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Physical activity and stomach cancer risk: The influence of intensity and timing during the lifetime

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ARTICLE INFO

Article history:
Received 27 October 2006
Received in revised form
17 November 2006
Accepted 27 November 2006

Keywords:
Stomach cancer
Gastric carcinoma
Recreational physical activity
Exercise
Cancer prevention
Cancer epidemiology

ABSTRACT

Physical inactivity is linked to risk for cancers of the colon, breast, lung and endometrium, but few data exist on this association with stomach cancer. We evaluated the association between recreational physical activity and incident stomach cancer in a case-control study. The data yielded odds ratios suggestive of ~20–40% reduced risk of stomach cancer when comparing more frequent (3+ times/week) to less frequent (<1/month) strenuous activities. The magnitudes of the associations for strenuous physical activities were consistent across the teens, early 30s, and early 50s. Compared to the least active quartile, the second, third, and fourth quartiles of average lifetime strenuous physical activity yielded odds ratios of 0.82, 0.69, and 0.58 (95% CI, 0.41–0.83), respectively. Odds ratios for moderate activity generally suggested a modest, but not statistically significant, inverse association. Increased strenuous physical activity, throughout the lifespan, was associated with decreased risk of incident stomach cancer.

1. Introduction

Physical activity is associated with reduced risk of cancers of the colon, breast, lung, and endometrium although the consistency and magnitude of risk reduction vary by cancer site.[1–4] Whether physical activity reduces the risk of other cancers remains less clear. Sparse evidence exists on the link between physical activity and risk of stomach cancer, as illustrated in two recent monographs[5,6] on diet and physical activity. The few studies that have evaluated the association between physical activity and stomach cancer have yielded inconsistent findings, but generally suggest no association or only a weakly decreased risk.[7–17] Because stomach cancer is now relatively rare in most developed areas, many previous cohort studies had a small number of cancer cases, perhaps lending to the equivocal findings. Likewise, several previous studies relied on occupational, not recreational, measures of physical activity, which may be differentially related to the disease or more susceptible to confounding factors.

In data from a nationwide case-control study from Canada, we investigated the risk of stomach cancer associated with recreational physical activity during various life periods. Potential confounders included a host of lifestyle, occupational, and demographic factors, including diet, income, education, body mass index (BMI), smoking status and occupational exposures.

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Abbreviations: BMI, body mass index; NECSS, National Enhanced Cancer Surveillance Study.
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doi:10.1016/j.ejca.2006.11.011

2. Materials and methods

The Canadian National Enhanced Cancer Surveillance Study (NECSS) was a large population based case-control investigation established by Health Canada and eight provincial cancer registries to improve the understanding of various types of cancer in Canada, including carcinoma of the stomach. Since the physical activity (and some of the covariate) questionnaire items were different in the province of Ontario and the remaining seven provinces, the data were considered separately for this report. The Ontario sample comprised 545 cases and 1387 controls. The remaining National sample comprised 636 cases and 3100 controls from the provinces of Newfoundland, Nova Scotia, Prince Edward Island, Manitoba, Saskatchewan, Alberta and British Columbia. In all eight provinces combined, 2813 stomach cancer cases were identified (960 females and 1853 males). Questionnaires were mailed to 1872 of the 2813 cases. The remaining were either not eligible for the study ($n = 603$), not contacted ($n = 63$), or physicians refused contact/unable to locate ($n = 273$). 1181 questionnaires were returned by stomach cancer cases (63.1% response rate). Overall, 8060 controls were invited to participate; 5030 controls returned the questionnaire (62.4% response rate).

Cancer cases were identified and histologically verified through pathology records at each provincial cancer registry. During the enrolment period, five of the eight provincial cancer registries met the North American Association of Central Cancer Registries' gold standard for completeness, with estimates of >95%; one registry met the silver standard of >90%; the two remaining registries had estimates of 82% and 88%. For all sites, the death certificate only (DCO) cases ranged from 0.1% to 3.6%. The DCO percentages for stomach cancer, however, were higher (0.3–4.7), which is common for cancers with poorer survival.[18]

Cases were eligible if diagnosed with stomach cancer (International Classification of Diseases 9th revision code (ICD9) of 151.0–151.9) between the start of 1995 and the end of 1997, aged 20–74 years, and resided in the applicable province at the time of cancer diagnosis. Physician consent was required to contact cases. Self-administered questionnaires were sent to eligible participants and post-card or telephone follow-up was used when needed. Slightly greater than 95% of cases were contacted within 6 months of diagnosis. Ethics review boards in each province approved the study.

Controls were a random sample of residents in each province, aged 20–74 years. Various databases were used to identify potential control subjects, including random digit dialling, property assessment rolls, and health care records, as described elsewhere.[19] The sampling strategy successfully identified at least one control for each case across all 5-year age and sex strata.

2.1. Physical activity measurement

In Ontario the self-administered questionnaire included separate items for combined strenuous and moderate recreational physical activities. Examples cited for the combined strenuous activity measure included cycling, jogging and swimming (average MET[20] value: 7.96). Examples cited for the combined moderate activity measure included brisk walking, gardening and social dancing (average MET value: 4.31). The physical activity matrix sought information on participants' physical activity during mid-teens, early 30s, early 50s and the period about two years prior to interview/diagnosis (e.g. recent activity). Frequency of physical activity for this report included less than once per month, one to three times per month, one or two times per week and three or more times per week. For the lifetime average indices, midpoints of categories were selected and all categories were converted to a common weekly unit (e.g. 1–3 times per month = 0.46 times per week).

Lifetime averages of strenuous and moderate physical activity were calculated from all non-missing physical activity responses. We selected the average of all reported physical activity frequencies, instead of the cumulative total of activities, to overcome the issue of missing responses. The subjects were categorised into quartiles based on the variable distribution among controls.

In the remaining seven provinces, the subjects were asked only about recent recreational physical activity, and to indicate seasonality, frequency, and typical duration for each of 12 common activities. Activities with MET[20] values above 6 were considered strenuous, while activities with MET values between 3 and 6 were considered moderate. The seasonality, frequency and average MET values were used to estimate a relative activity score for each subject. The subjects were categorised into quartiles based on the distribution among controls.

2.2. Covariates

The self-administered questionnaire also requested information about an extensive array of medical, demographic and lifestyle variables. Given the strong evidence for a link between dietary factors and stomach cancer risk,[5,6] we thoroughly assessed the dietary questionnaire items for confounding on physical activity. Relevant to these analyses were the 69 food and beverage items reported during the reference period. Individual food items, including fruits and vegetables, did not materially influence the parameter estimates for physical activity. Given the strong correlation between food items, factor analysis was used to aggregate them into interpretable dietary patterns.[21–25]

Other potential confounders included age, sex, education and body mass index (BMI: weight (kg) divided by height squared (m^2)). Two BMI indices were used for this analysis: first, the recent BMI was calculated from body weight during the reference period (BMI-recent); second, the subjects' highest non-pregnancy body weight was used to estimate maximum lifetime BMI (BMI-max). Both BMI values were categorised as per World Health Organization criteria.[26] Additional potential confounders included cigarette smoking (current, ever and never; and pack-years of cigarette smoking), occupational and household exposures to 19 carcinogenic substances (e.g. asbestos, arsenic, pesticides and herbicides), education, household income and exposure to tobacco smoke during childhood.

In the Ontario sample only, other covariates included cancer history in first-degree relatives, exposure to tobacco smoke during childhood and occupational physical activity: 'sitting activity', 'light activity', 'moderate activity' and 'strenuous activity' during the early 20s, early 30s, early 50s, and about two years prior to interview. Among women only, other variables included the use of oral contraceptives and postmenopausal hormones.

2.3. *Statistical analyses*

To evaluate the association between physical activity and stomach cancer risk, we computed odds ratios (OR) and their corresponding 95% confidence intervals (95% CI) from unconditional logistic regression models with SAS software (version 9.1, SAS Institute, Cary, North Carolina, USA). All covariates were categorised as shown in Table 1. The odds ratios and confidence intervals in Table 2 were from models that adjusted for age and sex only, and from fully adjusted models that included age, sex, BMI-recent, smoking status, education and the western diet pattern score (as derived from factor analysis). Over 100 variables, including 69 individual food items and five separate food-groups (e.g. total fruit/vegetable intake), were assessed as potential confounders on the association between lifetime strenuous physical activity and stomach cancer risk. No variable affected the parameter estimates for strenuous physical activity by 10% or greater. The covariates in this report were selected from similar reports in the literature and because of their relatively minor (<10%) confounding influences on the main physical activity variables.

Sex was modelled as a potential effect modifier with physical activity; a cross-product term for sex and lifetime strenuous physical activity was not statistically significant. Sex was therefore simply included as a covariate in all logistic regression models. Added justification for combining males and females came from the similar cut-points for the quartiles of strenuous and moderate physical activity indices, and the fact that none of the female-specific variables (e.g. oral contraceptive use) were confounders of the main associations.

3. Results

Education was inversely linked with stomach cancer; age, male sex and a western diet pattern were linked with

Table 1 – The bivariate and age and sex-adjusted associations between selected covariates and risk of stomach cancer

Measure	Cases		Controls		Crude		Age and sex adjusted	
	Frequency (#)	%	Frequency (#)	%	Odds ratio	95% CI	Odds ratio	95% CI
Age								
20–39 years	16	2.9	171	12.3	1		1	
40–49 years	52	9.5	255	18.4	2.18	(1.21–3.94)	2.65	(1.46–4.84)
50–59 years	107	19.6	218	15.7	5.25	(2.99–9.20)	5.64	(3.19–9.94)
60–69 years	193	35.4	438	31.6	4.71	(2.75–8.08)	4.74	(2.75–8.16)
70+ years	177	32.5	305	22.0	6.20	(3.60–10.70)	6.33	(3.65–10.96)
Sex								
Female	166	30.5	726	52.3	1		1	
Male	379	69.5	661	47.7	2.50	(2.00–3.10)	2.41	(1.94–2.99)
Body mass index, 2 years ago								
<18.5	13	2.4	29	2.1	1.37	(0.70–2.68)	1.57	(0.77–3.22)
18.5–24.99	213	39.1	650	46.9	1		1	
25–29.99	222	40.7	513	37.0	1.32	(1.06–1.65)	1.01	(0.80–1.28)
30+	89	16.3	187	13.5	1.45	(1.08–1.95)	1.21	(0.89–1.65)
Missing	8	1.5	8	0.6				
Education								
<12 years of grade school	258	47.3	459	33.1	1		1	
12 or 13 years of grade school	88	16.2	243	17.5	0.64	(0.48–0.86)	0.84	(0.62–1.14)
1 or 2 years of college	82	15.1	251	18.1	0.58	(0.43–0.78)	0.78	(0.57–1.06)
3 or 4 years of college	64	11.7	251	18.1	0.45	(0.33–0.62)	0.57	(0.41–0.80)
5 or more years of college	52	9.5	180	13.0	0.51	(0.36–0.73)	0.59	(0.41–0.85)
Missing	1	0.2	3	0.2				
Western dietary pattern (quartiles)								
1 (least 'western' like)	113	20.7	346	25.0	1		1	
2	114	20.9	347	25.0	1.01	(0.75–1.36)	1.05	(0.77–1.43)
3	140	25.7	347	25.0	1.24	(0.93–1.65)	1.26	(0.94–1.71)
4	178	32.7	347	25.0	1.57	(1.19–2.08)	1.61	(1.20–2.17)

Results from the Ontario sample.

Table 2 – Risk of incident stomach cancer and physical activity over various life periods

Measure	Cases		Controls		Age and sex adjusted		Covariate adjusted[a]	
	Frequency (#)[b]	%	Frequency (#)[b]	%	Odds ratio	95% CI	Odds ratio	95% CI
Strenuous activity in mid-teens								
<1/months	98	18.0	219	15.8	1		1	
1–3/months	36	6.6	123	8.9	0.70	(0.44–1.10)	0.67	(0.42–1.07)
1–2/week	96	17.6	237	17.1	0.92	(0.65–1.31)	1.01	(0.70–1.44)
3+/week	231	42.4	677	48.8	0.72	(0.54–0.97)	0.73	(0.54–0.99)
P_{trend}					0.06		0.09	
Strenuous activity in early 30s								
<1/months	171	31.4	363	26.2	1		1	
1–3/months	77	14.1	216	15.6	0.72	(0.52–1.00)	0.77	(0.55–1.09)
1–2/week	114	20.9	277	20.0	0.84	(0.62–1.13)	0.87	(0.64–1.18)
3+/week	93	17.0	312	22.5	0.59	(0.43–0.80)	0.63	(0.46–0.86)
P_{trend}					0.002		0.007	
Strenuous activity in early 50s								
<1/months	200	36.7	372	26.8	1		1	
1–3/months	60	11.0	126	9.1	0.85	(0.59–1.21)	0.86	(0.59–1.24)
1–2/week	49	9.0	130	9.4	0.73	(0.50–1.06)	0.82	(0.56–1.21)
3+/week	60	11.0	156	11.3	0.71	(0.50–1.01)	0.80	(0.56–1.15)
P_{trend}					0.03		0.21	
Average lifetime strenuous activity								
1st quartile	165	30.3	325	23.4	1		1	
2nd quartile	129	23.7	324	23.4	0.79	(0.59–1.05)	0.82	(0.61–1.11)
3rd quartile	122	22.4	373	26.9	0.66	(0.49–0.88)	0.69	(0.51–0.93)
4th quartile	71	13.0	271	19.6	0.55	(0.39–0.77)	0.58	(0.41–0.83)
P_{trend}					0.0002		0.0011	
Moderate activity in mid-teens								
<1/months	51	9.4	124	8.9	1		1	
1–3/months	58	10.6	109	7.9	1.39	(0.87–2.23)	1.41	(0.87–2.28)
1–2/week	66	12.1	226	16.3	0.78	(0.50–1.21)	0.81	(0.51–1.27)
3+/week	304	55.8	808	58.3	0.92	(0.64–1.33)	0.96	(0.66–1.40)
P_{trend}					0.23		0.17	
Moderate activity in early 30s								
<1/months	63	11.6	113	8.2	1		1	
1–3/months	68	12.5	180	13.0	0.75	(0.49–1.16)	0.82	(0.52–1.28)
1–2/week	108	19.8	293	21.1	0.72	(0.48–1.07)	0.74	(0.49–1.11)
3+/week	258	47.3	653	47.1	0.70	(0.49–1.00)	0.74	(0.52–1.07)
P_{trend}					0.08		0.13	
Moderate activity in early 50s								
<1/months	69	12.7	108	7.8	1		1	
1–3/months	68	12.5	118	8.5	0.88	(0.57–1.36)	0.94	(0.60–1.46)
1–2/week	91	16.7	209	15.1	0.68	(0.46–1.02)	0.74	(0.49–1.11)
3+/week	206	37.8	431	31.1	0.76	(0.54–1.09)	0.84	(0.59–1.21)
P_{trend}					0.13		0.40	
Average lifetime moderate activity								
1st quartile	159	29.2	352	25.4	1		1	
2nd quartile	143	26.2	349	25.2	0.97	(0.73–1.28)	1.03	(0.77–1.37)
3rd quartile	108	19.8	346	25.0	0.69	(0.51–0.92)	0.74	(0.54–1.00)
4th quartile	116	21.3	286	20.6	0.94	(0.70–1.27)	0.99	(0.73–1.34)
P_{trend}					0.22		0.40	

Results from the Ontario sample.

a Models include terms for sex, age, recent BMI, education, smoking status and western diet pattern, in addition to physical activity.

b Totals may not add as in text due to missing information.

increased risks of the disease (Table 1). Controls reported more physical activity than did cases on all indices of strenuous physical activity (Tables 2–4). Strenuous physical activity across periods of the lifespan (mid-teens, early 30s, and early 50s) and the lifetime physical activity average demonstrated consistent inverse associations with stomach cancer risk in all logistic regression models. Odds ratios for the most active group relative to the least active group suggested ~20–40% reduced risks of stomach cancer. In almost all instances, the odds ratios were attenuated (but remained statistically significant) after additional adjustment for BMI-recent, education, smoking status and diet.

Table 3 – Risk of incident stomach cancer and recent physical activity

(Number of cases/controls)	Ontario sample (545/1387)					National sample (637/3100)			
	Age and sex adjusted		Covariate adjusted[a]			Age and sex adjusted		Covariate adjusted[a]	
	Odds ratio	95% CI	Odds ratio	95% CI		Odds ratio	95% CI	Odds ratio	95% CI
Strenuous activity 2 years ago									
<1/months	1		1		1st quartile	1		1	
1–3/months	0.56	(0.38–0.86)	0.59	(0.39–0.89)	2nd quartile	0.83	(0.63–1.10)	0.84	(0.62–1.12)
1–2/week	0.62	(0.43–0.89)	0.66	(0.45–0.96)	3rd quartile	0.65	(0.51–0.82)	0.69	(0.54–0.88)
3+/week	0.52	(0.37–0.73)	0.57	(0.40–0.80)	4th quartile	0.61	(0.48–0.77)	0.67	(0.53–0.86)
P_{trend}	<0.0001		0.0003			<0.0001		0.0003	
Moderate activity 2 years ago									
<1/months	1		1		1st quartile	1		1	
1–3/months	0.62	(0.41–0.93)	0.68	(0.45–1.04)	2nd quartile	0.88	(0.68–1.12)	0.83	(0.64–1.07)
1–2/week	0.71	(0.50–1.01)	0.77	(0.54–1.10)	3rd quartile	0.82	(0.64–1.05)	0.85	(0.66–1.10)
3+/week	0.73	(0.54–0.99)	0.82	(0.60–1.12)	4th quartile	1.06	(0.84–1.34)	1.09	(0.85–1.39)
P_{trend}	0.16		0.59			0.72		0.44	

Results from the Ontario and National study samples.
a Models include terms for sex, age, recent BMI, education, smoking status and western diet pattern, in addition to physical activity.

Table 4 – The age and sex-adjusted and multivariate adjusted associations between physical activity indices and risk of stomach cancer by sub-site of tumour location

(Number of cases/controls)	Cardia stomach cancer (144/1387)				Non-cardia stomach cancer (401/1387)			
	Age and sex adjusted		Covariate adjusted[a]		Age and sex adjusted		Covariate adjusted[a]	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Average lifetime strenuous activity								
1st quartile	1		1		1		1	
2nd quartile	0.77	(0.48–1.24)	0.84	(0.51–1.37)	1.23	(0.89–1.68)	1.31	(0.95–1.82)
3rd quartile	0.51	(0.31–0.85)	0.55	(0.32–0.93)	0.82	(0.59–1.14)	0.88	(0.62–1.23)
4th quartile	0.52	(0.30–0.90)	0.60	(0.34–1.07)	0.69	(0.48–1.01)	0.73	(0.50–1.07)
P_{trend}	0.004		0.03		0.22		0.05	
Average lifetime moderate activity								
1st quartile	1		1		1		1	
2nd quartile	0.85	(0.53–1.35)	0.92	(0.57–1.48)	1.02	(0.74–1.40)	1.08	(0.78–1.49)
3rd quartile	0.54	(0.32–0.90)	0.64	(0.38–1.09)	0.74	(0.53–1.03)	0.78	(0.56–1.10)
4th quartile	0.74	(0.44–1.24)	0.85	(0.50–1.44)	1.02	(0.73–1.42)	1.05	(0.75–1.47)
P_{trend}	0.07		0.28		0.56		0.69	

Results from the Ontario sample.
a Models include terms for sex, age, BMI, education, smoking status and western diet pattern, in addition to physical activity.

Odds ratios for moderate physical activity were consistently below one; in almost all instances, however, confidence intervals included unity. Occupational physical activity was not a confounder on recreational activity and it was not associated with risk of stomach cancer (data not shown). Separate logistic regression models were calculated by sex; these were not materially different than the sex-combined results, but owing to smaller sample sizes and decreased precision of the estimates, they were not presented. When lifetime strenuous and moderate physical activities were included in the same multivariate model, the results for the most active relative to the least active groups were very similar to results from separate models shown in Table 2. When both strenuous and moderate average lifetime activity variables were included in the same model, more frequent lifetime strenuous activity was associated with a 42% reduced risk of stomach cancer (OR: 0.58; 95% CI: 0.40–0.84), whereas more frequent lifetime moderate activity was not associated with risk of stomach cancer (OR: 1.13; 95% CI: 0.82–1.57). When strenuous activity during the various life periods was included in the same multivariate model, comparisons of the most active relative to the least active categories of strenuous activity during the mid-teens, early 30s and early 50s resulted in odds ratios of 0.86 (95% CI: 0.46–1.2), 0.68 (95% CI: 0.45–1.01) and 1.03 (95% CI: 0.68–1.57), respectively. When moderate activities during the various life periods were included in the same multivariate model, comparisons of the most active relative to the least active categories of moderate activity during the mid-teens, early 30s and early 50s resulted in odds ratios of 1.22 (95% CI: 0.75–1.97), 0.68 (95% CI: 0.41–1.13) and 0.98 (95% CI: 0.63–1.50), respectively.

In both the National and the Ontario samples, recent strenuous physical activity was inversely associated with stomach cancer risk such that high levels of strenuous physical activity yielded odds ratios from 0.52 to 0.67, and their corresponding confidence limits did not include unity (Table 3). Moderate activity indicated a similar, but not statistically significant, pattern of reduced risk in both samples.

Stratification by subsite (cardia versus non-cardia) yielded similar, but not identical, results (Table 4). These results must be interpreted with caution given the smaller numbers and lack of precision in the risk estimates. We have data on histologic subtype (e.g. diffuse versus intestinal) for some cases; however, stratified analyses were not conducted among these subgroups because *a priori* calculations suggested insufficient statistical power.

4. Discussion

In data from a large population based case-control study in Canada, we observed statistically significant inverse associations between strenuous recreational physical activity and risk of incident stomach cancer. Odds ratios suggested ~20–40% reduced risks of stomach cancer for participants who reported strenuous activity at least three times per week relative to inactive participants. The protective association persisted across several periods of the lifespan, and was most strong for average physical activity across the lifespan and for activity conducted during the fourth decade of life. Physical activity of moderate intensity also had an inverse association with stomach cancer, but the associations were largely not statistically significant.

Evidence is inconsistent on the link between occupational physical activity and stomach cancer. In an ecologic comparison of cancer mortality rates, 10 deaths from stomach cancer were reported among agricultural workers, whereas 20 deaths were expected from population mortality rates.[8] That farmwork requires a high level of energy expenditure was one of several explanations for this observation, but personal-level measures of physical activity were not provided. Inactivity at work, as assessed from occupation title, was associated with increased risk of stomach cancer among males in Missouri, controlling for age and smoking (OR: 1.4; 95% CI: 0.9–2.2).[14] Others have reported no association between occupational physical activity and stomach cancer risk.[13] Recent work suggested that an index of average occupational physical activity was equivalently associated with risk of cardia (OR: 0.76; 95% CI: 0.49–1.18) and non-cardia (OR: 0.77; 95% CI: 0.52–1.14) stomach cancers.[7]

Previous evidence of an association between recreational physical activity and stomach cancer was similarly inconsistent. Physical activity was associated with a non-statistically significant ~40–70% reduced risk of stomach cancer in a cohort of British men.[9] In data from a mixed case group of about 150 cases with cancers of the oesophagus, gastric cardia, and gastric non-cardia, and 132 controls, participation in active sports and physical exercise more than once a week was associated with decreased risk of cancer, but the data were not shown and reported as 'not statistically significant'.[11] Null associations for recreational physical activity, as assessed by relative walking pace and participation in leisure sports, were reported in a cohort study of over 18,000 men, among them, 72 died from stomach cancer.[10]

The reasons for these inconsistent findings are hard to verify. Measurement of physical activity is complex, and at least some of the mixed results are likely explained by differences in exposure measurement and intensity cut-offs. Occupational studies, for instance, frequently use job titles as proxies for work-related physical activity or energy expenditure. These crude indices may be prone to misclassification.[27] Further, as discussed by others,[7] the potential inverse correlation between occupational and recreational physical activities may be responsible for null results in some studies. There was no correlation, however, between lifetime measures of occupational and strenuous recreational activities in our Ontario data (Spearman correlation coefficient: −0.03; *p*-value: 0.26).

The definition of physical activity is another potential source of the discordant results between studies. One study, for example, defined physical activity according to self-reports of participants' walking pace relative to men of their own age. Other measures of physical activity have used weighted sums of typical activity during a 24-hour period, and resting heart rate.[15] Period of the lifecourse also differs markedly between studies. Cohort studies often evaluate physical activity at one time only, thereby potentially missing a true association since activity levels often vary over a lifetime.[28,29] To our knowledge, ours is the first study on physical activity and stomach cancer to use a measure of recreational

physical activity that included measures of frequency, intensity, and timing during various periods of the lifespan.

Both response and recall bias are possible explanations for our findings, but less likely given the consistency between samples and dose–response nature of our results. For our results to be caused by recall bias, our case group would need to under-report strenuous physical activity and/or our control group would need to over-report strenuous physical activity. Likewise, for participation bias to be responsible for our findings the participating cases would need to be relatively less active than non-participating cases and/or the participating controls would need to be relatively more active than the non-participating controls. The control series in our sample reported similar age and sex specific physical activity levels as did respondents in nationwide public health surveys of recreational physical activity,[30] suggesting that our control series was not more physically active than members of the general population at the time of data collection. But differences in physical activity measurement make direct comparisons difficult. Further, this was a general cancer and the environment study, and given the large number of cases and controls involved in this study from a wide range of age and socio-demographic strata, and the lack of associations with moderate and occupational activity measures, we feel the influence of recall or participation bias was likely minimal. We acknowledge that in the absence of physical activity data from non-participants, however, we cannot entirely rule out this potential bias.

Reverse causation must be considered as a potential source of bias in our results of recent physical activity; although participants' were requested to report activity levels about two years prior to diagnosis, it is possible that undiagnosed disease would attenuate their recent physical activity levels. Our findings from earlier periods in the lifespan (e.g. mid-teens and early 30s), where undiagnosed disease would be highly unlikely, strengthen the overall weight of our findings for strenuous physical activity, as they would not be influenced by reverse causation.

Our results indicated that stomach cancer risk was inversely associated with strenuous recreational physical activity over several periods of the lifespan, while moderate physical activity was only weakly associated with reduced risk of stomach cancer. These results suggest a threshold for intensity of physical activity: relatively strenuous physical activity (e.g. enough to induce sweating or accelerated breathing) may be required to confer protection against stomach cancer. Such an intensity level could be achieved by jogging or cycling with sufficient effort to induce sweating for three or more hours a week. Future work is needed to confirm if a threshold exists. Alternatively, these results may simply demonstrate the complexity in accurately classifying moderate physical activity.

Mechanistic studies are also required to support the plausibility of a protective effect; potential studies should distinguish between localised (e.g. through a physical activity mediated amelioration of inflammation on the stomach epithelium, perhaps through reduced concentration of PGE_2 levels, as previously shown in rectal mucosa[31]) and systemic effects (e.g. through modification of steroid hormones, insulin-like growth factors, insulin resistance, immune function, and/or lipid metabolism). A small randomised trial of a physical activity intervention with stomach cancer patients suggested an improvement in natural killer cell activity among 17 exercisers versus 18 controls,[32] suggesting improved immune system function from exercise. Exercise has also been shown to positively influence gastric hormones with potential chemopreventative effects on bile acids and interleukin 1.[33]

Future work should also assess effect modification by subsite (gastric cardia versus non-cardia) and subtype (diffuse versus intestinal); we did not have sufficient statistical power to adequately assess effect modification by subsite or subtype, but we present stratified results for the former nonetheless. Although these results need to be confirmed in future work, the indication that strenuous physical activity is linked to reduced stomach cancer risk adds further support to the vital public health role of recreational physical activity in preventing chronic diseases such as cancer.

Conflict of interest statement

None declared.

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