Amount, Type, and Timing of Recreational Physical Activity in Relation to Colon and Rectal Cancer in Older Adults: the Cancer Prevention Study II Nutrition Cohort

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Abstract

Physical activity has consistently been associated with lower risk of colon cancer, but information is limited on the amount, type, and timing of activities. The relationship between physical activity and rectal cancer is unclear. We examined characteristics of recreational physical activity in relation to colon and rectal cancer in the Cancer Prevention Study II Nutrition Cohort of 70,403 men and 80,771 women (median age, 63 years); 940 colon and 390 rectal cancers were identified from enrollment in 1992 to 1993 through August 1999. The multivariate-adjusted rate ratios (95% confidence intervals) associated with any recreational physical activity compared with none were 0.87 (0.71-1.06) for colon cancer and 0.70 (0.53-0.93) for rectal cancer. Colon cancer risk decreased significantly with increasing total hours (P for trend without reference group = 0.007) and metabolic equivalent hours (P for trend = 0.006) per week of activities. No clear decrease in rectal cancer risk was seen with increasing hours per week of physical activity. Rate ratios (95% confidence intervals) were 0.72 (0.52-0.98) for <2 hours, 0.68 (0.47-0.97) for 2 to 3 hours, 0.59 (0.41-0.83) for 4 to 6 hours, and 0.83 (0.59-1.16) for ≥7 hours per week of physical activity compared with none. Past exercise, as reported in 1982, was not associated with risk of either colon or rectal cancer. We conclude that increasing amounts of time spent at recreational physical activity are associated with substantially lower risk of colon cancer and that recreational physical activity is associated with lower risk of rectal cancer in older men and women. (Cancer Epidemiol Biomarkers Prev 2004;3(12):2187–95)

Introduction

Physical activity is an attractive cancer preventive strategy because it potentially benefits many health end points in addition to reducing the risk of certain cancers. Comprehensive reviews have noted a consistent association between increased physical activity and lower risk of colon cancer (1-3) and colorectal adenomas (4-10). Prospective (11-26) and case-control (27-38) studies of men have typically found, with few exceptions (13, 20, 22, 26), a statistically significant 40% lower risk of colon or colorectal cancer among the most active compared with the least active. Studies of women have been less consistent, generally finding a statistically nonsignificant 10% to 20% lower risk of colon or colorectal cancer associated with increased physical activity (10, 11, 13, 15, 17, 18, 20, 21, 23, 24). The results of prospective (14, 16, 20, 25) and case-control (29-31, 34, 39) studies of rectal cancer and total or recreational physical activity in men or women have not been consistent; studies have reported an inverse association (14, 30, 34, 39), no

association (25, 29, 31), or higher risk of rectal cancer associated with greater activity (16, 20).

More information is needed about the characteristics (amount, type, and timing) of physical activity necessary to affect colon and rectal cancer risk. The temporal relationship between physical activity and reduced risk of colon or rectal cancer is important both for biological understanding and for encouraging physical activity among older adults, yet few studies have determined physical activity at different time points in life. Whereas the association with colon cancer has been stronger with recent activity than with past activity (40), this may reflect the greater potential for measurement error when past activity is characterized only by recall.

We examined how the characteristics (amount, type, and timing) of recreational physical activity affect its association with colon or rectal cancer incidence among older adults in the Cancer Prevention Study II (CPS II) Nutrition Cohort. Because this cohort is a subset of the larger CPS II Mortality Cohort established in 1982, participants had prospectively reported data on physical activity and several other covariates on a questionnaire completed 10 years before enrollment in the Nutrition Cohort.

Materials and Methods

Study Population. The CPS II Nutrition Cohort of 86,404 men and 97,786 women was established in 1992 to

1993 as a subset of the 1,184,657 participants of the CPS II Mortality Cohort assembled in 1982 (41). Mortality Cohort participants in 1982 completed a self-administered questionnaire with information on exercise at work or play, diet, medical history, and other lifestyle habits. The 1992 Nutrition Cohort includes men and women ages 50 to 74 years residing in 1 of 21 states with population-based cancer registries that ascertained at least 90% of incident cancers by 1990. Median age at Nutrition Cohort entry in 1992 to 1993 was 63 years.

The Nutrition Cohort 1992 to 1993 questionnaire obtained information on physical activity, diet, medical history, and other lifestyle habits. Dietary assessment was based on a modified 68-item Block food frequency questionnaire (42); nutrient intakes were estimated using the Dietary Analysis System version 3.8a (43). This cohort was recontacted in 1997 and 1999 with self-administered questionnaires to update information on newly diagnosed cancers, medical history, and lifestyle factors. A pilot study linking Nutrition Cohort participants to state cancer registries found that cohort members were highly capable (sensitivity of 0.93) of self-reporting a previous cancer diagnosis (44). Mortality follow-up of the entire Nutrition Cohort is ongoing through automated linkage with the National Death Index for date and cause of death (41). CPS II Nutrition Cohort participants on the average reported higher educational attainment and more health conscious behaviors than the general U.S. population (41). All aspects of the CPS II Nutrition Cohort study protocol have been approved by the Emory University Institutional Review Board.

This study includes Nutrition Cohort members enrolled in 1992 to 1993; study observation period for each participant ended with the occurrence of one of the following: diagnosis of colon or rectal cancer, death, or August 31, 1999. Excluded from the study were persons who (1) were not known to be deceased but failed to respond to both 1997 and 1999 questionnaires (4.5%), (2) reported a colon or rectal cancer not subsequently verified by pathology report (0.2%), (3) reported a personal history of colon or rectal cancer at baseline (1.5%), or (4) reported missing or uninterpretable data for exercise level in 1982 (0.9%), recreational activities in 1992 (1.5%), body mass index (BMI; 1.3%), or dietary intake (8.1%). After exclusions, this study population consists of 70,403 men and 80,771 women, representing 82% of the CPS II Nutrition Cohort.

Incident Colon and Rectal Cancer. This study included 940 colon cancers (C18.0, C18.2-C18.9) and 390 cancers of the rectosigmoid junction or rectum (C19.0-C20.9) diagnosed between enrollment and August 31, 1999. Of these, 1,033 cases were self-reported colon or rectal cancers on the 1997 or 1999 questionnaires and verified by medical record abstraction (76%) or linkage with state cancer registries when medical records were unavailable (24%). Two hundred ninety-five cases were identified from the National Death Index linkage as interval cancer cases, defined as deaths with colon or rectal cancer recorded on death certificate among study participants who died after completing a questionnaire and did not report colon or rectal cancer on that questionnaire. We were able to verify 241 (82%) of the 295 interval cancer cases through cancer registry linkage. Subsite-specific analyses were conducted on

505 proximal (cecum to splenic flexure) and 339 distal (descending to sigmoid colon) colon cancers, excluding colon cancers with overlapping or not otherwise specified site codes.

Recreational Physical Activity. CPS II Nutrition Cohort participants reported in 1992 to 1993 the average number of hours per week (0, 1-3, 4-6, or ≥7) spent at seven recreational activities (walking, jogging/running, lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing) in the year before study enrollment (1991-1992). Activities other than walking were grouped together as "other activity." We categorized participants by report of any recreational activity; persons who reported no recreational activity served as the reference group for all analyses.

We computed total hours per week spent at recreational activities by summing the reported time spent at each activity (assigning the value of 0 for "none," 1.25 for "1-3," 5 for "4-6," and 7 for "≥7" hours per week) and then grouping participants into six exposure levels (no activity, <2, 2-3, 4-6, 7, or ≥8 hours per week). The 7 and ≥8 hours per week categories were combined for some analyses. Metabolic equivalent (MET) hours per week were estimated by multiplying the number of hours per week spent at each activity by its assigned MET intensity (45): walking (3.5), jogging/running (7.0), lap swimming (7.0), tennis or racquetball (6.0), bicycling/stationary bike (4.0), aerobics/calisthenics (5.0), and dancing (4.5). After summing across all activities, participants were grouped into six exposure levels (no activity, <7, 7-13, 14-23, 24-29, or ≥30 MET hours per week). We further examined gradients in hours per week (<4, 4-6, ≥7) spent at walking only and at a combination of walking plus other activities.

Past activity (none, slight, moderate, or heavy) was reported by participants in 1982 (10 years prior to Nutrition Cohort enrollment in 1992) in response to the question "How much exercise do you get (work or play)?" The "slight" category was used as the reference group due to the small number of persons who reported "none" to past activity; these two groups were combined for analyses of recent activity stratified by past activity.

Covariate Information. Potential confounders were chosen based on their observed association with colon and rectal cancer and with recreational physical activity (Table 1). Covariates included in final models for colon and rectal cancer were age (single years), education (some high school, high school graduate, some college or trade school, college graduate or postgraduate work, or unknown), cigarette smoking (never, former, current, ever smoker not specified, or status unknown), alcohol (nondrinker, <1 daily drink, 1 daily drink, ≥2 daily drinks, or unknown), red (including processed) meat intake (in quintiles), energy-adjusted total folate (in quintiles), energy-adjusted total dietary fiber (in quintiles), multivitamin use in 1982 (nonuser, occasional user, regular user, or status unknown), and hormone replacement therapy use in women (nonuser, former user, current user, ever user not specified, or status unknown). Multivariate-adjusted models of recent recreational activity and exercise level in 1982 were adjusted for one another, except in models stratified by past exercise. Other variables evaluated for potential confounding were race, family history of colorectal cancer, use of

Table 1. Selected characteristics of study participants by total hours per week of recreational physical activity in the year before study enrollment, CPS II Nutrition Cohort men and women, 1992-1993

Recreational physical activity in the year before study enrollment (total h/wk)	Men (n = 70,403)					Women (n = 80,771)				
	0	<2	2-3	4-6	≥7	0	<2	2-3	4-6	≥7
No. participants	8,545	20,022	11,535	15,368	14,933	7,471	25,959	16,139	17,873	13,329
Median h/wk	0	1.3	2.5	5.0	7.5	0	1.3	2.5	5.0	8.3
Median MET h/wk	0	4.4	10.6	17.5	30.1	0	4.4	10.6	17.5	31.9
Low or no exercise reported in 1982 (%)	32	34	27	23	16	43	34	27	22	15
Median age at cohort enrollment	63	64	63	65	65	62	62	62	62	62
Race, non-White (%)	2	2	2	2	2	3	2	3	2	3
Education, none beyond high school (%)	41	27	19	23	25	45	37	31	34	33
Gained >4.545 kg between 1982 and 1992 (%)	26	23	19	19	16	40	35	34	30	27
BMI (median, kg/m^2)	26.5	26.3	25.8	25.8	25.5	25.9	25.1	24.7	24.2	23.9
Tendency to gain weight at the waist (%)	70	75	75	73	70	52	53	53	51	49
Current cigarette smoking (%)	17	9	5	7	8	13	8	7	7	8
Alcohol, ≥2 daily drinks (%)	15	12	11	12	13	6	5	5	5	6
Aspirin, current use (%)	46	51	54	54	53	38	40	42	40	40
Multivitamin use in 1982, ≥15 d/mo (%)	15	20	23	21	22	22	25	29	27	29
Current hormone replacement therapy use (%)						28	32	35	33	33
Total energy intake (median, cal)	1,818	1,698	1,672	1,681	1,763	1,303	1,297	1,296	1,282	1,320
Energy-adjusted total fiber (median, g)	11	12	13	13	13	9	10	11	11	12
Energy-adjusted total folate (median, μg)	273	307	339	331	347	256	297	351	339	365
>7 servings of red meat/wk (%)	43	32	25	27	29	17	13	11	10	10

NOTE: Proportions standardized to the age distribution of the CPS II Nutrition Cohort.

aspirin or other analgesics, vegetable and fruit intake, and total calcium intake. These factors had negligible effect on the relationship between recreational activity and colon or rectal cancer and were not included in final models. We examined BMI (<18.5, 18.5-24, 25-29, 30-39, ≥40 kg/m^2) and total daily energy intake (in quintiles) but did not include these in final models due to their potential to be intermediate in the relationship between physical activity and lower risk of colon or rectal cancer, although their inclusion made little difference in risk estimates.

Statistical Methods. We estimated age- and multivariate-adjusted colon and rectal cancer incidence rate ratio (RR) and 95% confidence interval (95% CI) using Cox proportional hazards modeling. Ps for linear trend were estimated by modeling the number of hours or MET hours per week of total or specific types of activities as continuous variables, with and without the reference group. We examined effect measure modification by exercise level reported in 1982 (none or slight, moderate or heavy), change in body weight as reported in 1982 and 1992 (lost weight to having gained up to 4.545 kg, gained >4.545 kg, or 10 lb), BMI in 1992 (<25, 25-29, ≥30 kg/m^2), cigarette smoking (never, former, and current), aspirin use (nonuser and current user), and total daily energy intake (median intake or below, above median intake). Statistical interaction between covariates and any activity was evaluated using the likelihood ratio test. The Wald statistic was used to test for homogeneity of stratum-specific RRs associated with proximal and distal colon cancers and with hours of activity by type of activity. Analyses were done using SAS; all Ps were two sided and considered significant at 0.05.

Results

Participant Characteristics by Recreational Physical Activity. During the study period, 536 colon and 247 rectal cancers were identified among men and 404 colon and 143 rectal cancers among women. Forty-eight percent of colon cancers among men originated proximal to the splenic flexure compared with 60% among women.

Twelve percent of men and 9% of women reported no recreational physical activity in the year before study enrollment, 46% of men and 47% of women reported walking as the only recreational activity, 6% of men and 5% of women reported engaging only in activities other than walking, and 36% of men and 39% of women reported walking plus at least one other activity including (in order of decreasing frequency) bicycling/stationary biking, aerobics/calisthenics, dancing, lap swimming, tennis or racquetball, or jogging/running.

Compared with men and women reporting any recreational activity in the past year, persons who reported none were more likely to report lower educational attainment, current cigarette smoking, greater consumption of red meat, and lower consumption of total folate and fiber (Table 1); they were also less likely to report long-term multivitamin use on a regular basis (≥15 days per month). Men who reported no activity were also more likely to report two or more daily alcoholic drinks and higher median daily energy intake compared with men reporting any activity; women who reported no activity were the least likely to report hormone replacement therapy use. In both men and women, increasing amount of physical activity reported in 1992 to 1993 was inversely associated with median BMI, with the proportion of persons reporting little or no exercise in 1982 and with weight gain of >4.545 kg between 1982 and 1992.

Amount of Recreational Physical Activity and Colon Cancer Incidence. Men who reported any recreational physical activity in 1992 to 1993 had an 18% lower risk of colon cancer (multivariate-adjusted RR, 0.82; 95% CI, 0.64-1.04); women who reported any activity were not at lower risk compared with those reporting none (Table 2).

Table 2. Any activity, total hours, and MET h/wk of recreational physical activity and colon cancer incidence, number of cases, age- and multivariate-adjusted RR and 95% CI, CPS II Nutrition Cohort men and women, 1992-1993 to 1999

Recreational physical activity in year before study enrollment	Men			Women			Men and women
	No. cases	Age-adjusted RR (95% CI)	Multivariate-adjusted RR (95% CI)*	No. cases	Age-adjusted RR (95% CI)	Multivariate-adjusted* RR (95% CI)	Multivariate-adjusted* RR (95% CI)
Total	536			404			
No activity	79	1.00 (reference)	1.00 (reference)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)
Any reported activity†	457	0.72 (0.57-0.91)	0.82 (0.64-1.04)	365	0.92 (0.66-1.28)	0.98 (0.70-1.37)	0.87 (0.71-1.06)
Recreational physical activity† (h/wk)							
No activity	79	1.00 (reference)	1.00 (reference)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)
<2	164	0.83 (0.63-1.08)	0.91 (0.69-1.19)	136	0.97 (0.68-1.39)	1.01 (0.70-1.44)	0.94 (0.75-1.16)
2-3	72	0.62 (0.45-0.86)	0.72 (0.52-1.01)	80	0.94 (0.64-1.37)	1.01 (0.68-1.49)	0.83 (0.65-1.07)
4-6	124	0.76 (0.58-1.01)	0.86 (0.64-1.15)	92	0.92 (0.63-1.34)	0.97 (0.66-1.43)	0.89 (0.71-1.12)
7	59	0.71 (0.50-0.99)	0.77 (0.54-1.08)	34	0.99 (0.62-1.56)	1.03 (0.65-1.65)	0.85 (0.64-1.12)
≥8	38	0.51 (0.35-0.75)	0.58 (0.39-0.87)	23	0.60 (0.36-1.01)	0.65 (0.39-1.11)	0.60 (0.44-0.83)
P for trend, with and without reference group		0.001, 0.02	0.007, 0.03		0.07, 0.07	0.14, 0.11	0.002, 0.007
Recreational physical activity† (MET h/wk)							
No activity	79	1.00 (reference)	1.00 (reference)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)
<7	158	0.82 (0.63-1.07)	0.90 (0.68-1.18)	135	0.98 (0.69-1.40)	1.02 (0.71-1.46)	0.93 (0.75-1.16)
7-13	68	0.72 (0.52-1.00)	0.83 (0.59-1.16)	63	0.91 (0.61-1.36)	0.98 (0.65-1.47)	0.88 (0.68-1.13)
14-23	106	0.67 (0.50-0.90)	0.75 (0.55-1.01)	96	0.94 (0.65-1.37)	1.00 (0.68-1.47)	0.84 (0.66-1.06)
24-29	77	0.79 (0.58-1.09)	0.86 (0.63-1.19)	38	0.89 (0.57-1.40)	0.94 (0.60-1.48)	0.89 (0.68-1.15)
≥30	48	0.52 (0.36-0.74)	0.60 (0.41-0.87)	33	0.70 (0.44-1.12)	0.77 (0.48-1.24)	0.65 (0.49-0.87)
P for trend, with and without reference group		0.0006, 0.008	0.005, 0.02		0.07, 0.08	0.15, 0.12	0.002, 0.006

*Models included age, education, exercise level in 1982, cigarette smoking, alcohol, red meat, folate, fiber, multivitamin use in 1982, and hormone replacement therapy (women). Models of men and women combined also included sex.

†Included walking, jogging/running, lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing.

Statistically significant decreasing risk of colon cancer was associated with increasing hours (P for trend without reference group = 0.007) or MET hours (P for trend = 0.006) per week of total activities in men and women combined (Table 2). The decrease in risk with greater amount of activity was observed predominantly among men; no dose-response was observed among women. Significantly lower risk of colon cancer was observed at >7 hours or ≥30 MET hours per week of activity; the RR (95% CI) among men were 0.58 (0.39-0.87) for those reporting >7 hours and 0.60 (0.41-0.87) for ≥30 MET hours per week of activities. Although the RR estimates were lower among men than women within each exposure level, there were no statistically significant differences by sex.

Adjusting for BMI in addition to other covariates made little difference in the RR estimates associated with hours or MET hours per week of activity in men or women. The multivariate-adjusted RRs (95% CIs) for colon cancer in models that included BMI were 0.95 (0.76-1.18) for men and women reporting <2 hours, 0.85 (0.66-1.08) for 2 to 3 hours, 0.91 (0.72-1.15) for 4 to 6 hours, 0.87 (0.66-1.14) for 7 hours, and 0.62 (0.45-0.85) for ≥8 hours per week.

Amount by Type of Recreational Physical Activity and Colon Cancer Incidence. People who reported increasing hours of walking without other activities were not at lower risk of colon cancer compared with those who reported no recreational physical activity (Table 3). The strongest inverse association between colon cancer risk and physical activity was observed among men and women who reported walking plus other activities (P for trend without reference group = 0.03). Among men, the RRs (95% CIs) were 0.74 (0.53-1.03) for those reporting <4 hours, 0.86 (0.59-1.26) for 4 to 6 hours, and 0.53 (0.36-0.79) for ≥7 hours per week of walking plus other activities. The corresponding RRs (95% CIs) estimates among women were 0.99 (0.66-1.46) for those reporting <4 hours, 0.72 (0.43-1.19) for 4 to 6 hours, and 0.59 (0.36-0.97) for ≥7 hours per week. For men and women combined, the RR estimate associated with reporting ≥7 hours of walking plus other activities was significantly lower than that associated with reporting ≥7 hours of walking only (P for homogeneity = 0.009). Persons who reported engaging in other activities without walking were not at reduced risk of colon cancer; the number of people in this category was too small for stable estimates or further analyses.

Past and Recent Physical Activity and Colon Cancer Incidence. Less than 30% of men and women reported none or slight physical activity at work or play in 1982 (10 years before Nutrition Cohort enrollment). We found little evidence that past activity was associated with lower risk of colon cancer. Compared with those who in 1982 reported slight exercise, the RRs (95% CIs) for colon cancer were 1.12 (0.66-1.90) for reporting none, 1.01 (0.87-1.18) for moderate, and 1.12 (0.87-1.44) for heavy level of exercise.

Among men and women who reported being inactive (none or slight exercise) in 1982 (Table 4), report of any recreational physical activity in the year before study enrollment in 1992 to 1993 (considered recently active) was associated with 16% lower risk of colon cancer

Table 3. Hours of recreational physical activity and colon cancer incidence by type of activity, number of cases, age- and multivariate-adjusted RR and 95% CI, CPS II Nutrition Cohort men and women, 1992-1993 to 1999

Recreational physical activity in year before study enrollment	Men			Women			Men and women
	No. cases	Age-adjusted RR (95% CI)	Multivariate-adjusted* RR (95% CI)	No. Cases	Age-adjusted RR (95% CI)	Multivariate-adjusted* RR (95% CI)	Multivariate-adjusted* RR (95% CI)
Type of recreational physical activity (h/wk)							
No activity	79	1.00 (reference)	1.00 (reference)	39	1.00 (reference)	1.00 (reference)	1.00 (reference)
Walking only							
<4	143	0.80 (0.61-1.05)	0.87 (0.66-1.15)	125	0.98 (0.68-1.40)	1.00 (0.70-1.44)	0.91 (0.73-1.14)
4-6	72	0.77 (0.56-1.06)	0.83 (0.60-1.16)	60	1.04 (0.69-1.56)	1.08 (0.71-1.63)	0.92 (0.71-1.18)
≥7	51	0.84 (0.59-1.19)	0.88 (0.61-1.25)	25	1.15 (0.70-1.91)	1.18 (0.71-1.95)	0.96 (0.72-1.29)
P for trend, with and without reference group		0.39, 0.91	0.34, 0.84		0.47, 0.46	0.41, 0.46	0.76, 0.79
Walking plus other activities[†]							
<4	70	0.64 (0.46-0.88)	0.73 (0.53-1.02)	76	0.92 (0.63-1.36)	0.99 (0.67-1.47)	0.83 (0.64-1.06)
4-6	45	0.75 (0.52-1.08)	0.85 (0.58-1.24)	26	0.67 (0.41-1.11)	0.72 (0.43-1.19)	0.79 (0.58-1.06)
≥7	43	0.46 (0.32-0.67)	0.53 (0.36-0.78)	27	0.55 (0.33-0.89)	0.59 (0.36-0.98)	0.55 (0.40-0.74)
P for trend, with and without reference group		0.0004, 0.11	0.02, 0.16		0.01, 0.05	0.07, 0.07	0.003, 0.03

*Models included age, education, exercise level in 1982, cigarette smoking, alcohol, red meat, folate, fiber, multivitamin use in 1982, and hormone replacement therapy (women). Models of men and women combined also included sex.
[†] Included walking, jogging/running, lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing.

(RR, 0.84; 95% CI, 0.59-1.20) compared with report of no activity. Among men and women who reported being active (moderate or heavy exercise) in 1982, report of any recreational physical activity in the year before study enrollment (considered the continuously active) was associated with 13% lower risk of colon cancer (RR, 0.87; 95% CI, 0.68-1.10) compared with those reporting no activity. The RR associated with reporting ≥7 hours per week of physical activity in the year before study enrollment was identical in people who reported being inactive in 1982 (RR, 0.74; 95% CI, 0.44-1.25) and those who reported being active in 1982 (RR, 0.74; 95% CI, 0.56-0.99), but a significant dose-response was seen only among the continuously active (P for trend = 0.01).

Proximal and Distal Colon Cancer and Rectal Cancer. Although the inverse association between physical activity and colon cancer risk was somewhat stronger for proximal than distal colon cancer, the differences by subsite were not statistically significant (Table 5). We observed a 30% lower risk of rectal cancer among men and women who reported any recreational activity in the year before study enrollment than in those who reported none (Table 5). Rectal cancer risk decreased among those reporting modest amounts of total activity but not among people who reported the highest amounts of activity. The lower risk of rectal cancer associated with modest amounts of activity was similar for walking only or walking plus other activities (Table 5).

Table 4. Any and hours per week of recreational physical activity and colon cancer incidence, by exercise level reported in 1982, number of cases and multivariate-adjusted RR and 95% CI, CPS II Nutrition Cohort men and women, 1992-1993 to 1999

Recreational physical activity in the year before study enrollment (1991-1992)	Exercise level reported in 1982			
	None or slight		Moderate or heavy	
	No. cases	Multivariate-adjusted* RR (95% CI)	No. cases	Multivariate-adjusted* RR (95% CI)
Total	233		707	
Recreational physical activity				
No activity	38	1.00 (reference)	80	1.00 (reference)
Any activity[†]	195	0.84 (0.59-1.20)	627	0.87 (0.68-1.10)
Recreational physical activity[†] (h/wk)				
No activity	38	1.00 (reference)	80	1.00 (reference)
<2	92	0.90 (0.61-1.32)	208	0.93 (0.72-1.21)
2-3	37	0.78 (0.49-1.23)	115	0.85 (0.64-1.14)
4-6	43	0.83 (0.53-1.29)	173	0.91 (0.69-1.19)
≥7	23	0.74 (0.44-1.25)	131	0.74 (0.56-0.99)
P for trend, with and without reference group		0.28, 0.43		0.007, 0.01

*Models included age, sex, education, exercise level in 1982, cigarette smoking, alcohol, red meat, folate, fiber, multivitamin use in 1982, and hormone replacement therapy (women).
[†] Included walking, jogging/running, lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing.

Table 5. Any and hours per week of recreational physical activity and incident cancer of the proximal colon, distal colon, and rectum, number of cases and multivariate-adjusted RR and 95% CI, CPS II Nutrition Cohort men and women, 1992-1993 to 1999

Recreational physical activity in the year before study enrollment	Men and women					
	Proximal colon		Distal colon		Rectosigmoid and rectum	
	No. cases	Multivariate-adjusted* RR (95% CI)	No. cases	Multivariate-adjusted* RR (95% CI)	No. cases	Multivariate-adjusted* RR (95% CI)
Total	505		339		390	
Recreational physical activity						
No activity	67	1.00 (reference)	41	1.00 (reference)	63	1.00 (reference)
Any activity†	438	0.77 (0.59-1.01)	298	0.91 (0.65-1.28)	327	0.70 (0.53-0.93)
Recreational physical activity† (h/wk)						
No activity	67	1.00 (reference)	41	1.00 (reference)	63	1.00 (reference)
<2	156	0.83 (0.62-1.10)	110	1.00 (0.69-1.43)	112	0.72 (0.52-0.98)
2-3	80	0.73 (0.52-1.01)	54	0.87 (0.57-1.32)	60	0.68 (0.47-0.97)
4-6	123	0.85 (0.62-1.15)	74	0.89 (0.60-1.32)	68	0.59 (0.41-0.83)
≥7	79	0.63 (0.45-0.88)	60	0.82 (0.55-1.24)	87	0.83 (0.59-1.16)
P for trend, with and without reference group		0.008, 0.03		0.15, 0.20		0.73, 0.45
Type of recreational activities (h/wk)						
No activity	67	1.00 (reference)	41	1.00 (reference)	63	1.00 (reference)
Walking only						
<4	145	0.84 (0.62-1.12)	95	0.93 (0.64-1.35)	100	0.71 (0.51-0.97)
4-6	70	0.82 (0.58-1.15)	48	0.97 (0.63-1.48)	41	0.60 (0.40-0.90)
≥7	38	0.83 (0.56-1.25)	30	1.08 (0.67-1.73)	36	0.89 (0.59-1.34)
P for trend, with and without reference group		0.44, 0.90		0.84, 0.56		0.44, 0.70
Walking plus other activities						
<4	74	0.69 (0.49-0.97)	54	0.89 (0.59-1.35)	57	0.67 (0.46-0.97)
4-6	44	0.80 (0.54-1.18)	22	0.71 (0.42-1.21)	23	0.53 (0.33-0.87)
≥7	39	0.50 (0.33-0.75)	24	0.55 (0.33-0.92)	46	0.72 (0.49-1.08)
P for trend, with and without reference group		0.008, 0.12		0.15, 0.27		0.30, 0.32

*Models included age, sex, education, exercise level in 1982, cigarette smoking, alcohol, red meat, folate, fiber, multivitamin use in 1982, and hormone replacement therapy (women).
†Included walking, jogging/running, lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing.

Recreational Physical Activity and Colon Cancer Incidence Stratified by Covariates. We observed significant modification of the RR for colon cancer associated with any activity by aspirin use in men and women (P for interaction = 0.02). Compared with those reporting none, the RRs (95% CIs) associated with reporting any recreational activity were 0.65 (0.48-0.86) among current users of aspirin and 1.04 (0.78-1.38) among nonusers. Although not statistically different, the inverse association between colon cancer and any activity was stronger among persons who reported having gained ≤4.545 kg weight between 1982 and 1992 (compared with having gained >4.545 kg) and who reported below median total daily energy intake (compared with median intake or above). We observed no statistically significant effect modification by BMI, history of chronic diseases (diabetes, cardiovascular, or pulmonary diseases), or current use of hormone replacement therapy (women).

Discussion

In this cohort of older adults in the United States, increasing amounts of recent recreational physical activity were associated with lower risk of colon cancer,

even when the activity began later in life. Our results also showed that recreational physical activity was associated with significantly lower risk of rectal cancer in older men and women.

The significant dose-response relationship of decreasing colon cancer risk with increasing hours and MET hours per week of physical activity among men in this study has been reported by some but not all prospective studies (11-26). Ten (11, 12, 14, 15-17, 19, 23-25) of 14 studies of men reported significantly reduced risk of colon cancer with physical activity; seven of these studies (11, 15-17, 19, 23, 24) presented data beyond dichotomized activity levels. Whereas these seven studies generally showed lower risk with increasing activity, only three studies of men (15, 19, 24) reported a significant dose-response relationship; all three studies included the inactive (reference) group in trend analyses. Three (12, 20, 21) of the 10 prospective studies of women reported lower colon cancer risk with increasing physical activity; only one study of women (21) reported a statistically significant dose-response relationship. Case-control studies have generally reported significant test for trend in men but not in women (34-37). One study (39) reported a statistically significant dose-response relationship between colon cancer risk and long-term vigorous physical activity in men and women.

Physical activity has been variably defined in published studies by amount (11, 31, 32, 35, 36, 38), frequency (22, 24, 32, 40), intensity (25-27, 33), or amount weighed by intensity (14-16, 19, 21, 24, 26, 34, 39). Most prospective studies, however, have not quantified the amount of specific types of activities associated with lower colon cancer risk. A British study (26), one of the few that reported risk estimates associated with walking only, reported a statistically nonsignificant 25% lower risk of colorectal cancer associated with walking for ≥40 minutes per day. Previous studies that reported only MET hours, or a similarly weighed index, are difficult to interpret for public health recommendations due to the inability to separate amount from intensity of activities. For example, 30 MET hours per week of activities may correspond to 8.6 hours of walking (assuming 3.5 METs) or 4.3 hours of swimming (assuming 7 METs).

In the CPS II Nutrition Cohort, reporting increasing amounts of walking plus other activities was associated with significantly lower risk of colon cancer in both men and women, with a clear gradient in lower risk seen even among women. The lack of a clear reduction in risk among persons who reported any or increasing amounts of walking only was unexpected and may be partly explained by our inability to assess the pace of walking, physical fitness, or disability in this elderly cohort. It is possible that participants in this study who reported walking as the only recreational physical activity were physically unable to engage in other activities or walked at a slower pace than persons who reported engaging in walking and other activities. We had limited statistical power to examine colon or rectal cancer risk in relation to increasing amounts of other activities, because <6% of participants reported engaging in these activities without walking. Whereas our results suggest that engaging in walking and activities more intense than walking may be necessary to substantially lower colon cancer risk in older men and women, we recognize the need for more refined assessment of the intensity of walking and other activities in elderly populations.

An important question concerns whether recreational physical activity begun later in life is associated with lower risk of colon cancer. In our study, recent activity is more strongly associated with reduced risk of colon cancer than past activity. Furthermore, increasing amounts of recent activity are associated with lower risk of colon cancer regardless of past activity level. Although these data suggest that physical activity begun later in life may be beneficial with respect to colon cancer, we had limited statistical power to examine these relations because <30% of participants reported little or no activity in the past. The lack of an association with past activity is consistent with some (16, 22, 40) but not all published studies (33). One case-control study (40) found no association between early adulthood activity and colon cancer; another study reported lower risk of colon cancer associated with long-term vigorous but not moderate activity (33). Two prospective studies (16, 22) have reported on physical activity information collected at different time points. Neither the Physicians' Health Study (22) nor the Harvard College Alumni study (16) found an inverse association with past physical activity. Whereas these findings support the hypothesis that physical activity may play a more important role later in the continuum of colon carcinogenesis (2), they should

be interpreted cautiously because the lack of an inverse association with past activity may also be related to the generally crude measurement of past physical activity in this and other studies. Better measurements of physical activity, collected prospectively, are needed to evaluate the timing of physical activity in relation to colon and rectal cancer risk.

Few prospective studies have reported on physical activity and colon cancer by subsite (11, 20, 21); two studies have shown a stronger inverse association between physical activity and distal colon cancers (11, 21), whereas a third reported no difference by subsite in men and a stronger inverse association with proximal colon cancer in women (20). Case-control studies have not reported differences in the inverse association by colon subsite (32-36, 39). No statistically significant difference was observed between proximal and distal colon cancer risk in this study, but we had limited statistical power to examine subsite differences by sex.

The significantly lower risk of rectal cancer associated with recreational physical activity in this study is consistent with the results of a recent large case-control study (39) but is inconsistent with previous prospective studies (14, 16, 20, 25) that have generally reported null results. We observed no linear decrease in rectal cancer risk with increasing recreational physical activity; risk decreased with increasing amounts of activity but not at the highest level of activity, consistent with previous case-control studies (31, 34, 46). Only one large case-control study (39) has reported a significant dose-response relationship between increasing vigorous activity and decreasing risk of rectal cancer in men and women.

Several biological mechanisms have been proposed for the role of physical activity in colorectal carcinogenesis. Physical activity may reduce stool transit time, causing decreased exposure of the intestinal epithelium to carcinogens or mutagens. However, stool transit time has not been convincingly shown to be associated with colorectal cancer risk (47, 48). A related hypothesis is that exercise increases water intake, which has been associated with reduced risk of colorectal adenoma and cancer (49, 50). Physical activity also has been proposed to reduce colon cancer risk by reducing body weight or through mechanisms independent of body composition (1, 51). Physical inactivity and central adiposity are both associated with insulin resistance and the hyperinsulinemic state and may affect colon cancer risk through growth factors (52-54). Our results are consistent with physical activity being independently associated with colon cancer and not acting primarily through BMI. However, we did not have a measure of central adiposity. Nevertheless, our results support the importance of energy balance through physical activity and caloric intake (55) as suggested by the somewhat stronger inverse association with colon cancer seen among persons who reported modest daily energy intake and body weight maintenance. It is also possible that physical activity may play an anti-inflammatory role by acting directly on the immune system or through its effect on obesity (56), which is considered by some to cause low-grade systemic inflammation (57) and is associated with elevated serum levels of several inflammatory markers (57-59). Increased physical activity is associated with lower concentrations of C-reactive protein and fibrinogen

(60, 61) and can induce several cytokine inhibitors and anti-inflammatory cytokines (59). Human and experimental studies show that cytokine expression and function are critical in regulating colonic epithelial cell growth, differentiation, and migration and in maintaining overall mucosal integrity (62-66). The significant interaction between physical activity and aspirin use in lowering colon cancer risk in this study lends support to an anti-inflammatory role of physical activity.

Limitations of these data include our inability to assess the frequency (times per week) separately from the duration (hours each time) of physical activity, participants' physical fitness or disability, and our limited statistical power to examine colon cancers by subsite of origin or rectal cancers by sex. Our measures of physical activity were self-reported and not validated, and we had limited numbers of people who reported higher amounts of other activities. We had no information on the intensity at which participants did each of the recreational physical activities and may have misclassified participants who engaged in activities not listed among the seven activities on our questionnaire. Strengths of this study include the ability to evaluate multiple potential confounders and effect modifiers. The prospective design of this study also enabled us to assess the importance of past and recent physical activity, change in body weight, and other covariates using data collected 10 years apart.

Our results show that increasing amounts of recreational physical activity are associated with substantially lower risk of colon cancer and that recreational physical activity is associated with significantly lower risk of rectal cancer in older men and women. We conclude that recreational physical activity should be an integral part of any colorectal cancer prevention program in older adults.

Acknowledgments

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