Recreational Physical Activity and Cancer Risk in Subsites of the Colon (the Nord-Trøndelag Health Study)

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Abstract

Physical activity may reduce colon cancer risk, but the underlying mechanisms remain unclear. Relating physical activity to cancer risk in anatomic segments of the colon may advance our understanding of possible mechanisms. We conducted a prospective study of 59,369 Norwegian men and women who were followed up for cancer incidence and mortality. Cox proportional hazards models were used to estimate multivariably adjusted hazard ratios (HR) and 95% confidence intervals (95% CI). All statistical tests were two sided. During 17 years of follow-up, 736 colon cancers and 294 rectal cancers were diagnosed. Overall, we found an inverse association between recreational physical activity and colon cancer risk, but subsite analyses showed that the association was confined to cancer in the transverse and sigmoid colon. The adjusted HR, comparing people who reported high versus no physical activity, was 0.44 (95% CI, 0.25-0.78) for cancer in the transverse colon and 0.48 (95% CI, 0.31-0.75) for cancer in the sigmoid colon. The corresponding HR for cancer mortality was 0.33 (95% CI, 0.14-0.76) for the transverse colon and 0.29 (95% CI, 0.15-0.56) for the sigmoid colon. For rectal cancer, there was no association with physical activity in these data. In conclusion, the inverse association of recreational physical activity with cancer risk and mortality in the transverse and sigmoid segments of the colon may point at increased colon motility and reduced fecal transit time as possible underlying mechanisms. (Cancer Epidemiol Biomarkers Prev 2008;17(1):183–8)

Introduction

Recent reviews (1, 2) and a meta-analysis (3) conclude that physically active people have a lower risk of colon cancer compared with physically inactive people. For rectal cancer, however, the data show no clear association with physical activity (1, 2).

The underlying mechanisms for the effect of physical activity on colon cancer risk are not known, but several plausible pathways have been suggested (4). Physical activity appears to accelerate colonic transit time (5-7), suggesting that exercise may reduce exposure to fecal carcinogens in the colon. Also, effects of exercise related to insulin levels (8, 9), insulin-like growth factors, bile acids, and prostaglandins have been proposed (4).

By relating physical activity to cancer risk in anatomical segments of the colon, our understanding of possible mechanisms may be advanced (4, 10, 11). A few prospective studies (12-17) have assessed the relation of recreational physical activity with risk of subsite-specific colon cancer, but these studies classified subsites as cancer of the right or left colon or, alternatively, from the proximal or distal parts of the colon. Data on the risk of cancer at more exact anatomical subsites related to recreational activity have not been presented previously. Four studies related to occupational physical activity have been published, but with inconsistent results (18-21).

Based on information on a large cohort of Norwegian men and women who have been followed up for ~17 years, we had a sufficiently large number of colon cancer cases to prospectively study the separate associations of recreational physical activity, indicated by frequency, duration, and intensity of regular exercise, with the incidence of, and mortality from, cancer in the ascending, transverse, descending, and sigmoid segments of the colon as well as rectal cancer.

Materials and Methods

Study Population. In Nord-Trøndelag County in Norway, all inhabitants 20 years old and older were invited to participate in the Nord-Trøndelag Health Study between 1984 and 1986. Among 85,100 eligible individuals, 75,043 (88.2%) accepted the invitation and attended a clinical examination (36,769 men and 38,274 women). They filled in a questionnaire that was included with the invitation, and at the clinical examination, they were given a second questionnaire to complete at home and return in a prestamped envelope. Briefly, information was collected on a range of lifestyle and health-related factors, including measures of physical activity, smoking, alcohol consumption, and education. The

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clinical examination included standardized measurements of body height and weight in addition to blood pressure, heart rate, and blood glucose.

In the present analysis, we excluded 805 men and 1,089 women with known prevalent cancer at baseline. Among the remaining 73,149 participants, 13,046 failed to return the second questionnaire that included information on physical activity and 734 had incomplete information on other potentially confounding factors. This study is therefore based on cancer follow-up of 29,295 men and 30,074 women.

We compared those who responded to the questionnaire with nonresponders on some key factors and found that the groups were similar in terms of both colon cancer incidence [hazard ratio (HR) in nonresponders compared with responders, 1.07; 95% confidence interval (95% CI), 0.90-1.28] and variables such as age (mean age, responders 49.2 years versus nonresponders 48.8 years), sex (50.8% men versus 51.0% women), and body mass index (25.2 versus 25.1 kg/m^2).

Follow-up. The unique 11-digit identity number of Norwegian citizens was used to link individuals from the Nord-Trøndelag Health Study to information on cancer incidence at the Cancer Registry of Norway. Follow-up time was calculated from the date of attendance at the clinical examination until the date of cancer diagnosis (of all sites), date of emigration, date of death, or to the end of follow-up, December 31, 2002, whichever came first. Colon and rectal cancers were registered according to the *International Classification of Diseases, Seventh Edition* (ICD-7; codes 153 and 154, respectively). We subdivided colon cancers according to subsite as either ascending colon (including cecum and appendix, codes 153.0 and 153.6, respectively), transverse colon (including hepatic and splenic flexures, code 153.1), descending colon (code 153.2), or sigmoid colon (code 153.3). Cases with nonspecific subsite (code 153.8), overlapping subsite (code 153.7), or subsite in the rectosigmoid junction (code 153.4) were not included as cases in the subsite analyses and were censored at the time of diagnosis. Previous studies have assessed physical activity in relation to the proximal and distal parts of the colon, and for comparison with these studies, we reanalyzed the data, subdividing the cancers as proximal (ICD-7 codes 153.0, 153.1, and 153.6) or distal (ICD-7 codes 153.2 and 153.3).

In the analysis of colorectal cancer mortality, we included deaths where colon or rectal cancer was recorded as the underlying cause of death (Cause of Death Registry at Statistics Norway; ICD-9 code 153-154 and ICD-10 code C18-C20). We also used information from the Cancer Registry in these analyses (*a*) to ensure that we only studied deaths from incident colon and rectal cancers (that is, cancers diagnosed after the baseline measure of physical activity) and (*b*) to be able to study deaths according to anatomical subsite, as anatomical site is not routinely recorded on death certificates.

The study was approved by the Norwegian Data Inspectorate, the Norwegian Board of Health, and the Regional Committee for Ethics in Medical Research.

Physical Activity. At baseline, the participants were asked to complete a questionnaire that included frequency, duration, and intensity of recreational physical activity in a week (that is, walking, skiing, swimming, or other sports). The frequency question allowed five response options (0, <1, 1, 2-3, and ≥4 times; coded 1-5), and participants who reported exercising at least once a week were also asked about the average duration (<15, 15-30, 31-60, and >60 minutes; coded 1-4) and intensity (light, moderate, and vigorous; coded 1-3) of the activity. Among people who exercised once a week or more, we constructed a summary score of frequency, duration, and intensity. The score summarized each participant's responses to give equal weight to each measure according to the following equation: $1/5 \times$ frequency $+ 1/4 \times$ duration $+1/3 \times$ intensity. This approach gave a maximum score of 1.0 for each of the three components of the summary score. The median score value was 2.02 for men and 1.83 for women (range, 1.18-3.00). A summary score below the median was classified as low activity, whereas a score at the median or above was classified as high activity.

Statistical Analyses. We used Cox proportional hazards models to compute HRs of colon or rectal cancer, where people who reported different levels of physical activity were compared with the reference group of people who reported no physical activity. Precision of the estimates was assessed by 95% CI. Our basic models were age adjusted using attained age as the time variable. In addition, we adjusted for body mass index (<18.5, 18.5-24.9, 25.0-29.9, and ≥30.0 kg/m^2), smoking status (never, former, current, and unknown), use of alcohol (frequency last 2 weeks: 0, 1-4, ≥5, total abstainer, and unknown), marital status (married, unmarried, widowed, and divorced/separated), and education (<10, 10-12, and ≥13 years and unknown). Trend tests across categories of physical activity were calculated by treating the categories as ordinal variables in the Cox proportional hazards model. The overall analyses of total colon and rectal cancers were conducted separately for men and women, whereas in the analyses of subsites of the colon, men and women were combined (all *P* values for interaction were higher than 0.10). Additionally, we tested the heterogeneity of the estimated HRs for different subsites.

We also related physical activity to colon and rectal cancer mortality. The analyses were similar to those conducted for cancer risk. Additionally, we calculated the total attributable fraction based on these results (22), and we explored whether physical activity reported before diagnosis was related to survival from colon cancer.

In separate analyses, we evaluated the potential influence of preclinical disease at baseline by excluding cases that occurred during the first 3 years of follow-up. All statistical tests were two sided, and all statistical analyses were performed using Stata for Windows version 9.2 (StataCorp, 1985-2006).

Results

The characteristics of study participants at baseline are presented in Table 1. During 17 years of follow-up (918,085 person-years), 736 cases of colon cancer (346 in men and 390 in women) and 294 cases of rectal cancer (170 in men and 124 in women) were diagnosed among the 59,369 study participants. Among colon cancer cases, 267 originated from the ascending segment of the colon (31% of male and 40% of female cases), 124 from the transverse colon (18% of male and 17% of female cases),

Table 1. Characteristics of the study population according to summary score of recreational physical activity

Characteristic	No activity	<1 per wk	Low summary score (less than median)	High summary score (equal to or more than median)
No. participants (% of total)*	8,096 (13.6)	16,068 (27.1)	16,473 (27.8)	16,984 (28.6)
Mean (range) age at baseline, y	56.1 (20-101)	45.0 (20-98)	51.5 (21-95)	46.2 (20-92)
Mean (range) age at colorectal cancer diagnosis, y	74.5 (35-95)	67.9 (40-91)	73.4 (35-93)	71.7 (38-92)
Mean (SD) physical activity score			1.7 (0.2)	2.2 (0.3)
Mean (SD) body mass index, kg/m^2	25.9 (4.6)	25.2 (4.0)	25.3 (3.7)	24.6 (3.5)
Sex (% men)	48.0	51.1	55.1	44.0
Alcohol (% drinking last 2 wk)	30.7	47.0	42.0	45.3
Education (% college/university)	3.1	8.6	10.0	13.9
Marital status (% married)	63.0	72.9	72.2	69.3

NOTE: Summary score combining information on frequency, duration, and intensity among those who exercised once a week or more (low score defined as less than median and high score defined as equal to or more than median).

*Due to missing values on duration and intensity, the number of participants does not exactly correspond to the total number of participants in the study (n = 59,369).

50 from the descending colon (7% of male and 6% of female cases), 214 from the sigmoid colon (31% of male and 27% of female cases), and 38 cases originated from the rectosigmoid segment (7% of male and 4% of female cases). Forty-three (6%) cases could not be classified according to anatomical subsite. During the same follow-up period, we identified 382 persons (190 men and 192 women) who had died from colon cancer and 151 (88 men and 63 women) who had died from rectal cancer. Among these deaths, 121 were caused by cancer of the ascending colon, 60 from cancer of the transverse colon, 31 from cancer of the descending colon, and 100 deaths from cancer of the sigmoid colon.

Each measure of physical activity (frequency, duration, and intensity) showed inverse but moderate associations with colon cancer risk (Table 2). The inverse associations were strongest for the physical activity score that summarized the information on frequency, duration, and intensity (P_{trend} = 0.06 in men and 0.03 in women). Thus, the adjusted HR for colon cancer among people who reported high versus no physical activity was 0.69 (95% CI, 0.48-0.98) among men and 0.72 (95% CI, 0.53-0.98) among women.

For rectal cancer risk, there was no evidence of a linear association with physical activity in either men (P_{trend} = 0.89) or women (P_{trend} = 0.74). The adjusted HR associated with a high summary score compared to no physical activity was 1.12 (95% CI, 0.65-1.96) among men and 1.01 (95% CI, 0.58-1.75) among women (data not shown).

There was strong statistical evidence that HRs for the association of exercise with colon cancer risk varied depending on the anatomical site of the cancer (P from test of heterogeneity of HRs for different subsites < 0.001). There were particularly strong inverse associations for cancer in the transverse (P_{trend} = 0.004) and sigmoid (P_{trend} < 0.001) segments of the colon (Table 3). The adjusted HR comparing subjects with a high summary score with those who reported no activity were 0.44 (95% CI, 0.25-0.78) for cancer in the transverse colon and 0.48 (95% CI, 0.31-0.75) for cancer in the sigmoid colon. There were no clear associations for cancer in the ascending or descending segments of the colon.

For comparison with previous studies, the subsites were collapsed into cancers of the proximal or distal colon. By comparing the highest with the lowest level of physical activity, we found a stronger inverse association with distal (adjusted HR, 0.56; 95% CI, 0.37-0.83) than with proximal colon cancer (adjusted HR, 0.81; 95% CI, 0.59-1.10).

In a supplementary analysis, we excluded the first 3 years of follow-up to evaluate whether preclinical colon cancer at baseline could have influenced our findings, but the results were not substantially different from using the whole follow-up period. The HR, comparing people with high versus no physical activity, was 0.42 (95% CI, 0.23-0.78) for risk of cancer in the transverse colon and 0.54 (95% CI, 0.33-0.89) for cancer in the sigmoid colon (data not shown). We also evaluated whether stage at diagnosis varied between subsites of colon cancer but found only minor differences in the proportion who presented with metastases at diagnosis (74% of cases from the ascending colon, 74% from the transverse colon, 76% from the descending colon, and 66% from the sigmoid colon).

For colon cancer mortality, there was a strong inverse association with physical activity (P_{trend} < 0.001; Table 4). The adjusted HR for colon cancer death, comparing people with high versus no activity, was 0.56 (95% CI, 0.41-0.78). For deaths related to cancer in subsites of the colon, there were strong inverse associations for the transverse (P_{trend} = 0.002) and sigmoid (P_{trend} < 0.001) colon but no evidence of any association for the ascending and descending colon. Comparing people with high versus no physical activity, the adjusted HR was 0.33 (95% CI, 0.14-0.76) for the transverse colon and 0.29 (95% CI, 0.15-0.56) for the sigmoid colon.

In additional analysis of survival from colon cancer, we found that increasing level of physical activity was related to longer survival (P_{trend} = 0.006). The adjusted HR of people who reported the highest versus the lowest level of physical activity before diagnosis was 0.65 (95% CI, 0.47-0.91). After additional adjustment for stage at diagnosis (that is, metastatic or localized cancer), this association was somewhat attenuated (HR, 0.75; 95% CI, 0.53-1.05). Due to limited statistical power, survival analysis was not conducted for specific subsites of colon cancer.

Assuming that the findings for colon cancer mortality reflect causal relations, ~28% of colon cancer deaths that occurred in the population could have been avoided providing that all people were in the highest category of physical activity.

Table 2. HR of colon cancer incidence according to recreational physical activity, stratified by sex

Physical activity	Men				P_{trend}	Women				P_{trend}
	No. person-years	No. cases	Crude HR	Adjusted HR (95% CI)		No. person-years	No. cases	Crude HR	Adjusted HR (95% CI)	
No activity	53,344	60	1.00	1.00 (Reference)	—	56,445	79	1.00	1.00 (Reference)	—
Frequency per week										
<1	130,427	75	0.84	0.84 (0.60-1.19)	—	128,181	84	0.92	0.91 (0.66-1.25)	—
1	107,225	74	0.83	0.82 (0.58-1.17)	—	126,317	80	0.81	0.79 (0.57-1.09)	—
2-3	99,350	69	0.79	0.81 (0.57-1.15)	—	106,337	67	0.68	0.66 (0.47-0.92)	—
≥4	52,465	68	0.75	0.77 (0.54-1.09)	0.18	57,137	80	1.02	0.99 (0.72-1.36)	0.35
Minutes per exercise										
<15	25,459	39	1.08	1.07 (0.71-1.60)	—	36,717	44	0.87	0.85 (0.59-1.23)	—
15-30	85,910	78	0.81	0.80 (0.57-1.12)	—	122,860	98	0.84	0.81 (0.60-1.09)	—
31-60	122,150	71	0.68	0.68 (0.48-0.97)	—	137,873	82	0.78	0.73 (0.53-1.01)	—
>60	76,141	50	0.73	0.74 (0.50-1.08)	0.02	32,029	24	0.90	0.84 (0.53-1.34)	0.10
Intensity										
Low	132,085	170	0.82	0.83 (0.62-1.12)	—	210,754	198	0.80	0.77 (0.59-1.01)	—
Moderate/high	171,174	72	0.73	0.74 (0.52-1.06)	0.11	115,998	48	0.97	0.89 (0.60-1.32)	0.33
Summary score*										
Low	133,365	129	0.85	0.85 (0.62-1.16)	—	116,283	108	0.89	0.86 (0.64-1.01)	—
High	117,420	68	0.67	0.69 (0.48-0.98)	0.06	157,472	97	0.77	0.72 (0.53-0.98)	0.03

NOTE: The Cox regression model used attained age as the time variable and included the following covariates in fully adjusted models: body mass index (<18.5, 18.5-24.9, 25.0-29.9, or ≥30.0 kg/m^2), smoking status (never, former, current, or unknown), alcohol consumption (0, 1-4, or ≥5 times last 2 weeks, total abstainer, or unknown), education (<10, 10-12, or ≥13 years or unknown), and marital status [married, unmarried, widow(er), or divorced/separated]. P_{trend} gives the P from linear trend tests using the physical activity categories as an ordinal variable in the Cox model.
*Summary score combining information on frequency, duration, and intensity among those who exercised once a week or more (low score defined as less than median and high score defined as equal to or more than median).

Discussion

In this prospective study of men and women, there were strong inverse associations between recreational physical activity and risk of cancer in the transverse and sigmoid colon but no association for cancer in the ascending and descending colon. Similarly, we found strong inverse associations with colon cancer mortality that were also confined to the transverse and sigmoid colon.

An inverse association of physical activity with colon cancer risk has been reported in many studies (1-3). However, no previous study has assessed the association of recreational physical activity with cancer risk in anatomically defined segments of the colon. Other prospective studies have reported on cancer originating in the proximal (right) or distal (left) parts of the colon, but results from these studies have not been consistent (12-17, 23, 24). A few studies of occupational physical activity have included information on anatomical segments of the colon and reported reduced risk, either related to the transverse (19-21), sigmoid (19, 21), or descending (18) colon.

Our results suggest that the effect of physical activity on colonic transit time may underlie its association with

Table 3. HR of subsite-specific colon cancer incidence according to recreational physical activity

Anatomic localization	No activity (109,789 person-years)	<1 per wk (258,608 person-years)	Low score* (249,649 person-years)	High score* (274,892 person-years)	P_{trend}
Total colon					
No. cases	139	159	237	165	—
Adjusted HR (95% CI)	1.00 (Reference)	0.88 (0.70-1.12)	0.87 (0.70-1.08)	0.73 (0.58-0.92)	0.009
Ascending colon					
No. cases	45	43	89	75	—
Adjusted HR (95% CI)	1.00 (Reference)	0.80 (0.52-1.23)	1.06 (0.74-1.53)	1.05 (0.72-1.54)	0.41
Transverse colon					
No. cases	30	28	39	21	—
Adjusted HR (95% CI)	1.00 (Reference)	0.75 (0.44-1.28)	0.66 (0.41-1.08)	0.44 (0.25-0.78)	0.004
Descending colon					
No. cases	6	12	18	12	—
Adjusted HR (95% CI)	1.00 (Reference)	1.41 (0.52-3.83)	1.47 (0.57-3.75)	1.13 (0.41-3.07)	0.93
Sigmoid colon					
No. cases	45	58	64	38	—
Adjusted HR (95% CI)	1.00 (Reference)	0.88 (0.59-1.32)	0.68 (0.46-1.01)	0.48 (0.31-0.75)	<0.001

NOTE: The Cox regression model used attained age as the time variable and included the following covariates: sex, body mass index (<18.5, 18.5-24.9, 25.0-29.9, or ≥30.0 kg/m^2), smoking status (never, former, current, or unknown), alcohol consumption (0, 1-4, or ≥5 times last 2 weeks, total abstainer, or unknown), education (<10, 10-12, or ≥13 years or unknown), and marital status [married, unmarried, widow(er), or divorced/separated]. P_{trend} gives the P from linear trend tests using the physical activity categories as an ordinal variable in the Cox model.
*Summary score combining information on frequency, duration, and intensity among those who exercised once a week or more (low score defined as less than median and high score defined as equal to or more than median).

Table 4. HR of death from subsite-specific colon cancer according to recreational physical activity

Anatomic localization	No activity (113,443 person-years)	<1 per wk (265,453 person-years)	Low score* (258,151 person-years)	High score* (282,294 person-years)	P_{trend}
Total colon					
No. deaths	85	84	125	72	—
Adjusted HR (95% CI)	1.00 (Reference)	0.87 (0.64-1.18)	0.79 (0.59-1.04)	0.56 (0.41-0.78)	<0.001
Ascending colon					
No. deaths	23	18	41	31	—
Adjusted HR (95% CI)	1.00 (Reference)	0.71 (0.38-1.33)	1.03 (0.61-1.74)	0.96 (0.55-1.67)	0.75
Transverse colon					
No. deaths	17	15	14	19	—
Adjusted HR (95% CI)	1.00 (Reference)	0.73 (0.36-1.49)	0.40 (0.19-0.82)	0.33 (0.14-0.76)	0.002
Descending colon†					
No. deaths	2	8	10	9	—
Adjusted HR (95% CI)	0.31 (0.07-1.50)	1.00 (Reference)	0.82 (0.32-2.11)	0.85 (0.32-2.24)	0.40
Sigmoid colon					
No. deaths	28	26	29	13	—
Adjusted HR (95% CI)	1.00 (Reference)	0.78 (0.45-1.35)	0.51 (0.30-0.87)	0.29 (0.15-0.56)	<0.001

NOTE: The Cox regression model used attained age as the time variable and included the following covariates: sex, body mass index (<18.5, 18.5-24.9, 25.0-29.9, or ≥30.0 kg/m^2), smoking status (never, former, current, or unknown), alcohol consumption (0, 1-4, or ≥5 times last 2 weeks, total abstainer, or unknown), education (<10, 10-12, or ≥13 years or unknown), and marital status [married, unmarried, widow(er), or divorced/separated]. P_{trend} gives the P from linear trend tests using the physical activity categories as an ordinal variable in the Cox model.

*Summary score combining information on frequency, duration, and intensity among those who exercised once a week or more (low score defined as less than median and high score defined as equal to or more than median).

† Reference group changed to those who exercised <1 per week due to small number of deaths among subjects who reported no activity.

colon cancer risk. Physical activity stimulates colon motility and facilitates defecation and may thus reduce stool transit time through the bowel (5-7) and consequently reduce the contact time of potential fecal carcinogens with colonic mucosal surface. Bile acids may be carcinogenic (25) and promote tumor growth (26), and it has been reported that cholecystecomized patients are at increased risk of colon cancer (27).

Most studies of segmental colonic transit time only distinguish between right and left colon (28, 29), but in a study of healthy children, the transverse and rectosigmoid colon were identified as relatively slow transit segments (30). The transverse colon seems to be an area of storage and mixing of bowel content (31), whereas the rectosigmoid colon has been characterized as a segment with slow transit time in studies of elderly people (32, 33). Despite limited evidence, this may suggest a particular potential for physical activity to accelerate transportation of carcinogenic components in the transverse and sigmoid parts of the colon. In a study of body mass index and colon cancer risk, positive associations were restricted to the transverse and sigmoid colon, suggesting that cancer risk in these segments may be more modifiable than other parts of the colon (34).

The strong inverse associations of physical activity with colon cancer death were also restricted to the transverse and sigmoid colon. This may suggest that physical activity not only influences disease risk but may also slow down disease progression after diagnosis. This may also be supported by the finding that increasing level of physical activity was related to longer survival from colon cancer; however, due to limited statistical power, survival analyses according to subsites of colon cancer could not be conducted. It is possible that different mechanisms may underlie associations with incidence and survival. Two recent prospective studies from the United States have also shown that exercise could be associated with reduced cancer recurrence and mortality among colon cancer patients (35, 36), but neither these studies did assess survival by subsite of the colon.

We also estimated the proportion of colon cancer deaths that could potentially be prevented, assuming that the association with physical activity is causal. If all people in the study were at the highest score of physical activity, ~28% of the deaths could be avoided. It should be noted that to qualify for the highest category of physical activity, all that was required was exercise of moderate to vigorous degree of intensity once a week, with usual duration of at least 30 minutes.

This cohort consists of the majority of adults in a stable, homogeneous population in Norway. The population is well suited for follow-up studies partly because of excellent end-point registries in the country and partly because of the unique identification number allocated to each citizen. The reporting of cancer is mandatory and regulated by law, and to achieve a high degree of completeness and high data quality, the material of the Cancer Registry is matched against the Cause of Death Registry (37).

Our information on recreational physical activity was based on questionnaires that allow for subjective interpretation of the questions and individual perception of the activity; thus, misclassification of physical activity can be influenced by many factors, such as age, social context, and seasonal variation (38). However, validation studies have shown that questionnaires may be useful in classifying people into broad categories of physical activity (e.g., low, moderate, or highly active) but less appropriate for quantifying energy expenditure (39). The questions on duration and intensity of physical activity in this study have been validated previously against measured oxygen uptake and heart rate and found to perform well (40).

The precision of the estimates of relative risk and the consistent gradual reduction in risk of colon cancer with increasing level of physical activity speak against chance as a likely explanation for our results. It could be argued that preclinical disease could have influenced the measures of physical activity, but exclusion of the first 3 years of follow-up gave essentially unchanged results.

It is also conceivable that testing for colonic polyps by colonoscopy could be unevenly distributed among people in different categories of physical activity and therefore could have biased the estimates of relative risk. However, colorectal screening in Norway is restricted to families with a strong history of colorectal cancer, and there is no indication that these families have particular patterns of physical activity.

Nonetheless, biased estimates due to confounding by unmeasured or unknown factors cannot be excluded in this type of study. Adjustment for dietary factors could, for example, be of importance; unfortunately, no dietary information was available from this cohort. However, recent cohort studies of physical activity and risk of colon cancer show no or minimal effect of adjustment for dietary factors (14, 16, 17).

In conclusion, these data show that recreational physical activity reduced the risk of colon cancer incidence and mortality in both men and women, but the reduction in risk was only present in the transverse and sigmoid segments of the colon (that is, the parts of the colon that may be defined as slow transit segments). These results suggest that enhanced colon motility and accelerated bowel transit may be a likely mechanism for the effect of physical activity on colon cancer risk.

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