Independent and joint associations of weightlifting and aerobic activity with all-cause, cardiovascular disease and cancer mortality in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial

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ABSTRACT

Objectives Both aerobic moderate to vigorous physical activity (MVPA) and muscle-strengthening exercise (MSE) are recommended, but the mortality benefits of weightlifting, a specific type of MSE, are limited.

Methods In the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, we used Cox proportional hazards regression to calculate hazard ratios (HRs) and 95% CIs for the associations between weightlifting and mortality, adjusting for demographics, lifestyle and behavioural risk factors. The sample included 99 713 adults who completed the follow-up questionnaire that assessed weightlifting who were subsequently followed up through 2016 to determine mortality (median 9, IQR 7.6–10.6 years).

Results Mean age at the follow-up questionnaire was 71.3 (IQR 66–76) years, 52.6% female, with mean body mass index of 27.8 (SD 4.9) kg/m^2. Weightlifting was associated with a 9% lower risk of all-cause mortality (HR=0.91 (95% CI 0.88 to 0.94)) and CVD mortality (0.91 (95% CI 0.86 to 0.97)) after adjusting for MVPA. Joint models revealed that adults who met aerobic MVPA recommendations but did not weightlift had a 32% lower all-cause mortality risk (HR=0.68 (95% CI 0.65 to 0.70)), while those who also reported weightlifting 1–2 times/week had a 41% lower risk (HR=0.59 (95% CI 0.54 to 0.64)), both compared with adults reporting no aerobic MVPA or weightlifting. Without adjustment for MVPA, weightlifting was associated with lower cancer mortality (HR=0.85 (95% CI 0.80 to 0.91)).

Conclusion Weightlifting and MVPA were associated with a lower risk of all-cause and CVD mortality, but not cancer mortality. Adults who met recommended amounts of both types of exercise appeared to gain additional benefit.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Aerobic activity has consistently been shown to be associated with lower mortality, but the relationship with weightlifting behaviour independently and together with moderate to vigorous physical activity (MVPA) on mortality outcomes is less understood.

WHAT THIS STUDY ADDS

⇒ MVPA-adjusted models revealed inverse trends between increasing categories of weightlifting and decreased risk of all-cause, cardiovascular disease (CVD) and cancer mortality (all p for trend <0.01).
⇒ Weightlifting in older adults was independently associated with lower all-cause and CVD mortality, and only associated with cancer mortality without adjustment for MVPA.
⇒ Among adults reporting no aerobic MVPA, any weightlifting was associated with 9–22% lower all-cause mortality.
⇒ Lower all-cause mortality was observed in older adults doing either aerobic or weightlifting exercise, but the lowest mortality risk was seen among adults who reported both types of exercise.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our finding that mortality risk appeared to be lowest for those who participated in both types of exercise provides strong support for current recommendations to engage in both aerobic and muscle-strengthening activities.
⇒ The weightlifting-associated mortality benefit shown here provides initial evidence to clinicians and other health professionals that older adults would probably benefit from adding weightlifting exercises to their physical activity routines.

INTRODUCTION

Both aerobic and muscle strengthening physical activities are recommended for all adults to maximise health and increase longevity.[1] [1] Aerobic physical activity is voluntary movement that increases energy expenditure above baseline levels and can be completed within the domains of transportation, leisure and recreation, or household activities of daily living. Muscle-strengthening exercise (MSE) is defined as activities that increase or maintain muscular strength and endurance, balance or body composition.[2] Weightlifting, whether using free weights or machines, is one of the most common types of MSE and has high recall validity as a self-reported exposure.[3] The 2018 Physical Activity Guidelines recommend that all adults complete at least 150–300 min/week of moderate-intensity aerobic physical activity, or 75–150 min/week of vigorous intensity aerobic activity or an equal combination of the two—commonly abbreviated as MVPA (moderate to vigorous physical activity). Importantly, all adults are also recommended to complete at least 2 days per week of MSE for all major muscle groups.[1 4] Recent prevalence estimates from the Behavioural Risk Factor Surveillance Survey indicate that approximately 65% of Americans met aerobic MVPA guidelines in 2015–2016.[5 6] Data from the National Health Interview Survey indicate approximately 28% of respondents reported sufficient MSE, and 24% of respondents met both the aerobic and MSE guidelines.[7]

Although both aerobic MVPA and MSE are recommended for health benefits, most research has focused on aerobic MVPA.[2] Most evidence for the health benefits of MSE come from clinical studies with specific populations and short-term outcomes rather than from prospective observational studies with longer follow-up. Aerobic MVPA is consistently linked to lower mortality[8]; however, few observational studies have examined the association between MSE and mortality. Only 10 prospective epidemiologic studies have examined MSE and mortality, yielding a mean risk reduction for any MSE (compared with none) of 20–25% for all-cause mortality.[9 10] A limitation of previous studies of MSE and mortality include the use of aggregated exposures (eg, sessions/week, hours/week), which are often dichotomised into meeting/not meeting guidelines. This dichotomy, while sometimes useful, may obscure underlying dose–response associations between MSE and mortality. As such, the dose–response relationship between MSE and mortality has yet to be fully characterised including more detailed options of weightlifting frequency. Furthermore, the specific benefits of weightlifting on mortality are insufficiently studied, and they are important to examine with the popularity and specificity of weightlifting.

Given the few prospective observational studies and heterogenous assessments of MSE, the evidence base for the impact of weightlifting on mortality is quite limited. This study aimed to examine the relationship between weightlifting and all-cause mortality, evaluating both independent and joint associations with aerobic MVPA. We also included analyses of cardiovascular disease (CVD) and cancer mortality to examine common causes of death. We hypothesised that weightlifting would be associated with lower mortality.

METHODS

Study population and patient involvement

The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial was initiated in 1993 and includes 154 897 men and women aged 55–74 who were randomised into an intervention screening or control arm across 10 different cancer centres in the United States, including University of Colorado Health Sciences Centre, Lombardi Cancer Research Centre of Georgetown University, Pacific Health Research Institute, Henry Ford Health System, University of Minnesota School of Public Health/Virginia L Piper Cancer Institute, Washington University School of Medicine, University of Pittsburgh/Pittsburgh Cancer Institute/Magee-Women's Hospital, University of Utah School of Medicine, Marshfield (Wisconsin) Medical Research and Education Foundation, and the University of Alabama at Birmingham. In 2006 (13 years into the trial) follow-up questionnaires were sent to 104 002 participants. Many of those questions overlapped with the baseline questionnaire; however, the follow-up questionnaire included information not captured at baseline, including weightlifting. Cancer incidence and mortality of the cohort participants is updated regularly, with the most recent outcomes verified through December 2016. Ethical review was completed by National Cancer Institute and each of the 10 study sites. Informed consent was collected from all participants; the full trial details have been described elsewhere.[11] In this prospective cohort study for broad cancer screening, patients were not intimately involved in design or implementation of the trial or of these results.

Exposure assessment for weightlifting and aerobic MVPA

The follow-up questionnaire had a specific prompt on weightlifting, asking if the participant had done any weightlifting in the past 12 months (less than once per month, one to three times per month, one to two times per week, three to six times per week, and seven or more times per week; see online supplemental material 1 for copy of questionnaire). With these provided categorical response options, weightlifting was modelled as an ordinal categorical variable. Participants were not asked about weightlifting duration per session.

The follow-up questionnaire also asked about frequency and duration of both moderate and strenuous intensity physical activity over the past year. Moderate intensity was described as 'activity where you worked up a light sweat or increased your breathing and heart rate to moderately high levels'. Adults reported the average number of days per week of moderate activity, as well as duration in category options of less than 15 min, 16–19 min, 20–29 min, 30–39 min, or 40 min or more. Strenuous activity was described as 'activity strenuous enough to work up a sweat or increase your breathing and heart rate to very high levels' with the same response options as the moderate intensity, reported over the past year. Although the questionnaire used the term 'strenuous' activity, we will use the term vigorous for this investigation as the physiological cues about the intensity (sweating and breathing intensity) are consistent with vigorous intensity definitions, and also, 'vigorous' aligns with the Physical Activity Guidelines for Americans. Using these frequency and duration estimates, four groups were generated based on total minutes of MVPA, including (1) inactive 0 min/week; (2) insufficient aerobic MVPA, 1–149 min/week; (3) meeting guidelines, 150–300 min/week moderate or an equivalent amount of vigorous activity; and (4) highly active, 301 or more min/week of moderate or an equivalent amount of vigorous activity.

Outcome assessment for mortality

Mortality data was collected from annual study update questionnaires, reports from relatives and family members, from their physicians, or via linkage with the National Death Index. Once notification of a death occurred, PLCO screening centres acquired a death certificate. Primary and underlying causes of death were derived, coded and recorded in PLCO databases. We evaluated death from any cause as primary outcome (n=28 477 deaths). Additional outcomes included deaths from CVD (ICD-9 codes based on standard groupings for CVD, codes 200–400 (n=18 472) and cancer deaths (ICD-9 codes 100) (n=16 659). All-cause mortality was the primary outcome, we also included analyses of CVD and cancer mortality to examine associations with the most common causes of death.

Covariates

Demographic and lifestyle covariates were selected from existing literature of mortality and weightlifting associations.[12–15] All covariates were assessed at follow-up unless otherwise specified for time invariant variables (ie, race and ethnicity, education and sex). Questionnaires collected data on demographics, health behaviour, including tobacco and alcohol use, personal health history, as well as self-reported height and weight.

Statistical analysis

The following covariates were selected based on knowledge of the literature and directed acyclic graphs to select potential confounders. Variables included in the final regression model were: age (years); sex (male, female); education (<high school, high school graduate, some college, and ≥college graduate); body mass index (BMI) (<18.5, 18.6–24.9, 25–29.9, 30–34.9, ≥35 kg/m^2), alcohol (g/day, based on quartile distribution); self-reported race and ethnicity (Hispanic, non-Hispanic Black, non-Hispanic White, and all other identities); smoking status (never, former, current); total number of self-reported comorbidities from health history questionnaire (sum of arthritis, diabetes, emphysema, heart attack, hypertension, osteoporosis or stroke). Participants with missing data on physical activity were excluded from analysis (n=4289).

HR and 95% CIs for weightlifting and mortality were estimated using Cox proportional hazards regression with age as our time metric. For weightlifting and mortality risk analyses, those who reported no weightlifting in the last 30 days prior to follow-up questionnaire (non-weightlifters) were the reference group. Participants contributed person-time from completing the follow-up questionnaire until death (event) or the end of follow-up (censored, 2016), whichever came first. We used inverse probability selection weights to account for adults who did not consent to additional follow-up. The proportional hazards assumption was checked using visual inspection of the proportional hazards assumption, with no violations observed in the models for primary weightlifting exposures.

Spearman rank correlation coefficients were calculated across weightlifting and MVPA categories. We considered for main findings, HR and 95% CIs from the multivariate model, which provides information on the association between weightlifting and mortality, independent of confounders and MVPA. Weightlifting was modelled based on response options from the survey (no weightlifting, less than once per month, 1–3 times/month, 1–2 times/week, 3–6 times/week and ≥7 times/week). However, owing to the small number of deaths (n=198) in the highest weightlifting category (≥7 times/week), the top two categories (3–6 times/week and ≥7 times/week) of weightlifting frequency were combined. To estimate the direct (main) effect of weightlifting on mortality, models were run without adjustment for MVPA. Statistical models were also constructed to examine the independent influence of both activities (main effects) and separately, conducted within groups of combined MVPA and weightlifting levels (joint effects). Stratified models were formed for further examination of main effects of weightlifting within aerobic MVPA strata.

Associations between weightlifting and cause-specific mortality (CVD, cancer) were calculated using Fine and Grey competing risks Cox regression.[16] We conducted two sensitivity analyses. The first was an evaluation of the primary weightlifting–mortality associations without adjustment for inverse probability selection weights. Second, to evaluate potential reverse causality, all models were run excluding deaths that occurred within the first 2 years of follow-up.

Effect modification of the association between weightlifting and all-cause mortality by age, sex, smoking, education, race, and BMI categories was evaluated using multiplicative interaction terms, with statistical significance assessed by type III Wald test p value for the cross-product term. All statistical tests were two-sided, and p values of less than 0.05 were considered statistically significant; analyses were performed using SAS 9.4 (Cary, North Carolina, USA).

RESULTS

Demographics

Of the 99 713 adults eligible for the current analysis, 28 477 deaths were observed over an average of 9.6 years of follow-up time. Mean age at the start of follow-up was 71.3 (median 71, IQR 66–76) years, with mean BMI of 27.8 (median 26.6, IQR 23.9–29.7) kg/m^2. Twenty-three percent of adults reported any weightlifting activity at follow-up and 16% of the sample reported weightlifting regularly between one to six times per week. Thirty two percent of the sample was sufficiently active, either meeting (23.6%) or exceeding (8.0%) the aerobic MVPA guidelines. Full demographic characteristics are presented by weightlifting responses in table 1.

Correlation

Spearman rank correlation coefficients between any weightlifting (binary yes/no) and aerobic MVPA categories were 0.28 ($p<0.05$). Correlation between levels of weightlifting categories (frequency as reported) and aerobic MVPA categories were 0.27 ($p<0.05$). Correlations between weightlifting and aerobic MVPA were not substantively different for men (r=0.27, $p<0.05$) or women (r=0.30, $p<0.05$). Cross frequency of MVPA and weightlifting categories are found in table 2.

Weightlifting and aerobic MVPA with and without mutual adjustment

Overall, adults who reported any weightlifting had a 9% lower all-cause mortality risk (HR=0.91 (95% CI 0.88 to 0.94); table 3) after adjustment for aerobic MVPA. Similar lower mortality risks were observed for CVD mortality (HR=0.91 (95% CI 0.86 to 0.97)) but not for cancer mortality. Adults who reported weightlifting 1–2 times/week had 14% lower all-cause mortality. MVPA-adjusted models revealed inverse trends between increasing categories of weightlifting and decreased risk of all-cause, CVD and cancer mortality (all p for trend <0.01). Adults who reported meeting the aerobic guideline had a 32% lower risk (HR=0.68 (5% CI 0.65 to 0.70)) with mutual adjustment for weightlifting. Results presented are for the inverse probability selection weight-adjusted models, and analyses with and without weighted adjustments yielded comparable results. Furthermore, sensitivity testing excluding deaths within the first 2 years did not yield appreciably different point estimates, therefore the results presented here include all deaths in follow-up. Supplemental table 2 in online supplemental material 1 shows further sensitivity testing of sequential modeling of covariates from table 3.

Joint associations with weightlifting and aerobic MVPA

Among non-weightlifters, any level of aerobic MVPA was associated with 24% to 34% lower all-cause mortality (eg, meeting guidelines, HR=0.68 (95% CI 0.65 to 0.70)) with reference group no MVPA and no weightlifting (table 4). Among adults reporting no aerobic MVPA, any weightlifting was associated with 9% to 22% lower mortality (eg, 1–2 times/week, HR=0.80 (95% CI 0.71 to 0.92)). Notably, compared with adults with neither MVPA nor weightlifting, those who reported both types of exercise tended to have lower mortality than with either exercise behaviour alone. For example, adults who reported at least recommended MVPA levels with weightlifting 1–2 times/week

Table 1 Study sample demographics by levels of weightlifting as reported

Demographics	None n=76,428 (76.8%)	Less than 1 times/ month n=1454 (1.5%)	1–3 times/month n=4208 (4.2%)	1–2 times/week n=8441 (8.5%)	3–6 times/week* n=8359 (8.4%)	≥7* times/week n=589 (0.6%)
Age at randomisation	62.3 (5.2)	60.6 (4.8)	60.8 (4.8)	61.1 (4.9)	61.6 (4.9)	63.2 (5.3)
Age at follow-up	71.4 (5.9)	69.5 (5.7)	69.8 (5.6)	70.2 (5.7)	70.8 (5.6)	72.6 (6.2)
No of comorbidities	1.3 (1.2)	1.1 (1.2)	1.1 (1.1)	1.0 (1.1)	1.0 (1.1)	1.2 (1.2)
BMI (kg/m^2)						
<18.5	2956 (3.9%)	56 (3.9%)	147 (3.6%)	312 (3.8%)	312 (3.8%)	34 (5.8%)
18.5–24.9	22 804 (30.4%)	488 (34.0%)	1593 (38.4%)	3509 (42.2%)	3505 (42.6%)	245 (41.9%)
25–29.9	31 391 (41.8%)	635 (44.2%)	1710 (41.2%)	3299 (39.7%)	3235 (39.3%)	211 (36.1%)
30–34.9	12 706 (16.9%)	193 (13.4%)	522 (12.6%)	927 (11.1%)	936 (11.4%)	73 (12.5%)
≥35	5212 (6.9%)	64 (4.5%)	174 (4.2%)	264 (3.2%)	236 (2.9%)	21 (3.6%)
Sex						
Men	35 737 (46.8%)	654 (45.0%)	1938 (46.1%)	3847 (45.6%)	4604 (55.1%)	347 (58.9%)
Women	40 691 (53.2%)	800 (55.0%)	2270 (53.9%)	4594 (54.4%)	3755 (44.9%)	242 (41.1%)
Race						
White	68 447 (91.4%)	1292 (91.0%)	3767 (91.2%)	7644 (92.5%)	7495 (91.3%)	526 (91.3%)
Black	2474 (3.3%)	49 (3.5%)	115 (2.8%)	183 (2.2%)	158 (1.9%)	13 (2.3%)
Hispanic	1073 (1.4%)	26 (1.8%)	73 (1.8%)	115 (1.4%)	175 (2.1%)	15 (2.6%)
Other	2914 (3.9%)	53 (3.7%)	176 (4.3%)	325 (3.9%)	385 (4.7%)	22 (3.8%)
Smoking						
Never	35 309 (46.9%)	652 (45.5%)	1935 (46.7%)	3813 (45.7%)	3649 (44.2%)	292 (50.1%)
Former	544 (7.4%)	63 (4.4%)	183 (4.4%)	308 (3.7%)	323 (3.9%)	22 (3.8%)
Current	34 386 (45.7%)	717 (50.0%)	2023 (48.9%)	4218 (50.6%)	4286 (51.9%)	269 (46.1%)
Alcohol intake						
None	28 (0.1%)	0 (0%)	2 (0.1%)	3 (0.1%)	3 (0.1%)	0 (0%)
<0.2 g/day	8703 (25.6%)	127 (20%)	371 (19.9%)	688 (18.3%)	688 (18.8%)	69 (24.5%)
0.2–1.39 g/day	8388 (24.6%)	143 (22.5%)	422 (22.6%)	774 (20.6%)	793 (21.7%)	69 (25.5%)
1.4–10.7 g/day	8725 (25.6%)	181 (28.5%)	508 (27.3%)	1102 (29.4%)	1009 (27.6%)	61 (22.5%)
>10.7 g/day	8209 (24.1%)	184 (29.0%)	561 (30.1%)	1185 (31.6%)	1170 (31.9%)	72 (26.6%)
Education						
<High school	4445 (5.9%)	19 (1.3%)	82 (2.0%)	161 (2.0%)	226 (2.8%)	39 (6.8%)
High school	18 400 (24.6%)	176 (12.4%)	585 (14.2%)	1113 (13.5%)	1258 (15.4%)	105 (18.3%)
College	26 250 (35.1%)	444 (31.3%)	1345 (32.6%)	2633 (31.9%)	2579 (31.5%)	188 (32.8%)
>College	25 653 (34.3%)	779 (54.9%)	2114 (51.2%)	4346 (52.7%)	4134 (50.4%)	242 (42.2%)
Aerobic MVPA groups						
None (0 min)	27 792 (36.7%)	466 (32.2%)	881 (21.1%)	757 (9.0%)	509 (6.1%)	76 (13.0%)
Some (1–149 min)	27 871 (36.8%)	592 (40.9%)	1923 (46.0%)	3603 (48.9%)	2416 (29.1%)	144 (24.5%)
Meets (150–300 min)	15 173 (20.1%)	326 (22.5%)	1096 (26.2%)	3261 (38.9%)	3553 (42.8%)	171 (29.1%)
Exceeds (>301 min)	4847 (6.4%)	64 (4.4%)	284 (6.8%)	780 (9.3%)	1834 (22.1%)	196 (33.4%)

*For regression analysis, these top two categories of 3–6 times/week and ≥7 times/week were combined owing to the small number of deaths in these categories.
BMI, body mass index; MVPA, moderate–vigorous physical activity.

had 41% to 47% lower risk (eg, meets aerobic and 1–2 times/week, HR=0.59 (0.54 to 0.64)), compared with the common reference group of no aerobic or weightlifting exercise. This finding suggests that the two types of exercise have an additive mortality benefit.

Table 2 Cross frequency of adults within each aerobic physical activity and weightlifting levels

Weightlifting frequency	No MVPA	Some MVPA	Meets MVPA	Exceeds MVPA
Never	27 792 (17.9%) 9918	27 871 (18.0%) 7245	15 173 (9.8%) 3540	4847 (3.1%) 1114
Less than once/month	466 (0.3%) 125	592 (0.4%) 106	326 (0.2%) 59	64 (0.04%) 8
One to three times/ month	881 (0.6%) 247	1923 (1.2%) 381	1096 (0.7%) 197	284 (0.2%) 41
One to two times/ week	757 (0.3%) 226	3603 (1.6%) 780	3261 (2.3%) 579	780 (1.2%) 116
Three to six times/ week	509 (0.3%) 177	2416 (1.6%) 634	3553 (2.3%) 721	1834 (1.2%) 385
≥7 times/week	76 (0.05%) 35	144 (0.09%) 60	171 (0.1%) 52	196 (0.1%) 51

Total number (n) and percent sample (%) presented, with total number of deaths per cell.
MVPA, moderate to vigorous physical activity.

Weightlifting stratified by aerobic MVPA

Stratified analyses are presented as supplemental material (online supplemental material 1). When restricting analyses within strata of aerobic MVPA (none, some, meets, exceeds), inverse all-cause mortality hazard reductions were observed for unit increase of weightlifting (Supplemental table 2, HR=0.98, 0.97, 0.98, 0.95, respectively).

Effect modification

Education, smoking, BMI, race and ethnicity did not significantly modify the associations between weightlifting and all-cause mortality. We did find statistical evidence for heterogeneity by sex, indicating a stronger association of weightlifting and mortality in women (table 5).

DISCUSSION

In this large cancer screening trial, consistent independent and joint weightlifting mortality reductions were observed.

Table 3 Muscle strengthening and aerobic exercise associated with all-cause and cause-specific mortality with and without mutual adjustment (HR and 95% CIs)

		All-cause mortality HR (95% CI)		CVD mortality HR (95% CI)		Cancer mortality HR (95% CI)	
	Deaths (n)	Model A	Model A+MVPA*	Model A	Model A+MVPA	Model A	Model A+MVPA
Weightlifting Yes (vs no)	3835	0.79 (0.76 to 0.81)	0.91 (0.88 to 0.94)	0.76 (0.76 to 0.80)	0.91 (0.86 to 0.97)	0.85 (0.80 to 0.91)	0.96 (0.90 to 1.02)
Weightlifting frequency							
Never	22 086	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Less than once/month	300	0.82 (0.74 to 0.92)	0.84 (0.76 to 0.94)	0.84 (0.70 to 1.03)	0.86 (0.71 to 1.05)	0.88 (0.72 to 1.07)	0.91 (0.75 to 1.11)
One to three times/month	874	0.80 (0.75 to 0.85)	0.85 (0.79 to 0.91)	0.82 (0.73 to 0.92)	0.89 (0.79 to 0.99)	0.80 (0.71 to 0.90)	0.85 (0.75 to 0.96)
One to two times/week	1712	0.76 (0.73 to 0.80)	0.86 (0.82 to 0.91)	0.73 (0.97 to 0.79)	0.85 (0.78 to 0.93)	0.88 (0.81 to 0.96)	0.97 (0.89 to 1.06)
Three to 7+times/week	2123	0.79 (0.75 to 0.82)	0.93 (0.89 to 0.98)	0.76 (0.71 to 0.82)	0.95 (0.88 to 1.03)	0.81 (0.75 to 0.88)	0.93 (0.85 to 1.01)
Per unit increase in weightlifting category		0.93 (0.92 to 0.94)	0.97 (0.96 to 0.98)	0.92 (0.91 to 0.94)	0.97 (0.96 to 0.99)	0.95 (0.93 to 0.96)	0.98 (0.96 to 0.99)
P for trend		<0.0001	<0.0001	<0.0001	0.002	<0.0001	0.03
MVPA groups							
None	11 203		1.00 (ref)		1.00 (ref)		1.00 (ref)
Some	9574		0.76 (0.74 to 0.78)		0.73 (0.69 to 0.77)		0.78 (0.74 to 0.82)
Meets	5365		0.68 (0.65 to 0.70)		0.65 (0.62 to 0.69)		0.70 (0.66 to 0.75)
Exceeds	1788		0.66 (0.63 to 0.70)		0.65 (0.60 to 0.71)		0.70 (0.64 to 0.77)

Weighted estimates to the whole cohort are presented.
Model A adjusted for age at follow-up questionnaire, sex, education, smoking, alcohol intake, current body mass index category, race and number of comorbidities.
*These results include covariates from model A plus each group of aerobic activity guidelines (inactive 0 min of activity, insufficient 1–149 min of activity, meets guidelines 150–300 min of activity, highly active >301 minutes of activity).
CVD, cardiovascular disease; MVPA, moderate–vigorous physical activity.

Weightlifting and aerobic MVPA were both independently associated with lower all-cause and CVD mortality. However, lower risk was not apparent for cancer mortality. Observed associations between weightlifting and all-cause mortality did not appear to vary by the participant factors we examined other than sex. We found statistical evidence that the weightlifting all-cause mortality association was stronger in women. Joint models revealed 32% lower all-cause mortality with meeting aerobic MVPA guidelines without any weightlifting; conversely, weightlifting 1–2 times/week was associated with 20% lower all-cause mortality without any aerobic MVPA. Reporting both MVPA and weightlifting together were associated with a 41% lower all-cause mortality. In joint models, our data show that weightlifting with most levels of aerobic MVPA was associated with 15–47% lower all-cause mortality.

We focused on weightlifting, a type of MSE, but 10 prospective observational studies have examined the MSE–mortality association. Five publications were able to categorise respondents into those meeting MSE guidelines of at least two sessions/week, often revealing a lower mortality with MSE.[17–21] Other studies were able to dichotomise into those who report any (vs those who do not) MSE,[22 23] and other studies used total duration (instead of frequency) of muscle-strengthening activity.[24–26] Prospective investigations using duration exposures (eg, hours/week) for MSE are difficult to translate into meeting the physical activity guidelines since those are delivered in session frequency, not duration. Our results are specific to weightlifting and may not fully capture all MSE, which prevented us from categorising our results as meeting MSE guidelines. Furthermore, the questionnaire response options from the PLCO cohort do not map exactly the two sessions per week option (ie, options of 1–2 sessions/week and 3–6 sessions/week). Of previously published studies, none exclusively used weightlifting as the exposure. Six studies[18 19 21 24–26] used prompts on weightlifting with strength training as MSE assessments, whereas four studies[17 20 22 23] used a broader definition of muscle-strengthening activities or strength-promoting exercise. Our study adds knowledge on weightlifting exercise, but we recognise that it is not the only modality of MSE, which might also include calisthenics, Pilates and plyometrics. Our findings support the joint mortality benefits of MSE (via weightlifting) along with aerobic activity, in amounts that approximate current physical activity guidelines,[1 4] although we were unable to explicitly test the two sessions/week recommendation directly.

There are several potential pathways by which weightlifting could be associated with mortality, including the influence of

Table 4 Joint models of aerobic activity and weightlifting for all-cause mortality risk

		Aerobic activity			
		No MVPA	Some MVPA	Meets MVPA	Exceeds MVPA
Weightlifting	None	1.00 reference	0.76 (0.73 to 0.78)	0.68 (0.65 to 0.70)	0.66 (0.62 to 0.70)
	<1 time/month	0.78 (0.66 to 0.93)	0.65 (0.54 to 0.78)	0.67 (0.52 to 0.85)	0.51 (0.27 to 0.99)
	1–3 times/month	0.85 (0.75 to 0.97)	0.65 (0.59 to 0.72)	0.56 (0.49 to 0.62)	0.55 (0.41 to 0.74)
	1–2 times/week	0.80 (0.71 to 0.92)	0.67 (0.63 to 0.72)	0.59 (0.54 to 0.64)	0.53 (0.44 to 0.63)
	3–>7 times/week	0.91 (0.80 to 1.04)	0.73 (0.68 to 0.79)	0.61 (0.57 to 0.65)	0.63 (0.57 to 0.69)

Models adjusted for age at questionnaire (where weightlifting was assessed), sex, education, smoking, alcohol intake, current body mass index, race, and number of comorbidities. Aerobic moderate to vigorous physical activity (MVPA) categories are none (0 min per week), some (1–149 min/week), meets (150–300 min/week) and exceeds (>301 min/week). P value for the weightlifting* aerobic activity term was 0.69.
HR and 95% CIs are presented, weighted estimates to the whole cohort.

Table 5 Effect modification of the weightlifting (yes, no) all-cause mortality association by strata of relevant covariates*

Covariate stratification HR (95% CI)	P value interaction term
Age	
Under 71 years: 1.08 (1.07 to 1.09) Older than, including 71: 1.11 (1.11 to 1.12)	0.85
Sex	
Men: 0.96 (0.90 to 1.03) Women: 0.82 (0.75 to 0.90)	0.001
Smoking	
Never: 0.88 (0.91 to 0.95) Current: 0.95 (0.89 to 1.03)	0.50
Self-reported racial identity	
White: 0.91 (0.86 to 0.96) Non-White: 0.81 (0.65 to 1.02)	0.06
Education	
No college: 0.91 (0.84 to 0.98) College plus: 0.93 (0.89 to 0.97)	0.79
Body mass index	
<24.9 kg/m^2: 0.77 (0.50 to 1.12) 25 to 29.9 kg/m^2: 0.97 (0.90 to 1.06) 30.0+kg/m^2: 0.84 (0.73 to 0.97)	0.31

*HR and 95% CIs are presented, weighted estimates to the whole cohort.

weightlifting on body composition, leading to more lean mass and thus improved function.[27] Total lean mass is also independently associated with lower mortality risk, with studies examining the muscle's role in both endocrine and paracrine functions, and how that can influence health.[28] Finally, weightlifting, in particular, could be a socially related behaviour in that those who weightlift participate in social networks, assuming that this behaviour is done in a gym with others.[29] However, it is important to acknowledge that consistent weightlifting is associated with other improvements, including functional strength gains and improved musculoskeletal health.[30] These are hypotheses as due to the nature of this study we cannot fully examine these potential relationships.

Our study has some limitations. It is a single observational study which cannot alone establish causality but nevertheless adds value to the evidence base. There may be measurement error associated with recall of weightlifting behaviour; however, self-reported recall is an appropriate assessment technique for prospective observational studies.[3] Our study has a single-time assessment of a time-varying behaviour, which is a limitation. We did not have repeated measures to capture changes in behaviour over time, thus serial measurement with longer follow-up time would be informative in future studies. This analysis was limited by the lack of specific details about weightlifting that could be informative for a dose–response investigation, including training intensity, training load, volume (set and repetitions), and for how long the adult has been participating in weightlifting. Given the exposure categories provided we are unable to perfectly harmonise weightlifting frequency of at least 2 days per week from the Physical Activity Guidelines. We had limited observations for the highest level of weightlifting frequency (≥7 days/week) and mortality, therefore we combined categories to ensure we had appropriate statistical power. Finally, this study might not be generalisable to other racial and ethnic groups or younger study populations given that the PLCO study population was predominantly non-Hispanic White with mean age of 71 years at the follow-up questionnaire assessment.

Strengths of our investigation include the size of the population and the unique exposure and frequency assessment of weightlifting. The cohort updates the cancer incidence and mortality data regularly, which allows for cancer mortality for independent and joint associations of weightlifting and MVPA. Our analysis used inverse probability selection weights to combat losses to follow-up, including those who did not consent to the follow-up questionnaire. Our sensitivity analyses restricted to those who died after the first 2 years of follow-up did not change our results, which lowers the potential for confounding by poor health status. Finally, our results are generalisable to a primarily non-Hispanic White, older adult population, demonstrating the beneficial weightlifting–mortality association.

In conclusion, participants who took part in weightlifting had a lower risk of mortality after accounting for aerobic MVPA, and the combination of weightlifting and aerobic MVPA provided more benefit than either type of exercise alone. Our study provides support for weightlifting as a health behaviour associated with longevity for older adults at varying levels of aerobic MVPA participation. Importantly, these findings support meeting both the aerobic MVPA and muscle strengthening (including weightlifting) recommendations, especially targeting older adults who do not weightlift but may be currently aerobically active to maximise health and mortality outcomes. Future studies are needed to more clearly define the MSE–mortality dose–response relationship and to better understand if the associations observed in this report hold in diverse populations. Additionally, future work should include more precise estimates of MSE (including weightlifting) to include both frequency, intensity and duration estimates to improve our understanding of the dose–response relationship for mortality and other health-related outcomes.

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Ethics approval This study involves human participants and the PLCO Cancer Screening Trial was approved by the institutional review board at the National Cancer Institute and at the 10 participating study centers including University of Colorado Health Sciences Center, Lombardi Cancer Research Center of Georgetown University, Pacific Health Research Institute, Henry Ford Health System, University of Minnesota School of Public Health/Virginia L. Piper Cancer Institute, Washington University School of Medicine, University of Pittsburgh/Pittsburgh Cancer Institute/Magee-Women's Hospital, University of Utah School of Medicine, Marshfield (Wisconsin) Medical Research and Education Foundation, and the University of Alabama at Birmingham. Participants gave informed consent to participate in the study before taking part.

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