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INTERACTIVE EFFECTS OF AEROBIC FITNESS, STRENGTH AND OBESITY ON MORTALITY IN MEN

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Abstract

Introduction—Low aerobic fitness, low muscular strength, and obesity have been associated with premature mortality, but their interactive effects are unknown. This study examined interactions among these common, modifiable factors, which may help inform more effective preventive interventions.

Methods—A national cohort study was conducted of all 1,547,478 military conscripts in Sweden during 1969–1997 (97–98% of all 18-year-old males each year). Aerobic fitness, muscular strength, and body mass index (BMI) measurements were examined in relation to all-cause and cardiovascular mortality through 2012 (maximum age 62). Data collection/analysis were in 2015–2016.

Results—Low aerobic fitness, low muscular strength, and obesity at age 18 were independently associated with higher all-cause and cardiovascular mortality in adulthood. The combination of low aerobic fitness and muscular strength (lowest vs. highest tertiles) was associated with 2-fold all-cause mortality (adjusted hazard ratio, 2.01; 95% CI, 1.93–2.08; $P < 0.001$; mortality rates per 100,000 person-years, 247.2 vs. 73.8), and 2.6-fold cardiovascular mortality (2.63; 2.38–2.91;

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Conflicts of interest

None.

$P < 0.001$; 43.9 vs. 8.3). These factors also had positive additive and multiplicative interactions in relation to all-cause mortality (their combined effect exceeded the sum or product of their separate effects; $P < 0.001$), and were associated with higher mortality even among men with normal BMI.

Conclusions—Low aerobic fitness, low muscular strength, and obesity at age 18 were associated with increased mortality in adulthood, with interactive effects between aerobic fitness and muscular strength. These findings suggest that preventive interventions should begin early in life and include both aerobic fitness and muscular strength, even among those with normal BMI.

INTRODUCTION

Physical inactivity and obesity are among the leading global risk factors for disability and premature mortality.¹ Currently 1 in 3 adults worldwide do not meet public health guidelines for physical activity,² and more than one-third are overweight or obese.³ These factors increase the risk of coronary heart disease, type 2 diabetes, and cancer (especially breast and colon cancers), and by conservative estimates cause 6–10 million deaths annually worldwide.^{1, 3, 4}

Because these risk factors are common, modifiable, and have high public health impacts, a better understanding of their interactive effects is needed to inform lifestyle interventions and clinical counseling. There are several important gaps in current knowledge. Although physical activity has been widely studied,^{5, 6} objective measurements of physical fitness may be stronger and more informative risk factors,⁷ and are better indicators of habitual physical activity than self-reported activity.⁸ Prior studies have reported that low aerobic fitness,^{9–11} low muscular strength,^{12–14} and obesity¹⁵ are associated with premature mortality. However, no studies have examined additive and multiplicative interactions among these common exposures in relation to mortality. Most studies also have examined these exposures in mid-adulthood and not earlier in life. As a result, the interactive effects of early-life aerobic fitness, muscular strength, and obesity on mortality in adulthood remain unknown. Such knowledge may help inform earlier and more effective interventions in susceptible subgroups.

The authors sought to address these knowledge gaps by conducting a large cohort study to examine the interactive effects of aerobic fitness, muscular strength, and body mass index (BMI) in late adolescence on mortality in adulthood. In particular, they hypothesized that low aerobic fitness and low muscular strength would have positive interactive effects on mortality, because such effects have been found for common diseases that are known contributors to premature mortality, such as type 2 diabetes,¹⁶ hypertension,¹⁷ and stroke.¹⁸

METHODS

Study Population

The authors identified 1,547,478 males who underwent a military conscription examination in Sweden during 1969–1997. All 18-year-old males nationally were conscripted each year except for 2–3% who either were incarcerated or had severe chronic medical conditions or disabilities documented by a physician. Aerobic fitness, muscular strength, and BMI measurements were obtained using the Swedish Military Conscription Registry, which

contains information from a 2-day standardized physical and psychological examination required for all conscripts starting in 1969. This study was approved by the Regional Ethics Committee of Lund University in Sweden (No. 2010/476). The collection and analysis of secondary data were conducted in 2015–2016.

Aerobic Fitness, Muscular Strength, and BMI Ascertainment

Aerobic fitness was measured as the maximal aerobic workload using a standard well-validated electrically-braked stationary bicycle ergometer test. Following a warm-up period, each conscript performed 5–10 minutes of exercise on a stationary bicycle at a starting work rate of 75 to 175 Watts (determined by a sliding scale based on body weight), and increasing by 25 Watts/minute until volitional exhaustion. Maximal aerobic workload was calculated as the power output in Watts before the last intensity increase, plus the prorated output for the last stage.¹⁹ Maximal aerobic workload is highly correlated with maximal oxygen uptake (VO_2 max; correlation ~ 0.9),²⁰ and its measurement using this bicycle ergometer test is highly reproducible, with a test-retest correlation of 0.95.²¹ Muscular strength was measured as the weighted sum of maximal knee extension (weighted $\times 1.3$), elbow flexion (weighted $\times 0.8$), and hand grip (weighted $\times 1.7$), each measured in Newtons, using standard well-validated isometric dynamometer tests. Each dynamometer test was performed three times and the maximum value was recorded for analysis, except when the last value was highest, in which case testing was repeated until strength values stopped increasing.²² BMI was calculated using standardized height and weight measurements as weight in kilograms divided by the square of height in meters. All testing equipment was calibrated daily.^{19, 22}

Aerobic fitness and muscular strength were examined alternatively as continuous variables or categorical variables in tertiles (aerobic fitness in Watts: low [<240], medium [$240\text{--}288$], high [289]; muscular strength in Newtons: low [<1900], medium [$1900\text{--}2170$], high [2171]), while adjusting for body size and other covariates (as described below). BMI was examined alternatively as a continuous or categorical variable using Centers for Disease Control and Prevention (CDC) definitions for children and adolescents aged 2 to 19 years to facilitate comparability with US studies: “overweight” is defined as 85th and <95th percentile and “obesity” as 95th percentile on the CDC’s 2000 sex-specific BMI-for-age growth charts, which correspond to BMI 25.6 and <29.0 and BMI 29.0, respectively, for 18-year-old males.²³ As alternatives to BMI, height and weight were examined simultaneously in a separate model, as continuous or categorical (height: <175 , $175\text{--}184$, 185 cm; weight: <60 , $60\text{--}79$, 80 kg) variables.

Mortality Ascertainment

All men were followed up for all-cause and cardiovascular disease (CVD) mortality from the date of the military conscription examination through December 31, 2012. Mortality and cause of death were identified using the Swedish Death Registry, which includes information on all deaths in Sweden with compulsory reporting nationwide. CVD was classified according to the *International Classification of Diseases (ICD-7: 330–334, 400–467; ICD-8/9: 390–459; ICD-10: I00–I99)*.

Adjustment Variables

Other variables that may be associated with physical fitness, BMI, and mortality were obtained from the Swedish Military Conscription Registry and national census data, which were linked using an anonymous personal identification number. The following were used as adjustment variables: year of the military conscription examination (modeled simultaneously as a continuous and categorical [1969–1979, 1980–1989, 1990–1997] variable to account for potential linear and non-linear effects); highest education level attained during the study period (<12, 12–14, 15 years); neighborhood socioeconomic status at baseline (SES, included because neighborhood SES characteristics have been associated with physical fitness and BMI²⁴ and with mortality^{25, 26}; composed of an index that includes low education level, low income, unemployment, and social welfare receipt, as previously described,²⁷ and categorized as low [<-1 SD from the mean], medium [-1 to 1 SD], or high [>1 SD]); and family history of CVD in a parent or sibling (yes or no, identified from the Swedish Hospital Registry during 1964–2012 and the Swedish Outpatient Registry during 2001–2012, using the same diagnosis codes noted above).

Missing data for each variable were imputed using a standard multiple imputation procedure based on the variable's relationship with all other covariates and mortality.²⁸ Missing data were relatively infrequent for aerobic fitness (5.7%), muscular strength (5.0%), height (7.2%), weight (7.3%), education level (0.4%), and neighborhood SES (9.1%). As an alternative to multiple imputation, sensitivity analyses were performed after restricting to men with complete data for all variables ($N=1,361,083$; 88.0%).

Statistical Analysis

Cox proportional hazards regression was used to compute hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between aerobic fitness, muscular strength, or BMI and all-cause or CVD mortality. The Cox model time scale was elapsed time since the military conscription examination (which also corresponds to attained age because baseline age was the same [18 years] for all conscripts). Individuals were censored at emigration ($n=87,450$; 5.7%). Two models were performed for each outcome, all-cause and CVD mortality: the first was unadjusted, and the second included year of the military conscription examination, aerobic fitness, muscular strength, BMI, education level, neighborhood SES, and family history of CVD (as defined above). The proportional hazards assumption was evaluated by graphical assessment of log-log plots, which showed a good fit in all models.

Interactions among aerobic fitness, muscular strength, and/or BMI were examined on both the additive and multiplicative scale in relation to all-cause or CVD mortality. Additive interactions were assessed using the “relative excess risk due to interaction” (RERI: two-way interaction, $RERI_{HR} = HR_{11} - HR_{10} - HR_{01} + 1$; three-way interaction, $RERI_{HR} = HR_{111} - HR_{100} - HR_{010} - HR_{001} + 2$).^{29, 30} Multiplicative interactions were assessed using the ratio of HRs (two-way interaction, $HR_{11} / [HR_{10} \times HR_{01}]$; three-way interaction, $HR_{111} / [HR_{100} \times HR_{010} \times HR_{001}]$).²⁹ All statistical tests were 2-sided and used an α -level of 0.05. All analyses were conducted using Stata version 14.1.

RESULTS

Among the 1,547,478 males in this cohort, 64,343 (4.2%) died from any cause and 10,381 (0.7%) died from CVD in 43.7 million person-years of follow-up (mean follow-up, 28.2 years). The median age at the end of follow-up was 47.2 years (mean 47.4, SD 7.9, range 19.0 to 62.0). The median age at death from any cause was 54.9 years (mean 52.6, SD 7.0, range 18.0 to 62.0), and at death from CVD was 56.3 years (mean 54.7, SD 5.8, range 18.0 to 62.0). Table 1 shows all-cause and CVD mortality rates by aerobic fitness, muscular strength, BMI, and other potential risk factors.

Main Effects of Aerobic Fitness, Muscular Strength, and BMI

Low aerobic fitness was associated with increased all-cause and CVD mortality, after adjusting for BMI, muscular strength, and other factors (Table 2, lowest vs. highest tertile, adjusted HR for all-cause mortality: 1.58; 95% CI, 1.53–1.63; $P<0.001$; CVD mortality: 1.81; 1.67–1.96; $P<0.001$). Low muscular strength also was associated (but less strongly) with increased all-cause mortality (adjusted HR: 1.27; 95% CI, 1.24–1.30; $P<0.001$) and CVD mortality (1.43; 1.36–1.51; $P<0.001$). When modeled as continuous variables, both aerobic fitness and muscular strength had strong inverse linear trends across their full distribution in relation to all-cause or CVD mortality ($P<0.001$; Table 2). When they were alternatively examined after standardizing for body weight (i.e., Watts or Newtons per kg of body weight), the risk estimates were similar to those from the main analysis that adjusted for BMI as a covariate.

Obesity also was associated with increased all-cause mortality (adjusted HR 1.58; 95% CI, 1.51–1.66; $P<0.001$) and was the strongest risk factor for CVD mortality (>3-fold risk), relative to normal BMI (Table 2). When both height and weight were modeled as an alternative to BMI, high weight was associated with increased all-cause and CVD mortality, whereas tallness was modestly protective against both outcomes (Table 2, adjusted models). In sensitivity analyses that were restricted to men with no missing data, all risk estimates were very similar to the main results (data not shown).

Interactions in Relation to All-Cause Mortality

The interactive effects of aerobic fitness and muscular strength on all-cause mortality are shown in Table 3. The combination of low aerobic fitness and low muscular strength was associated with highest mortality, which was 2-fold relative to men with high aerobic fitness and high muscular strength (adjusted HR, 2.01; 95% CI, 1.93–2.08; $P<0.001$; absolute mortality rates per 100,000 person-years, 247.2 vs. 73.8). Low aerobic fitness was associated with increased mortality irrespective of muscular strength (HRs 1.41 to 1.86; Table 3, right-most column); whereas low muscular strength was associated with very slightly increased mortality among men with high or medium aerobic fitness, and 1.4-fold mortality among those with low aerobic fitness (lower part of Table 3: “HRs for low muscular strength within strata of aerobic fitness”). There was a positive interaction between low aerobic fitness and low (or medium) muscular strength on both the additive and multiplicative scale (i.e., their combined effect exceeded the sum or product of their separate effects; $P<0.001$). Figure 1 shows the probability of premature death from any cause among men at the 25th, 50th, and

75th percentiles of muscular strength across the full distribution of aerobic fitness, after adjusting for BMI and other covariates. The non-parallel curves, particularly at the lower range of aerobic fitness, reflect a positive interaction.

Low aerobic fitness and obesity had no interactions in relation to all-cause mortality (eTable 1 and eFigure 1). Low muscular strength and obesity had a negative interaction on both the additive and multiplicative scale in relation to all-cause mortality (i.e., their combined effect was less than the sum or product of their separate effects; eTable 2 and eFigure 2). The presence of all 3 risk factors (low aerobic fitness, low muscular strength, and obesity) was associated with a 2.4-fold all-cause mortality (adjusted HR, 2.42; 95% CI, 2.05 to 2.86; $P<0.001$; based on 147 deaths among men with all 3 risk factors; eTable 3).

Interactions in Relation to CVD Mortality

A similar pattern was seen for these exposures in relation to CVD mortality. The combination of low aerobic fitness and low muscular strength was associated with highest (2.6-fold) CVD mortality, relative to men with high aerobic fitness and high muscular strength (absolute CVD mortality rates per 100,000 person-years, 43.9 vs. 8.3). These factors had a positive interaction on the additive ($P<0.001$) but not multiplicative ($P=0.12$) scale (eTable 4).

Low aerobic fitness and obesity had a weakly positive additive interaction in relation to CVD mortality ($P=0.04$; eTable 5). The combination of low aerobic fitness and obesity was associated with >5-fold CVD mortality, relative to men with high aerobic fitness and normal BMI (adjusted HR, 5.63; 95% CI, 4.83 to 6.56; $P<0.001$; absolute CVD mortality rates per 100,000 person-years, 105.3 vs. 6.5; eTable 5). Low muscular strength and obesity had no interactions in relation to CVD mortality (eTable 6). The presence of all 3 risk factors (low aerobic fitness, low muscular strength, and obesity) was associated with a nearly 7-fold CVD mortality (adjusted HR, 6.97; 95% CI, 5.18 to 9.36; $P<0.001$; based on 51 CVD deaths among men with all 3 risk factors; eTable 7).

DISCUSSION

Interactive Effects on All-Cause Mortality

In this large national cohort study, low aerobic fitness, low muscular strength, and obesity at age 18 were independently associated with higher all-cause mortality in adulthood, after adjusting for each other, family history of CVD, and socioeconomic factors. Either low aerobic fitness or low muscular strength was associated with increased mortality even among men with normal BMI. Furthermore, these factors had a positive additive and multiplicative interaction (i.e., their combined effect on mortality exceeded the sum or product of their separate effects).

To our knowledge, this is the first study to examine not only the independent effects of these exposures on mortality, but also additive and multiplicative interactions. Additive interactions are often unexamined despite being more informative about public health impact.^{31, 32} Previous studies have reported similar main effects of aerobic fitness,^{9–11} physical inactivity,^{5, 6} or BMI¹⁵ on mortality. Most have suggested that high aerobic fitness

is associated with lower mortality irrespective of BMI level.^{9–11} Fewer studies have examined muscular strength in relation to mortality,^{12–14} and to our knowledge none has examined its potential interaction with aerobic fitness. The present study reports not only important independent effects of these factors at age 18 on mortality in adulthood, but strong additive and multiplicative interactions between low aerobic fitness and muscular strength. The additive interaction indicates that low aerobic fitness accounted for more deaths among men with low (or medium) vs. high muscular strength. If the observed associations are causal, they imply that preventive interventions should begin early in life and include not only weight control but both aerobic fitness and muscular strength, even among persons with normal BMI. Furthermore, improvements in aerobic fitness would be expected to have the greatest public health impact among those with low muscular strength.

Interactive Effects on CVD Mortality

Similar relationships but stronger in magnitude were found for CVD mortality. Men with all 3 of the study exposures (obesity and lowest tertile of aerobic fitness and muscular strength) had a nearly 7-fold CVD mortality. These exposures have previously been associated with several underlying causes of CVD in this cohort, including type 2 diabetes,¹⁶ hypertension,¹⁷ stroke,¹⁸ and ischemic heart disease (In Press). These common conditions are major contributors to shortened life expectancy in this population and worldwide, and are emphasized by the UN as important threats to global health.³³

These findings underscore the need to promote physical fitness more proactively and consistently throughout the health care system.³⁴ Physical exercise is an essential first-line treatment for most chronic diseases³⁵ and plays a key role in reducing health care expenditures.³⁶ Brief counseling on physical exercise has been shown to be efficient, clinically effective, and cost-effective, yet remains under-utilized in clinical practice.³⁴ Prescribed interventions should include not only weight control and aerobic exercise but muscular strength training, which is independently linked with better cardiovascular prognosis and survival.³⁷

Strengths and Limitations

Strengths of this study include its large national cohort design with prospective ascertainment of aerobic fitness, muscular strength, and BMI. The national cohort design prevented selection bias, and the use of objectively measured exposures prevented bias that may result from self-reporting. Well-validated measures of aerobic fitness and muscular strength were examined that are likely better indicators of CVD risk and prognosis than physical activity.^{38, 39} The analyses were adjusted for other common risk factors, including family history and both individual and neighborhood-level socioeconomic factors, which also were prospectively ascertained and not self-reported.

Limitations included the measurement of aerobic fitness, muscular strength, and BMI at only one age (18 years), which prevented examination of changes in these factors over time. Information was lacking on smoking, which is potentially related to the exposures of interest (particularly aerobic fitness) as well as mortality. However, aerobic fitness (VO₂ max) has been reported to be only 7% lower in 18-year-old male smokers compared with non-

smokers⁴⁰; thus smoking is unlikely to account for more than a small proportion of the observed association between aerobic fitness and mortality. Other potentially important confounders or mediators such as alcohol use, chronic diseases, and medications were not examined. Because this study was based on Swedish military conscripts, the cohort consisted entirely of men, whose median attained age at the end of follow-up was 47 years (maximum 62). Other studies will be needed to examine these relationships in women and with additional follow-up to older ages.

CONCLUSIONS

In this large national cohort study, low aerobic fitness, low muscular strength, and obesity at age 18 were independently associated with increased mortality in adulthood, with interactive effects between aerobic fitness and muscular strength. These findings suggest that these early-life factors may contribute to premature mortality in adulthood. If causal, they imply that preventive interventions should begin early in life and include not only weight control but both aerobic fitness and muscular strength, even among persons with normal BMI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Probability of premature death from any cause by aerobic fitness and muscular strength at age 18 years (median attained age 47 years, maximum 62 years), adjusted for BMI and other covariates.

Table 1

Mortality rates by aerobic fitness, muscular strength, BMI, and other potential risk factors.

Risk Factor	Still Living	Died from Any Cause		Died from CVD	
	n (%)	n (%)	Rate ^a	n (%)	Rate ^a
Total	1,483,135 (100.0)	64,343 (100.0)	146.0	10,381 (100.0)	23.7
Aerobic fitness (tertiles)					
Low	474,707 (32.0)	36,643 (57.0)	218.0	6,536 (63.0)	39.2
Medium	501,349 (33.8)	19,198 (29.8)	127.0	2,923 (28.2)	19.4
High	507,079 (34.2)	8,502 (13.2)	68.7	922 (8.9)	7.7
Muscular strength (tertiles)					
Low	486,328 (32.8)	24,597 (38.2)	175.4	3,953 (38.1)	28.5
Medium	501,357 (33.8)	22,195 (34.5)	142.5	3,730 (35.9)	24.1
High	495,450 (33.4)	17,551 (27.3)	121.5	2,698 (26.0)	18.8
BMI					
Normal	1,368,478 (92.3)	59,037 (91.8)	144.4	9,112 (87.8)	22.4
Overweight	81,255 (5.5)	3,413 (5.3)	150.9	744 (7.2)	33.1
Obese	33,402 (2.3)	1,893 (2.9)	208.0	525 (5.1)	57.8
Height (cm)					
<175 (5 ft. 9 in.)	331,535 (22.4)	15,340 (23.8)	154.6	2,405 (23.2)	24.4
175–184	873,645 (58.9)	40,310 (62.7)	154.0	6,579 (63.4)	25.3
185 (6 ft. 1 in.)	277,955 (18.7)	8,693 (13.5)	109.4	1,397 (13.4)	17.6
Weight (kg)					
<60 (132 lbs.)	182,713 (12.3)	9,051 (14.1)	157.8	1,265 (12.2)	22.2
60–79	1,101,126 (74.2)	47,658 (74.1)	145.2	7,461 (71.9)	22.9
80 (176 lbs.)	199,296 (13.4)	7,634 (11.8)	138.8	1,655 (15.9)	30.2
Education (years)					
<12	212,632 (14.3)	24,212 (37.6)	334.2	3,703 (35.7)	51.6
12–14	656,222 (44.3)	27,405 (42.6)	144.0	4,375 (42.1)	23.1
15	614,281 (41.4)	12,726 (19.8)	71.9	2,303 (22.2)	13.1
Neighborhood SES					

Risk Factor	Still Living	Died from Any Cause		Died from CVD	
		n (%)	Rate ^a	n (%)	Rate ^a
Low	227,045 (15.3)	12,349 (19.2)	177.5	1,938 (18.7)	27.9
Medium	977,583 (65.9)	44,652 (69.4)	151.5	7,426 (71.5)	25.4
High	278,507 (18.8)	7,342 (11.4)	96.3	1,017 (9.8)	13.4
Family history of CVD					
No	522,100 (35.2)	17,148 (26.7)	123.9	2,185 (21.0)	15.8
Yes	961,035 (64.8)	47,195 (73.3)	156.2	8,196 (79.0)	27.4

^a Mortality rate per 100,000 person-years.

BMI = body mass index, CVD = cardiovascular disease, SES = socioeconomic status.

Table 2

Associations between aerobic fitness, muscular strength, BMI, or other risk factors and mortality.

Risk Factor	All-Cause Mortality						CVD Mortality					
	Unadjusted			Adjusted ^a			Unadjusted			Adjusted ^a		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Aerobic fitness (tertiles)												
Low	2.13	2.08, 2.19	<0.001	1.58	1.53, 1.63	<0.001	2.57	2.39, 2.76	<0.001	1.81	1.67, 1.96	<0.001
Medium	1.39	1.36, 1.43	<0.001	1.22	1.19, 1.25	<0.001	1.54	1.42, 1.66	<0.001	1.26	1.16, 1.36	<0.001
High	1.00			1.00			1.00			1.00		
Per 100 Watts (trend test)	0.48	0.47, 0.49	<0.001	0.55	0.54, 0.57	<0.001	0.42	0.40, 0.44	<0.001	0.46	0.44, 0.49	<0.001
Muscular strength (tertiles)												
Low	1.38	1.35, 1.41	<0.001	1.27	1.24, 1.30	<0.001	1.42	1.35, 1.49	<0.001	1.43	1.36, 1.51	<0.001
Medium	1.10	1.08, 1.12	<0.001	1.01	0.99, 1.03	0.29	1.15	1.09, 1.20	<0.001	1.10	1.04, 1.16	<0.001
High	1.00			1.00			1.00			1.00		
Per 1000 Newtons (trend test)	0.70	0.69, 0.71	<0.001	0.73	0.71, 0.75	<0.001	0.63	0.59, 0.67	<0.001	0.58	0.55, 0.62	<0.001
BMI												
Normal	1.00			1.00			1.00			1.00		
Overweight	1.13	1.10, 1.17	<0.001	1.17	1.13, 1.22	<0.001	1.70	1.57, 1.83	<0.001	1.90	1.76, 2.05	<0.001
Obese	1.63	1.56, 1.71	<0.001	1.58	1.51, 1.66	<0.001	3.22	2.95, 3.52	<0.001	3.42	3.13, 3.75	<0.001
Per 1 BMI unit (trend test)	1.01	1.01, 1.02	<0.001	1.03	1.02, 1.04	<0.001	1.06	1.05, 1.07	<0.001	1.08	1.07, 1.09	<0.001
Height (cm)												
<175	0.99	0.97, 1.01	0.19	0.97	0.95, 0.99	0.002	0.95	0.90, 0.99	0.03	1.02	0.97, 1.07	0.53
175–184	1.00			1.00			1.00			1.00		
185	0.73	0.71, 0.75	<0.001	0.87	0.85, 0.89	<0.001	0.73	0.69, 0.77	<0.001	0.80	0.76, 0.85	<0.001
Per 5 cm (trend test)	0.92	0.91, 0.93	<0.001	0.96	0.95, 0.97	<0.001	0.92	0.91, 0.94	<0.001	0.91	0.90, 0.93	<0.001
Weight (kg)												
<60	1.01	0.98, 1.03	0.66	0.79	0.77, 0.81	<0.001	0.87	0.82, 0.92	<0.001	0.63	0.59, 0.68	<0.001
60–79	1.00			1.00			1.00			1.00		
80	1.04	1.01, 1.06	0.003	1.21	1.18, 1.24	<0.001	1.52	1.44, 1.60	<0.001	2.01	1.90, 2.13	<0.001
Per 5 kg (trend test)	1.01	1.01, 1.02	<0.001	1.06	1.05, 1.07	<0.001	1.12	1.11, 1.13	<0.001	1.18	1.17, 1.19	<0.001

Risk Factor	All-Cause Mortality						CVD Mortality					
	Unadjusted			Adjusted ^a			Unadjusted			Adjusted ^a		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Education (years)												
<12	2.03	1.99, 2.06	<0.001	1.89	1.85, 1.92	<0.001	1.80	1.72, 1.88	<0.001	1.60	1.53, 1.67	<0.001
12-14	1.00			1.00			1.00			1.00		
15	0.48	0.47, 0.49	<0.001	0.51	0.50, 0.52	<0.001	0.53	0.51, 0.56	<0.001	0.59	0.56, 0.62	<0.001
Per higher category (trend)	0.49	0.48, 0.50	<0.001	0.52	0.51, 0.53	<0.001	0.55	0.53, 0.56	<0.001	0.61	0.59, 0.62	<0.001
Neighborhood SES												
Low	1.12	1.10, 1.14	<0.001	1.08	1.06, 1.10	<0.001	1.03	0.98, 1.08	0.26	1.01	0.96, 1.06	0.72
Medium	1.00			1.00			1.00			1.00		
High	0.69	0.67, 0.70	<0.001	0.88	0.86, 0.90	<0.001	0.60	0.57, 0.64	<0.001	0.78	0.73, 0.83	<0.001
Per higher category (trend)	0.80	0.79, 0.81	<0.001	0.91	0.89, 0.92	<0.001	0.80	0.78, 0.83	<0.001	0.90	0.87, 0.93	<0.001
Family history of CVD												
No	1.00			1.00			1.00			1.00		
Yes	1.09	1.07, 1.11	<0.001	1.00	0.98, 1.02	0.97	1.33	1.27, 1.40	<0.001	1.20	1.15, 1.26	<0.001

Note: Boldface indicates statistical significance ($p < 0.05$).

^aThe model included year of military conscription examination, aerobic fitness, muscular strength, BMI, education, neighborhood SES, and family history of CVD. Height and weight were modeled simultaneously as an alternative to BMI in a separate model. The reference category for all variables is indicated by an HR of 1.00.

BMI = body mass index, CVD = cardiovascular disease, HR = hazard ratio, SES = socioeconomic status.

Table 3
Interactions between aerobic fitness and muscular strength in relation to all-cause mortality.^a

Muscular strength (tertiles)	Aerobic fitness (tertiles)				HRs for medium aerobic fitness within strata of muscular strength	HRs for low aerobic fitness within strata of muscular strength
	High	Medium	Low			
	Rate (no. deaths) ^b	Rate (no. deaths) ^b	Rate (no. deaths) ^b	Rate (no. deaths) ^b	HR (95% CI)	HR (95% CI)
High	73.8 (4,541)	136.7 (7,482)	195.3 (5,528)	1.41 (1.35, 1.47); P<0.001	1.21 (1.17, 1.26); P<0.001	1.21 (1.17, 1.26); P<0.001
Medium	64.9 (2,241)	122.8 (6,484)	196.9 (13,470)	1.52 (1.47, 1.58); P<0.001	1.22 (1.18, 1.27); P<0.001	1.27 (1.21, 1.34); P<0.001
Low	68.8 (1,720)	119.9 (5,232)	247.2 (17,645)	2.01 (1.93, 2.08); P<0.001	1.37 (1.32, 1.43); P<0.001	1.27 (1.20, 1.34); P<0.001
HRs (95% CI) for medium muscular strength within strata of aerobic fitness	0.96 (0.91, 1.01); P=0.11	1.01 (0.98, 1.04); P=0.60	1.08 (1.04, 1.11); P<0.001			
HRs (95% CI) for low muscular strength within strata of aerobic fitness	1.08 (1.02, 1.14); P=0.008	1.13 (1.09, 1.18); P<0.001	1.42 (1.38, 1.47); P<0.001			
Interaction on additive scale for low vs. high tertiles: RERI (95% CI)			0.52 (0.44, 0.59); P<0.001			
Interaction on multiplicative scale for low vs. high tertiles: Ratio of HRs (95% CI)			1.32 (1.23, 1.40); P<0.001			

Note: Boldface indicates statistical significance ($p<0.05$).

^aHRs are adjusted for year of military conscription examination, BMI, education, neighborhood SES, and family history of CVD.

^bMortality rate per 100,000 person-years, and total number of deaths.

BMI = body mass index, CVD = cardiovascular disease, HR = hazard ratio, RERI = relative excess risk due to interaction, SES = socioeconomic status.