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Body Mass Index and Colon Cancer in a National Sample of Adult US Men and Women

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The evidence supporting obesity as a risk factor for colon cancer remains inconclusive, especially among women. The author studied the association between obesity and colon cancer in a nationally representative cohort of men and women aged 25–74 years who participated in the First National Health and Nutrition Examination Survey from 1971 to 1975 and were subsequently followed up through 1992. Among the 13,420 persons included in the analytic sample, 222 incident cases of colon cancer were identified. Height and weight were measured during the baseline examination. Compared with participants whose body mass index was less than 22 kg/m^2, the hazard ratios were 1.79 (95% confidence interval (CI): 0.87, 3.71), 1.86 (95% CI: 0.86, 4.03), 2.47 (95% CI: 1.14, 5.32), 3.72 (95% CI: 1.68, 8.22), and 2.79 (95% CI: 1.22, 6.35) for participants with a body mass index of 22–<24 kg/m^2, 24–<26 kg/m^2, 26–<28 kg/m^2, 28–<30 kg/m^2, and ≥30 kg/m^2, respectively. The hazard ratios were similar for men and women. Subscapular skinfold thickness, but not triceps skinfold thickness, was positively associated with colon cancer incidence among men but not women, after adjustment for body mass index and other possible confounders. These results strongly support the hypothesis that excess body weight is a risk factor for colon cancer among both men and women. *Am J Epidemiol* 1999;150:390–8.

body mass index; colonic neoplasms; follow-up studies; obesity; risk factors

Colon cancer is the third most common cancer among both men and women in the United States. For 1995, the American Cancer Society estimated that about 45,500 men and 49,000 women would be newly diagnosed with colon cancer and that about 46,400 Americans would die from this disease (1). Various dietary components, reproductive history and factors, use of nonsteroidal anti-inflammatory agents, tobacco use, hormone use, physical activity, and obesity have been studied as possible risk factors for colon cancer (2). Despite the number of prospective (3–25) and case-control studies (26–51) that have examined the association between obesity and colon cancer in greater or lesser detail, the evidence for obesity as a risk factor is not viewed as conclusive (52). Studies of colon or colorectal adenomas also have been inconclusive (21, 46, 53–65). Some have suggested that obesity represents a surrogate marker for dietary excess, a sedentary lifestyle, or some other unmeasured factor. Because the prevalence of obesity has increased dramatically since the late 1970s (66), it is important to characterize its associated morbidity and mortality burden, including possibly colon cancer.

The National Health and Nutrition Examination Survey (NHANES) Epidemiologic Follow-up Study offers several advantages when examining the relation between obesity and colon cancer. The study includes a large cohort that is representative of the civilian noninstitutionalized population of the United States. It contains large numbers of women, the follow-up period covers almost 20 years, and weight and height were measured in a standardized fashion at entry into the study. Therefore, the goals of this study were to examine the association between body mass index and colon cancer in a national sample of men and women and to estimate the population attributable fraction of obesity-associated colon cancer. Because few studies have shown that obesity also is related to colon cancer in women, one of the major goals of this study was to examine this relation among women.

MATERIALS AND METHODS

Between 1971 and 1975, the first NHANES survey (NHANES I) was conducted (67–70). A representative national sample of the noninstitutionalized civilian population was obtained by using a multistage, stratified sampling design. NHANES I participants who were aged 25 years or older were followed up through 1992 (71, 72).

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Abbreviations: CI, confidence interval; ICD-9-CM, *International Classification of Diseases*, Ninth Revision, Clinical Modification; NHANES, National Health and Nutrition Examination Survey.

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Incident cases of colon cancer were identified from health care facility records and death certificates by using *International Classification of Diseases,* Ninth Revision, Clinical Modification (ICD-9-CM) code 153. Participants or their proxies were asked about hospitalizations during the study period. If any were reported, permission was obtained to abstract certain data such as admission and discharge dates and diagnoses. Photocopies of pathology reports for patients with malignancies were also requested. Medical records were recoded by trained medical coders by using ICD-9-CM codes. Up to 10 diagnostic fields were abstracted from the hospital discharge summary or medical records face sheet. In addition, nursing home administrators were requested to provide information on the dates and reasons for admission. Deaths were identified through searches of the National Death Index and of Health Care Financing Administration enrollee files and through other tracing mechanisms. A participant was considered deceased only if a death certificate had been received or a proxy interview had been completed to verify the death. Through 1992, death certificates had been obtained for 97 percent of deceased participants. The date of onset was chosen as the earlier occurrence of death from colon cancer or hospitalization for this condition.

At baseline, participants were weighed under controlled conditions in mobile examination trailers by using a self-balancing scale that recorded their weight to within 0.11 kg (0.25 pounds). Examination clothing consisted of disposable paper uniforms and foam-rubber slippers. The weight of this clothing was not subtracted from the participants' measured weight, but it varied between 0.09 kg and 0.27 kg (0.2–0.6 pounds). By using the weight and height for each participant, the author created six levels of body mass index: <22 kg/m^2, 22–<24 kg/m^2, 24–<26 kg/m^2, 26–<28 kg/m^2, 28–<30 kg/m^2, and ≥30 kg/m^2.

The subscapular and triceps skinfolds were measured to the nearest millimeter. The distribution of the entire sample was used, and quintiles were constructed for both skinfolds and the subscapular/triceps skinfold ratio.

Covariates in the analysis were age, race (non-White, White), education (years), cigarette smoking (never, former, current), serum cholesterol concentration (mg/dl), recreational exercise (much, moderate, little or no exercise), nonrecreational exercise (very active, moderately active, quite inactive), and alcohol consumption (0, 1–2, ≥3 drinks per day). For smoking, the author used a variable that was constructed in part from responses obtained during the baseline interview and in part from the first follow-up interview (73, 74). Two questions were used to create the categories of smoking: "Have you smoked at least 100 cigarettes during your entire life?" and "Do you smoke cigarettes now?" Cholesterol was measured by using a modification of the Abell-Kendall method. Dietary information was collected from 11,348 participants through a single 24-hour dietary recall questionnaire and a 19-question food frequency questionnaire. For the group of analyses that included dietary covariates, the author added data on total energy and fat intake, collected from a single 24-hour dietary recall, and fruit and vegetable intake (<1, 1–2, >2–3, >3 per day) determined from a single dietary frequency question.

Persons who indicated that they had been operated on for a tumor of the stomach, bowel, or colon were excluded from the analysis, as were persons who were lost to follow-up for all attempted contacts or for whom data on any of the study variables were missing. Person-time was calculated for each participant from the time of entry into the study until one of the following conditions occurred: 1) the participant developed colon cancer, 2) the participant died or left the study, or 3) follow-up was completed in 1992. By using direct standardization, age-adjusted incidence rates were standardized to the age distribution from the 1980 US Census. The independent association between body mass index and colon cancer was examined with proportional hazard models. To account for the complex sampling design, SUDAAN software was used for all analyses except for evaluation of proportionality assumptions, which were done with SAS software (75, 76). Population attributable fractions for multiple-category exposures were calculated with the following formula presented by Kleinbaum et al. (77):

$$1 - \sum_{i=0}^{k} p_{ci}/\mathrm{IDR}$$

where p_{ci} is the estimated proportion of cases in the ith exposure category ($i = 0, \ldots, k$) and IDR is the incidence density ratio for the ith exposure category.

RESULTS

Consecutively excluding participants for various reasons left 222 participants for analysis, as follows: 1) lost to follow-up: 13,861 participants, 232 persons with colon cancer; 2) missing body mass index: 13,855 participants, 232 persons with colon cancer; 3) operation for a tumor of the stomach, bowel, or colon at baseline: 13,660 participants, 226 persons with colon cancer; and 4) missing data for covariates: 13,420 participants, 222 persons with colon cancer. Of the participants who had colon cancer, 57 were identified from death certificates and 165 from institutional records.

For 545 of the 546 participants who were lost to follow-up and whose body mass index was determined at baseline, the unadjusted and age-adjusted body mass index means were 24.8 kg/m^2 and 25.4 kg/m^2, respectively. For 13,855 of the 13,861 participants who were not lost to follow-up and who had a body mass index determination, the unadjusted and age-adjusted body mass index means were 25.6 kg/m^2 ($p = 0.022$) and 25.5 kg/m^2 ($p = 0.768$), respectively. The mean age of participants who were lost to follow-up was about 11 years less than that of the others.

Baseline characteristics, at the inception of the study, of participants who developed colon cancer and of those who remained free of this disease are presented in table 1. Age-adjusted incidence rates of colon cancer among men were somewhat higher than those among women. The lowest incidence rates among both men and women occurred among the leanest participants, those whose body mass index was <22 kg/m^2 (table 2). As body mass index increased, the incidence rates increased steadily and peaked for participants whose body mass index was 28–<30 kg/m^2. This association between body mass index and colon cancer was confirmed in proportional hazards analysis that included various covariates. When body mass index was examined as a continuous variable, the hazard ratio was 1.06 per unit of body mass index (95 percent confidence interval (CI): 1.03, 1.10). The hazard ratios were very similar for both men and women. Furthermore, none of the interaction terms between body mass index and age, race, educational attainment, cholesterol level, or level of physical activity reached statistical significance, suggesting that the hazard ratios for these variables were similar.

To examine the possible confounding effects of several dietary factors on the hazard ratios, the author repeated the proportional hazards regression analyses by including total energy intake, fat intake, and fruit and vegetable intake in the models. Because dietary information was not collected from all participants, the analytic sample included 10,402 participants, of whom 179 developed colon cancer. In general, hazard ratios changed little. Compared with participants whose body mass index was <22 kg/m^2, the hazard ratios were 1.67 (95 percent CI: 0.69, 4.06), 2.28 (95 percent CI: 0.92, 5.68), 2.50 (95 percent CI: 0.91, 6.83), 3.56 (95 percent CI: 1.42, 8.97), and 3.37 (95 percent CI: 1.25, 9.10) for participants whose body mass indexes were 22–<24 kg/m^2, 24–<26 kg/m^2, 26–<28 kg/m^2, 28–<30 kg/m^2, and ≥30 kg/m^2, respectively.

When the author used the hazard ratios from table 2 and the body mass index distribution from the first phase of NHANES III, conducted from 1988 to 1991, the population attributable fraction for multiple levels of a body mass index of ≥22 kg/m^2 was 53 percent for persons aged 25–74 years (52 percent for men and 54 percent for women). This calculation was made by using as the reference category persons whose body mass index was <22 kg/m^2.

Among men, the risk for colon cancer was elevated among those with a triceps skinfold thickness of >20 mm versus ≤20 mm (table 3). Although the hazard ratio for the fourth quintile of triceps skinfold thickness was significantly elevated compared with the lowest quintile, the hazard ratio for the highest quintile failed to achieve statistical significance. Among women, none of the skinfold thickness parameters was significantly associated with colon cancer after adjustment for multiple covariates, including body mass index.

DISCUSSION

In this study of a nationally representative sample of the US population, body mass index at entry into the study was strongly predictive of colon cancer over a 19-year follow-up period. These results agree with those of other prospective studies that have reported on the relation between obesity and colon cancer among men (3, 4, 6, 7, 9–11, 18, 19, 21–23). However, in contrast to some other studies, this study also found a strong association between body mass index and colon cancer among women.

Among prospective studies, about 20 accounts of 15 different study populations have reported on the association between some measure of obesity and colon cancer, but in only a relative few was this association the focus of the study (3–25). Although the majority of these studies support the hypothesis that obesity is in some fashion associated with an increased risk for colon cancer, especially among men, comparisons among these studies are difficult because of the choice of measures of obesity such as relative weight and body mass index, the manner in which these variables were used in the analyses (continuous or categorical), and the choice of reference categories. At least 12 prospective studies included women but not all presented separate estimates of the risk for obesity-associated colon cancer (3, 5, 6, 9–14, 19, 20, 24). Only in three of these studies was a significant positive association reported between body mass index and colon cancer incidence (10, 20, 25). In these studies, the estimated relative risks were about 1.4–1.8 for the highest category of body mass index compared with the lowest category. In contrast, the hazard ratios in the present study were much larger.

The relation between obesity and colon cancer also has been examined in case-control studies (26–51). Positive findings were reported in most (27, 29, 33,

TABLE 1. Baseline characteristics of study participants, by colon cancer status, First National Health and Nutrition Examination Survey, 1971–1975

Characteristic	Participants who developed colon cancer		Participants who remained free of colon cancer	
	Sample size	Age-adjusted %* (SE†)	Sample size	Age-adjusted %* (SE)
Age (years)‡				
25–44	20	11.3 (2.5)	5,849	46.7 (0.7)
45–64	73	55.1 (4.2)	3,837	41.2 (0.8)
≥65	129	33.7 (3.9)	3,512	12.1 (0.6)
Sex				
Male	104	51.4 (8.4)	5,402	47.9 (0.6)
Female	118	48.6 (8.4)	7,796	52.1 (0.6)
Race				
Black	29	13.7 (8.1)	1,919	9.3 (0.7)
White	193	86.3 (8.1)	11,133	89.6 (0.7)
Other	0		146	1.1 (0.2)
Education (years)				
<12	128	45.9 (8.1)	5,812	34.6 (0.8)
≥12	94	54.1 (8.1)	7,386	65.4 (0.8)
Smoking status				
Current	61	29.5 (7.7)	4,885	41.0 (0.6)
Former	41	27.8 (8.9)	2,215	17.4 (0.4)
Never	120	42.7 (7.6)	6,098	41.6 (0.6)
Cholesterol (mg/dl)				
<200	54	37.2 (7.5)	4,587	36.4 (0.8)
200–239	69	38.5 (7.8)	4,408	33.6 (0.6)
≥240	99	24.3 (3.3)	4,203	30.0 (0.6)
Recreational exercise				
Much exercise	39	24.4 (8.1)	2,358	20.6 (0.7)
Moderate exercise	76	36.7 (7.6)	5,028	39.1 (0.8)
Little or no exercise	107	38.9 (7.9)	5,811	40.3 (1.1)
Nonrecreational exercise				
Very active	88	40.3 (7.9)	5,674	44.9 (0.8)
Moderately active	110	38.6 (6.9)	6,165	45.3 (0.7)
Quite inactive	24	21.0 (7.3)	1,358	9.8 (0.4)
Body mass index (kg/m^2)				
<22	28	13.6 (6.3)	3,216	24.2 (0.4)
22–<24	41	11.6 (4.0)	2,332	18.2 (0.4)
24–<26	36	9.8 (2.4)	2,211	17.3 (0.5)
26–<28	40	20.4 (6.6)	1,987	15.5 (0.4)
28–<30	35	15.9 (4.6)	1,286	9.6 (0.3)
≥30	42	28.8 (8.5)	2,166	15.2 (0.4)
Alcoholic drinks per day				
<1	188	74.4 (7.7)	11,045	79.8 (0.8)
1–2	21	22.0 (7.7)	1,329	12.1 (0.6)
≥3	13	3.6 (1.3)	824	8.1 (0.4)

* Weighted estimate.
† SE, standard error.
‡ Age-specific results.

35–40, 43, 47, 50, 51) but not all (26, 28, 30–32, 34, 41, 42, 44–46, 48). Of the studies of 15 populations that reported results separately for men, seven publications found a statistically significant positive association between obesity and colon cancer, seven did not support this association, and one provided no statistical testing. Of the studies of 16 populations that reported results separately for women, six publications found a statistically significant positive association between obesity and colon cancer, nine did not support this association, and one provided no statistical testing. Prior to 1990, most of the case-control studies used

TABLE 2. Age-adjusted incidence rates of and risk for colon cancer as a function of baseline body mass index, National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1971–1992

Baseline body mass index (kg/m²)	No. of incident cases of colon cancer	Person-years of follow-up	Crude incidence rate*	Age-adjusted incidence rate*	Hazard ratio (95% confidence interval)†
			Entire sample		
<22	28	53,475	30	37	1.00
22–<24	41	38,919	63	73	1.79 (0.87, 3.71)
24–<26	36	36,610	76	74	1.86 (0.86, 4.03)
26–<28	40	32,635	105	96	2.47 (1.14, 5.32)
28–<30	35	21,122	153	144	3.72 (1.68, 8.22)
≥30	42	34,904	107	111	2.79 (1.22, 6.35)
			Men		
<22	13	13,485	42	46	1.00
22–<24	16	14,189	61	82	1.58 (0.57, 4.36)
24–<26	18	16,844	71	78	1.59 (0.59, 4.25)
26–<28	24	17,588	103	93	2.41 (<1.00, 5.82)
28–<30	19	9,966	147	163	3.72 (1.41, 9.83)
≥30	14	10,335	110	156	2.95 (0.99, 8.74)
			Women		
<22	15	39,990	25	33	1.00
22–<24	25	24,731	65	68	2.03 (0.80, 5.17)
24–<26	18	19,766	82	70	2.17 (0.78, 6.04)
26–<28	16	15,047	107	90	2.49 (0.83, 7.47)
28–<30	16	11,155	160	131	3.64 (1.27, 10.46)
≥30	28	24,568	105	99	2.74 (1.04, 7.25)

* Per 100,000 person-years; weighted estimates.

† Adjusted for age, sex (except for sex-specific analyses), race, education, smoking status, serum cholesterol concentration, recreational exercise, nonrecreational exercise, and alcohol consumption.

weights that antedated the interview or diagnosis of persons with colon cancer by 3 years or less. More recent case-control studies have examined the relation of body mass index at different ages with colon cancer.

Studies of obesity and colon or colorectal polyps have presented mixed findings (21, 46, 53–65). About half of the studies show a positive association between body mass index or some other anthropometric measure and large-bowel polyps.

For men, several studies have reported relative risks of a magnitude similar to the hazard ratios reported in this study (9, 10, 19). Under the assumption that increasing body mass index increases the risk for colon cancer, the form of the relation between body mass index and colon cancer risk has not been well established. The data from the NHANES Epidemiologic Follow-up Study suggest a reasonably linear relation up to a body mass index of 30 kg/m²; above 30 kg/m², the hazard ratio no longer increases. Possibly the hazard ratio for the 28–30 kg/m² group is abnormally high, or the risk does indeed level off at higher levels of body mass index. However, the sample size also was the smallest in the ≥30 kg/m² group. Several authors have reported relative risks for models that included body mass index as a continuous variable. Klatsky et al. reported a hazard ratio of 1.04 (95 percent CI: 1.02, 1.06) (13), Kreger et al. found a hazard ratio of 1.09 (95 percent CI: 1.00, 1.18) (17), Lee and Paffenbarger found a hazard ratio of 1.08 (95 percent CI: 1.04, 1.13) (18), and Chyou et al. reported a hazard ratio of 1.06 (95 percent CI: 1.03, 1.10) (23). However, the issue of a possible nonlinear relation was not explored in those reports. In comparison, the author found a hazard ratio of 1.06 (95 percent CI: 1.03, 1.10) per kg/m² in the present study.

Researchers also have examined whether the association between obesity and colon cancer varies by tumor site. For example, some studies have suggested that the association between body mass index and colon cancer is especially strong for tumors of the descending colon and sigmoid (37, 38, 43). However, this finding was not supported by other studies (10, 15, 17, 35, 36). Although colon subsite ICD-9-CM codes were available for most of the participants in the NHANES Epidemiologic Follow-up Study who were hospitalized with colon cancer, only a few death certificates contained the information needed to determine which part of the colon was affected. Therefore, analyses for specific colon sites were not performed.

TABLE 3. Hazard ratios from proportional hazards regression analysis for skinfolds and colon cancer incidence, National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, 1971–1992

Skinfolds	Hazard ratio (95% confidence interval)					
	Total		Men		Women	
	Adjusted for multiple covariates* (no. of cancers = 220; no. in sample = 13,395)	Adjusted for multiple covariates and body mass index (no. of cancers = 220; no. in sample = 13,392)	Adjusted for multiple covariates (no. of cancers = 102; no. in sample = 5,499)	Adjusted for multiple covariates and body mass index (no. of cancers = 102, no. in sample = 5,497)	Adjusted for multiple covariates (no. of cancers = 118; no. in sample = 7,896)	Adjusted for multiple covariates and body mass index (no. of cancers = 118; no. in sample = 7,895)
Subscapular quintiles (mm)						
2–10	1.00	1.00	1.00	1.00	1.00	1.00
>10–14.5	1.25 (0.66, 2.38)	1.10 (0.59, 2.05)	1.45 (0.61, 3.43)	1.50 (0.64, 3.52)	1.14 (0.48, 3.43)	0.95 (0.40, 2.25)
>14.5–20	1.23 (0.64, 2.37)	1.00 (0.52, 1.93)	1.82 (0.79, 4.16)	1.91 (0.79, 4.65)	0.83 (0.34, 4.16)	0.62 (0.24, 1.56)
>20–26.5	1.97 (0.99, 3.95)	1.47 (0.73, 2.94)	3.48 (1.51, 8.05)	3.73 (1.51, 9.26)	1.06 (0.44, 8.05)	0.65 (0.27, 1.59)
>26.5–66	1.89 (0.95, 3.75)	1.16 (0.49, 2.72)	2.79 (1.07, 7.27)	3.11 (0.68, 14.23)	1.28 (0.54, 7.27)	0.55 (0.20, 1.50)
Continuous (per 10 mm)	1.02 (1.00, 1.04)	1.00 (0.97, 1.03)	1.04 (1.01, 1.06)	1.03 (0.98, 1.08)	1.01 (0.99, 1.04)	0.98 (0.94, 1.02)
	(no. of cancers = 221; no. in sample = 13,411)	(no. of cancers = 221; no. in sample = 13,408)	(no. of cancers = 104; no. in sample = 5,505)	(no. of cancers = 104; no. in sample = 5,503)	(no. of cancers = 117; no. in sample = 7,906)	(no. of cancers = 117; no. in sample = 7,905)
Triceps quintiles (mm)						
2–10	1.00	1.00	1.00	1.00	1.00	1.00
>10–14	1.00 (0.51, 1.99)	0.87 (0.43, 1.74)	0.99 (0.46, 2.15)	0.84 (0.37, 1.91)	0.99 (0.20, 4.79)	0.87 (0.18, 4.13)
>14–19	1.23 (0.64, 2.35)	0.98 (0.48, 1.99)	1.33 (0.61, 2.91)	1.02 (0.39, 2.63)	0.94 (0.27, 3.28)	0.75 (0.22, 2.61)
>19–26	1.45 (0.78, 2.71)	1.01 (0.49, 2.05)	0.88 (0.27, 2.83)	0.58 (0.15, 2.32)	1.43 (0.34, 6.01)	1.01 (0.24, 4.19)
>26–65	1.51 (0.73, 3.12)	0.79 (0.30, 2.10)	2.65 (0.69, 10.20)	1.18 (0.18, 7.60)	1.25 (0.30, 5.20)	0.69 (0.15, 3.17)
Continuous (per 10 mm)	1.02 (1.00, 1.05)	1.00 (0.96, 1.03)	1.04 (0.99, 1.09)	1.01 (0.94, 1.09)	1.01 (0.99, 1.04)	0.98 (0.94, 1.03)
	(no. of cancers = 219; no. in sample = 13,392)	(no. of cancers = 219; no. in sample = 13,389)	(no. of cancers = 102; no. in sample = 5,499)	(no. of cancers = 102; no. in sample = 5,497)	(no. of cancers = 117; no. in sample = 7,893)	(no. of cancers = 117; no. in sample = 7,892)
Subscapular/triceps ratio quintiles						
0.16–0.67	1.00	1.00	1.00	1.00	1.00	1.00
>0.67–0.90	1.05 (0.60, 1.85)	0.90 (0.52, 1.56)	0.67 (0.16, 2.88)	0.69 (0.16, 2.90)	1.10 (0.58, 2.08)	0.93 (0.49, 1.76)
>0.90–1.14	0.93 (0.49, 1.77)	0.74 (0.39, 1.37)	0.64 (0.16, 2.59)	0.64 (0.16, 2.58)	0.93 (0.44, 1.95)	0.71 (0.35, 1.45)
>1.14–1.5	0.87 (0.46, 1.64)	0.67 (0.36, 1.23)	0.59 (0.16, 2.11)	0.55 (0.15, 2.03)	0.98 (0.45, 2.11)	0.71 (0.34, 1.47)
>1.5–6.67	1.27 (0.59, 2.70)	0.95 (0.46, 1.97)	0.88 (0.24, 3.29)	0.81 (0.22, 3.05)	1.11 (0.20, 6.04)	0.88 (0.17, 4.52)

* Multiple covariates: age, sex (except for sex-specific analyses), race, education, smoking status, serum cholesterol concentration, recreational exercise, nonrecreational exercise, and alcohol consumption.

Only one other prospective study appears to have examined the relation between skinfold thickness and colon cancer incidence (22). In that study of men, no significant association was observed between subscapular skinfold thickness, triceps skinfold thickness, or the ratio of the two and colon cancer incidence. Although skinfold thickness was not positively associated with colon cancer in women in the NHANES Epidemiologic Follow-up Study, subscapular skinfold thickness appeared to be associated positively with colon cancer in men, although the hazard ratio failed to achieve significance.

This study is subject to several limitations. The outcome variable, colon cancer, was derived from health care facility records and death certificates, which resulted in some degree of misclassification. Little is known about the validity of ICD-9-CM codes specified on hospital records to indicate colon cancer. However, colon cancer appears to be overcoded and rectal cancer undercoded on death certificates (78, 79). Using data from the Surveillance, Epidemiology, and End Results Program as the gold standard, Chow and Devesa reported that colon cancer deaths were overreported by 19.9 percent during 1975–1976, 26.5 percent during 1980–1981, and 26.1 percent during 1985–1986 (79). If misclassification of colon cancer was similar at each level of body mass index, some attenuation of the hazard ratios might have occurred. However, the author is not aware of data showing that misclassification of colon cancer on death certificates and hospitalization records varies according to body mass index.

Some researchers have adjusted for a family history of colon cancer or a history of a previous colonoscopy or sigmoidoscopy. No such information was collected in NHANES I. It is uncertain whether these variables would confound the relation between obesity and colon cancer. It also is possible that the analysis did not control adequately for the effect of physical activity, as this information was derived from two broad questions. However, these physical activity variables were shown in the same data set to predict the future occur-

rence of cancer (80). Adjustment for total energy and fat intake may have been incomplete in the set of analyses that included dietary data, as this information was obtained from a single 24-hour recall. A diagnostic bias could have affected the results if colon cancer was diagnosed more readily in overweight participants than in participants whose weights were within acceptable limits. However, there is no information to support or refute this possibility.

The role of obesity in the pathogenesis of colon cancer is not well understood. Obesity may be a marker for one or more risk factors for colon cancer. For example, body weight for each person is largely a function of the net effects of energy expenditure and energy consumption. Given the difficulty of measuring both physical activity and dietary intake accurately, body weight could represent a more accurate method of determining the cumulative effects of these two variables. If obesity is a risk factor, it may act as a promoter of carcinogenesis; body mass index was not associated with colon adenomas smaller than 1 cm, whereas it was with larger adenomas and with colon cancer (21). McKeown-Eyssen (81) and Giovannucci (82) have proposed that hyperinsulinemia may be one of the factors responsible for the increased colon cancer risk. They base their reasoning on the following lines of evidence: insulin has growth factor properties, normal and malignant colon cells have insulin receptors, cell culture studies have shown that insulin stimulates the growth of colonic epithelial cells, insulin is a mitogen of tumor cell growth in vitro, and obesity results in insulin resistance, which is characterized by hyperinsulinemia as long as the pancreatic β-cells remain competent. Furthermore, McKeown-Eyssen also suggested that serum levels of glycerides and glucose, which tend to be higher in obese persons, may affect fecal bile acids, which have been implicated in the pathogenesis of colon cancer (81).

To solidify the current research base, additional research is required on the association between weight and colon cancer risk among women. Such studies should include sufficient follow-up time and a large-enough number of endpoints to allow a full examination of the range of body mass index and colon cancer risk. In addition, the mechanisms through which obesity affects the risk for colon cancer need to be clarified. Research also is needed about critical periods during a person's life when obesity could pose especially high risks. Furthermore, the relation between weight change and colon cancer risk has not been well studied. If excessive weight is in fact related by some mechanism to the development of colon cancer and is not just a marker for one or more other factors, research is needed to determine the effect of deliberate weight loss on the risk for colon cancer.

Several factors argue that the association between obesity and colon cancer could be causal. The majority of epidemiologic studies indicate that obesity is associated with an increased risk for colon cancer, especially among men, although the magnitude of the association remains uncertain. The temporal directionality of the association is correct, several studies suggest a dose-response relation between obesity and colon cancer, and biologically plausible mechanisms have been suggested. If this association is indeed causal, the high prevalence of obesity in the United States at present may bode ill for future trends in the incidence of this disease.

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