon cancer. For fiber intake from fruits and from vegetables, no significant differences by tumor site were observed (data not shown).

Intakes of whole grain and refined grain foods were each not statistically associated with risk of colorectal cancer: the pooled multivariate RR in the highest quintile vs the lowest were 0.92 (95% CI, 0.84-1.00, P for trend = .21) for whole grain food and 1.01 (95% CI, 0.91-1.13, P for trend = .94) for refined grain food. Although the results did not significantly differ by tumor site for both whole and refined grain food intake, there was a suggestion that whole grain food intake was inversely associated with risk of rectal cancer (pooled multivariate RR=0.81; 95% CI, 0.65-1.00 in the highest quintile vs the lowest, P for trend = .07). In the analyses of grain foods, if dietary folate intake was not included as a covariate, the results did not change.

**COMMENT**

In this pooled analysis of 13 prospective cohort studies, we observed a statistically significant inverse association between dietary fiber intake and risk of colorectal cancer in the age-adjusted model. However, the overall association was attenuated and no longer statistically significant after ad-
justing for other colorectal cancer risk factors. When intakes of dietary fiber were examined separately by specific food sources, none were associated with risk of colorectal cancer. However, there was a suggestion that intake of dietary fiber from cereals and intake of dietary fiber from whole grain foods were both associated with a weak reduction in risk of rectal cancer.

The association between dietary fiber intake and risk of colorectal cancer has been inconsistent among observational studies and several factors may explain the disparity: potential biases in study design, failure to adjust for confounders, and differences in study populations. Inconsistent results also have been reported from randomized clinical trials of dietary fiber supplementation. In most case-control studies, the failure to adjust for confounders may contribute to the accumulation of discordant findings among studies. If the range of intake of a nutrient in a study is very narrow, a null association may be more likely observed. However, lack of variation in dietary fiber intake is unlikely to have accounted for the null association we found. In our analyses, the study-specific mean energy-adjusted dietary fiber intake was 9 to 20 g/d for men and 8 to 17 g/d for women in the lowest quintile and 23 to 41 g/d for men and 20 to 35 g/d for women in the highest quintile with a 1.8- to 3.0-fold difference in intakes between the two extreme quintiles across studies. This range is similar to the range observed in EPIC, which reported a statistically significant inverse association with dietary fiber intake. Mean dietary fiber intake in EPIC was 18 g/d for men and 16 g/d for women in the lowest quintile and 30 g/d for men and 24 g/d for women in the highest quintile (a 1.5- to 1.7-fold difference). In addition, when we used identical absolute intake cut points across studies, no association was observed for dietary fiber intake of at least 30 g/d vs 10 to less than 15 g/d, which is similar to the quintile definitions used in EPIC.

Because the Pooling Project is a retrospectively planned pooled analysis of the primary data, the food frequency questionnaires that were used to assess diet varied across studies. To take into account potential misclassification in dietary fiber intake that may arise from measurement error in energy intake, we calculated energy-adjusted intakes for each study. We also conducted analyses by categorizing dietary fiber intake using study-specific quintiles.
tamin/nonmineral supplement use, in-rectal cancer. Although misclassifi-
ration on the use of dietary fiber intake. However, misclassification could also have oc-
hood) or lifelong fiber intake on risk of colorectal cancer. Although misclassifi-
neasured only at baseline, we take was assessed only at baseline, we estimate dietary fiber intake during earlier life pe-
jective dietary fiber intake to risk of colorectal cancer above the lowest category of dietary intake.
Several limitations of our analysis should be considered. Fiber intake is likely to be measured with error be-
cause this has been related to lower risks of other chronic conditions such as heart disease and diabetes. 52

4%. 52 Therefore, failure to measure use of fiber supplements is unlikely to have led to substantial misclassification of dietary fiber intake.

A strength of the Pooling Project is that the individual data from each co-
hort were reanalyzed using a standard approach, which provided more flexi-
ility in examining dose-response relationships, confounding, and effect modiﬁcation than meta-analyses of the published literature, which frequently summarize risk estimates obtained for heterogeneous exposure categories with different adjustment for potential confounders. Also, we had high statistical power with over 8000 colorectal cancer cases, thus a substantial effect of fiber is unlikely to have been missed. In addition, in a subset of the studies we were able to correct for measurement error in dietary fiber intake using their valida-

Several limitations of our analysis should be considered. Fiber intake is likely to be measured with error because of errors in how study partici-

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REFERENCES