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The importance of vigorous-intensity, leisure-time physical activity in reducing cardiovascular disease mortality risk in the obese

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The importance of vigorous-intensity leisure-time physical activity in reducing cardiovascular disease mortality risk in the obese

Running head: Vigorous activity, obesity and mortality risk

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Abstract

Objective: To investigate the role of vigorous-intensity leisure-time physical activity in reducing cardiovascular disease (CVD) mortality risk in the obese.

Methods: Trained interviewers assessed physical activity and body mass index (BMI) in 59,005 adult participants (57 ± 12 years of age [mean $\pm$ SD]; 46.5% male) in the household-based surveillance studies, Health Survey for England and Scottish Health Survey. Mortality was ascertained from death certificates. Data were collected from January 1994 to March 2011. Cox proportional hazards models were adjusted for age, sex, smoking habit, total physical activity, longstanding illness, prevalent CVD, and occupation.

Results: There were 2,302 CVD deaths during 532,251 person-years of follow-up (9 ± 4 years). Some 25% of participants were categorized as obese ($\text{BMI} \geq 30 \text{ kg} \cdot \text{m}^{-2}$). Leisure-time physical activity was inversely associated and BMI was positively associated with CVD mortality. Compared to those who reported meeting physical activity guidelines, including some vigorous-intensity physical activity, and who had a normal BMI ($18.5\text{--}24.9 \text{ kg} \cdot \text{m}^{-2}$) (reference group), CVD mortality hazard ratio was not significantly different in the obese who also reported meeting physical activity guidelines, including some vigorous-intensity physical activities (1.25; 95% confidence interval: 0.50, 3.12). Compared to the reference group, CVD mortality hazard ratio was more than twofold in the obese who reported meeting physical activity guidelines, including only moderate-intensity physical activities (2.52; 95% CI: 1.15, 2.53).

Conclusion: This large, statistically powerful study suggests that vigorous-intensity leisure-time physical activity is important in reducing CVD mortality risk in the obese.

48 **Abbreviations**

49

50 BMI = body mass index

51 CI = confidence interval

52 CVD = cardiovascular disease

53 HR = hazard ratio

54 HSE = Health Survey for England

55 ICD = International Classification of Disease

56 MET = Metabolic equivalent

57 SHS = Scottish Health Survey

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58 Introduction

59

60 Compared to normal weight adults, cardiovascular disease (CVD) mortality risk is greater in
61 overweight adults and greater still in obese adults (1). The American College of Sports
62 Medicine and the American Heart Association recommend physical activity in the primary
63 prevention of morbidity and mortality in the general population (2); nonetheless, the
64 relationship between physical activity and CVD mortality in the obese is unclear. The inverse
65 association between physical activity and CVD mortality risk in the general population is
66 independent of body mass index (BMI) (3); however, few studies have been large enough to
67 investigate the association between physical activity and CVD mortality risk in the obese per
68 se (4). Compared to being inactive, any participation in vigorous-intensity physical activity is
69 associated with lower CVD mortality risk in the general population (3). Therefore, the
70 objective of the present study was to investigate the role of vigorous-intensity physical
71 activity in reducing CVD mortality risk in the obese using a pooled analysis of 11 population-
72 based cohorts.

73 **Methods**

74

75 *Participants*

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77 The methods used in Health Survey for England (HSE) and Scottish Health Survey (SHS) are
78 consistent and are described in detail elsewhere (5,6). Briefly, HSE and SHS are household-
79 based surveillance surveys in which households are selected using a multistage, stratified
80 probability design in order to be representative of the target populations of each country.
81 Stratification is based on geographical areas, not individual characteristics: postcode (zip
82 code) sectors are selected at the first stage and household addresses are selected at the second
83 stage. Participants in the present study were from surveys conducted in 1994 (HSE only),
84 1995 (SHS only), 1997 (HSE only), 1998 (HSE and SHS), 1999 (HSE only), 2003 (HSE and
85 SHS), 2004 (HSE only), 2006 (HSE only), and 2008 (HSE only). Participants aged 40 years
86 or older were included in the present study because it was deemed likely that congenital
87 abnormalities would be responsible for cardiac events in young individuals and lifestyle
88 would be responsible for such events in middle-aged and older adults (7). Data were collected
89 from January 1994 to March 2011. Local research ethics committees approved each survey
90 and participants gave written informed consent.

91

92 *Physical activity*

93

94 Trained interviewers asked about physical activity. Physical activity was assessed using an
95 established questionnaire that is described elsewhere (8). Briefly, the interviewer used the
96 questionnaire to enquire about the following aspects of the respondent’s physical activity in
97 the four weeks prior to the interview: frequency and duration of participation in domestic

physical activity ('light' and 'heavy' housework, gardening and 'do-it-yourself'); frequency, duration and pace of walking (slow, average, brisk or fast); frequency, duration and perceived intensity of participation in sports and exercise using a prompt card showing 10 main groupings, including cycling, swimming, jogging/running, football, rugby, tennis and squash (six open entries could also be recorded). The validity (9) and reliability (10) of the physical activity questionnaire are described elsewhere. A compendium was used to identify physical activity intensities according to metabolic equivalents (METs), where one MET represents resting energy expenditure (11). Light-intensity activities were of 1.5-2.9 METs, moderate-intensity activities were of 3.0-5.9 METs, and vigorous-intensity activities were of ≥ 6.0 METs. A MET-hour was computed by multiplying the MET score of an activity by the time (in hours). Total physical activity was computed by summing the MET-hours of all light-, moderate-, and vigorous-intensity activities. Only leisure-time physical activities were included in the present analysis, not occupational and routine domestic activities.

Obesity

Trained interviewers measured weight and height (6), and BMI was expressed as weight in kilograms divided by height in meters squared. Overweight was defined as a BMI of 25-<30 $\text{kg}\cdot\text{m}^{-2}$ and obese as a BMI of $\geq 30 \text{ kg}\cdot\text{m}^{-2}$ (12). Trained and qualified nurses measured waist circumference at the midpoint of the iliac crest and costal margin (lower rib). Obesity was defined as a waist circumference >102 cm in men and >88 cm in women (13).

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119 *Covariates*

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121 The trained interviewers also asked about age, sex, smoking habit, longstanding illness,
122 cardiovascular disease, occupation, and ethnicity. Socioeconomic status was determined from
123 participants' occupations using the four-group version of the Registrar General's
124 classification: professional and managerial occupations; skilled, non-manual occupations;
125 skilled manual occupations; and, routine and manual occupations.

126

127 *Mortality follow-up*

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129 The British National Health Service Central Registry flagged participants. Data for survivors
130 were censored to the end of 2009 (SHS) or the first quarter of 2011 (HSE). Diagnoses for the
131 primary cause of death were based on the International Classification of Diseases, Ninth
132 (ICD-9) and Tenth (ICD-10) Revisions. Codes corresponding to CVD mortality were 390-
133 459 for ICD-9 and I01-I99 for ICD-10.

134

135 *Statistical analysis*

136

137 Cox proportional hazards models were used to estimate the associations between physical
138 activity, obesity and CVD mortality risk. In keeping with prevailing guidelines (2), exposure
139 to physical activity was defined as at least 150 minutes per week of moderate-intensity
140 physical activity, at least 75 minutes per week of vigorous-intensity activity, or equivalent
141 combinations. We further distinguished between the physically active who reported taking
142 part in vigorous-intensity activity and those who did not in order to investigate the role of
143 physical activity intensity in reducing CVD mortality risk. The proportional hazards

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3 144 assumption was examined by comparing the cumulative hazard plots grouped on exposure;
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5 145 and, no appreciable violations were noted. Calendar time (months) was the timescale. Data
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7 146 from the underweight ($\text{BMI} < 18.5 \text{ kg} \cdot \text{m}^{-2}$) and those who died during the first 24 months of
8
9 147 follow-up were not used. Analyses were adjusted for age and sex (Model 1) and further
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11 148 adjusted for smoking habit, total physical activity, longstanding illness, prevalent CVD, and
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13 149 occupation (Model 2). The associations between physical activity, obesity and CVD mortality
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15 150 risk in those who reported never smoking was investigated in a sensitivity analysis. All
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17 151 analyses were performed using SPSS version 22 (IBM Inc.).
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Results

Supplemental Figure 1 shows the sample selection; 59,005 participants in HSE and SHS were included in the present study. Table 1 shows participants’ characteristics at baseline according to BMI. The average age was 57 years and was significantly different in the normal, overweight, and obese groups. Some 47% of participants were men and the proportions of men were lower in the normal BMI and obese groups. The average leisure-time physical activity level was higher in those with a normal BMI but there were considerable differences within each BMI group. The proportion of current smokers was higher in those with a normal BMI than those who were overweight or obese. The proportion in professional and managerial occupations was lower and the proportion in semi-skilled and unskilled manual occupations was higher in the obese group than the other groups. The proportions with longstanding illness and prevalent CVD were also higher in the obese group than the other groups. The proportion of CVD deaths during follow-up was 3.6% in the normal, 4.0% in the overweight, and 4.1% in the obese BMI groups. Supplemental Table 1 shows physical activity levels according to prevailing physical activity guidelines. Moderate-to vigorous-intensity physical activity was $327\pm354\text{ min}\cdot\text{wk}^{-1}$ (mean $\pm$ SD) in those who reported meeting the guidelines including some vigorous-intensity activity and $404\pm394\text{ min}\cdot\text{wk}^{-1}$ in those who reported meeting the guidelines including only moderate-intensity activity. Total physical activity was $50\pm43\text{ MET}\cdot\text{hr}\cdot\text{wk}^{-1}$ in those who reported meeting the guidelines including some vigorous-intensity activity and $48\pm47\text{ MET}\cdot\text{hr}\cdot\text{wk}^{-1}$ in those who reported meeting the guidelines including only moderate-intensity activity.

Table 2 shows mean waist girth values in men and women according to BMI and physical activity. Statistical significance was investigated in the obese. Compared to obese men who

177 reported meeting physical activity guidelines, including some vigorous-intensity physical
178 activity (reference group), waist girth was not significantly different in obese men who
179 reported meeting physical activity guidelines, including only moderate-intensity physical
180 activities (mean difference: 1.4 cm; 95% confidence interval, CI: -0.4, 3.2; $p=.54$). Compared
181 to the reference group, waist girth was not significantly different in obese men who were
182 active, but did not meet physical activity guidelines (mean difference: 1.1 cm; 95% CI: -0.2,
183 2.5; $p=0.36$). Compared to the reference group, waist girth was significantly different in
184 obese men who were inactive (mean difference: 3.2 cm; 95% CI: 2.0, 4.5; $p<.001$). Compared
185 to obese women who reported meeting physical activity guidelines, including some vigorous-
186 intensity physical activity (reference group), waist girth was not significantly different in
187 obese women who reported meeting physical activity guidelines, including only moderate-
188 intensity physical activities (mean difference: 1.2 cm; 95% CI: -1.0, 3.4; $p=.99$). Compared to
189 the reference group, waist girth was not significantly different in obese women who were
190 active, but did not meet physical activity guidelines (mean difference: 0.8 cm; 95% CI: -0.9,
191 2.6; $p=0.99$). Compared to the reference group, waist girth was significantly different in
192 obese women who were inactive (mean difference: 2.9 cm; 95% CI: 1.2, 4.5; $p<.001$).
193 Supplemental Table 2 shows that the correlation between waist girth and BMI was .85 to .86
194 in men and women of different physical activity levels.

195
196 There were 2,302 CVD deaths during 532,251 person-years of follow-up (9 ± 4 years). Table 3
197 shows the associations between BMI and CVD mortality. Compared to those with a normal
198 BMI (reference group), the fully-adjusted hazard ratio for CVD mortality was not
199 significantly different in the overweight (hazard ratio, HR: 0.97; 95% CI: 0.87, 1.07), but was
200 higher and significantly different in the obese (HR: 1.23; 95% CI: 1.10, 1.37). Waist girth
201 was measured in 45,259 participants and the fully-adjusted hazard ratio for CVD mortality

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202 was 1.18 (95% CI: 1.07, 1.29) in the obese compared to the non-obese. Compared to those
203 who were willing to have their waist girth measured, those who were unwilling were younger
204 (57.7 vs. 56.7 years, $p<.001$), were more likely to be women (53.2 vs. 54.4 %, $p=.007$), were
205 less physically active (86 vs. 59 minutes per week of moderate- and vigorous-intensity
206 physical activity, $p<.001$), and were of higher BMI (27.5 vs. 27.7 kg·m⁻², $p<.001$).
207
208 Table 4 shows the associations between physical activity, BMI, and CVD mortality.
209 Compared to those who reported meeting physical activity guidelines and who had a normal
210 BMI (reference group), the fully-adjusted hazard ratio for CVD mortality was not
211 significantly different in the overweight (HR: 1.41; 95% CI: 0.94, 2.10) or the obese (HR:
212 1.41; 95% CI: 0.84, 2.38) who also reported meeting physical activity guidelines. Compared
213 to the reference group, the full-adjusted hazard ratio for CVD mortality was not significantly
214 different in the overweight who reported doing less than the recommended amounts of
215 leisure-time physical activity (HR: 1.34; 95% CI: 0.92, 1.95), but was higher and
216 significantly different in the obese who reported doing less than the recommended amounts
217 of leisure-time physical activity (HR: 1.84; 95% CI: 1.21, 2.81). Compared to the reference
218 group, the fully-adjusted hazard ratio for CVD mortality was around twofold in those who
219 reported no leisure-time physical activity per week, including those with a normal BMI, the
220 overweight, and the obese. Supplemental Table 3 shows that the associations between
221 physical activity, BMI, and CVD mortality were similar in men and women. Supplemental
222 Table 4 shows that the associations between physical activity, obesity and CVD mortality risk
223 were also similar in those who reported never smoking.
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225 Table 5 shows the associations between leisure-time physical activity, BMI, and CVD
226 mortality in the physically active who reported taking part in vigorous-intensity activity and

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3 227 those who did not. Compared to those who reported meeting physical activity guidelines,
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5 228 including some vigorous-intensity physical activity, and who had a normal BMI (reference
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7 229 group), the fully-adjusted hazard ratio for CVD mortality was not significantly different in
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9 230 the overweight (HR: 1.85; 95% CI: 0.92, 3.70) or the obese (HR: 1.25; 95% CI: 0.50, 3.12)
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11 231 who also reported meeting physical activity guidelines, including some vigorous-intensity
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13 232 physical activity. Compared to the reference group, the fully-adjusted hazard ratio for CVD
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15 233 mortality was not significantly different in those with a normal BMI (HR: 1.45; 95% CI:
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17 234 0.70, 3.01) or the overweight (HR: 1.70; 95% CI: 0.86, 3.37) who reported meeting physical
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19 235 activity guidelines, including only moderate-intensity physical activities. Compared to the
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21 236 reference group, the fully-adjusted hazard ratio for CVD mortality was more than twofold in
22
23 237 the obese who reported meeting physical activity guidelines, including only moderate-
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25 238 intensity physical activities (HR: 2.52; 95% CI: 1.15, 2.53).
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Discussion

The objective of this study was to investigate the role of vigorous-intensity leisure-time physical activity in reducing CVD mortality risk in the obese. There were two main findings. First, in comparison to those who reported meeting prevailing physical activity guidelines, including some vigorous-intensity activity, and who had a normal BMI (reference group), CVD mortality risk was not significantly different in the obese who also reported meeting prevailing physical activity guidelines, including some vigorous-intensity activity. Second, in comparison with the reference group, CVD mortality risk was increased more than twofold in the obese who reported meeting physical activity guidelines, including only moderate-intensity physical activities. These findings indicate the importance of vigorous-intensity leisure-time physical activity in reducing CVD mortality risk in the obese.

Few investigators have reported the joint association between physical activity and overweight and obesity with mortality. Hu and colleagues (4) reported that, compared to those who were ‘moderately’ or ‘highly’ active and who had a BMI <30 kg·m⁻², CVD mortality hazard ratio was 2.09 (95% CI: 1.68, 2.59) in those who were inactive and who had a BMI ≥30 kg·m⁻² (physical activity was ‘moderate’ in those who reported moderate or high levels of either occupational or leisure-time physical activity; physical activity was ‘high’ in those who reported moderate or high levels of both occupational and leisure-time physical activity). Leitzman and colleagues (3) reported that, compared to the inactive who had a BMI ≥25 kg·m⁻², all-cause mortality hazard ratio was 0.60 (95% CI: 0.54, 0.66) in those who reported taking part in the recommended amount of moderate-intensity activity and who had a BMI ≥25 kg·m⁻², and 0.58 (95% CI: 0.52, 0.65) in those who reported taking part in the recommended amount of vigorous-intensity activity and who had a BMI ≥25 kg·m⁻² (the

recommended amount of moderate activity was equivalent to around 30 minutes on most days of the week; the recommended amount of vigorous activity was at least 20 minutes on three days of the week). Leitzman and colleagues (13) did not report the association between physical activity and all-cause mortality in the obese per se. Moholdt and colleagues (14) reported that physical activity was associated with reduced risk of mortality in overweight and obese adults with coronary heart disease. It is biologically plausible that physical activity reduces CVD mortality risk in the overweight and obese because exercise training improves a number of CVD risk factors independent of weight loss (15,16). For example, 24 weeks of aerobic exercise training improved 10 of 11 lipoprotein variables in overweight and obese adults with mild-to-moderate dyslipidemia who were counseled to maintain body weight (17).

Compared to normal weight adults (BMI 18.5-<25 kg·m⁻²), CVD mortality hazard ratio is 1.22 (95% CI: 1.20, 1.24) in overweight adults (BMI 25-<30 kg·m⁻²) (1). For BMI over 25 kg·m⁻², the CVD mortality hazard ratio per 5 kg·m⁻² higher BMI is 1.49 (95% CI: 1.45, 1.53) (1). It is alarming therefore that, if post 2000 BMI trends continue, there is virtually zero probability of meeting the World Health Organisation target of halting by 2025 the rise in obesity at its 2010 levels (18). Physical activity improves cardiorespiratory fitness (19) and it has been consistently shown that moderate to high levels of fitness attenuate, if not negate, the association between obesity and cardiovascular disease (16). This concept is known as the fat-but-fit paradigm and is present in one fifth of obese individuals (16). Physical inactivity cost global healthcare systems at least US\$54 billion in 2013 (20) and policymakers have been urged to take physical inactivity seriously (21). We agree with those who would have policies to increase physical activity and cardiorespiratory fitness (16,19,22). Vigorous-intensity exercise increases cardiorespiratory fitness more than the same amount of moderate-

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289 intensity exercise (19); And, there are two reasons to think that vigorous-intensity physical
290 activity was particularly important in the present study. First, total physical activity was
291 similar in participants who reported meeting the guidelines including some vigorous-intensity
292 activity and in participants who reported meeting the guidelines including only moderate-
293 intensity activity. Second, the reduction in CVD mortality risk in obese participants who
294 reported meeting the guidelines including some vigorous-intensity activity was independent
295 of total physical activity. Waist girth was not significantly different in obese men and women
296 who took part in vigorous-intensity activity and those who took part in only moderate-
297 intensity activity; however, magnetic resonance imaging and spectroscopy suggest that
298 visceral fat and liver fat are lower in men who are fat, fit and vigorously active (23).
299
300 The present study has some limitations. A causal relationship cannot be inferred from an
301 observational study. The possibility of reverse causation cannot be discounted, where those
302 with underlying disease are less likely to be physically active; however, data from the
303 underweight and those who died during the first 24 months of follow-up were not used; and,
304 the hazard ratios were adjusted for longstanding illness and prevalent CVD to address the
305 notion of reverse causation. Physical activity was self-reported; however, questionnaires are
306 still regarded as the mainstay of established surveillance studies like HSE and SHS (24).

307 **Conclusion**

308

309 Few studies are large enough to investigate the joint associations of physical activity and
310 obesity with CVD mortality. This large, statistically powerful study suggests that vigorous-
311 intensity leisure-time physical activity is important in reducing CVD mortality risk in the
312 obese.

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Conflicts of Interest

The authors have nothing to declare.

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Table 1. Participants’ characteristics at baseline according to body mass index^a

	Body mass index (n)			<i>P</i>
	Normal	Overweight (25,602)	Obese	
	(18,401)		(15,002)	
Age, years	56.3±12.3	57.9±11.8	57.8±11.2	<.001
Men, %	39	53	44	<.001
Physical activity, min·wk ⁻¹	93±238	83±257	52±160	<.001
Smoking, %				<.001
<i>Never</i>	45.3	45.1	46.0	
<i>Ex-smoker</i>	25.7	34.5	36.5	
<i>Current, <10 a day</i>	6.4	4.8	3.9	
<i>Current, 10-19 a day</i>	12.1	7.7	6.2	
<i>Current, ≥20 a day</i>	10.5	7.9	7.4	

Social occupation class, %				<.001
<i>Professional/managerial</i>	34.6	35.1	30.0	
<i>Skilled non-manual/manual</i>	42.0	42.1	42.3	
<i>Semi/unskilled manual</i>	23.2	22.3	27.4	
<i>Other (armed forces, etc.)</i>	0.4	0.4	0.3	
Longstanding illness, %	43.6	51.7	61.8	<.001
Prevalent CVD, %	6.1	8.7	10.6	<.001

^aBody mass index: normal is defined as 18.5-24.9 kg·m⁻²; overweight is defined as 25.0-29.9 kg·m⁻²; obese is defined as ≥ 30 kg·m⁻². Physical activity refers to moderate- and vigorous-intensity leisure-time physical activities. CVD is cardiovascular disease. Prevalent CVD defined as physician diagnosed angina, heart attack or stroke. CVD deaths refers to deaths during follow-up. Data from the underweight (BMI <18.5 kg·m⁻²) and those who died during the first 24 months of follow-up were not used. Differences across groups were tested using ANOVA for continuous data and chi-squared tests for categorical variables.

Table 2. Mean waist girth values in men and women according to body mass index and physical activity^a

Leisure-time physical activity	Men			Women		
	Normal BMI	Overweight	Obese	Normal BMI	Overweight	Obese
Meets guidelines, including some vigorous activity	87	96	109	76	85	99
Meets guidelines, including only moderate activity	88	98	110	76	86	100
Active, but not meeting guidelines	88	97	110	77	87	100
Inactive	88	99	112	77	88	102

^aValues are centimeters. Trained interviewers assessed physical activity and body mass index. Meeting prevailing guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity physical activity, or equivalent combinations. Body mass index (BMI): normal is defined as 18.5-24.9 kg·m⁻²; overweight is defined as 25.0-29.9 kg·m⁻²; obese is defined as ≥ 30 kg·m⁻². Trained and qualified nurses measured waist girth at the midpoint of the iliac crest and costal margin (lower rib).

Table 3. Cox proportional hazard ratios for the associations between body mass index and cardiovascular disease mortality

Body mass index ^a	Events/individuals	Model 1, HR (95% CI)	Model 2, HR (95% CI)
Normal	670/18401	1.0 (Reference)	1.0
Overweight	1015/25602	0.96 (0.87, 1.06)	0.97 (0.87, 1.07)
Obese	617/ 15002	1.28 (1.15, 1.43)	1.23 (1.10, 1.37)

^aBody mass index: normal is defined as 18.5-24.9 kg·m⁻²; overweight is defined as 25.0-29.9 kg·m⁻²; obese is defined as ≥ 30 kg·m⁻² (n=59,005). Model 1 adjusted for age and sex. Model 2 adjusted for age, sex, smoking, physical activity, longstanding illness, social occupation class, and prevalent CVD.

Table 4. Cox proportional hazard ratios for the associations between physical activity, body mass index, and cardiovascular disease mortality in adults age 40 years or older

Leisure-time physical activity	Body mass index ^a		
	Normal, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)
Meets guidelines	1.0 (Reference)	1.41 (0.94, 2.10)	1.41 (0.84, 2.38)
Does not meet guidelines	1.41 (0.94, 2.12)	1.34 (0.92, 1.95)	1.84 (1.21, 2.81)
None	2.02 (1.44, 2.84)	1.91 (1.36, 2.67)	2.44 (1.74, 3.42)

There were 2,302 cardiovascular disease events in 59,005 individuals. Those with a body mass index $<18.5 \text{ kg}\cdot\text{m}^{-2}$ and those who died in the first two years of follow-up were removed to guard against reverse causation. Models adjusted for age, sex, smoking, total physical activity, longstanding illness, social occupation class, and prevalent CVD. Meeting physical activity guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity activity, or equivalent combinations. ^aBody mass index: normal is defined as $18.5\text{-}24.9 \text{ kg}\cdot\text{m}^{-2}$; overweight is defined as $25.0\text{-}29.9 \text{ kg}\cdot\text{m}^{-2}$; obese is defined as $\geq 30 \text{ kg}\cdot\text{m}^{-2}$.

Table 5. Cox proportional hazard ratios for the associations between leisure-time physical activity, body mass index, and cardiovascular disease mortality in the physically active who reported taking part in vigorous-intensity activity and those who did not

Leisure-time physical activity ^a	Body mass index ^b		
	Normal, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)
Some vigorous	1.0 (Ref)	1.85 (0.92, 3.70)	1.25 (0.50, 3.12)
Moderate only	1.45 (0.70, 3.01)	1.70 (0.86, 3.37)	2.52 (1.15, 2.53)

There were 130 cardiovascular disease events. ^a6,799 participants reported meeting physical activity guidelines, including some vigorous-intensity physical activity; 4,163 participants reported doing at least 150 min·wk⁻¹ of leisure-time physical activity, including only moderate-intensity physical activities. Those with a body mass index <18.5 kg·m⁻² and those who died in the first two years of follow-up were removed to guard against reverse causation. Models adjusted for age, sex, smoking, total physical activity, longstanding illness, social occupation class, and prevalent CVD. ^bBody mass index: normal is defined as 18.5-24.9 kg·m⁻²; overweight is defined as 25.0-29.9 kg·m⁻²; obese is defined as ≥ 30 kg·m⁻².

Supplemental Figure 1. Flow chart showing sample selection.

Supplemental Table 1. Participants' physical activity levels according to prevailing physical activity guidelines^a

Leisure-time physical activity	Physical activity level (mean±SD)	
	Moderate- to vigorous-intensity, min·wk ⁻¹	Total, MET·hr·wk ⁻¹
Meets guidelines, including some vigorous activity	327±354	50±43
Meets guidelines, including only moderate activity	404±394	48±47
Active, but not meeting guidelines	54±37	20±24
Inactive	0	14±22

^aTrained interviewers assessed physical activity and meeting prevailing guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity physical activity, or equivalent combinations (Haskell et al., Circulation, 2007, 116, 1081-93). A compendium was used to identify physical activity intensities according to metabolic equivalents (METs), where one MET represents resting energy expenditure (Ainsworth et al., Med Sci Sports Exerc, 2011, 43, 1575-81). Light activities were of 1.5-2.9 METs, moderate activities were of 3.0-5.9 METs, and vigorous activities were of ≥6.0 METs. A MET-hour was computed by multiplying the MET score of an activity by the time (in hours). Total physical activity was computed by summing the MET-hours of all light, moderate, and vigorous activities. Compared with the inactive group, every other group is significantly different ($p<.001$).

Supplemental Table 2. Correlations between waist girth and body mass index in men and women according to physical activity level^a

Leisure-time physical activity	Men	Women
Meets guidelines	.85	.86
Active, but not meeting guidelines	.86	.85
Inactive	.86	.85

^aValues are partial correlations adjusted for age. Trained interviewers assessed physical activity and body mass index. Meeting prevailing guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity physical activity, or equivalent combinations (Haskell et al., Circulation, 2007, 116, 1081-93). Body mass index: normal is defined as 18.5-24.9 kg·m⁻²; overweight is defined as 25.0-29.9 kg·m⁻²; obese is defined as ≥ 30 kg·m⁻² (World Health Organization, Obesity and overweight. Fact sheet No 311. Geneva: WHO, 2016). Trained and qualified nurses measured waist girth at the midpoint of the iliac crest and costal margin (lower rib).

Supplemental Table 3. Cox proportional hazard ratios for the associations between physical activity, body mass index, and cardiovascular disease mortality in men and women age 40 years or older^a

Leisure-time physical activity	Body mass index		
	Normal, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)
<i>Men</i>			
Meets guidelines	1.0 (Reference)	1.26 (0.77, 2.06)	1.68 (0.90, 3.11)
Does not meet guidelines	1.17 (0.68, 2.01)	1.42 (0.89, 2.27)	1.99 (1.17, 3.39)
None	1.71 (1.11, 2.63)	1.68 (1.10, 2.56)	2.54 (1.66, 3.89)
<i>Women</i>			
Meets guidelines	1.0 (Reference)	1.63 (0.82, 3.23)	0.91 (0.32, 2.54)
Does not meet guidelines	1.79 (0.94, 3.39)	1.15 (0.62, 2.19)	1.80 (0.91, 3.56)
None	2.54 (1.45, 4.44)	2.40 (1.38, 4.19)	2.57 (1.46, 4.50)

^aThere were 1,242 cardiovascular disease events in 27,088 men and 1,060 cardiovascular disease events in 29,019 women. Those with a body mass index $<18.5 \text{ kg}\cdot\text{m}^{-2}$ and those who died in the first two years of follow-up were removed to guard against reverse causation. Models adjusted for age, sex, smoking, total physical activity, longstanding illness, social occupation class, and prevalent CVD. Meeting physical activity guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity activity, or equivalent combinations. Body mass index: normal is defined as $18.5\text{--}24.9 \text{ kg}\cdot\text{m}^{-2}$; overweight is defined as $25.0\text{--}29.9 \text{ kg}\cdot\text{m}^{-2}$; obese is defined as $\geq 30 \text{ kg}\cdot\text{m}^{-2}$.

Supplemental Table 4. Cox proportional hazard ratios for the associations between physical activity, body mass index, and cardiovascular disease mortality in non-smokers aged 40 years or older^a

Leisure-time physical activity	Body mass index		
	Normal, HR (95% CI)	Overweight, HR (95% CI)	Obese, HR (95% CI)
Meets guidelines	1.0 (Reference)	1.70 (0.86, 3.37)	1.84 (0.75, 4.51)
Does not meet guidelines	1.78 (0.89, 3.54)	1.41 (0.73, 2.71)	1.66 (0.79, 3.48)
None	2.28 (1.27, 4.10)	2.11 (1.18, 3.78)	2.94 (1.64, 5.30)

^aThere were 802 cardiovascular disease events in 25,561 men and women who reported never smoking. Those with a body mass index $<18.5 \text{ kg}\cdot\text{m}^{-2}$ and those who died in the first two years of follow-up were removed to guard against reverse causation. Models adjusted for age, sex, total physical activity, longstanding illness, social occupation class, and prevalent CVD. Meeting physical activity guidelines was defined as at least 150 minutes per week of moderate-intensity physical activity, at least 75 minutes per week of vigorous-intensity activity, or equivalent combinations. Body mass index: normal is defined as $18.5\text{--}24.9 \text{ kg}\cdot\text{m}^{-2}$; overweight is defined as $25.0\text{--}29.9 \text{ kg}\cdot\text{m}^{-2}$; obese is defined as $\geq 30 \text{ kg}\cdot\text{m}^{-2}$.