Leisure-Time Physical Activity, Body Size, and Colon Cancer in Women

María Elena Martínez, Edward Giovannucci, Donna Spiegelman, David J. Hunter, Walter C. Willett, Graham A. Colditz*

For the Nurses' Health Study Research Group

Background: **Physical inactivity and high body mass index (weight in kilograms divided by height in square meters) have been linked to increased risk of colon cancer. However, none of the few prospective studies in women has shown a statistically significant reduction in colon cancer incidence or mortality associated with increased leisure-time physical activity.** *Purpose:* **In this prospective study, we asked whether leisure-time physical activity, body mass index, or body fat distribution could significantly influence the risk of colon cancer in women.** *Methods:* **The participants in this study were enrolled in the Nurses' Health Study, which began in 1976. Every 2 years, the women provided additional personal information and information on medical risk factors and major medical events. The time spent per week at a variety of leisure-time physical activities was determined, and the time spent at each activity was multiplied by its typical energy expenditure, expressed in terms of metabolic equivalents or METs. The resulting values for each woman were added to yield an MET-hours-per-week score. Reported diagnoses of colon cancer were confirmed by review of hospital records and pathology reports. Relative risks and associated 95% confidence intervals were calculated.** *Results:* **In multivariate analyses that included body mass index, women who expended more than 21 MET-hours per week on leisure-time physical activity had a relative risk of colon cancer of 0.54 (95% confidence interval [CI] = 0.33-0.90) in comparison with women who expended less than 2 MET-hours per week. Women who had a body mass index greater than 29 kg/m^2 had a relative risk of colon cancer of 1.45 (95% CI = 1.02-2.07) in comparison with women who had a body mass index less than 21 kg/m^2. A tendency toward higher colon cancer risk was observed for increasing waist-to-hip ratio (relative risk = 1.48 [95% CI = 0.88-2.49] for comparison of the highest quintile ratio [>0.833] to the lowest [<0.728]).** *Conclusions and Implications:* **The significant inverse association between leisure-time physical activity and incidence of colon cancer in women in this study is consistent with what has been found in men. Recommendations to increase physical activity and maintain lean body weight should receive greater emphasis as part of a feasible approach to the prevention of colon cancer. [J Natl Cancer Inst 1997;89:948-55]**

Physical inactivity has been related to a higher risk of colon cancer (*1-37*), which is the second most common cause of cancer mortality in the United States (*38*). However, of the few prospective studies of physical activity and colon cancer in women (*8,13,17,18,26,30,37*), none has shown a statistically significant reduction in cancer incidence or mortality associated with increased leisure-time activity. Furthermore, relatively few studies have assessed colon cancer risk by anatomic subsite (*3,5,6,9,10,14,15,27,29,32,37*). Additional data (*39-52*) also support a direct association between body mass index (BMI) and colon cancer in men, but the evidence is weaker for women.

The considerably stronger evidence relating physical inactivity to a higher risk of colon cancer in men than in women is enigmatic. This divergence may reflect the scarcity of data for women or the inappropriateness for women of the activity instruments used. It is also possible that the adverse effects of inactivity on colon cancer risk differ by sex. Because of the paucity of data on women, we examined prospectively the relationship between leisure-time physical activity and the risk of colon cancer in the Nurses' Health Study. We also examined whether abdominal fat distribution, absolute weight, and weight change from age 18 years to adulthood are associated with the risk of colon cancer. We have previously published results on BMI and colon cancer in this cohort on the basis of 191 cases of cancer that occurred from 1976 through 1984 (*44*). Because of previous reports, we hypothesized that any influence of physical activity, body size, and fat distribution would be strongest for the distal colon.

Subjects and Methods

Nurses' Health Study Cohort

In 1976, 121 701 female registered nurses 30-55 years of age were enrolled in the Nurses' Health Study by return of a mailed questionnaire. Every 2 years, follow-up questionnaires are mailed to the participants to update information on risk factors and major medical events. The participants in the present study were women who were free of cancer (except non-melanoma skin cancer), ulcerative colitis, or Crohn's disease at the beginning of the follow-up period and who provided information on the risk factors of interest. The protocol for the study

*Affiliations of authors: M. E. Martínez, Department of Nutrition, Harvard School of Public Health, Boston, MA; E. Giovannucci, Department of Nutrition, Harvard School of Public Health, Channing Laboratory, Brigham and Women's Hospital, and Harvard Medical School, Boston; D. Spiegelman, Department of Epidemiology, Harvard School of Public Health; D. J. Hunter, G. A. Colditz, Channing Laboratory, Brigham and Women's Hospital, Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health; W. C. Willett, Department of Nutrition and Department of Epidemiology, Harvard School of Public Health, Channing Laboratory, Brigham and Women's Hospital, and Harvard Medical School.

Correspondence to: Graham A. Colditz, M.D., Dr.P.H., Channing Laboratory, Brigham and Women's Hospital, 181 Longwood Ave., Boston, MA 02115.

See ''Notes'' following ''References.''

was approved by the Human Research Committee of the Brigham and Women's Hospital in Boston, MA.

Assessment of Physical Activity

On the 1986 questionnaire, we included a section on recreational or leisure-time physical activity during the past year. Participants reported the average time per week spent for each of the following activities: walking or hiking outdoors (including walking while playing golf); jogging (slower than 10 minutes per mile); running (10 minutes per mile or faster); bicycling (including use of a stationary machine); lap swimming; playing tennis; playing squash or racquet ball; and calisthenics, aerobics, aerobic dance, or use of a rowing machine. In addition, each woman reported the number of flights of stairs that she climbed daily and her usual walking pace. The reported time spent at each activity per week was multiplied by its typical energy expenditure requirements expressed in metabolic equivalents (METs) (53) and added together to yield an MET-hours-per-week score. One MET, the energy expended while sitting quietly, is equivalent to 3.5 mL of oxygen uptake per kilogram of body weight per minute for a 70-kg adult. Body weight was not included in the derivation of energy expenditure of physical activity to avoid confounding the energy expenditure variable by body weight. We used the following MET values for each activity: jogging, 7.0; running, 12.0; bicycling, 7.0; swimming, 7.0; playing tennis, 7.0; playing squash or racquet ball, 9.0; calisthenics, aerobics, aerobic dance, or use of a rowing machine, 6.5; and climbing stairs, 8.0. Walking was assigned an MET value correspondent to the reported pace: easy, 2.5; normal, 3.0; brisk, 4.0; or very brisk, 4.5.

Several groups (54-56) have investigated the reliability and validity of questionnaires designed to assess physical activity, and instruments such as ours appear to be acceptably valid. We assessed the validity of the self-reported physical activity questionnaire in a sample of 147 nurses from another, similar cohort study by comparing this questionnaire with the average of four, 7-day activity diaries recorded over a 1-year period (57). The Pearson correlation coefficient between the MET-hour score measured by the questionnaire and the average of the diaries was .46. After adjustment for within-person variation in the diaries, the deattenuated correlation was .56.

Assessment of Body Size Parameters

In 1976, women reported their height. Body weight was reported in each biennial questionnaire. In 1980, 80% of the participants recorded their weight at age 18. In 1986, the nurses were instructed to measure (to the nearest quarter of an inch) their waist at the umbilicus and their hips at the largest circumference between the waist and thighs; the women took these measurements while they were standing and without bulky clothing (58). Sixty-nine percent of the participants provided circumference measures. This low response was due to the fact that the response to these questions was optional.

We used BMI (weight in kilograms divided by height in square meters) as the primary measure of adiposity, waist-to-hip ratio as the measure of relative distribution of fat, and waist circumference as an estimate of abdominal fat. BMI is minimally correlated with height in this population ($r = -.03$) and highly correlated with weight ($r = .86$) (59). We categorized women into groups with BMI corresponding to less than 21, 21-22.9, 23-24.9, 25-28.9, and 29 or more kg/m². We also calculated weight change from 18 years of age to 1980.

We evaluated the precision of self-reported anthropometric measures in a sample of 140 cohort members (58). Trained technicians visited the substudy participants twice, approximately 6 months apart, to measure current weight and waist and hip circumferences. The Pearson correlation between self-report and the average of the technicians' two measurements was .97 for weight, .87 for waist circumference, .81 for hip circumference, and .66 for waist-to-hip ratio.

Identification of Cases

The ascertainment of cases of colorectal cancer has been detailed elsewhere (60). On each biennial follow-up questionnaire, we asked whether cancer of the colon or rectum had been diagnosed during the previous 2 years. We also used the National Death Index and the U.S. Postal Service to identify fatalities; we estimate that more than 98% of deaths were ascertained (61). When a participant (or the next of kin for decedents) reported a diagnosis of cancer of the colon or rectum on our follow-up questionnaire, we asked her (or the next of kin) for permission to obtain hospital records and pathology reports pertaining to this diagnosis. A study physician blinded to the exposure information reviewed the medical records to extract information on the histologic type, the anatomic location, and the stage of the cancer. Proximal colon cancers were defined as those from the cecum to and including the splenic flexure, and distal colon cancers were defined as those in the descending and sigmoid colon. Cancers other than adenocarcinoma were excluded. In the analysis of colon cancer overall, we included cases lacking information for anatomic location, since analyses limited to cases with complete information yielded results virtually identical to those of analyses excluding these cases.

Statistical Analysis

Physical activity, waist circumference, and waist-to-hip ratio were analyzed in quintiles according to the distribution of the study population. BMI was categorized as described earlier, and change in weight from 18 years of age to 1980 was divided into informative increments on the basis of an examination of the distribution of values. Person-years of follow-up were computed from the date of return of the 1980 questionnaire (for BMI and change in weight from age 18 to 1980) or the 1986 questionnaire (for physical activity, waist circumference, and waist-to-hip ratio) to the date of colorectal cancer diagnosis, death from any cause, or May 31, 1992, whichever came first. Relative risks (RRs) and their 95% confidence intervals (CIs) were calculated with the lowest quintile as the reference for all variables except change in weight from age 18 to 1980, for which women with stable weight (±5 kg) were used as the reference group. A limited assessment of physical activity obtained in the 1980 questionnaire was used in the analysis of BMI.

We used the Mantel–Haenszel estimator and logistic regression models to adjust for age (across 5-year categories) and potentially confounding variables (62). A priori potential risk factors for colorectal cancer included in the models were age (in six categories), history of colorectal cancer in a parent or sibling, smoking (pack-years of smoking after smoking for a period of 35 years), aspirin use (times per week), intake of red meat, and alcohol consumption. We also included use of postmenopausal hormones (premenopausal status, never use, past use, or current use) in the models because these hormones are related to body fat distribution (63) and to colorectal cancer in this cohort. We used the median of each category as a continuous variable to calculate the tests for trend; the P values for these tests are two-sided.

Results

The 1980-1992 cohort for this study comprised 89 448 eligible women; 396 cases of colon cancer (185 distal, 159 proximal, and 52 unknown site) were identified during 1 012 375 person-years of follow-up. During 1986-1992, we identified 212 cases of colon cancer (97 distal, 88 proximal, and 27 unknown site) among 67 802 eligible participants who accrued 385 819 person-years of follow-up.

Compared with women who were less physically active, those who were more active consumed more energy, less total and animal fat, and more dietary fiber; they were also leaner and had a lower waist-to-hip ratio (Table 1). The most active group also included a lower proportion of women who were current smokers, a lower proportion of aspirin users, and a higher proportion of multivitamin users and users of postmenopausal hormones. There was no appreciable difference across physical activity quintiles for alcohol consumption, family history of colorectal cancer in first-degree relatives, previous endoscopy, or previous colorectal polyps.

Physical Activity

Walking, the most common type of leisure-time physical activity, was reported by 70% of the respondents. In multivariate analysis, the risk of colon cancer was inversely related to leisure-time physical activity (Table 2). Compared with women who expended less than 2 MET-hours per week, those who expended more than 21 MET-hours had an RR of 0.54 (95% CI = 0.33-

Table 1. Characteristics of the study population according to quintiles of MET-hours* per week

Characteristic†	MET-hours per week				
	<2	2-4	5-10	11-21	>21
Participants, No.	11 264	9032	11 651	10 641	10 287
Mean daily intake‡					
Energy, kcal	1710	1763	1787	1792	1804
Total fat, g	60.3	59.3	58.7	57.6	56.3
Animal fat, g	34.5	33.8	33.1	32.3	31.7
Dietary fiber, g	16.0	16.8	17.3	18.0	18.7
Alcohol, g	6.1	5.9	5.9	6.4	6.9
Mean body mass index, kg/m²§	26.0	25.3	25.0	24.5	24.0
Mean waist-to-hip ratio	0.796	0.788	0.783	0.778	0.773
Current smoker, %	26.4	22.5	19.6	16.4	16.8
History of colorectal cancer,‖ %	8.0	7.9	8.3	8.5	8.2
Aspirin use,¶ %	15.6	15.7	17.4	16.1	14.8
Multivitamin use, %	38.4	39.6	41.3	44.2	46.1
Postmenopausal hormone use, %	14.7	15.9	16.7	17.6	18.4
Previous endoscopy, %	17.2	17.2	17.2	17.9	17.8
Previous colorectal polyp, %	1.1	1.0	1.0	1.0	0.9

  *Metabolic equivalent (MET)-hours = sum of the average time per week spent in each leisure-time physical activity multiplied by the MET value for each activity; MET value = (caloric need/kilogram body weight per hour activity)/(caloric need/kilogram body weight per hour at rest).

  †Standardized for age at baseline.

  ‡Adjusted to total energy intake by regression analysis (except for alcohol).

  §Weight in kilograms/height in square meters.

  ‖History of colorectal cancer in a parent or sibling.

  ¶Regular use of aspirin from 1980 to 1984.

0.90; P for trend = .03). This inverse association was essentially limited to cancer of the distal colon; women in the highest quintile were approximately 70% less likely to develop cancer at this site (RR = 0.31; 95% CI = 0.12-0.77; P for trend = .01) than women in the lowest quintile. No significant trend was found for cancer of the proximal colon. Excluding BMI from the multivariate models had no appreciable effect on the results.

We assessed the relationship between colon cancer and the intensity of activity by looking at the amount of time spent doing activities of low, moderate, or high intensity. The intensity cat-

Table 2. Relative risk (RR) of colon cancer according to level of leisure-time physical activity (in MET-hours*) in 1986,† Nurses' Health Study, 1986-1992

	MET-hours per week					
	<2	2-4	5-10	11-21	>21	Two-sided P for trend‡
Person-years.	63 734	51 413	66 435	60 769	58 817	
Colon cancer§						
No. of cases	47	26	36	29	23	
Age-adjusted RR	1.00 (referent)	0.69	0.74	0.65	0.52	
Multivariate RR‖	1.00 (referent)	0.71	0.78	0.67	0.54	.03
95% CI¶	—	0.44-1.15	0.50-1.20	0.42-1.07	0.33-0.90	
Distal colon cancer						
No. of cases	21	15	17	14	6	
Age-adjusted RR	1.00 (referent)	0.89	0.78	0.70	0.31	
Multivariate RR‖	1.00 (referent)	0.92	0.81	0.71	0.31	.01
95% CI¶	—	0.48-1.79	0.43-1.55	0.36-1.41	0.12-0.77	
Proximal colon cancer						
No. of cases	19	8	15	11	13	
Age-adjusted RR	1.00 (referent)	0.53	0.76	0.61	0.73	
Multivariate RR‖	1.00 (referent)	0.54	0.79	0.62	0.77	.67
95% CI¶	—	0.23-1.22	0.40-1.56	0.30-1.32	0.38-1.58	

  *See footnote to Table 1 for definition and calculation of MET-hours.

  †Data were based on 67 802 respondents. Data on leisure-time physical activity were missing for 51 case patients and 84 651 person-years.

  ‡Test for trend was calculated by use of the median of each MET-hours per week category as a continuous variable in the multiple regression model.

  §Includes 22 cases lacking data on anatomic site.

  ‖Adjusted for age, cigarette smoking, family history of colorectal cancer, body mass index, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

  ¶CI = confidence interval.

egories were first created by including those activities corresponding to the range in METs for each category (<3 for low, 3-6 for moderate, and >6 for high). The amount of time spent in these activities was then categorized for the analyses. The multivariate RR for colon cancer for women who engaged in activities of moderate intensity for 1 hour or more per day was 0.69 (95% CI = 0.52-0.90) relative to women who participated in these activities for less than 1 hour per day. A similar reduction in risk was observed for activities of high intensity (RR = 0.61 [95% CI = 0.43-0.86] for ≥30 minutes per day compared with <30 minutes per day). There was no reduction in risk for activities of low intensity (RR = 1.54 [95% CI = 0.94-2.50] for ≥1 hour per day compared with <1 hour). When these variables were included in one multivariate model simultaneously, the RRs were only slightly attenuated.

Using data from our validation study (57), we corrected the estimated RRs and their respective 95% CIs for bias due to measurement error (64). For a difference of 30 MET-hours per week (approximately equal to 1 hour of brisk walking or 30 minutes of jogging or biking every day), the corrected RR adjusted for age, family history, and BMI was 0.38 (95% CI = 0.09-1.63) compared with the uncorrected value of 0.77 (95% CI = 0.52-1.13).

BMI and Weight Change From Age 18 Years to Adulthood

The RR for colon cancer associated with a BMI of greater than 29 kg/m^2 was 1.45 (95% CI = 1.02-2.07; P for trend = .04) (Table 3). Similar to the observation for physical activity, this increase in risk was due largely to a strong association with cancer of the distal colon. Women in the upper category of BMI were at almost twice the risk of developing cancer of the distal colon as those in the lower category (RR = 1.96; 95% CI =

1.18-3.25; P for trend = .004). The RR for proximal colon cancer associated with BMI was weaker, and no significant trend was observed. Excluding physical activity from the multivariate models made no appreciable difference in the overall results. When we conducted analyses for BMI excluding current smokers, the results were not appreciably altered. In these analyses, the RRs for the upper compared with the lower quintile of BMI were 1.48 (95% CI = 0.95-2.31) for colon cancer overall, 2.04 (95% CI = 1.14-3.69) for distal colon cancer, and 1.28 (95% CI = 0.56-2.92) for proximal colon cancer.

After adjustment for BMI at age 18, weight gain from 18 years of age to 1980 was not appreciably associated with a higher risk of colon cancer overall. For colon cancer overall, women who gained 20 kg or more from age 18 to 1980 had an RR of 1.08 (95% CI = 0.79-1.48) compared with those with stable weight (±5 kg); however, the corresponding RR for distal colon cancer was stronger (RR = 1.56; 95% CI = 0.97-2.49).

Waist-to-Hip Ratio and Waist Circumference

A tendency toward higher risk of colon cancer with increasing waist-to-hip ratio was observed (Table 4). Women in the highest quintile of waist-to-hip ratio had an RR for colon cancer of 1.48 (95% CI = 0.88-2.49) compared with women in the lowest quintile; however, the trend was not statistically significant (P = .16). The corresponding RR for distal colon cancer was stronger but less precise (RR = 1.79; 95% CI = 0.82-3.90; P for trend = .11). Although a positive association was also seen for cancer of the proximal colon, the point estimates were imprecise and no monotonic trend was observed. After adjustment for BMI, the results for waist-to-hip ratio were essentially unchanged.

Waist circumference was also positively, but not signifi-

Table 3. Relative risk (RR) of colon cancer according to body mass index (BMI*) in 1980,† Nurses' Health Study, 1980-1992

| | BMI, kg/m^2 | | | | | |
	<21	21-22.9	23-24.9	25-28.9	≥29	Two-sided P for trend‡
Person-years........................	215 722	246 238	203 842	200 472	140 048	
Colon cancer§						
No. of cases	57	94	78	91	73	
Age-adjusted RR	1.00 (referent)	1.32	1.21	1.35	1.58	
Multivariate RR‖	1.00 (referent)	1.31	1.16	1.29	1.45	.04
95% CI¶	—	0.94-1.82	0.82-1.63	0.92-1.80	1.02-2.07	
Distal colon cancer						
No. of cases	25	38	39	41	41	
Age-adjusted RR	1.00 (referent)	1.25	1.43	1.48	2.16	
Multivariate RR‖	1.00 (referent)	1.24	1.37	1.40	1.96	.004
95% CI¶	—	0.75-2.04	0.83-2.27	0.85-2.31	1.18-3.25	
Proximal colon cancer						
No. of cases	23	39	33	37	25	
Age-adjusted RR	1.00 (referent)	1.33	1.27	1.34	1.28	
Multivariate RR‖	1.00 (referent)	1.33	1.20	1.29	1.26	.54
95% CI¶	—	0.79-2.22	0.71-2.05	0.76-2.18	0.71-2.23	

*See Table 1 and text for definition and calculation of BMI.

†Data were based on 89 448 respondents; BMI data were missing for three case patients and 6053 person-years.

‡Test for trend was calculated by use of the median of each BMI category as a continuous variable in the multiple regression model.

§Includes 52 cases lacking data on anatomic site.

‖Adjusted for age, cigarette smoking, family history of colorectal cancer, leisure-time physical activity, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

¶CI = confidence interval.

cantly, associated with the risk of colon cancer. The RR for colon cancer overall was 1.48 (95% CI = 0.89-2.46) for women whose waist circumference was greater than 34 inches compared with women whose waist circumference was 27.5 inches or less; for distal colon cancer, the RR was 1.47 (95% CI = 0.71-3.06). After adjustment for BMI, the corresponding RRs were 1.16 (95% CI = 0.61-2.21) for colon cancer overall and 1.09 (95% CI = 0.42-2.79) for distal colon cancer.

Using validation data on waist and hip circumference (58), we corrected the estimated RRs and their CIs for bias due to measurement error. After adjustment for age, family history of colorectal cancer, and physical activity, the corrected RR for colon cancer overall associated with a difference in waist-to-hip ratio of 0.20 (approximately equal to the difference between the medians of the upper and lower quintiles) was 2.84 (95% CI = 0.39-20.51) compared with the uncorrected RR of 1.31 (95% CI = 0.91-1.90).

Discussion

In these prospective data, an increasing level of leisure-time physical activity was associated with a decrease in the incidence of colon cancer. As noted earlier, to our knowledge, none of the published prospective studies of women has reported a significant association between colon cancer incidence or mortality and recreational physical activity (8,13,18,26,30,37). It is difficult to address the discrepancy between the findings in these other studies and ours because of the wide variation in methodology. Some studies used colorectal cancer incidence as an end point (8,18,37), one focused on fatal colon cancer and considered a combination of activity at work and play (26), one suffered from a lack of power due to a small sample size (13), and one did not specifically target physical activity in the report (30). As shown in previous studies of men (5,15), including our own

study (29), and in studies of men and women (10,14,32), the protective effect was stronger for cancer of the distal colon than for cancer of the proximal colon; however, in one study (37), the association was stronger for cancer of the proximal colon. These findings are also consistent with those for distal colon adenomas in this cohort (65), where stronger effects were seen for large adenomas, suggesting that physical inactivity promotes the growth of these polyps. A higher BMI was also associated with a 50% increase in the risk of colon cancer and an almost doubled risk of distal colon cancer. In addition, waist-to-hip ratio, used as a measure of the relative distribution of body fat, was positively, but not significantly, associated with the risk of colon cancer.

Most published studies of physical activity and colon cancer in women (4,10,12-14,17,20-22,25,31,34-37) have used a measure of occupational activity or a combination of occupational and leisure-time activities. It is possible that ascertainment of occupational physical activity is better in men than in women. Slattery et al. (22) noted that the activities of housewives are usually excluded from this assessment. Since there are sometimes fewer women in jobs having higher occupational activity levels, these women are statistically uninformative or usually combined with those in lower activity levels because of small numbers (4,12,30), thus providing narrow levels of activity. In addition, to our knowledge, only five of the published studies assessing recreational activities (20,24,28,29,36) have applied a factor of energy expenditure, such as MET equivalents, which takes into account the intensity of the activities measured. We observed a reduction in the risk of colon cancer for women who engaged in moderate or vigorous activity, but no reduction was seen for activities of low intensity, such as easy-paced walking.

Several mechanisms for a protective effect of physical activity have been proposed (66). They include decreased gastroin-

Table 4. Relative risk (RR) of colon cancer according to waist-to-hip ratio in 1986,* Nurses' Health Study, 1986-1992

| | Waist-to-hip ratio | | | | | |
	<0.728	0.728-0.758	0.759-0.790	0.791-0.833	>0.833	Two-sided P for trend†
Person-years.	54 893	56 555	51 681	48 387	54 886	
Colon cancer‡						
No. of cases	21	29	24	38	49	
Age-adjusted RR	1.00 (referent)	1.19	0.99	1.46	1.59	
Multivariate RR§	1.00 (referent)	1.18	0.97	1.51	1.48	.16
95% CI‖	—	0.67-2.07	0.54-1.74	0.88-2.58	0.88-2.49	
Distal colon cancer						
No. of cases	9	17	9	17	24	
Age-adjusted RR	1.00 (referent)	1.64	0.90	1.55	1.91	
Multivariate RR§	1.00 (referent)	1.64	0.87	1.64	1.79	.11
95% CI‖	—	0.73-3.69	0.35-2.20	0.73-3.71	0.82-3.90	
Proximal colon cancer						
No. of cases	7	12	11	18	19	
Age-adjusted RR	1.00 (referent)	1.48	1.38	2.01	1.71	
Multivariate RR§	1.00 (referent)	1.45	1.30	2.06	1.66	.34
95% CI‖	—	0.57-3.68	0.50-3.35	0.86-4.96	0.69-3.99	

*Results based on 52 687 respondents to questionnaire on waist and hip circumference.

†Test for trend was calculated by use of the median of each waist-to-hip ratio category as a continuous variable in the multiple regression model.

‡Includes 18 cases lacking data on anatomic site.

§Adjusted for age, cigarette smoking, family history of colorectal cancer, leisure-time physical activity, postmenopausal hormone use, aspirin use, intake of red meat, and alcohol consumption.

‖CI = confidence interval.

testinal transit time, altered prostaglandin levels, improved immune function, changes in bile acid metabolism, and increased levels of gastrointestinal hormones that can lower gut transit time and bile acid excretion. Giovannucci (67) hypothesized that insulin resistance may be the factor by which other factors, such as physical inactivity and abdominal obesity, act to increase the risk of colon cancer. These factors are strong, independent determinants of insulin resistance and hyperinsulinemia (68-73); since insulin is an important growth factor for colonic mucosal cells and colonic cancer cells in vitro (74-76), hyperinsulinemia may mediate the effect of a sedentary lifestyle on the risk of colon cancer.

A major strength of this study, aside from its prospective nature, is the ability to control for other known or suspected risk factors for colon cancer. It is possible that physically active women have other healthy lifestyle factors, as was observed in this cohort of women. However, with control for these factors, the RRs were only slightly altered and remained statistically significant. Thus, leisure-time physical activity not only appears to be an indicator of a healthy lifestyle but also exerts an independent protective effect against colon cancer.

In conclusion, these prospective data show a significant reduction in the risk of colon cancer associated with a higher level of leisure-time physical activity in women. They also add to the current literature on the higher risk of colon cancer associated with a greater body size, particularly BMI. These risk factors appear to act independently of each other and of other risk factors for colon cancer. Consistent with some previous studies, these findings are stronger for left-sided colon cancer. Currently, 24% of the U.S. population engages in no physical activity (77). Another 54% is somewhat active but still fails to meet the current recommendations of engaging regularly in light-to-moderate physical activity for at least 30 minutes per day (78,79). Powell and Blair (80) estimate that 3500 deaths from colon cancer could be prevented if 50% of the people who are irregularly active engaged regularly in physical activity. Our own data suggest that engaging in activities of moderate intensity (i.e, walking at a normal or brisk pace) for 1 hour per day is associated with a 46% reduction in the risk of developing colon cancer. Thus, increasing physical activity levels may be an effective approach for reducing the burden of colon cancer in our society.

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