

# Does physical activity reduce the risk of developing peptic ulcers?

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## Abstract

**Background**—Although *Helicobacter pylori* has been identified as a major cause of chronic gastritis, not all infected patients develop ulcers, suggesting that other factors such as lifestyle may be critical to the development of ulcer disease.

**Aim**—To investigate the role physical activity may play in the incidence of peptic ulcer disease.

**Methods**—The subjects were men (8529) and women (2884) who attended the Cooper Clinic in Dallas between 1970 and 1990. The presence of gastric or duodenal ulcer disease diagnosed by a doctor was determined from a mail survey in 1990. Subjects were classified into three physical activity groups according to information provided at the baseline clinic visit (before 1990): active, those who walked or ran 10 miles or more a week; moderately active, those who walked or ran less than 10 miles a week or did another regular activity; the referent group consisting of those who reported no regular physical activity.

**Results**—With the use of gender specific proportional hazards regression models that could be adjusted for age, smoking, alcohol use, body mass index, and self reported tension, active men were found to have a significant reduction in risk for duodenal ulcers (relative hazard (95% confidence interval) for the active group was 0.38 (0.15 to 0.94) and 0.54 (0.30 to 0.96) for the moderately active group). No association was found between physical activity and gastric ulcers for men or for either type of ulcer for women.

**Conclusions**—Physical activity may provide a non-pharmacological method of reducing the incidence of duodenal ulcers among men.

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Keywords: alcohol; duodenal; exercise; gastric; ulcer; risk factors

Peptic ulcer disease is one of the most common disorders affecting the digestive system. In 1989, 10% of adult residents of the United States (an estimated 18 million people) reported ever having had ulcer disease diagnosed by a doctor, and about one third of those reported having an ulcer within the preceding year.<sup>1</sup> Since Marshall and Warren<sup>2</sup> suggested that *Helicobacter pylori* may play a role in gastritis associated diseases, it has been confirmed that *H pylori* infection is the major cause of chronic gastritis throughout the world. Expo-

sure to *H pylori* occurs in childhood and is common in many areas of the world. In the United States, the prevalence of *H pylori* infection is higher among blacks and among those in low education and low income groups, indicating that socioeconomic conditions may affect exposure.<sup>3</sup>

Although *H pylori* infection is common world wide, only a minority of infected patients develop ulcers.<sup>4,5</sup> A variety of host factors or cofactors, other than *H pylori*, are probably critical to the development of peptic ulcer disease in infected people.<sup>5-9</sup> Besides *H pylori*, smoking, alcohol consumption, and psychological stress have been identified as risk factors (or cofactors) for peptic ulcer disease,<sup>9-11</sup> suggesting that, even if *H pylori* is causal for some types of peptic ulcer disease, other factors may play an important contributing role.<sup>6-8</sup>

Although physical activity has been shown to provide numerous benefits for psychological and physical health,<sup>12</sup> studies of the effect of physical activity on the development of peptic ulcer disease, controlling for psychological tension, have not been reported. Physical activity could possibly affect peptic ulcer disease through several biological mechanisms including: (a) enhancing the immune system's ability to neutralise the effects of *H pylori*; (b) reducing excess acid secretion; (c) improving a person's ability to cope with stressful situations. The purpose of this study is to explore the relation between physical activity and peptic ulcer disease among men and women, controlling for age, smoking habits, alcohol use, body mass index, and psychological tension.

## Methods

### DATA SOURCES

Study subjects were selected from those who received a medical examination at the Cooper Clinic, in Dallas, Texas, between 1970 and 1990. All subjects completed a detailed questionnaire and underwent a clinical evaluation, including a physical examination by the doctor. Information obtained included personal characteristics—for example, age and sex—medical status, clinical measures, medical history, lifestyle habits (tobacco use, alcohol use, and physical activity), and a measure of psychological tension—that is, stress. Between 1970 and 1990, 36 605 people (28 315 men and 8290 women) were examined at least once. They came from all 50 states, and were predominantly male (80%) and white (97%). Participants were well educated and from middle to upper socioeconomic strata; more than 75% had graduated from college.

A mail back survey completed in 1990 asked for detailed self reported information on

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Table 1 Rate ratios of potential risk factors for self reported duodenal ulcers, Cooper Clinic, Dallas, Texas, 1970–1990

	Men			Women		
	Cases	Subjects	RR (95% CI)	Cases	Subjects	RR (95% CI)
Physical activity						
Active	6	2059	0.23 (0.10 to 0.55)	3	563	0.82 (0.21 to 3.28)
Moderately active	20	3686	0.43 (0.25 to 0.75)	4	1395	0.44 (0.13 to 1.56)
Referent	35	2784	1.00	6	926	1.00
	Trend test: $\chi^2=16.708$ , $p=0.001$			Trend test: $\chi^2=0.287$ , $p=0.592$		
Psychological tension						
High	22	1905	2.28 (1.32 to 3.92)	2	635	0.74 (0.16 to 3.42)
Low	31	6112	1.00	9	2116	1.00
Smoking						
Yes	52	3362	1.70 (1.03 to 2.80)	4	1043	0.78 (0.24 to 2.54)
No	29	5167	1.00	9	1841	1.00
Ethanol consumption						
Heavy	12	2059	0.82 (0.40 to 1.70)	1	325	0.67 (0.08 to 5.75)
Moderate	8	1507	0.75 (0.33 to 1.72)	1	369	0.59 (0.07 to 5.04)
Light	23	2421	1.34 (0.73 to 2.48)	6	1098	1.19 (0.37 to 3.90)
None	18	2542	1.00	5	1092	1.00
	Trend test: $\chi^2=0.813$ , $p=0.367$			Trend test: $\chi^2=0.036$ , $p=0.849$		
Age (years)						
>60	5	537	1.30 (0.49 to 3.41)	1	179	1.31 (0.15 to 11.13)
40.1 to 60	34	4927	0.96 (0.56 to 1.64)	7	1535	1.07 (0.34 to 3.35)
20 to 40	22	3065	1.00	5	1170	1.00
	Trend test: $\chi^2=0.059$ , $p=0.808$			Trend test: $\chi^2=0.049$ , $p=0.824$		
Body mass index						
Higher 25%	12	1923	0.89 (0.46 to 1.71)	1	618	0.38 (0.05 to 3.09)
Reference	33	4684	1.00	7	1650	1.00
Lower 25%	16	1922	1.18 (0.65 to 2.14)	5	616	1.91 (0.61 to 6.01)

RR, risk ratio.

illnesses and conditions diagnosed by a doctor. The questionnaires were sent to everyone who had ever attended the Cooper Clinic. The final response rate after multiple mailings was 63% (not including those questionnaires with incorrect addresses).

Subjects were included in this analysis if they were over age 20 at the first clinic visit, had a baseline examination between 1970 and 1990, and responded to a mailed questionnaire in 1990 (at least six months after their clinic examination). The 231 who had an ulcer diagnosis at their first clinic visit were excluded. The final sample size was 11 413 (8529 men and 2884 women).

#### OUTCOME VARIABLES

Although ulcers of the stomach (gastric ulcers) or of the upper intestine (duodenal ulcers) are grouped as peptic ulcers, they are distinct diseases with significant pathological differences. Therefore, in spite of the small number of new cases, peptic ulceration of the stomach and duodenum were distinguished in this study.

The presence of diagnosed ulcer disease was reported by participants in the follow up survey in 1990. Although the accuracy of self reported peptic ulcer disease diagnosed by a doctor is not known, this cohort has shown high sensitivity and specificity for diagnosed hypertension (98% and 99% respectively).<sup>13</sup> High sensitivity and specificity for hypertension have also been reported in other data sets of well educated adults (82% and 98% respectively).<sup>14</sup> A national survey in the United States found that about 75% of those who self reported ulcer disease had their diagnosis confirmed by a doctor.<sup>1</sup> Because of this evidence, we are unlikely to have large misclassification errors by using self report data on ulcer disease to classify these well educated people as to their disease status.

#### INDEPENDENT VARIABLES

Physical activity was assessed at baseline and determined by self reported regular walking and jogging and other activities. Subjects who did not participate in regular walking or jogging or any other leisure time physical activity were the referent group; those who walked or jogged up to 10 miles a week or reported regular participation in another activity were considered moderately active; and those who walked or jogged more than 10 miles a week were considered active.

In this analysis, current smokers were compared with those who had never smoked or who had quit smoking by the time of the baseline examination, which was before the ulcer diagnosis. Information on alcohol use was obtained at the baseline clinic examination, and the data converted to ethanol consumption as follows: 1.1 g for 1 oz of beer, 2.7 g for 1 oz of wine, and 15.1 g for 1 oz of spirits.<sup>15</sup> Ethanol consumption was categorised into four levels: none (reference level); 0.1–13.2 g a day (equivalent to one drink a day); 13.21–26.4 g a day (equivalent to two drinks a day); 26.41 g or more a day (equivalent to more than two drinks a day).

Psychological stress has been shown to have a strong effect on the gastrointestinal system, and there is some evidence that it may cause peptic ulcers.<sup>10</sup> To assess psychological tension as a marker for stress, we used the question (from the baseline record) "How would you classify yourself on the following tension and anxiety scale?" The five possible choices were: no tension or very relaxed; slight tension; moderate tension; high tension; very tense or highly strung. We identified people with high tension as those who reported either having high levels of tension or that they were very tense or highly strung.

Table 2 Rate ratios of potential risk factors for self reported gastric ulcers, Cooper Clinic, Dallas, Texas, 1970–1990

	Men			Women		
	Cases	Subjects	RR (95% CI)	Cases	Subjects	RR (95% CI)
Physical activity						
Active	19	2059	0.51 (0.30 to 0.87)	6	563	0.55 (0.22 to 1.37)
Moderately active	47	3686	0.71 (0.48 to 1.05)	18	1395	0.66 (0.35 to 1.27)
Referent	50	2784	1.00	18	926	1.00
	Trend test: $\chi^2=6.966$ , $p=0.008$			Trend test: $\chi^2=2.175$ , $p=0.140$		
Psychological tension						
High	36	1905	1.83 (1.22 to 2.75)	16	635	2.67 (1.39 to 5.11)
Low	63	6112	1.00	20	2116	1.00
Smoking						
Yes	56	3362	1.43 (1.01 to 2.06)	18	1043	1.32 (0.72 to 2.43)
No	60	5167	1.00	24	1841	1.00
Ethanol consumption						
Heavy	32	2059	0.86 (0.55 to 1.34)	6	325	1.26 (0.50 to 3.19)
Moderate	13	1507	0.48 (0.26 to 0.88)	6	369	1.11 (0.44 to 2.82)
Light	25	2421	0.57 (0.35 to 0.93)	14	1098	0.87 (0.43 to 1.77)
None	46	2542	1.00	16	1092	1.00
	Trend test: $\chi^2=0.797$ , $p=0.372$			Trend test: $\chi^2=0.237$ , $p=0.626$		
Age (years)						
>60	7	537	1.21 (0.54 to 2.72)	1	179	0.41 (0.05 to 3.06)
40.1 to 60	76	4927	1.43 (0.95 to 2.15)	25	1535	1.15 (0.64 to 2.22)
20 to 40	33	3065	1.00	16	1170	1.00
	Trend test: $\chi^2=1.836$ , $p=0.175$			Trend test: $\chi^2=0.167$ , $p=0.683$		
Body mass index						
Higher 25%	30	1923	1.18 (0.76 to 1.82)	4	618	0.38 (0.13 to 1.08)
Reference	62	4684	1.00	28	1650	1.00
Lower 25%	24	1922	0.94 (0.59 to 1.51)	10	616	0.96 (0.47 to 1.96)

RR, risk ratio.

Weight and height were measured on a standard doctor's scale at the first (baseline) clinic visit. Body mass index (BMI) was calculated as weight (kg)/height<sup>2</sup> (m<sup>2</sup>). BMI was divided into three levels: lowest 25% (cut off point 23.5), highest 25% (cut off point 27.4), and the middle group which served as the reference. Age and BMI were used as control variables. Other potential confounders such as race/ethnicity, socioeconomic status, and educational status were not included because most of the participants were white and well educated.

#### STATISTICAL ANALYSIS

Analyses were conducted using SAS software.  $\chi^2$  and trend tests were used to summarise categorical variables. Instantaneous relative risk (RR) was derived from the Cox proportional hazard model using the time of observation. Considering the differences between men and women in lifestyle, occupation, and other unmeasured factors that are difficult to control adequately in the models, we developed gender specific Cox regression models. Because of missing values for the psychological tension variable ( $n = 645$ ), Cox models were developed first for the whole population without including psychological tension as an independent variable. Subsequently, Cox models were developed for the subset of subjects who had been asked the psychological tension question. We included all variables in building each model to evaluate the effect of each variable while controlling for all others.

## Results

#### DESCRIPTIVE ANALYSES

After the omission of participants who had a diagnosis of peptic ulcer disease before the baseline visit and those who had missing information on physical activity patterns, ulcer diagnoses, smoking habits, alcohol use, weight,

or height, 11 413 people (8529 (74.7%) men and 2884 (25.3%) women) were available for study. The average age was 45 (range 20–87) years. Between the time of the baseline examination and the mail back survey, 61 men and 13 women developed new duodenal ulcers and 116 men and 42 women developed new gastric ulcers.

Tables 1 and 2 show a possible protective effect of both moderate and high levels of physical activity on the development of duodenal or gastric ulcers among men, and the  $\chi^2$  trend test suggests a dose-response trend for both duodenal ulcer ( $p = 0.001$ ) and gastric ulcer ( $p = 0.008$ ). Results also show that current smoking and high levels of tension were risk factors for duodenal ulcer (among men) and that high levels of tension were a risk factor for gastric ulcer for both men and women. For men, smoking was associated with an increased risk of gastric ulcers, but light and moderate amounts of alcohol consumption were protective, although the trend test for alcohol consumption was not statistically significant. The results shown in tables 1 and 2 are not adjusted for any of the covariates, nor are they adjusted for the length of observation.

#### COX PROPORTIONAL HAZARD MODELS

The results of the Cox proportional hazard models that include all of the potential risk factors except psychological tension were similar to those models that included psychological tension, which are reported here and shown in table 3. For men, inactivity and the presence of psychological tension were risk factors for duodenal ulcer. Also for men, smoking and psychological tension were positively associated with gastric ulcers; alcohol consumption had a U shaped relation, with moderate intake inversely associated with the development of gastric ulcer. For women, the only significant

Table 3 Cox proportional hazard model: risk ratio of all potential risk factors: Cooper Clinic, Dallas, Texas, 1970–1990

Factors	Men		Women	
	Duodenal ulcer HR (95% CI)	Gastric ulcer HR (95% CI)	Duodenal ulcer HR (95% CI)	Gastric ulcer HR (95% CI)
Moderately active	0.54 (0.30 to 0.96)	1.08 (0.69 to 1.69)	0.62 (0.15 to 2.53)	1.08 (0.51 to 2.27)
Active	0.38 (0.15 to 0.94)	1.01 (0.56 to 1.82)	1.47 (0.32 to 6.83)	1.19 (0.44 to 3.25)
High tension	1.97 (1.14 to 3.43)	1.57 (1.04 to 2.38)	0.66 (0.14 to 3.10)	2.52 (1.30 to 4.89)
Smoking	1.91 (1.09 to 3.35)	1.71 (1.13 to 2.58)	0.61 (0.15 to 2.45)	1.14 (0.57 to 2.28)
Ethanol (light)	1.90 (0.90 to 4.02)	0.65 (0.38 to 1.11)	1.93 (0.47 to 7.88)	1.11 (0.48 to 2.53)
Ethanol (moderate)	0.80 (0.31 to 2.05)	0.43 (0.22 to 0.83)	0.80 (0.08 to 7.88)	1.15 (0.41 to 3.23)
Ethanol (heavy)	0.77 (0.33 to 1.80)	0.72 (0.43 to 1.21)	2.56 (0.39 to 16.92)	1.28 (0.44 to 3.70)
Age (40–60 years)	1.07 (0.59 to 1.94)	1.24 (0.80 to 1.93)	0.63 (0.18 to 2.24)	1.13 (0.57 to 2.24)
Age (60.1+ years)	1.95 (0.72 to 5.33)	1.26 (0.52 to 3.05)	1.16 (0.13 to 10.22)	0.62 (0.08 to 4.73)
BMI (upper 25%)	1.13 (0.60 to 2.14)	1.04 (0.63 to 1.74)	2.00 (0.55 to 7.35)	1.25 (0.57 to 2.74)
BMI (lower 25%)	0.64 (0.29 to 1.40)	1.04 (0.64 to 1.70)	0.39 (0.05 to 3.28)	0.41 (0.14 to 1.21)

HR, hazard ratio; BMI, body mass index.

finding was that psychological tension was associated with gastric ulcer development.

### Discussion

Peptic ulcer disease is a common clinical problem. The lifetime risk of peptic ulcer disease is 5–10% in developed countries.<sup>1 16 17</sup> The pathophysiology of peptic ulcer is complicated and may involve overproduction of acid or pepsin, inadequate mucosal defences, or reflux of bile and pancreatic juice into the stomach.<sup>18</sup> Although *H pylori* is considered causal for peptic ulcer disease, infection is widespread in developed as well as developing countries, but few people actually develop peptic ulcers.<sup>4 19</sup> The epidemiological data for peptic ulcer disease do not suggest a single cause but instead multiple aetiological factors including socioeconomic indicators, psychosocial factors, *H pylori* infection, and cigarette smoking.<sup>9</sup>

There are several mechanisms through which physical activity may be involved in the pathogenesis of peptic ulcer disease, one of which may involve the immune system. Although epidemiological studies suggest that regular moderate physical activity is associated with a lower risk of bacterial infections (upper respiratory tract infections)<sup>20</sup> and experimental studies document an alteration in immune status in both athletes and non-athletes in response to exercise,<sup>21</sup> the issue is far from resolved. Even when these changes are documented, the immune system is not necessarily enhanced. In fact, overexertion of the physical system can have an overall negative effect on immune system parameters, similar to the proposed effect of stress. Because the experimental studies that show increases or decreases in a myriad of immune parameters have not been able to connect these results with clinical illness, this mechanism is hypothetical at this stage.<sup>22</sup>

Another potential mechanism through which physical activity may affect the development of ulcer disease is decreased acid secretion. A few studies report a decrease in basal or meal stimulated acid secretion with cycling and after exertion, leading to suggestions that exercise may assist in duodenal ulcer healing and maintenance of remission.<sup>23–25</sup> Regular physical activity (walking, gardening, or vigorous physical activity) has been found to be associated with a decreased risk for severe

gastrointestinal haemorrhage in older subjects with gastroduodenal ulcer or gastritis (RR = 0.4, 95% confidence interval (CI) = 0.3 to 0.7).<sup>26</sup> In our study, after confounding variables had been controlled for, physical activity was found to be inversely related to the incidence of duodenal, but not gastric, ulcers for men only. This finding may be consistent with other studies if the effect of reduced acid secretion is more important for the duodenum, but this is difficult to determine because most studies combine duodenal and gastric ulcers. Also, our study showed a similar effect of physical activity on both gastric and duodenal ulcers when evaluated without adjusting for other potential confounders.

Another potential mechanism by which physical activity can reduce the incidence of duodenal ulcers is through its effect on stress. The role of physical activity in reducing stress has not been clearly defined, probably because of the difficulty of developing a consistent definition of psychological stress. In cross sectional studies as well as clinical trials, moderate levels of physical activity have been associated with stress related emotions such as anxiety.<sup>27 28</sup> Although the data are not totally consistent at this point, there is some evidence that increases in physical conditioning or fitness enhances a person's ability to deal with the physiological response to psychological stress.<sup>29</sup>

A recent update concludes that stress is a major risk factor for peptic ulcer disease regardless of *H pylori* infection or non-steroidal anti-inflammatory drug use.<sup>30</sup> The relation between stress and peptic ulcer disease has been well established.<sup>10 30</sup> In a longitudinal study of adults in the United States,<sup>31</sup> after adjustment for age, sex, education, smoking status, and regular aspirin use, those who perceived themselves as stressed were 1.8 (95% CI = 1.3 to 2.5) times more likely to develop ulcers than those who did not. A graded relation between the perceived amount of stress and incidence of peptic ulcers was also shown. The results of our study, using self perceived tension as a marker for stress, support this viewpoint.

Not all studies have found a protective effect of physical activity on the development of ulcers. Katschinski and coauthors<sup>32</sup> found physical activity at work to be positively associated with duodenal ulcers. After the values had



been adjusted for age, sex, smoking, and social class, the subjects who reported high levels of physical activity at work had a higher risk of duodenal ulcer than those who reported sedentary activity at work (RR = 3.6, 95% CI = 1.3 to 7.8), but moderate activity at work was not associated with duodenal ulcer (RR = 1.3, 95% CI = 0.6 to 3.0). Although the data were controlled for social class, people who have jobs with high physical demands—that is, labourers—may also have high levels of stress or other lifestyle exposures—for example, *H pylori* infection—that were not considered in the analysis. In part, the inconsistencies found among these studies may reflect differences in the measurement of physical activity as well as other factors, such as the level of stress.

Two related behaviours, cigarette smoking and alcohol consumption, have been variously implicated as risk factors for peptic ulcer disease. As in other studies,<sup>1 11 35 34</sup> we found both gastric and duodenal ulcer disease to be strongly associated with cigarette smoking, even after controlling for other potential risk factors. Excessive alcohol consumption causes damage to the stomach or duodenum by impairing the integrity of the mucosal barrier.<sup>35</sup> However, in our study, we found a protective effect of moderate consumption of alcohol (one or two drinks a day) on the development of gastric ulcer in men even after controlling for tension. This finding suggests that some of the adverse effects of alcohol may be attributed to alcohol associated behaviour, such as smoking. A seroepidemiological study of smoking and alcohol consumption on serum pepsinogen I, pepsinogen II, or pepsinogen I/II ratio conducted among 13 381 employees using a questionnaire and serum test<sup>36</sup> concluded that current smoking elevated pepsinogen I and the I/II ratio, and drinking reduced pepsinogen I and II, but the effect was small. As in the current study, other studies found drinking alcohol to be either a protective factor or not associated with peptic ulcer.<sup>37-39</sup> Drinking moderate amounts of alcohol has also been shown to be protective against active infection with *H pylori*.<sup>40 41</sup> The possibility exists that alcohol consumption may be related to positive or negative risk factors, depending on the dose and type of drinking.

Weatherall and Shaper<sup>42</sup> found that mean BMI decreased with increasing levels of physical activity, and peptic ulcer disease was inversely related to BMI in 7735 middle aged overweight and obese men in 24 British towns. In the Cooper Clinic data, in a population of primarily normal weight people, we found no evidence of a relation between BMI and peptic ulcer disease.

Sonnenberg and Everhart<sup>1</sup> reported that age was not associated with gastric ulcer development in National Health Interview Survey data but was associated with duodenal ulcer development. We did not find age to be associated with either type of ulcer disease. One explanation for this variation is that peptic ulcer disease is a chronic condition and older populations may have a higher prevalence,

and, in our study, only new (incident) cases were analysed. Another explanation is that, if *H pylori* is a causal factor, older persons would have a longer window for exposure, and a higher prevalence among older persons may reflect an aging related decline in immune function. However, because the prevalence of *H pylori* is strongly associated with low income, low levels of education, and non-white race, and because our study participants were not in these risk groups, it is possible that, for these subjects, *H pylori* infection did not play a major role in the development of their peptic ulcer disease. This would also explain the lack of an effect of age on the development of peptic ulcers found in this study.

Our findings for women were different from those for men, and this may reflect a different level of intensity for the reported physical activity between men and women. Our study looked at type and duration of physical activity, but not intensity. In addition to intensity, the type of physical activity reported may not be representative of all the physical activity that women may do, including housework and child care. The small sample size for women (only 13 duodenal ulcer cases) was also a disadvantage for this study. Further analysis of other data sets will be required to clarify the potential relation between physical activity and peptic ulcers in women. If these findings hold, physical activity may prove to be a good candidate for non-pharmacological intervention to prevent the development of duodenal ulcers among men.

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Contributors: Y C developed the study hypothesis, designed and conducted analyses, and wrote the initial complete draft of the manuscript. C A M participated in augmenting the background, interpreting the results, and editing the manuscript. D R D developed the prospective data set and conducted preliminary analyses. S N B initiated the original cohort design and participated in developing the study hypothesis, interpreting the results, and editing the manuscript.

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### Take home message

Physical activity has numerous health benefits and may also represent a cost effective approach to the prevention of peptic ulcers. Furthermore, at the levels observed in this study among the moderately active group (walking or jogging less than 10 miles a week), possible adverse effects—for example, injuries—are minimised. However, in the general population, only about one third of adults undertake this much physical activity. Strategies to promote safe walking, jogging, and cycling may benefit many aspects of health in addition to the cardiovascular and musculoskeletal systems.