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Physical activity, obesity, and risk of colon and rectal cancer in a cohort of Swedish men

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ABSTRACT

We investigated the association between physical activity and colorectal cancer risk in a cohort of Swedish men. Information on physical activity was obtained at baseline in 1997 with a self-administered questionnaire from 45,906 men who were cancer-free at enrollment. During a mean follow-up of 7.1 years, 496 cases of colorectal cancer occurred. Leisure-time physical activity was inversely associated with colorectal cancer risk; the multivariate hazard ratio (HR) for 60 min or more per day of leisure-time physical activity compared with less than 10 min per day was 0.57 (95% CI 0.41–0.79; *P* for trend = 0.001). Results were similar for colon (HR = 0.56; 95% CI 0.37–0.83) and rectal cancer (HR = 0.59; 95% CI 0.34–1.02). Home/housework activity was inversely associated with colon cancer risk (HR = 0.68; 95% CI 0.48–0.96). No association was observed for work/occupational activity. These results support a role of physical activity in reducing the risk of colon and rectal cancer.

1. Introduction

Since Garabrant and colleagues[1] and Husemann and colleagues[2] reported an increased risk of colon and rectal cancer in individuals with a sedentary occupation, many studies have examined the role of physical activity in the etiology of colorectal cancer. In 2002, the International Agency for Research on Cancer concluded that there is sufficient evidence for a cancer-preventive effect of physical activity for colon cancer and inadequate evidence for rectal cancer.[3] Few cohort studies have reported on physical activity and colon cancer by subsite, and the findings are inconsistent.[4–9] Moreover, there is no consensus on the type and critical period of physical activity that might be necessary to reduce colorectal cancer risk.

We therefore examined prospectively the relation between physical activity (leisure-time, housework, and occupational) and risk of colon (overall and by subsite) and rectal cancer in a large population-based cohort of Swedish men. We also report findings on the association of anthropometric variables with colorectal cancer risk.

2. Materials and methods

2.1. Study population

The cohort of Swedish men (COSM) began in the autumn of 1997, when all men who were aged 45–79 years and who resided in the Västmanland and Örebro counties of central Sweden received a mailed questionnaire regarding

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demographics, anthropometry, physical activity, medical history, diet, and other potential risk factors for cancer. Of the 100,303 eligible men, 48,850 (49%) completed the questionnaire. The investigation was approved by the Regional Ethical Committee at the Karolinska Institute in Stockholm, Sweden. For the analyses, we excluded men with incorrect or missing national registration number and men diagnosed with cancer (except nonmelanoma skin cancer) prior to baseline. This left 45,906 men eligible for the analyses.

2.2. Assessment of physical activity

Participants reported their level of activity at work (mostly sitting down; sitting down about half of the time; mostly standing up; mostly walking, lifts, carry little; mostly walking, lifts, carry much; heavy manual labor), home/housework (<1, 1–2, 3–4, 5–6, 7–8, or >8 h per day), walking/bicycling (almost never, <20 min per day, 20–40 min per day, 40–60 min per day, 1–1.5 h per day, or >1.5 h per day), and exercise (<1, 1, 2–3, 4–5, or >5 h per week) in the year before study enrollment. The questionnaire also included questions on inactivity (watching TV/reading (<1, 1–2, 3–4, 5–6, or >6 h per day) and hours per day of sleeping and sitting/lying down (open questions). Total leisure-time physical activity (in min per day) was calculated by adding the time spent per day on walking/bicycling and exercising. The reported time spent at each activity per day was multiplied by its typical energy expenditure requirements expressed in metabolic equivalents (METs)[10] and added together to create a MET-hours per day (24-h) score, as described by Norman and colleagues.[11]

The validity of the assessment of physical activity as used in this cohort was tested among 111 men, aged 44–78 years, from the study area by comparison with two 7-day activity records, performed 6 months apart.[11] The Spearman correlation coefficients (adjusted for within- and between-person variation in the records) between the questionnaire and activity records were 0.4 for leisure-time physical activity (combined walking/bicycling and exercise), 0.6 for home/housework, 0.4 for work/occupation, and 0.6 for total activity score.[11]

2.3. Assessment of body size and other information

We used the questionnaire to obtain self-reported information on weight and height at age 20, and weight and waist circumference at baseline. We estimated body mass index (BMI) from weight and height (kg/height in m^2) as a measure of overall obesity. High validity has been observed for self-reported height ($r = 0.9$) and weight ($r = 0.9$) compared with actual measurement among Swedish men.[12] Waist circumference was used as an estimate of abdominal adiposity.

Diet was assessed with a food-frequency questionnaire that determined the frequency of consumption of 96 food items during the past year; details on the validity and reproducibility of this food-frequency questionnaire have been described elsewhere.[13] Information was also collected on dietary supplement use, smoking, family history of colorectal cancer, history of diabetes, and aspirin use.

2.4. Case ascertainment and follow-up

Incident cases of colon and rectal cancer were identified through computerised linkage of the study cohort to the National and Regional Swedish Cancer registers, both of which have been estimated to be almost 100% complete.[14] Complementary data concerning localisation of colonic carcinomas were obtained from the regional colon cancer registry of the Uppsala–Örebro region. Only adenocarcinomas were included in this analysis. Proximal colon cancers included tumours of the caecum, appendix, ascending colon, hepatic flexure, and transverse colon (codes 153.0, 153.1, and 153.4–153.6 of the International Classification of Diseases, 9th Revision). Distal colon cancers included tumours in the splenic flexure, descending colon, and sigmoid colon (codes 153.2, 153.3, and 153.7). Cancer of the rectum included tumours occurring at the rectosigmoid junction and rectum (codes 154.0 and 154.1). Ascertainment of deaths in the cohort and dates of migration was accomplished through linkage to the Swedish Death and Population registers at Statistics Sweden.

2.5. Statistical analysis

Follow-up time for each man was accrued from baseline to the date of diagnosis of colon or rectal cancer, death, migration, or June 30, 2005 whichever came first. We categorised men into five groups with BMI (kg/m^2) corresponding to <23.0, 23.0–24.9, 25.0–26.9, 27.0–29.9, and $\geqslant$30.0. The effect of weight change was assessed by subtracting the weight at age 20 from the weight at baseline. We created five categories of weight change: loss of 5 kg or more, loss or gain of less than 5 kg (reference), gain of 5–10 kg, gain of 11–20 kg, and gain of more than 20 kg. We used quintiles for weight, waist circumference, height, and total activity, and categories for specific activities.

Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using Cox proportional hazards models[15] stratified by age in months at baseline. All multivariate models included education, family history of colorectal cancer, history of diabetes, smoking, and aspirin use. Multivariate analyses of physical activity were also adjusted for BMI, and those of BMI, waist, weight, weight changes, and height were adjusted for leisure-time physical activity. Other variables evaluated for potential confounding were multivitamin supplement use and intakes of total energy, alcohol, dietary fiber, calcium, folate, fruits, vegetables, and red meat. Inclusion of these variables had negligible effect on the associations of physical activity or anthropometric variables with colorectal cancer risk, and they were not included in the final models. We tested the proportional hazard assumption using the likelihood ratio test; there was no departure from the assumption for any covariate in the final models.

Tests of linear trends across exposure categories were assessed by fitting ordinal exposure variables as continuous terms. The Wald statistic was used to test for homogeneity of the HRs for proximal colon, distal colon, and rectal cancer.[16] We used the likelihood ratio test to assess statistical interaction. All analyses were performed using the statistical software SAS (version 9.1; SAS Institute, Cary, NC). All statistical tests were two-sided.

3. Results

The distribution of potential confounders according to leisure-time physical activity and BMI is shown in Table 1. Compared with inactive men, men with higher levels of physical activity had lower BMI and were less likely to smoke. Men with low physical activity or with greater BMI were more likely to have a history of diabetes and to use aspirin. In addition, men with high BMI were less likely to have a post-secondary education.

During a mean follow-up of 7.1 years, 496 colorectal cancers were diagnosed. Of these, 309 were located in the colon (133 proximal colon, 138 distal colon, and 38 cancers at an unknown colonic subsite) and 190 in the rectum (3 cases were

Table 1 – Baseline characteristics of study participants by categories of leisure-time physical activity and BMI[a]

Characteristic	Leisure-time physical activity (min/day)[b]			BMI (kg/m^2)		
	<10	10–59	⩾60	<23.0	23.0–29.9	⩾30
Age, mean (years)	59.7	59.5	62.5	60.4	60.1	59.7
BMI, mean (kg/m^2)	26.7	25.9	25.5	21.6	25.9	32.5
Waist, mean (cm)	99.7	96.7	94.8	87.1	96.5	110.9
Post-secondary education (%)	12.1	17.0	15.4	21.9	16.0	11.0
Family history of colorectal cancer (%)	6.7	7.2	6.9	7.1	7.2	6.5
History of diabetes (%)	9.0	6.0	5.9	4.0	5.6	12.8
Current smokers (%)	33.8	24.6	22.4	27.6	24.1	24.9
Aspirin, regular use (%)	39.1	36.8	35.0	34.0	36.5	41.1

a All variables (except age) are age-standardised to the age-distribution of the cohort. BMI = body mass index.
b Combined walking/bicycling and exercise.

Table 2 – Hazard ratios and 95% confidence intervals of colorectal cancer by physical activity in the cohort of Swedish men (1998 – June 2005)[a]

Variable	Cases[b]	Person-years[b]	Age-adjusted HR	Multivariate HR[c]
Leisure-time activity (min/day)[d]				
<10	51	23,658	1.00	1.00
10–29	100	62,006	0.73 (0.52–1.03)	0.76 (0.54–1.06)
30–59	166	117,659	0.59 (0.43–0.81)	0.64 (0.47–0.89)
⩾60	174	112,838	0.52 (0.38–0.71)	0.57 (0.41–0.79)
P for trend			<0.0001	0.001
Home/housework (h/day)[e]				
<1	187	122,569	1.00	1.00
1–2	205	138,084	0.84 (0.68–1.02)	0.90 (0.73–1.10)
⩾3	77	45,326	0.75 (0.57–0.98)	0.81 (0.62–1.07)
P for trend			0.02	0.11
Work/occupation[f]				
Light	242	165,702	1.00	1.00
Moderate	164	97,039	0.93 (0.76–1.14)	0.99 (0.81–1.22)
Heavy	76	50,214	1.08 (0.83–1.39)	1.10 (0.84–1.44)
P for trend			0.85	0.58
Total activity score (MET-h/day)				
<37.9	98	61,804	1.00	1.00
37.9–40.7	80	63,549	0.82 (0.61–1.10)	0.84 (0.62–1.13)
40.8–44.8	105	63,120	0.97 (0.73–1.28)	1.00 (0.76–1.33)
⩾44.9	82	63,505	0.79 (0.59–1.07)	0.82 (0.60–1.10)
P for trend			0.27	0.38

a CI = confidence interval; HR = hazard ratio; MET = metabolic equivalent of energy expenditure (kcal/kg × h).
b The sum does not add up to the total owing to missing data.
c Multivariate models were stratified by age (in months) at baseline and adjusted for education (less than high school, high school graduate, or more than high school), family history of colorectal cancer (yes/no), history of diabetes (yes/no), smoking (never, past, or current smoker), aspirin use (yes/no), and body mass index (<23.0, 23.0–24.9, 25.0–29.9, or ⩾30.0 kg/m^2). Leisure-time physical activity, home/housework, and work/occupation were included simultaneously in the multivariate model.
d Combined walking/bicycling and exercise; the median MET values for the categories are 0.5, 1.4, 3.0, and 6.3 MET-h/day.
e The median MET values for the categories are 1, 3.8, and 8.8 MET-h/day.
f Light = mostly sitting down (7.4 MET-h/day) to sitting down half of the time (10.3 MET-h/day); moderate = mostly standing up (12.5 MET-h/day) to mostly walking, lifts, carry little (14.8 MET-h/day); heavy = mostly walking, lifts, carry much (17.1 MET-h/day) to heavy manual work (22.2 MET-h/day). Work/occupational activity levels were multiplied by 5.7 per day (8 h per day, 5 days per week).

diagnosed with both colon and rectal cancer). We observed an inverse association between leisure-time physical activity and risk of colorectal cancer (Table 2). Men who engaged in leisure-time physical activity for 60 min or more per day had a multivariate HR of 0.57 (95% CI 0.41–0.79) compared to men who engaged in leisure-time physical activity for less than 10 min per day. Excluding cases diagnosed during the first two years of follow-up did not change the results materially (multivariate HR = 0.56; 95% CI 0.38–0.82). The incidence rates, age-standardised to the age distribution in the cohort, were 246 and 134 per 100,000 persons per year in the lowest and highest categories of leisure-time physical activity. No significant associations were observed for home/housework, work/occupational activity, or total activity in multivariate analyses (Table 2).

Leisure-time physical activity was inversely associated with risk of both colon and rectal cancer (Table 3). Although the inverse association between leisure-time physical activity and colon cancer risk was somewhat stronger for distal than proximal colon cancer, the difference by subsite was not statistically significant (P for heterogeneity = 0.18). Home/housework was statistically significantly inversely associated with risk of colon cancer, whereas occupational and total activity was not associated with risk of any subsite (Table 3).

We also examined the relation between leisure-time physical activity at age 30 (reported retrospectively at baseline) and risk of colorectal cancer. The multivariate HR of colorectal cancer for men who engaged in leisure-time physical activity for 60 min or more per day at age 30 was 1.08 (95% CI 0.75–1.56) compared with those who engaged in such activity for less than 10 min per day at age 30.

We calculated the population attributable risk, i.e. the proportion of cases that would be avoided if the risk factor distribution of a high-risk group switched to that of a low-risk group, by using the prevalence of men who engaged in leisure-time physical activity for less than 30 min per day (27.4%; defined as high-risk group) and the multivariate HR for comparison of less than 30 min per day with 30 min per day or more (defined as low risk group). The population attributable risk was 9%.

Table 3 – Multivariate hazard ratios and 95% confidence intervals of proximal colon, distal colon, and rectal cancer by physical activity in the cohort of Swedish men (1998 – June 2005)[a]

Variable	Colon[b]		Proximal colon		Distal colon		Rectum	
	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]
Leisure-time activity (min/day)[e]								
<10	34	1.00	12	1.00	19	1.00	17	1.00
10–29	55	0.66 (0.43–1.02)	26	0.98 (0.49–1.97)	25	0.51 (0.28–0.93)	45	0.91 (0.51–1.59)
30–59	111	0.68 (0.46–1.01)	49	0.90 (0.47–1.73)	48	0.50 (0.29–0.87)	58	0.61 (0.35–1.06)
⩾60	107	0.56 (0.37–0.83)	45	0.72 (0.37–1.40)	45	0.40 (0.22–0.70)	67	0.59 (0.34–1.02)
P for trend		0.01		0.17		0.01		0.01
Home/housework (h/day)[f]								
<1	128	1.00	55	1.00	57	1.00	61	1.00
1–2	120	0.75 (0.58–0.97)	56	0.78 (0.53–1.14)	52	0.78 (0.53–1.15)	86	1.21 (0.87–1.70)
⩾3	46	0.68 (0.48–0.96)	16	0.50 (0.29–0.89)	23	0.86 (0.52–1.41)	31	1.08 (0.69–1.69)
P for trend		0.01		0.02		0.39		0.62
Work/occupation[g]								
Light	145	1.00	62	1.00	66	1.00	99	1.00
Moderate	113	1.17 (0.91–1.52)	46	1.14 (0.76–1.69)	53	1.25 (0.85–1.82)	52	0.75 (0.53–1.06)
Heavy	41	1.03 (0.72–1.47)	21	1.26 (0.75–2.11)	14	0.79 (0.43–1.42)	35	1.16 (0.78–1.74)
P for trend		0.51		0.33		0.91		0.99
Total activity score (MET-h/day)								
<37.9	59	1.00	27	1.00	28	1.00	39	1.00
37.9–40.7	53	0.93 (0.64–1.36)	22	0.90 (0.51–1.59)	23	0.82 (0.47–1.44)	29	0.74 (0.46–1.21)
40.8–44.8	68	1.07 (0.75–1.53)	28	0.95 (0.56–1.64)	32	1.12 (0.67–1.89)	37	0.88 (0.55–1.39)
⩾44.9	47	0.79 (0.53–1.17)	30	0.71 (0.39–1.29)	19	0.70 (0.38–1.27)	35	0.86 (0.53–1.37)
P for trend		0.41		0.32		0.47		0.66

a CI = confidence interval; HR = hazard ratio; MET = metabolic equivalent of energy expenditure (kcal/kg × h).
b Including 38 colon cancers at an unknown subsite in the colon.
c The sum does not add up to the total owing to missing data.
d Multivariate models were stratified by age (in months) at baseline and adjusted for education (less than high school, high school graduate, or more than high school), family history of colorectal cancer (yes/no), history of diabetes (yes/no), smoking (never, past, or current smoker), aspirin use (yes/no), and body mass index (<23.0, 23.0–24.9, 25.0–29.9, or ⩾30.0 kg/m^2). Leisure-time physical activity, home/housework, and work/occupation were included simultaneously in the multivariate model.
e Combined walking/bicycling and exercise; the median MET values for the categories are 0.5, 1.4, 3.0, and 6.3 MET-h/day.
f The median MET values for the categories are 1, 3.8, and 8.8 MET-h/day.
g Light = mostly sitting down (7.4 MET-h/day) to sitting down half of the time (10.3 MET-h/day); moderate = mostly standing up (12.5 MET-h/day) to mostly walking, lifts, carry little (14.8 MET-h/day); heavy = mostly walking, lifts, carry much (17.1 MET-h/day) to heavy manual work (22.2 MET-h/day). Work/occupational activity levels were multiplied by 5.7 per day (8 h per day, 5 days per week).

There were statistically significant positive associations of BMI and weight with risk of colorectal cancer (Table 4). When analysed as continuous variables, the multivariate HR of colorectal cancer for an increment of 1 BMI unit (1 kg/m^2) was 1.04 (95% CI: 1.01–1.07) and the multivariate HR for an increment of 5 kg in weight was 1.05 (95% CI 1.02–1.09). Waist circumference was weakly positively associated with the risk of colorectal cancer (Table 4). Colorectal cancer risk was not associated with height (multivariate HR = 1.03; 95% CI: 0.73–1.44, for ⩾183 versus <172 cm) or weight change over lifetime (multivariate HR = 1.16; 95% CI 0.81–1.65, for gain of more than 20 kg compared with loss or gain of less than 5 kg). The associations for BMI, weight, and waist did not differ significantly by cancer site (Table 5).

To eliminate preclinical cases that might have experienced weight loss before completing the questionnaire, we did analyses that excluded the first 2 years of follow-up. Associations of BMI and weight with risk of colorectal cancer were strengthened in these lag analyses; the multivariate HRs for the highest versus the lowest category were 1.65 (95% CI 1.09–2.51) for BMI and 1.65 (95% CI 1.15–2.38) for weight.

To evaluate the possibility of an interaction between physical activity and BMI in relation to colorectal cancer, we classified participants according to both leisure-time physical activity and BMI. The decreased risk of colorectal cancer associated with increased levels of leisure-time physical activity was observed across all categories of BMI (P for interaction = 0.33; Fig. 1). There was also no statistically significant interaction between leisure-time physical activity and age (<65 or ⩾65 years; P for interaction = 0.61), smoking status (never, past, or current; P for interaction = 0.84), or aspirin use (yes or no; P for interaction = 0.83).

4. Discussion

In this large population-based prospective cohort of Swedish men, we observed that increased amounts of leisure-time physical activity were associated with reduced risk of both colon and rectal cancer. Findings of this study also confirm direct associations of BMI and weight with colorectal cancer risk.

The reduction in colon cancer risk associated with increasing amounts of recent leisure-time physical activity in this study is consistent with the results from the majority of previous prospective and case-control studies.[3,17] A meta-analysis estimated an approximately 20–40% lower risk of colon cancer for high versus low leisure-time physical activity.[17]

Evidence suggest that the etiologic factors for cancers of the proximal and distal colon may differ.[18,19] For example, there are various molecular and clinical differences between the two subsites that may influence the susceptibility to environmental factors.[19] We found that the inverse relationship between leisure-time physical activity and risk of colon cancer was stronger for distal colon than for proximal colon,

Table 4 – Hazard ratios and 95% confidence intervals of colorectal cancer by BMI, body weight, and waist circumference in the cohort of Swedish men (1998 – June 2005)[a]

Variable	Cases[b]	Person-years[b]	Age-adjusted HR	Multivariate HR[c]
BMI (kg/m^2)				
<23.0	70	57,097	1.00	1.00
23.0–24.9	111	79,423	1.13 (0.83–1.52)	1.13 (0.84–1.53)
25.0–26.9	114	78,190	1.23 (0.91–1.65)	1.20 (0.89–1.62)
27.0–29.9	107	64,956	1.39 (1.03–1.89)	1.32 (0.97–1.80)
⩾30.0	59	30,977	1.71 (1.20–2.42)	1.54 (1.08–2.21)
P for trend			0.001	0.01
Weight (kg)[d]				
<72	81	57,221	1.00	1.00
72–76	92	58,732	1.21 (0.90–1.63)	1.18 (0.87–1.60)
77–82	104	66,406	1.31 (0.98–1.76)	1.26 (0.93–1.70)
83–89	97	61,497	1.37 (1.02–1.84)	1.28 (0.94–1.75)
⩾90	114	67,396	1.65 (1.24–2.20)	1.48 (1.09–2.03)
P for trend			0.001	0.02
Waist (cm)[d]				
<88	47	44,165	1.00	1.00
88–92	67	53,831	1.10 (0.76–1.60)	1.06 (0.73–1.55)
93–97	95	56,784	1.38 (0.97–1.96)	1.32 (0.92–1.88)
98–103	96	54,462	1.46 (1.03–2.08)	1.37 (0.96–1.96)
⩾104	102	52,928	1.44 (1.02–2.05)	1.29 (0.90–1.85)
P for trend			0.01	0.03

a BMI = body mass index; CI = confidence interval; HR = hazard ratio.
b The sum does not add up to the total owing to missing data.
c Multivariate models were stratified by age (in months) at baseline and adjusted for education (less than high school, high school graduate, or more than high school), family history of colorectal cancer (yes/no), history of diabetes (yes/no), smoking (never, past, or current smoker), aspirin use (yes/no), and leisure-time physical activity (<10, 10–29, 30–59, or ⩾60 min/day).
d Multivariate hazard ratios also adjusted for height (in quintiles).

Table 5 – Multivariate hazard ratios and 95% confidence intervals of proximal colon, distal colon, and rectal cancer by BMI, body weight, and waist circumference in the cohort of Swedish men (1998 – June 2005)[a]

Variable	Colon[b]		Proximal colon		Distal colon		Rectum	
	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]	Cases[c]	HR (95% CI)[d]
BMI (kg/m²)								
<23.0	47	1.00	19	1.00	23	1.00	25	1.00
23.0–24.9	72	1.11 (0.77–1.61)	29	1.09 (0.61–1.96)	29	0.92 (0.53–1.59)	39	1.08 (0.65–1.80)
25.0–26.9	65	1.07 (0.73–1.56)	30	1.19 (0.66–2.13)	31	1.09 (0.63–1.89)	49	1.35 (0.83–2.19)
27.0–29.9	61	1.15 (0.78–1.70)	27	1.19 (0.65–2.17)	29	1.18 (0.67–2.07)	46	1.53 (0.93–2.51)
⩾30.0	39	1.60 (1.03–2.48)	15	1.43 (0.71–2.88)	17	1.49 (0.78–2.84)	21	1.44 (0.79–2.61)
P for trend		0.08		0.32		0.16		0.06
Weight (kg)[e]								
<72	49	1.00	22	1.00	21	1.00	33	1.00
72–76	70	1.50 (1.04–2.18)	22	0.98 (0.54–1.79)	38	1.99 (1.15–3.42)	23	0.71 (0.42–1.22)
77–82	61	1.22 (0.83–1.81)	29	1.20 (0.68–2.14)	23	1.11 (0.60–2.05)	43	1.29 (0.80–2.07)
83–89	54	1.19 (0.79–1.78)	22	0.94 (0.51–1.76)	27	1.51 (0.82–2.76)	43	1.40 (0.86–2.26)
⩾90	69	1.50 (1.01–2.24)	35	1.52 (0.85–2.73)	27	1.39 (0.75–2.60)	46	1.47 (0.90–2.42)
P for trend		0.23		0.20		0.71		0.02
Waist (cm)[e]								
<88	31	1.00	12	1.00	12	1.00	17	1.00
88–92	47	1.19 (0.75–1.87)	16	1.05 (0.49–2.23)	27	1.78 (0.90–3.54)	20	0.84 (0.44–1.61)
93–97	51	1.15 (0.73–1.80)	24	1.35 (0.67–2.73)	25	1.55 (0.77–3.12)	45	1.67 (0.95–2.95)
98–103	55	1.28 (0.82–2.00)	25	1.41 (0.70–2.85)	22	1.46 (0.71–2.98)	41	1.58 (0.89–2.81)
⩾104	68	1.44 (0.93–2.24)	33	1.66 (0.84–3.27)	26	1.62 (0.80–3.27)	35	1.24 (0.68–2.25)
P for trend		0.09		0.08		0.47		0.16

a BMI = body mass index; CI = confidence interval; HR = hazard ratio.
b Including 38 colon cancers at an unknown subsite in the colon.
c The sum does not add up to the total owing to missing data.
d Multivariate models were stratified by age (in months) at baseline and adjusted for education (less than high school, high school graduate, or more than high school), family history of colorectal cancer (yes/no), history of diabetes (yes/no), smoking (never, past, or current smoker), aspirin use (yes/no), and leisure-time physical activity (<10, 10–29, 30–59, or ⩾60 min/day).
e Multivariate hazard ratios also adjusted for height (in quintiles).

which is consistent with results of most of the previous prospective studies[4–6,9] but not all.[7,8]

Our finding of a lower risk of rectal cancer associated with increased amounts of leisure-time physical activity is in agreement with results of a recent large prospective cohort study.[7] In the Cancer Prevention Study II Nutrition Cohort with over 150,000 women and men, 390 individuals were diagnosed with rectal cancer during 7 years of follow-up.[7] In this cohort, a statistically significant 30% reduction in rectal cancer risk was observed for any recreational physical activity compared with none.[7] In a cohort of male Finnish smokers,[20] a statistically significant inverse association was observed between occupational activity and risk of rectal cancer; however, leisure-time physical activity was not associated with risk of either colon or rectal cancer. Other prospective studies have not observed any significant association between leisure-time or total physical activity and risk of rectal cancer,[4,8,20,21] but were limited by a small number of cases (ranging from 44 to 104). Results from case-control studies of physical activity and rectal cancer have also been inconsistent. In a meta-analysis of studies published through 2001, the summary results from case-control studies showed a nonsignificant 12–13% reduced risk of rectal cancer for high versus low physical activity (all types combined).[17] In a recent large population-based case-control study (with 952 rectal cancer cases) that was not included in the meta-analysis, high levels of leisure-time physical activity was associated with a statistically significant 30–40% lower risk of rectal cancer.[22]

Our results related to obesity and physical activity may be explained, biologically, within the axis of insulin resistance and hyperinsulinemia. Obesity is a major determinant of insulin resistance, and physical activity (independently of influencing body mass) increases insulin sensitivity and reduces insulin levels.[23] Insulin is an important growth factor of colonic epithelial cells and is a mitogen of tumour cell growth *in vitro*.[23] Supporting a role of insulin in colorectal carcinogenesis, epidemiologic studies have shown an increased risk of colorectal cancer associated with high circulating levels of insulin and C-peptide (a marker of insulin secretion)[24–27] and chronic insulin therapy.[28] In addition, a recent meta-analysis showed that diabetes was associated with a statistically significant increased risk of both colon and rectal cancer,[29] suggesting that hyperinsulinemia may be implicated in both colon and rectal cancer. Other proposed mechanisms for a protective role of physical activity on colon cancer include decreased gastrointestinal transit time, improved immune function, changes in bile acid metabolism, and altered prostaglandin levels.[30]

Findings from this study suggest that recent physical activity may be more beneficial with regard to colorectal cancer than physical activity early in adulthood (age 30).

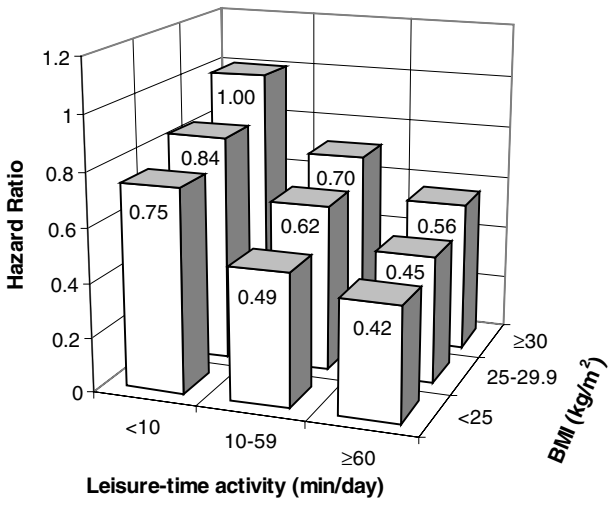

Fig. 1 – Multivariate hazard ratios of colorectal cancer by leisure-time physical activity and body mass index (BMI). Multivariate models were stratified by age (in months) at baseline and adjusted for education (less than high school, high school graduate, or more than high school), family history of colorectal cancer (yes/no), history of diabetes (yes/no), smoking (never, past, or current smoker), and aspirin use (yes/no). The nine hazard ratios with 95% confidence intervals are as follows: 1.00 (reference), 0.70 (0.36–1.38), 0.56 (0.26–1.23), 0.84 (0.42–1.66), 0.62 (0.34–1.13), 0.45 (0.24–0.84), 0.75 (0.36–1.55), 0.49 (0.26–0.90), and 0.42 (0.22–0.78).

Although one case-control study found a reduction in colon cancer risk associated with long-term vigorous activity,[31] most studies have not observed inverse associations with early adulthood activity.[7,21,32,33]

Strengths of the present study include a population-based and prospective design, a large sample size, and validated data on different types of physical activity, including leisure-time, housework, and occupational activity. Because of the large sample size, we could investigate associations by subsites in the colon and with rectal cancer with reasonable statistical power. Other strengths of the study include the virtually complete cohort follow-up and the detailed information on potential confounders. A limitation of this study is that measures of physical activity and body size were self-reported, which could lead to misclassification of exposures. However, because information on exposures was collected before the diagnosis of colorectal cancer, any misclassification would most likely have attenuated rather than exaggerated any true relationships and thus is unlikely to explain the observed associations.

In summary, results from this prospective study support the hypothesis of a protective role of leisure-time physical activity against colon cancer. Furthermore, our findings suggest that increased amounts of time spent at leisure-time physical activity may reduce the risk of rectal cancer.

Conflict of interest statement

None declared.

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