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Vegetable and Fruit Consumption and Risks of Colon and Rectal Cancer in a Prospective Cohort Study

The Netherlands Cohort Study on Diet and Cancer

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The relation between vegetable and fruit consumption and colorectal cancer risk was comprehensively assessed in the Netherlands Cohort Study on Diet and Cancer using a validated 150-item food frequency questionnaire. After 6.3 years of follow-up (1986–1992), over 1,000 incident cases of colorectal cancer were registered. Using case-cohort analysis, the authors calculated rate ratios and 95% confidence intervals adjusted for age, alcohol intake, and family history of colorectal cancer. For colon cancer, no statistically significant associations with total vegetable intake or total fruit intake were found. However, among women, an inverse association was observed with vegetables and fruits combined (for the highest quintile vs. the lowest, the rate ratio was 0.66 (95% confidence interval: 0.44, 1.01)). *Brassica* vegetables and cooked leafy vegetables showed inverse associations for both men and women. Among women and, to a lesser extent, among men, inverse associations were stronger for distal colonic tumors than for proximal colonic tumors. For rectal cancer, no statistically significant associations were found for vegetable consumption or fruit consumption or for specific groups of vegetables and fruits; only *Brassica* vegetables showed a positive association in women. As in other cohort studies, the observed inverse relation between vegetable and fruit consumption and occurrence of colorectal cancer was less strong than relations reported in case-control studies. *Am J Epidemiol* 2000;152:1081–92.

cohort studies; colonic neoplasms; dietary fiber; fruit; rectal neoplasms; vegetables

Several investigators have summarized epidemiologic data considering the effect of vegetable and fruit consumption on cancer risk (1–4). In the most recent review by Steinmetz and Potter (4), 15 of the 21 case-control studies examined showed statistically significant inverse associations between one or more vegetable/fruit categories and colon cancer risk. Four of the studies did not show significant inverse associations for any vegetable/fruit category, and in two studies statistical significance was not reported. The protective effect of vegetables seemed to be most clear for raw vegetables and the green types. The case-control evidence did not support a protective effect of legumes against colon cancer. For cancer of the rectum, eight out of 13 studies showed significant inverse associations; two did not show associations, and in three studies, significance was not reported. The evidence of a protective effect on rectal cancer was most consistent for cruciferous vegetables.

To date, data from 11 prospective cohort studies on vegetable/fruit consumption (or on fiber from vegetables/fruits) and risk of (fatal) colon or rectal cancer or colorectal adenoma have been published. Two studies examined Seventh-Day Adventists (5, 6), one examined Japanese-American men residing in Hawaii (7), and one examined vegetarians and health-conscious people (8). Furthermore, data have been published from the Nurses' Health Study (9, 10), the Second Cancer Prevention Study (11), the Leisure World Study (12), the Iowa Women's Health Study (13), the Health Professionals Follow-up Study (14–16), the New York University Women's Health Study (17), and the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (18). Only statistically nonsignificant inverse associations between vegetable or fruit consumption and colorectal cancer risk have been found. With two exceptions (8, 18), all data from cohort studies that have been published so far have come from the United States. Only three studies published data on both men and women, in separate analyses (5, 11, 12). Most studies focused on colon cancer or colorectal cancer, not allowing for separate conclusions regarding rectal cancer. Four studies presented data on more than one vegetable item (6, 12, 13, 18).

With 6.3 years of follow-up, the Netherlands Cohort Study on Diet and Cancer has accrued over 1,000 colorectal cancer cases. This large number has enabled us to study the relation between intake of vegetables and fruits (including subgroup analyses) and colorectal cancer risk in both men and women with a Western European diet. We were able to perform separate analyses for colon and rectal cancer and for specific subsites in the colon. Because the association

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Abbreviations: CI, confidence interval; RR, rate ratio.

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between consumption of *Allium* vegetables and colorectal carcinoma risk has already been examined in the Netherlands Cohort Study (19), specific analyses for these vegetables were not included in the present paper.

MATERIALS AND METHODS

The Netherlands Cohort Study

The Netherlands Cohort Study on Diet and Cancer is a prospective cohort study that was started in September 1986. The study design has been reported in detail elsewhere (20). In brief, the cohort included 62,573 women and 58,279 men aged 55–69 years at the beginning of the study who originated from 204 Dutch municipalities with computerized population registries. A self-administered mailed questionnaire on dietary habits, lifestyle, smoking, personal and family history of cancer, and demographic data was completed at baseline. Accumulation of person-time in the cohort has been estimated through biennial vital status follow-up of a subcohort of 1,688 men and 1,812 women who were randomly selected after baseline exposure measurement. No subcohort members were lost to follow-up.

Identification of cases of colon and rectal cancer

The method of record linkage used to obtain information on cancer incidence has been described previously (21). In short, follow-up for incident cancer has been established by computerized record linkage of the entire cohort with all regional cancer registries in the Netherlands and with PALGA, a national database of pathology reports. For prevention of random and systematic coding errors, the questionnaire data of all cases and subcohort members have been key-entered twice and processed blinded with respect to case/subcohort status.

The food frequency questionnaire

The dietary section of the questionnaire was a 150-item semiquantitative food frequency questionnaire. The questionnaire concentrated on habitual consumption of food and beverages during the year preceding the start of the study. With regard to vegetable consumption, participants were asked to report their frequency of consumption of 15 cooked vegetables and four raw vegetables, both in summer and in winter. For most vegetables, the questionnaire explicitly specified whether the vegetable was eaten raw or cooked. On the basis of results from the Dutch Nutrition Survey (22), onions and sweet peppers were considered to be eaten cooked, while tomatoes were considered to be eaten raw. Participants could indicate their frequency of consumption by choosing one of six categories ranging from "never or less than once per month" to "three to seven times per week."

Participants were asked about usual serving sizes only for string beans and cooked endive; the mean of these values served as an indicator for the serving sizes of all cooked vegetables. Subjects who did not report their usual serving sizes were assigned a default value. For subjects with only one reported serving size, the individual serving size was derived using a conversion factor. Both the default value and the conversion factor were derived from a pilot study. For tomatoes and sweet peppers, participants were asked to report their consumption in number of pieces per week and per month, respectively, for both summer and winter.

With regard to fruit consumption, participants were asked to report frequencies (varying from "never or less than once per month" to "six or seven times per week") and amounts consumed for oranges, mandarins, grapefruits, grapes, bananas, apples/pears, and strawberries. Using standard sizes, we converted these frequencies and amounts to grams per day.

An open-ended question on other food eaten regularly was also included. Participants could write down how often they ate such a food per week and how much they ate on each occasion.

The food frequency questionnaire was validated against a 9-day diet record. Spearman correlation coefficients for vegetables and fruits were 0.60 and 0.38, respectively. Vegetable consumption appeared to be slightly overestimated and fruit consumption to be underestimated by the food frequency questionnaire as compared with the diet records (23).

Study population

After exclusion of 1) cases who reported prevalent cancer at baseline (other than nonmelanoma skin cancer), 2) cases without microscopically confirmed cancer, 3) cases with incident carcinoma in situ, and 4) cases with colon and rectal cancers other than carcinoma (sarcoma, lymphoma, cancers of unspecified morphology), 659 incident colon carcinoma cases and 375 rectal carcinoma cases were available for analyses, using the first 6.3 years of follow-up. Cases with prevalent cancer other than nonmelanoma skin cancer were excluded from the subcohort as well, which left 1,716 women and 1,630 men for analysis. Furthermore, subjects with incomplete or inconsistent dietary data were excluded from the analyses. These subjects included 1) those who left 60 or more (out of 150) questionnaire items blank *and* ate fewer than 35 items at least once per month and 2) those who left one or more item blocks (groups of items, e.g., beverages) blank. Additional details are given elsewhere (23).

Questions on vegetable consumption appeared early in the food frequency questionnaire. This led to some subjects' making mistakes on these particular items (e.g., improbably high summed frequencies for vegetable consumption, errors in separate consumption frequencies for summer and winter, and improbably high (or low) reported portion sizes), while items on other food groups appearing further along in the questionnaire were filled out without problems. In order to check the quality of the responses to the vegetable questions, we computed a vegetable error index. When the vegetable error index exceeded a certain value, i.e., more than three errors, that subject was excluded from the analyses of vegetable consumption. For vegetable consumption, the final analysis was based on a total of 587 colon cancer cases

(313 men and 274 women), 323 rectal cancer cases (201 men and 122 women), and 2,953 subcohort members (1,456 men and 1,497 women). For fruit consumption, the final analysis was based on 620 colon cancer cases (332 men and 288 women), 344 rectal cancer cases (217 men and 127 women), and 3,123 subcohort members (1,525 men and 1,598 women).

Data analysis

Analyses were performed for total vegetable consumption, total fruit consumption, consumption of vegetables and fruits combined, consumption of individual vegetables and fruits as listed in the questionnaire, and consumption of vegetable/fruit groups (raw vegetables, cooked vegetables, legumes, *Brassica* vegetables, cooked and raw leafy vegetables, and citrus fruit). "Total vegetable consumption" is the summed total for all vegetables mentioned in the questionnaire and in the open-ended question. Although results on *Allium* vegetables are not reported separately, they were included in total vegetable consumption. For analysis of vegetable consumption, potatoes and mature beans were not included.

Subjects were classified into quintiles, tertiles, or categories of vegetable or fruit consumption (g/day), depending on the data distribution in the subcohort. Analyses were performed using the case-cohort approach (24). In this approach, cases are enumerated for the entire cohort, while person-years at risk for the cohort are estimated using the subcohort sample.

We computed age-adjusted rate ratios for colon and rectal cancer (and their 95 percent confidence intervals) using the GLIM statistical package (25). Exponentially distributed survival times were assumed in the follow-up period. Since standard software was not available for case-cohort analysis, we developed specific macros to account for the additional variance introduced by sampling from the cohort instead of using the entire cohort (26). Tests for trends in rate ratios were based on two-sided likelihood ratio tests. Total energy consumption, alcohol intake, smoking, physical activity, body mass index (reported weight (kg) divided by reported height (m) squared), and family history of colorectal cancer were evaluated as potential confounders. In our study, family history of colorectal cancer and alcohol intake were related to colorectal cancer, and we adjusted for these factors in a multivariate model. Rate ratios for the mean daily quantities of specific vegetables and fruits consumed were calculated for continuous variables (g/day) and are expressed in increments of 25 g/day. This increment corresponds to a consumption frequency of approximately once per week for a cooked vegetable. The independent contribution of each specific vegetable was assessed through analyses in which all other vegetables or fruits were included in the model simultaneously.

Separate analyses were conducted for colon and rectal carcinoma in males and females. For colon cancer, subgroup analyses were performed for proximal and distal colon carcinomas. Analyses were repeated after exclusion of cases diagnosed during the first 2 years of follow-up.

RESULTS

Table 1 presents mean vegetable and fruit consumption, by sex, for cases with incident colon and rectal cancer and for members of the subcohort. Mean daily fruit consumption among subcohort members was more than 40 g higher for women than for men, whereas differences in vegetable consumption were less striking. Consumption of vegetables by male colon and rectal cancer cases was not different from that of subcohort members, whereas fruit consumption was slightly higher among male colon cancer cases than in the subcohort. For women, both vegetable consumption and fruit consumption were lower among colon cancer cases than among subcohort members. For female rectal cancer cases, vegetable consumption was higher and fruit consumption was lower than that of subcohort members.

For subcohort members, vegetable and fruit consumption was calculated for strata of the most important potential confounders: alcohol intake and family history of colorectal cancer (table 2). Vegetable consumption was calculated for subcohort members in different quintiles of fruit consumption, and fruit consumption was calculated for subcohort members in different quintiles of vegetable consumption. Fruit consumption was higher in the higher age groups for both men and women. For vegetable consumption, no age effect was found. Vegetable consumption was higher with increasing alcohol intake in men, and this trend was even stronger in women. For fruit consumption, no association with alcohol intake was found. Small differences in vegetable and fruit consumption were found between people with and without a family history of colorectal cancer. In both men and women, higher fruit consumption was associated with higher vegetable consumption.

Tables 3 and 4 present rate ratios for colon and rectal cancer, respectively, according to quintiles of vegetable consumption, fruit consumption, and the combination of vegetable and fruit consumption. Rate ratios were adjusted both for age only and for age, family history of colorectal cancer, and alcohol intake. In women, nonsignificant inverse associations with colon cancer were found for fruit consumption and consumption of vegetables/fruits combined. However, a nonsignificant positive association with rectal cancer was found for vegetable consumption in women. Among men, no inverse associations were found for colon or rectal cancer, and fruit consumption even showed a slight positive trend for colon cancer.

Vegetables and fruits were divided into groups, and rate ratios were calculated for quintiles of consumption using the multivariate model (table 5). For colon cancer in men, negative associations were seen for *Brassica* vegetables (rate ratio (RR) for the highest quintile vs. the lowest (hereafter called high/low RR) = 0.76 (95 percent confidence interval (CI): 0.51, 1.13), p trend = 0.11) and for cooked leafy vegetables (high/low RR = 0.75 (95 percent CI: 0.50, 1.13), p trend = 0.05). In women, *Brassica* vegetables and cooked leafy vegetables also showed the strongest negative associations with colon cancer (high/low RR = 0.51 (95 percent CI: 0.33, 0.80), p trend = 0.004, and high/low RR = 0.62 (95 percent CI: 0.40, 0.96), p trend = 0.06, respectively). With regard to rectal cancer, no associations with

TABLE 1. Daily vegetable and fruit consumption (in grams) among male and female cases with colon and rectal cancer and members of a subcohort randomly selected at baseline, Netherlands Cohort Study, 1986–1992

	Men						Women					
	Colon cancer		Rectal cancer		Subcohort		Colon cancer		Rectal cancer		Subcohort	
	Mean	SD*	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Vegetable consumption	(*n* = 313)		(*n* = 201)		(*n* = 1,456)		(*n* = 274)		(*n* = 122)		(*n* = 1,497)	
Total vegetables†	184.7	77.6	186.5	74.5	187.1	76.3	182.4	69.6	200.2	77.6	191.0	74.5
Cooked vegetables	151.1	68.3	149.2	60.5	150.8	63.1	143.2	55.2	155.1	60.7	149.5	59.3
Raw vegetables	33.6	24.6	37.3	29.6	36.2	29.0	39.1	26.5	45.0	32.3	41.5	29.8
Subgroups												
Brassica vegetables	31.6	20.2	32.7	19.4	32.7	20.3	27.4	16.9	33.5	20.2	31.6	20.0
Brussels sprouts	7.6	6.8	7.7	6.5	7.7	6.7	6.7	5.7	7.6	7.8	7.7	7.4
Cauliflower	14.2	10.4	14.2	10.3	14.6	11.1	12.0	8.3	15.8	10.9	13.9	10.5
Cabbage (white/green)	6.5	8.6	7.3	8.7	7.2	8.2	6.0	6.6	7.0	7.7	6.9	8.0
Kale	3.2	3.3	3.6	3.3	3.3	3.4	2.7	3.0	3.1	3.6	3.2	3.4
Legumes‡	37.3	25.5	36.3	27.2	34.7	23.0	28.3	18.3	30.4	19.0	30.7	20.7
String beans	21.5	16.1	20.5	13.6	20.5	15.3	17.8	12.8	18.0	11.8	19.5	14.7
Broad beans	4.9	7.3	4.1	5.6	4.7	7.2	4.2	5.5	5.7	7.7	4.3	6.6
Leafy vegetables, cooked	20.2	15.8	21.7	16.5	21.6	16.0	19.4	14.1	22.6	15.7	21.3	14.9
Spinach	9.4	8.8	9.7	9.4	9.6	8.9	8.3	7.5	10.2	8.7	9.4	8.3
Endive	10.8	10.4	12.0	10.2	12.0	10.8	11.1	10.1	12.4	10.8	11.8	10.2
Leafy vegetables, raw	9.8	8.2	9.5	8.3	9.9	9.2	9.6	8.1	10.6	9.8	10.1	8.4
Endive	1.9	3.6	2.0	3.8	2.4	4.9	2.3	3.7	3.1	4.8	2.5	4.3
Lettuce	7.9	7.1	7.5	6.4	7.6	6.7	7.3	6.8	7.5	6.9	7.6	6.6
Other vegetables												
Carrots, cooked	8.8	8.3	8.7	7.6	9.0	8.9	8.8	7.7	9.0	7.6	8.9	8.6
Carrots, raw	1.7	5.1	2.2	7.5	2.1	7.8	2.9	8.5	3.7	10.6	3.5	9.4
Sweet peppers	2.6	4.5	2.5	4.3	2.5	4.0	3.3	6.0	3.9	5.5	3.3	4.9
Sauerkraut§	5.8	5.2	5.9	4.8	5.9	5.5	5.5	4.6	6.4	7.3	5.7	4.9
Tomatoes	18.4	19.2	20.9	22.4	19.5	20.0	22.8	19.3	26.7	20.7	23.5	20.3
Beetroot	7.5	8.1	7.6	7.9	7.7	8.7	7.7	7.5	8.3	7.6	8.1	7.7
Mushrooms	3.2	4.5	3.2	3.6	3.2	3.9	3.6	4.1	4.3	4.6	3.7	4.4
Gherkins	1.3	3.3	1.8	4.1	1.9	8.1	1.3	5.1	1.4	4.4	1.8	6.6
Rhubarb	2.6	7.3	1.9	3.3	2.2	5.7	2.3	5.2	1.8	3.6	2.4	5.4
Fruit consumption	(*n* = 332)		(*n* = 217)		(*n* = 1,525)		(*n* = 288)		(*n* = 127)		(*n* = 1,598)	
Total fruit	160.4	104.2	154.8	122.5	154.4	111.8	187.0	121.9	184.9	101.5	196.1	118.9
Citrus fruit	68.6	74.2	61.8	70.4	64.8	69.8	90.4	76.8	92.6	68.5	88.2	73.2
Mandarins	3.1	6.4	3.4	6.0	3.8	7.2	5.8	8.9	6.4	11.6	5.5	8.9
Oranges and fresh orange juice	43.1	52.8	43.9	59.4	40.6	51.1	57.9	58.6	55.5	49.2	55.9	55.8
Grapefruits and fresh grapefruit juice	8.6	25.1	6.6	20.0	6.6	21.7	12.2	31.0	12.7	25.1	11.4	26.3
Orange/grapefruit juice (processed)¶	13.7	47.8	7.9	20.3	13.8	38.2	14.3	33.9	18.0	32.8	15.3	35.4
Grapes	4.0	6.7	3.5	6.4	3.9	8.5	5.3	9.2	4.0	7.8	5.0	9.7
Bananas	12.3	21.9	9.8	22.0	12.9	25.0	9.8	19.5	9.7	19.6	12.9	26.8
Apples, pears	70.7	74.9	70.3	85.2	67.4	74.6	76.8	75.5	75.0	66.9	84.2	82.0
Strawberries	6.2	7.3	5.8	5.9	6.8	7.8	7.3	7.5	8.4	8.5	8.1	8.6
Other fruit juices¶	9.3	30.7	5.5	19.5	7.8	28.7	12.4	32.0	9.5	32.1	12.8	34.2

* SD, standard deviation.
† Includes fruits and vegetables noted in an open-ended question on frequently consumed items not listed in the questionnaire.
‡ Also includes dried pulses.
§ Not included in the *Brassica* vegetable group because potential anticancer agents are destroyed by processing.
¶ Not included in total fruit.

TABLE 2. Mean daily consumption of vegetables and fruits in a subcohort randomly selected at baseline, according to several characteristics, Netherlands Cohort Study, 1986–1992

Characteristic	Vegetable consumption*						Fruit consumption*					
	Men (*n* = 1,456)			Women (*n* = 1,497)			Men (*n* = 1,525)			Women (*n* = 1,598)		
	No.	Mean (g/day)	SD†	No.	Mean (g/day)	SD	No.	Mean (g/day)	SD	No.	Mean (g/day)	SD
Age (years)												
55–59	562	185	78	570	192	75	582	148	109	616	192	125
60–64	505	189	75	520	194	74	534	154	111	548	198	114
65–69	389	187	76	407	186	74	409	165	116	434	199	116
Alcohol intake (g/day)‡												
0	219	176	87	457	184	77	231	158	106	488	199	124
0.1–4	290	185	75	526	190	72	304	173	132	563	195	114
5–14	405	180	69	263	198	73	422	156	103	278	196	114
15–29	327	193	69	131	203	77	341	144	102	137	181	120
≥30	202	205	88	50	219	73	210	141	117	53	198	112
Family history of colorectal cancer												
No	1,377	187	77	1,415	191	74	1,441	154	112	1,511	196	120
Yes	79	184	67	82	193	82	84	155	113	87	191	99
Quintile of vegetable/fruit consumption§												
1 (low)	293	165	70	214	166	69	299	128	100	314	158	113
2	287	184	75	288	180	72	303	140	103	302	188	106
3	296	182	69	303	189	73	298	150	103	319	187	107
4	292	194	73	325	199	69	300	159	103	304	204	112
5 (high)	288	210	87	367	209	80	325	192	134	359	238	136

* Total numbers differ for vegetable and fruit consumption because of an extra exclusion criterion for analysis of vegetable consumption.
† SD, standard deviation.
‡ Numbers do not total 2,953 (vegetable consumption) or 3,123 (fruit consumption) because of missing values.
§ Total vegetable consumption by quintile of fruit consumption, and total fruit consumption by quintile of vegetable consumption.

consumption of particular groups of vegetables or fruits were found in men. In women, a positive association found with vegetables was strongest for vegetables in the *Brassica* group (high/low RR = 1.66 (95 percent CI: 0.94, 2.94), p trend = 0.05).

Table 6 presents rate ratios from models containing all confounders for 25-g/day increments in consumption of specific vegetables and fruits, both with and without additional adjustment for other vegetables or other fruits. Among men, statistically significant negative associations with colon cancer were found for cooked endive in both models; among women, significant negative associations were found for cauliflower and spinach in the model that included adjustment for other cooked vegetables. In the model that did not include other vegetables, negative associations of brussels sprouts, cabbage, and string beans with colon cancer in women were borderline significant. With regard to rectal cancer, significant positive associations were found among women for cauliflower and broad beans in both models.

Colon cancer cases were classified according to site of occurrence (proximal vs. distal), and for each site rate ratios were calculated for total vegetable and fruit consumption, total vegetable consumption, total fruit consumption, and consumption of *Brassica* vegetables (the most notable vegetable group in table 6). Overall, the incidence of cancer in the distal colon seemed to be more influenced by vegetable consumption than was incidence in the proximal colon. Regarding cancer of the distal colon in women, statistically significant negative associations were found for all vegetables and fruits (high/low RR = 0.44 (95 percent CI: 0.23, 0.82), p trend = 0.01), for total vegetables (high/low RR = 0.64 (95 percent CI: 0.36, 1.17), p trend = 0.04), and for *Brassica* vegetables (high/low RR = 0.47 (95 percent CI: 0.25, 0.89), p trend = 0.02) (table 7). In men, only *Brassica* vegetables showed a statistically significant negative association with distal colon cancer (high/low RR = 0.68 (95 percent CI: 0.41, 1.15), p trend = 0.02). When the analyses of total vegetable consumption and total vegetable/fruit consumption were repeated with *Brassica* vegetables included in the model, the inverse association with total vegetable consumption was lost but the inverse relation between total vegetable/fruit consumption and cancer of the distal colon was maintained for women (results not shown). Rate ratios for increasing quintiles of total vegetable/fruit intake were 1.0, 0.66, 0.77, 0.65, and 0.53, respectively. Therefore, for women, negative associations with vegetable consumption could be interpreted as being mainly due to consumption of *Brassica* vegetables.

DISCUSSION

After 6.3 years of follow-up in the Netherlands Cohort Study on Diet and Cancer, some evidence was found for an inverse association between consumption of vegetables and/or fruit in general and the incidence of colon (but not rectal) cancer. As was noted above, case-control studies tend to report clearly negative associations between vegetable and fruit consumption and colon or rectal cancer, but evi-

TABLE 3. Rate ratios for colon cancer according to quintiles of vegetable and/or fruit consumption in men and women, Netherlands Cohort Study, 1986–1992

Quintile of consumption	Median intake (g/day)	No. of cases	Person-years of observation	Age-adjusted rate ratio		Multiply adjusted rate ratio*	
				RR†	95% CI†	RR	95% CI
Men							
Total vegetables and fruits							
1 (low)‡	177	62	1,739	1.00		1.00	
2	257	55	1,694	0.86	0.57, 1.29	0.85	0.57, 1.28
3	319	66	1,777	1.01	0.69, 1.49	1.00	0.67, 1.47
4	393	65	1,715	1.00	0.68, 1.48	1.00	0.68, 1.48
5 (high)	519	64	1,748	0.96	0.65, 1.43	0.95	0.64, 1.41
p-trend				0.85		0.90	
Total vegetables							
1 (low)‡	100	65	1,713	1.00		1.00	
2	144	64	1,765	0.96	0.65, 1.41	0.96	0.65, 1.42
3	175	61	1,745	0.94	0.64, 1.39	0.92	0.62, 1.36
4	214	65	1,761	1.00	0.68, 1.47	0.98	0.66, 1.44
5 (high)	285	57	1,689	0.89	0.60, 1.32	0.85	0.57, 1.27
p-trend				0.65		0.45	
Total fruit							
1 (low)‡	34	56	1,817	1.00		1.00	
2	91	75	1,765	1.41	0.96, 2.07	1.40	0.95, 2.06
3	136	50	1,811	0.90	0.59, 1.36	0.91	0.60, 1.38
4	187	74	1,823	1.25	0.85, 1.84	1.29	0.87, 1.90
5 (high)	286	76	1,840	1.31	0.89, 1.93	1.33	0.90, 1.97
p-trend				0.28		0.22	
Women							
Total vegetables and fruits							
1 (low)‡	208	71	1,794	1.00		1.00	
2	298	42	1,714	0.62	0.41, 0.94	0.63	0.41, 0.97
3	370	54	1,765	0.77	0.52, 1.14	0.77	0.52, 1.15
4	444	54	1,770	0.76	0.52,1.12	0.77	0.51, 1.14
5 (high)	578	45	1,762	0.65	0.43, 0.97	0.66	0.44, 1.01
p-trend				0.08		0.10	
Total vegetables							
1 (low)‡	107	64	1,775	1.00		1.00	
2	147	48	1,701	0.80	0.53, 1.20	0.83	0.54, 1.26
3	181	59	1,837	0.92	0.63, 1.36	0.95	0.64, 1.42
4	220	47	1,759	0.78	0.52, 1.17	0.79	0.52, 1.20
5 (high)	293	48	1,733	0.80	0.53, 1.20	0.83	0.54, 1.26
p-trend				0.25		0.31	
Total fruit							
1 (low)‡	65	45	1,324	1.00		1.00	
2	124	59	1,779	0.96	0.63, 1.46	0.95	0.62, 1.45
3	177	49	1,821	0.79	0.51, 1.23	0.78	0.50, 1.22
4	237	66	2,028	0.91	0.60, 1.38	0.91	0.60, 1.38
5 (high)	343	61	2,404	0.72	0.48, 1.10	0.73	0.48, 1.11
p-trend				0.10		0.12	

* Adjusted for age, family history of colorectal cancer, and category of alcohol intake.
† RR, rate ratio; CI, confidence interval.
‡ Reference category.

dence from cohort studies that has been published thus far is less strong.

In review articles, studies showing at least one significant inverse association are generally treated as being supportive of the hypothesis that vegetables and fruits protect against colorectal cancer. Thus, studies with a negative association for one vegetable/fruit group but positive associations for other vegetable/fruit groups will often be categorized as presenting negative associations. Although this may bias conclusions about the strength of the protective effect of veg-

TABLE 4. Rate ratios for rectal cancer according to quintiles of vegetable and/or fruit consumption in men and women, Netherlands Cohort Study, 1986–1992

Quintile of consumption	Median intake (g/day)	No. of cases	Person-years of observation	Age-adjusted rate ratio		Multiply adjusted rate ratio*	
				RR†	95% CI†	RR	95% CI
Men							
Total vegetables and fruits							
1 (low)‡	177	47	1,743	1.00		1.00	
2	257	34	1,694	0.72	0.45, 1.14	0.72	0.44, 1.15
3	319	31	1,779	0.63	0.39, 1.02	0.63	0.39, 1.02
4	393	43	1,716	0.90	0.58, 1.39	0.90	0.57, 1.41
5 (high)	519	44	1,760	0.89	0.57, 1.38	0.88	0.56, 1.37
p-trend				0.94		0.90	
Total vegetables							
1 (low)‡	100	42	1,717	1.00		1.00	
2	144	39	1,765	0.91	0.57, 1.44	0.89	0.56, 1.43
3	175	39	1,746	0.93	0.58, 1.47	0.88	0.55, 1.41
4	214	39	1,761	0.92	0.58, 1.46	0.87	0.54, 1.39
5 (high)	285	40	1,703	0.96	0.61, 1.52	0.88	0.55, 1.41
p-trend				0.89		0.58	
Total fruit							
1 (low)‡	34	50	1,822	1.00		1.00	
2	91	48	1,771	1.00	0.65, 1.52	0.99	0.64, 1.52
3	136	32	1,818	0.64	0.40, 1.02	0.65	0.40, 1.05
4	187	42	1,824	0.81	0.52, 1.26	0.84	0.54, 1.31
5 (high)	286	43	1,842	0.84	0.54, 1.29	0.85	0.55, 1.32
p-trend				0.22		0.29	
Women							
Total vegetables and fruits							
1 (low)‡	208	20	1,797	1.00		1.00	
2	298	24	1,706	1.26	0.68, 2.33	1.27	0.69, 2.35
3	370	26	1,765	1.32	0.72, 2.42	1.33	0.73, 2.43
4	444	22	1,771	1.10	0.59, 2.06	1.08	0.58, 2.03
5 (high)	578	23	1,766	1.17	0.63, 2.17	1.17	0.63, 2.17
p-trend				0.81		0.84	
Total vegetables							
1 (low)‡	107	16	1,778	1.00		1.00	
2	147	24	1,706	1.59	0.83, 3.05	1.56	0.81, 2.99
3	181	22	1,837	1.37	0.70, 2.65	1.35	0.69, 2.61
4	220	25	1,759	1.64	0.86, 3.14	1.60	0.84, 3.06
5 (high)	293	28	1,735	1.85	0.98, 3.49	1.78	0.94, 3.38
p-trend				0.07		0.09	
Total fruit							
1 (low)‡	65	16	1,324	1.00		1.00	
2	124	21	1,784	0.96	0.49, 1.88	0.95	0.48, 1.87
3	177	29	1,827	1.31	0.70, 2.47	1.31	0.70, 2.48
4	237	33	2,030	1.29	0.70, 2.41	1.30	0.69, 2.41
5 (high)	343	20	2,413	0.67	0.34, 1.31	0.67	0.34, 1.33
p-trend				0.41		0.44	

* Adjusted for age, family history of colorectal cancer, and category of alcohol intake.
† RR, rate ratio; CI, confidence interval.
‡ Reference category.

etable/fruit consumption on colorectal cancer, there is no doubt about the overall conclusion that negative associations have been observed in most case-control studies.

Comparison of the present data with results from other cohort studies is complicated by the fact that different studies use different endpoints (e.g., colon cancer, rectal cancer, colorectal cancer, or adenomas of the colon or rectum) or sex groups, and some present results from pooled analyses. In addition, only a few studies have conducted analyses using more than one variable to reflect vegetable or fruit intake.

TABLE 5. Rate ratios* for colon and rectal cancer according to consumption of specific groups of vegetables and fruits in men and women, Netherlands Cohort Study, 1986–1992

Quintile or category of consumption	Men					Women				
	Median intake (g/day)	Colon cancer		Rectal cancer		Median intake (g/day)	Colon cancer		Rectal cancer	
		RR†	95% CI†	RR	95% CI		RR	95% CI	RR	95% CI
Cooked vegetables										
1 (low)‡	79	1.00		1.00		80	1.00		1.00	
2	115	0.94	0.64, 1.39	0.89	0.56, 1.41	115	0.66	0.43, 1.02	1.08	0.58, 2.00
3	143	0.85	0.57, 1.26	0.76	0.47, 1.22	142	0.96	0.65, 1.43	0.70	0.35, 1.38
4	175	0.92	0.62, 1.36	0.77	0.48, 1.24	174	0.87	0.58, 1.31	1.38	0.77, 2.48
5 (high)	234	0.94	0.64, 1.39	0.96	0.61, 1.51	227	0.75	0.49, 1.14	1.34	0.74, 2.42
p-trend		0.72		0.67			0.43		0.18	
Raw vegetables										
1 (low)‡	7	1.00		1.00		10	1.00		1.00	
2	19	0.56	0.37, 0.84	0.71	0.43, 1.17	25	0.95	0.63, 1.42	0.82	0.42, 1.56
3	30	0.88	0.61, 1.27	1.00	0.63, 1.56	37	0.92	0.60, 1.39	1.40	0.78, 2.51
4	44	0.77	0.53, 1.13	0.93	0.59, 1.47	50	0.68	0.43, 1.06	0.92	0.48, 1.75
5 (high)	73	0.79	0.54, 1.16	0.93	0.58, 1.47	76	1.02	0.67, 1.54	1.24	0.67, 2.26
p-trend		0.47		0.91			0.53		0.42	
Legumes										
1 (low)‡	11	1.00		1.00		10	1.00		1.00	
2	22	0.95	0.65, 1.40	0.89	0.56, 1.42	18	0.65	0.42, 1.00	1.07	0.57, 2.00
3	30	0.83	0.55, 1.25	0.90	0.56, 1.46	26	1.02	0.68, 1.51	1.40	0.77, 2.57
4	40	1.02	0.69, 1.51	1.07	0.67, 1.69	37	0.86	0.57, 1.29	1.44	0.79, 2.62
5 (high)	62	1.13	0.77, 1.64	0.92	0.58, 1.47	58	0.79	0.52, 1.20	1.01	0.53, 1.94
p-trend		0.41		0.97			0.58		0.59	
Brassica vegetables										
1 (low)‡	11	1.00		1.00		11	1.00		1.00	
2	21	1.00	0.69, 1.46	0.73	0.45, 1.18	20	0.60	0.40, 0.89	0.83	0.44, 1.57
3	29	0.82	0.56, 1.22	0.79	0.49, 1.26	28	0.85	0.58, 1.25	1.28	0.70, 2.33
4	40	0.91	0.62, 1.32	0.95	0.61, 1.48	38	0.66	0.44, 0.99	1.01	0.53, 1.90
5 (high)	58	0.76	0.51, 1.13	0.88	0.56, 1.39	58	0.51	0.33, 0.80	1.66	0.94, 2.94
p-trend		0.11		0.94			0.004		0.05	
Leafy vegetables, cooked										
1 (low)‡	4	1.00		1.00		4	1.00		1.00	
2	12	1.05	0.72, 1.52	0.86	0.53, 1.39	12	0.99	0.67, 1.48	1.00	0.55, 1.84
3	19	0.79	0.53, 1.18	1.19	0.76, 1.88	19	0.94	0.62, 1.41	1.30	0.73, 2.32
4	27	0.84	0.57, 1.25	1.00	0.62, 1.60	27	1.03	0.69, 1.53	1.02	0.55, 1.88
5 (high)	41	0.75	0.50, 1.13	0.88	0.54, 1.44	41	0.62	0.40, 0.96	1.16	0.65, 2.07
p-trend		0.05		0.86			0.06		0.61	
Leafy vegetables, raw										
Low‡	3	1.00		1.00		3	1.00		1.00	
Medium	8	0.97	0.71, 1.31	1.13	0.79, 1.62	8	0.82	0.59, 1.14	0.82	0.51, 1.32
High	18	1.02	0.75, 1.38	0.95	0.66, 1.39	18	0.98	0.71, 1.35	1.11	0.70, 1.75
p-trend		0.92		0.83			0.85		0.64	
Citrus fruit										
1 (low)‡	0	1.00		1.00		8	1.00		1.00	
2	17	0.95	0.64, 1.41	0.74	0.47, 1.18	38	0.95	0.62, 1.45	0.96	0.51, 1.79
3	41	0.95	0.64, 1.40	1.00	0.65, 1.54	79	1.22	0.82, 1.81	1.08	0.59, 1.97
4	83	1.08	0.74, 1.58	0.81	0.52, 1.27	111	0.94	0.62, 1.45	1.27	0.70, 2.30
5 (high)	167	1.09	0.75, 1.59	0.77	0.49, 1.20	187	1.00	0.66, 1.52	1.16	0.63, 2.12
p-trend		0.44		0.33			0.99		0.38	

* The model included age, family history of colorectal cancer, and category of alcohol intake.
† RR, rate ratio; CI, confidence interval.
‡ Reference category.

In the present study, negative associations with vegetable and fruit consumption were more pronounced for women than for men. Similar differences have been observed in all other cohort studies presenting data on both men and women (5, 11, 12). It has been suggested that this could be attributed to greater accuracy of female food intake data, since traditionally women have been responsible for food preparation (12). Our questionnaire was validated against dietary records, and correlation coefficients for vegetables and fruits did not differ between the sexes (23).

In our study, more detailed analyses of groups of vegetables and of specific vegetables and fruits did show negative associations with *Brassica* vegetables and cooked leafy vegetables for colon cancer in both men and women. *Brassica* vegetables are known to have cancer-preventive effects (27). It has been suggested that the protective effect may be

TABLE 6. Rate ratios for colon and rectal cancer according to consumption of individual vegetables and fruits (continuous variables), per 25-g/day increment, in men and women: Netherlands Cohort Study, 1986–1992*

	Mean intake in subcohort (g/day)	Colon cancer				Rectal cancer			
		Men		Women		Men		Women	
		Rate ratio†	Adjusted rate ratio‡	Rate ratio†	Adjusted rate ratio‡	Rate ratio†	Adjusted rate ratio‡	Rate ratio†	Adjusted rate ratio‡
Total vegetables	189.7	0.98		0.97		0.99		1.05	
Cooked vegetables	150.8	1.00		0.96		0.98		1.05	
Brussels sprouts	7.7	0.87	0.94	0.61	0.89	0.89	0.99	0.89	0.53
Cauliflower	14.2	0.90	0.97	0.62	0.69	0.92	0.91	1.62	1.73
Cabbage	7.0	0.74	0.76	0.69	0.76	1.00	1.03	1.14	1.10
Spinach	9.5	0.96	1.09	0.63	0.76	1.02	1.04	1.31	1.18
Endive, cooked	11.9	0.72	0.68	0.87	1.03	0.97	0.99	1.15	0.94
Beetroot	7.9	0.94	1.02	0.96	1.16	1.01	1.06	1.28	1.17
String beans	20.0	1.08	1.18	0.79	0.85	0.96	0.98	0.88	0.67
Broad beans	4.5	1.02	1.02	0.89	1.22	0.67	0.64	1.89	1.98
Kale	3.3	0.71	0.76	0.39	0.56	1.60	2.02	0.91	0.71
Carrots, cooked	8.9	0.99	1.07	1.05	1.28	0.97	0.96	1.20	1.08
Sweet peppers	2.9	1.48	1.69	1.15	1.26	1.03	1.03	2.02	1.83
Sauerkraut	5.8	0.89	1.15	0.80	1.27	0.97	0.92	1.31	1.24
Rhubarb	2.3	1.32	1.37	0.89	0.90	0.78	0.76	0.56	0.57
Mushrooms	3.5	1.13	0.97	0.94	1.02	0.99	1.02	2.39	1.70
Gherkins	1.9	0.65	0.66	0.74	0.77	0.95	0.91	0.69	0.58
Raw vegetables	38.9	0.91		0.96		1.03		1.11	
Endive	2.4	0.50	0.49	0.96	2.00	0.54	0.51	2.16	2.00
Carrots	2.8	0.75	0.78	0.89	1.07	1.02	1.05	1.20	1.07
Lettuce	7.6	1.18	1.43	0.88	0.80	0.93	0.95	0.99	0.80
Tomatoes	21.5	0.93	0.93	0.97	1.18	1.10	1.11	1.20	1.18
Total fruit	175.7	1.00		0.98		1.00		1.00	
Citrus fruit	76.8	1.01		1.01		0.98		1.01	
Mandarins	4.7	0.68	0.69	1.18	1.26	0.86	0.96	1.40	1.61
Oranges/fresh orange juice	48.4	1.00	1.00	1.01	1.01	1.02	1.02	0.98	0.98
Grapefruits/fresh grapefruit juice	9.1	1.07	1.07	1.03	1.04	0.98	0.99	1.03	1.05
Grapes	4.5	0.97	1.08	1.02	1.08	0.83	0.92	0.62	0.58
Bananas	12.9	0.98	0.99	0.88	0.88	0.88	0.90	0.77	0.77
Apples, pears	76.0	1.01	1.01	0.97	0.97	1.01	1.01	0.97	0.97
Strawberries	7.5	0.70	0.71	0.70	0.68	0.61	0.64	0.99	1.14
Orange/grapefruit juice	14.5	1.00	1.00	0.99	0.99	0.86	0.87	1.05	1.07
Other fruit juices	10.4	1.04	1.04	0.99	1.00	0.91	0.93	0.87	0.87

* Results are presented with and without adjustment for consumption of other cooked or raw vegetables, or other fruits.
† Adjusted for age, alcohol intake, and family history of colorectal cancer.
‡ Additionally adjusted by simultaneous inclusion of items in the cooked vegetable group, the raw vegetable group, and the fruit group, respectively.

partly due to these vegetables' relatively high content of glucosinolates, of which certain hydrolysis products have shown anticarcinogenic properties (28). However, other cohort studies that have presented data on *Brassica* vegetables have found no association or a positive association. No association was found for colon cancer in the Iowa Women's Health Study (13) or for adenoma in the Health Professionals Follow-up Study (16); a positive association with colorectal cancer was found among male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (18).

For rectal cancer, inverse associations with vegetable and/or fruit consumption were not found in either sex. Associations even tended to be positive for total vegetable consumption and consumption of *Brassica* vegetables in women.

Separate analyses on subsites of the colon showed stronger inverse relations of vegetable consumption with cancer of the distal colon than with cancer of the proximal colon. For women, similar results on subsites were found in the Iowa Women's Health Study (13). The fiber in vegetables and fruits might dilute concentrations of carcinogens by increasing fecal bulk in the distal part of the colon. In the other prospective study that presented data on colon subsites, the Nurses' Health Study, investigators reported no effect of total dietary fiber (the only variable included in separate analyses) on either subsite (10).

TABLE 7. Rate ratios for colon cancer according to quintiles of vegetable and/or fruit consumption in men and women, by subsite: Netherlands Cohort Study, 1986–1992*

Quintile of consumption	Men				Women			
	Proximal colon		Distal colon		Proximal colon		Distal colon	
	RR†	95% CI†	RR	95% CI	RR	95% CI	RR	95% CI
	(*n* = 148)		(*n* = 153)		(*n* = 138)		(*n* = 116)	
Total vegetables and fruits								
1 (low)‡	1.00		1.00		1.00		1.00	
2	0.93	0.53, 1.63	0.73	0.42, 1.30	0.61	0.34, 1.10	0.63	0.36, 1.11
3	1.01	0.58, 1.75	1.05	0.62, 1.76	0.82	0.48, 1.41	0.71	0.42, 1.22
4	1.07	0.62, 1.84	1.00	0.59, 1.71	0.91	0.54, 1.54	0.57	0.32, 1.01
5 (high)	0.89	0.51, 1.56	1.04	0.62, 1.75	0.89	0.52, 1.51	0.44	0.23, 0.82
p-trend	0.89		0.53		0.90		0.01	
Total vegetables								
1 (low)‡	1.00		1.00		1.00		1.00	
2	1.01	0.58, 1.77	0.89	0.53, 1.49	0.76	0.42, 1.36	0.75	0.43, 1.33
3	1.11	0.64, 1.92	0.82	0.48, 1.38	0.96	0.56, 1.65	0.95	0.56, 1.61
4	1.13	0.65, 1.97	0.88	0.53, 1.49	1.11	0.65, 1.89	0.43	0.22, 0.83
5 (high)	1.03	0.59, 1.81	0.76	0.27, 1.30	0.99	0.57, 1.72	0.64	0.36, 1.17
p-trend	0.78		0.33		0.58		0.04	
Brassica vegetables								
1 (low)‡	1.00		1.00		1.00		1.00	
2	1.26	0.73, 2.17	0.96	0.59, 1.56	0.70	0.42, 1.17	0.56	0.32, 1.00
3	1.02	0.57, 1.81	0.79	0.47, 1.32	0.76	0.44, 1.29	1.06	0.64, 1.77
4	1.38	0.82, 2.32	0.57	0.33, 0.99	0.82	0.49, 1.39	0.53	0.28, 0.98
5 (high)	0.93	0.52, 1.66	0.68	0.41, 1.15	0.57	0.32, 1.02	0.47	0.25, 0.89
p-trend	0.96		0.02		0.12		0.02	
	(*n* = 159)		(*n* = 160)		(*n* = 144)		(*n* = 122)	
Total fruit								
1 (low)‡	1.00		1.00		1.00		1.00	
2	1.44	0.86, 2.43	1.28	0.74, 2.21	0.88	0.50, 1.54	1.07	0.57, 2.00
3	0.78	0.43, 1.41	1.04	0.59, 1.83	0.65	0.36, 1.19	1.01	0.54, 1.90
4	1.21	0.71, 2.05	1.38	0.81, 2.37	0.77	0.44, 1.35	1.04	0.57, 1.92
5 (high)	1.20	0.71, 2.05	1.49	0.88, 2.54	0.81	0.47, 1.39	0.59	0.30, 1.13
p-trend	0.76		0.11		0.43		0.09	

* The model included age, family history of colorectal cancer, and category of alcohol intake.
† RR, rate ratio; CI, confidence interval.
‡ Reference category.

Alcohol intake and family history of colorectal cancer were included in the analyses, because these variables showed an effect on colon and/or rectal cancer risk. Subjects in the highest category of alcohol intake (≥30 g/day) had an increased risk of colorectal cancer compared with abstainers (rate ratios were 2.2 for rectal cancer in both sexes, 1.5 for colon cancer in men, and 1.8 for colon cancer in women). Having a family history of colorectal cancer doubled the risks for colon and rectal cancer in men and for colon cancer in women, whereas it did not seem to be associated with rectal cancer risk in women. Rate ratios for age were 1.09 for colon cancer and 1.07 for rectal cancer per 1-year increment. Adjustment for pack-years of cigarettes smoked, leisure time physical activity, body mass index, and total energy consumption did not influence estimated rate ratios and thus were not included in the model.

Surprisingly, we found that increased alcohol intake was related to higher vegetable consumption among both men and women in the subcohort. This was not a direct effect of socioeconomic status, because in stratified analyses the relation was found within each socioeconomic subgroup (data not shown). Additional analyses revealed that this relation resulted from a larger reported serving size of vegetables, not a higher frequency of consumption, among subjects with a higher alcohol intake. In addition, the reported serving size of meat appeared to be higher among these subjects. However, adjustment for alcohol intake did not change rate ratio estimates importantly.

Generally, information bias—i.e., changes in the reported dietary habits of cases due to their disease—is largely avoided in prospective studies, since dietary habits are reported before the disease is diagnosed. However, in the Netherlands Cohort Study, vegetable and fruit consumption might have been influenced by the presence of latent colorectal cancer. We think this is unlikely, because neither vegetable consumption nor fruit consumption differed between colon and rectal cancer cases detected during the first 2 years of follow-up and cases detected in later years. Actually, repeating the analyses after exclusion of cases detected during the first 2 years of follow-up did not affect the results importantly.

Other circumstances might have been responsible for obscuring associations between vegetable consumption and colorectal cancer risk. However, with 514 male and 396 female colorectal cancer cases, the power of this study should have been sufficiently large to detect important associations. In addition, the possibility of selection bias due to exposure-related loss to follow-up can be excluded, since the completeness of follow-up for cancer incidence was estimated at more than 96 percent and no subcohort members were lost to follow-up. Another reason for our not finding a clear postulated association between vegetable consumption and colorectal cancer incidence might be that the dietary habits assessed by our questionnaire do not sufficiently reflect dietary intakes in previous decades, the time span needed for development of colorectal cancer. To avoid this problem, researchers in the Nurses' Health Study (10) and the Health Professionals Follow-up Study (14, 16) focused on colorectal adenomatous polyps; as precursors of colon cancer, such polyps antedate the clinical diagnosis of colorectal cancer by an average of 10 years (29). Initially, dietary fiber from all sources (vegetables, fruits, and grains) was significantly associated with a lower risk of colorectal adenoma in men (14); but with longer follow-up and multivariate analyses, only fiber from fruit, not that from vegetables or cereals, appeared to be protective (16). However, incident adenomatous polyps (those appearing after a "clean" endoscopy prior to the start of the study) did show inverse associations for fiber from fruit (but not fiber from vegetables). Fruits and folate-rich vegetables showed significant inverse associations with adenomatous polyps of the distal colon (16). No association of fiber from vegetables or fruit with distal colorectal adenomas was found for women (10).

Could the assessment of vegetable or fruit consumption itself have biased the results obtained? To minimize the amount of uninformative data, in addition to the general dietary exclusion criteria, we excluded subjects who appeared not to have understood how to fill in the questions on vegetable consumption, which appeared in the first part of the food frequency questionnaire; those subjects were defined by an extreme score on the vegetable error index. Vegetable intakes are generally considered difficult to assess with food frequency questionnaires (as well as with other methods of dietary assessment), particularly if portion sizes have to be estimated. In our validation study, the correlation coefficient for total vegetable consumption was 0.4 (21); this is quite low but is comparable to the figures reported for many other prospective studies, including the Dutch part of the EPIC Study (European Prospective Investigation into Cancer and Nutrition) (30) and the study of Japanese-American men in Hawaii (31). One reason for the low correlation may be a relative lack of true contrast in frequencies of total vegetable consumption among our subjects, because the Dutch are accustomed to eating only one hot meal per day, almost always including vegetables. Coefficients of variation for total vegetable consumption are approximately 40 percent for both men and women. A consequence of a relatively large measurement error, resulting in an attenuation of the estimated rate ratio, is underestimation of the inverse association between total vegetable consumption and colorectal cancer. Because of individual preferences, contrast in consumption frequencies is much higher for specific vegetables (coefficient of variation ~100 percent). Therefore, a smaller error is expected for the assessment of specific vegetables, and inverse associations with colon and/or rectal cancer will be less likely to be obscured. It was not possible to assess validity for specific vegetables in our validation study, since 9 days of dietary records are not sufficient for estimating the consumption frequency of specific vegetables. For fruit consumption, more contrast is observed than for vegetables (coefficient of variation = 73 percent for men and 61 percent for women), and portion sizes are easier to estimate, reducing the measurement error.

Another explanation that must be considered in interpreting these results is that unmeasured or unknown factors may have caused some confounding. However, it is unlikely that such factors had a great impact on the association between vegetable or fruit consumption and colon or rectal cancer incidence. Because of multiple comparisons, chance might have played a role in our findings, particularly in the analyses of specific vegetables.

The present analyses confirm that, especially for men, the evidence for a protective effect of vegetables on risks of colon and rectal cancer is less strong in cohort studies than in case-control studies. From these data, it cannot be concluded in general that increased vegetable or fruit consumption will lead to a considerable decrease in colorectal cancer risk, although *Brassica* vegetables were exceptional in showing rather strong negative associations with colon cancer in both sexes. However, with regard to rectal cancer, *Brassica* vegetables appear to enhance risk in women. No conclusion can be drawn about the protective effect of increasing consumption of vegetables among subjects with very low vegetable or fruit consumption, since these people were not well represented in the cohort. Likewise, we cannot exclude the possibility that vegetables and fruits play a more important role among subjects with certain dietary habits, such as very high meat consumption. Further analyses will be necessary to test these hypotheses.

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