Original research

Lifetime high occupational physical activity and total and cause-specific mortality among 320 000 adults in the NIH-AARP study: a cohort study

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ABSTRACT

Objectives We examined the associations of history and duration in high occupational physical activity (OPA) with long-term total and cause-specific mortality.

Methods The sample included 322 126 participants (135 254 women) from the National Institutes of Health–AARP Diet and Health Study, established in 1995–1996. History and duration in high OPA were reported by participants. All-cause, cardiovascular, cancer and other cause mortality records available through 31 December 2011.

Results The prevalence of high OPA was 52.1% in men and 16.1% in women. During 13.6 years (SD, 3.3) of follow-up, 73 563 participants (25 219 women) died. In age-adjusted models, the risk of death was higher among men (HR 1.14, 95% CI 1.12 to 1.16) and women (HR 1.22, 95% CI 1.18 to 1.26) with a history of high OPA. However, these associations were substantially attenuated in women (HR 1.04, 95% CI 1.00 to 1.07, an 81.8% attenuation) and eliminated in men (HR 1.02, 95% CI 0.99 to 1.04, 85.7% attenuation) after multivariable adjustments. Similar important attenuation results were found when examining duration in high OPA, as well as using cause-specific deaths as the outcomes. Educational attainment and smoking patterns were the main contributors in the excess mortality among people working in highly physically active jobs in both men and women.

Conclusion Participating in high OPA was not consistently associated with a higher mortality risk, after adjustments for education and smoking factors. Workers in high OPA should be aware that they might not be getting all well-known health benefits of being physically active if they are only very active at work.

INTRODUCTION

Although there is convincing evidence that physical activity can improve chances of survival, much of this evidence is limited to studies of physical activity that takes place during leisure time.[1] Whether these well-known health benefits also hold for occupational physical activity (OPA)—activity taking place as a part of work—has recently been questioned.[2] In contrast with earlier studies by Morris et al[3] and by Paffenbarger et al,[4] new evidence indicates that high OPA (eg, carrying heavy loads, using heavy tools, walking long distances,

Key messages

What is already known about this subject?
► Despite early studies in 50s and 70s, two systematic reviews with meta-analysis in 2012 and 2019, and an umbrella review in 2020 it is still unclear whether high occupational physical activity is associated with lower survival.
► There is a need to provide clearer evidence on the role of high occupational physical activity on mortality, taken into account previous study limitations.

What are the new findings?
► In this study of ~320 000 adults and more than 73 000 deaths, history and duration in high occupational physical activity were associated with a higher mortality risk in both men and women in unadjusted models.
► After adjusting for potential measured confounders, mainly educational level and smoking, the positive associations between occupational physical activity and mortality were in most instances eliminated.
► These findings do not support that daily physical activity undertaken in the work domain provides survival benefits, as might be understood from statements in the current physical activity guidelines suggesting that physical activity in all domains provide health benefits.

How might this impact on policy or clinical practice in the foreseeable future?
► The increased mortality risk among workers that engage in high occupational physical activity versus individuals less active at work could be explained by detrimental socioeconomic, behavioural, and environmental factors that are more prevalent in this population.
► Workers in high occupational physical activity should be aware that they might not be getting all well-known health benefits of being physically active if they are only very active at work.

digging, shovelling, mining) may not improve survival and in some instances has appeared to be associated with increased mortality risk.[5]

A recent systematic review and meta-analysis, including 17 studies with data from 193 696 participants, found that high OPA was associated with an 18% increased risk of all-cause mortality in men.[5] This finding contrasts with the established notion that being physically active is associated with better health. However, the evidence supporting a 'physical activity paradox',[6 7] that is, where workers in high OPA having lower survival, in contrast to seminal works in 50s and 70s showing health benefits, has important limitations. For example, there is a lack of evidence from long-term exposure to high OPA. Also, most studies on this topic have limited or no adjustment for important covariates such as socioeconomic status, education and other lifestyles such as tobacco consumption and leisure time physical activity, and no examination of long-term and cause-specific deaths.[2]

There are many people worldwide who engage in high OPA, hence it is of public and occupational health interest to provide new evidence while overcoming previous studies limitations.[2] In the present study, we used data from a large prospective study with detailed information on many relevant confounding factors—the National Institutes of Health (NIH)-AARP Diet and Health Study—to examine the associations between history and duration (ie, years) in high OPA with all-cause mortality and cause-specific mortality among US adults.

METHODS
Study population
The NIH-AARP Diet and Health Study cohort has been described in detail elsewhere.[8] In brief, the AARP is a large organisation, comprises both men and women aged 50 years and over. The organisation focuses on many health issues and maintains regular communications with members through its magazine and bulletin. Between 1995 and 1996, a total of 617 119 AARP members, aged 50–71 years, were invited to participate in the study by mail and confirm acceptance by returning a mailed lifestyle and diet questionnaire. Participants resided in six states (California, Florida, Louisiana, New Jersey, North Carolina and Pennsylvania) and two metropolitan areas (Atlanta and Detroit). Of the respondents, 566 398 completed this baseline questionnaire adequately. Within 6 months of the baseline questionnaire, an additional risk factor questionnaire was mailed to 539 213 participants that reported not having colorectal cancer, breast cancer, prostate cancer or renal disease in the baseline questionnaire and 334 905 participants returned this questionnaire.

Among those who returned the risk factor questionnaire we excluded 12 194 participants whose questionnaires were completed by a spouse or other surrogate correspondent, 2620 who did not provide information on OPA, and 33 who died before their completed risk factor questionnaire was received. The final sample for this study included 322 126 (135 254 women) participants. All participants provided informed consent by completing and returning the baseline questionnaire.

Assessment of exposure
History of high OPA was assessed with a positive response to the following question included in the risk factor questionnaire: Have you ever had a job that required physically demanding work (that is, one that required you to do very heavy labor, such as carry heavy loads, walk long distances, or dig)? In addition, the total number of years in high OPA were also reported by participants with a positive response to the previous question and with the following five

options: (1) <1 year, (2) 1–2 years, (3) 3–5 years, (4) 6–9 years and (5) ≥10 years.

Assessment of mortality
Death and specific causes of death were obtained through follow-up with linkage to the National Death Index. All-cause mortality was the primary outcome variable. We also used the International Classification of Diseases, 9th Revision (ICD-9), and ICD, 10th Revision (ICD-10) codes to classify the underlying cause of death (obtained from death certificates) as follows: cancer (ICD-9, 140–239; ICD-10, C00–C97 and D00–D48), cardiovascular disease (ICD-9, 390–398, 401–404, 410–438, and 440–448; ICD-10, I00–I13, I20–I51 and I60–I78), and other causes. Follow-up time (years) was calculated starting the follow-up from the risk factor questionnaire until the date of death or 31 December 2011.

Assessment of covariates
Information on age, sex, educational level (<8 years, 8–11 years, 12 years or completed high school, posthigh school or some college, and completed college or postgraduate), currently married (yes vs no), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic and Asian/Pacific Islander/Native American), smoking (never, former ≤20 cigs/day, former >20 cigs/day, current ≤20 cigs/day and current >20 cigs/day), body mass index (<18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, 35.0–39.9 and ≥40 kg/m^2) were self-reported. Cardiometabolic (ie, hypercholesterolaemia, hypertension and diabetes) and chronic conditions (ie, coronary heart disease, stroke, cancer excluding colorectal cancer, breast cancer and prostate cancer, osteoporosis, and pulmonary emphysema) as diagnosed by a physician (yes vs no) were reported by the study participants. To further characterise socioeconomic status, we included a neighbourhood socioeconomic deprivation index based on 19 census variables developed using principal component analysis (sex-specific fifths).[9] Participation in leisure time physical activity was determined as hours/week spent in moderate to vigorous leisure activities (rarely, never, weekly but <1 hour, 1–3 hours/week, 4–7 hours/week and >7 hours/week) in the previous 10 years.[9] Total energy intake (calories), alcohol intake (g/day) and diet quality by the Healthy Eating Index 2015 (0–100 score) were calculated from the AARP 124-item food frequency questionnaire that assess dietary intake over the past year and was included in the baseline questionnaire.[10]

Statistical analysis
A history (never, ever) and duration (never (0 years), <1 year, 1–2 years, 3–5 years, 6–9 years and ≥10 years) in high OPA were the two main variables used for the analyses. All analyses were conducted separately for men and women.

Descriptive characteristics according to high OPA categories were presented as mean (with SD) or %. HRs and 95% CIs for total mortality associated with high OPA (never or 0 year as the reference category) were estimated using Cox proportional-hazards regression models, with follow-up time as the underlying time metric. We performed a basic model including age as covariate, and then we fitted three sequential multivariable adjusted models including socioeconomic factors, other lifestyle variables and health conditions, respectively. Specifically, the first multivariable model was adjusted for age, deprivation index, educational level, race and marital status. The second model was adjusted for covariates included in the first model 1 plus energy intake, Healthy Eating Index, smoking status, alcohol

intake, leisure time moderate to vigorous physical activity and body mass index categories. The final model was adjusted with covariates included in the second model plus diabetes, hypertension, hypercholesterolaemia, coronary heart disease, stroke, cancer (excluding colorectal cancer, breast cancer and prostate cancer), osteoporosis and pulmonary emphysema. HRs and 95% CIs for cause-specific mortality associated with high OPA were also estimated using Cox proportional hazards regression using the same basic and variable adjusted models, except for model 3, that excluded potential mediator variables of such specific mortality (ie, cardiometabolic risk factors (diabetes, hypertension, hypercholesterolaemia), and cardiovascular diseases (coronary heart disease and stroke) for cardiovascular deaths and cancer for cancer deaths).

For each covariate, and when applicable, we included an indicator for missing data in the regression models; the highest missing information in each covariate was 5%. To examine the extent to which the associations between high OPA and mortality are attributable to main covariates we calculated the percentage of excess risk explained by covariates using the formula $(\mathrm{HR}_{\mathrm{age\text{-}adjusted}} - \mathrm{HR}_{\mathrm{multivariable\ model\ 3}})/(\mathrm{HR}_{\mathrm{age\text{-}adjusted}} - 1) \times 100$.[11]

We also performed some additional analyses on the primary outcome. First, we identified which covariates explained the greatest excess risk in the association between high OPA and mortality by comparing the age-adjusted model with a model adjusted for age plus one individual variable using the aforementioned formula. Second, the main associations with mortality risk were stratified by socioeconomic factors, lifestyle behaviours, cardiometabolic risk factors and chronic health conditions. Finally, residual confounding by unmeasured confounders were addressed by calculating the E-value.[12]

We tested the proportional hazards assumption by modelling the interaction of follow-up time with high OPA and observed no significant deviations. Analyses were conducted with the use of STATA software, V.14.1. Statistical tests were two sided, and p values of less than 0.05 were considered to indicate statistical significance.

Patient and public involvement

Participants were not involved in the design and implementation of the study protocols or in setting research questions and the outcome measures. No participants were asked to advise on interpretation or writing up of findings.

RESULTS

The prevalence of ever having been exposed to high OPA or more years worked in high OPA was greater in men than women (table 1). In both men and women, those who worked more time in high OPA had lower education and a higher deprivation index compared with those who never worked in these jobs. Among men, those with a history of high OPA had a greater prevalence of cardiometabolic risk factors, chronic conditions and a lower adherence to healthy lifestyles. Women with a history of high OPA also had higher prevalence of obesity, chronic conditions and lower adherence to some healthy lifestyles.

During 13.6 years (SD, 3.3) of follow-up (total person-years, 4 380 914), 48 344 men and 25 219 women died. In age-adjusted models, the risk of death was higher among men and women with a history of high OPA (HR 1.14, 95% CI 1.12 to 1.16, and HR 1.22, 95% CI 1.18 to 1.26, respectively) (figure 1). However, after adjustment in multivariable models, the associations were substantially attenuated in women (HR 1.04, 95% CI 1.00 to 1.07, an 82% attenuation) and eliminated in men (HR 1.02, 95% CI 0.99 to 1.04, 86% attenuation).

Participants who reported a longer duration in high OPA had a higher risk for mortality after adjusting for age alone, but associations were notably attenuated after multiple adjustments (figure 2). Age-adjusted models showed that in men there was a J-shape dose–response association between duration in high OPA and mortality and that the greatest mortality risk was among those with ≥10 years, compared with those that never had high OPA (HR 1.29, 95% CI 1.26 to 1.31). Risk was substantially attenuated after adjusting for other covariates. In the final multivariable model, participants with 1–2 years of high OPA had a 5% reduced risk for all-cause mortality (HR 0.95, 95% CI 0.92 to 0.99) while participants with ≥10 years of high OPA were at slightly higher risk for mortality (HR 1.06, 95% CI 1.04 to 1.09, a 79% attenuation) when compared with men who never had high OPA. In women, we found that any duration of high OPA was associated with an increased risk of mortality but not in a clear dose-response manner, compared with women who never had high OPA. Associations were attenuated and no longer significant after multivariable adjustments (eg, HR 1.03, 95% CI 0.98 to 1.07 in ≥10 years, an 87% attenuation).

The associations of high OPA and deaths from cancer, cardiovascular disease and other causes were also examined (table 2). In these analyses, we found similar results to deaths of all causes. That is, there were clear associations of a history and longer duration in high OPA in age-adjusted models, but these associations were progressively attenuated or disappeared after multiple adjustments; the greatest increased risk was found for death from cardiovascular disease among men with ≥10 years in high OPA (HR 1.09, 95% CI 1.05 to 1.14, a 73% attenuation from the age-adjusted model). Associations were attenuated after adjusting for other covariates.

We further examined how each single variable alone included in the same multivariable model were associated with all-cause mortality (online supplemental table S1). In men, educational level and smoking contributed the most to the attenuations in the high OPA-mortality associations (online supplemental table S1). Including only age, educational level and smoking in the same model was enough to almost eliminate the increased mortality risk due to history (HR 1.02, 95% CI 1.00 to 1.04, an 86% attenuation) or long duration (HR 1.08, 95% CI 1.05 to 1.10, a 72% attenuation) in high OPA. In women, smoking, educational level were also the two variables that explained the higher mortality attributed to high OPA, but to a lower extent when compared with men (online supplemental table S2); in addition, the deprivation index explained the higher mortality of high OPA. With only some exceptions, similar associations between high OPA and all-cause mortality were also observed in strata of all covariates; for example, we found a few positive interactions these are possibly attributable to the large sample sizes (online supplemental tables S3 and S4). The joint association of high OPA and leisure-time physical activity only showed consistent and markedly reduced HRs with high levels of leisure-time physical activity (online supplemental table S5). E-values estimates and the E-values for the lower confident limit suggest that substantial unmeasured confounding might reduce the observed association or its CI to null in the associations that remain significant (online supplemental figure S1).

DISCUSSION

In this prospective cohort study of ∼320 000 US adults and more than 73 000 deaths, we observed positive associations between high OPA and deaths of any cause in both men and women. However, after adjusting for potential confounders, including

Table 1 Baseline characteristics of the study participants according to history and duration of high occupational physical activity, by sex

	Never	Ever					
	0 years	<1 year	1–2 years	3–5 years	6–9 years	≥10 years	Total (ever)
Men, n (%)	89 582 (47.9)	7847 (4.2)	13 722 (7.4)	19 681 (10.5)	12 135 (6.5)	43 905 (23.5)	97 290 (52.1)
Age, years	62.8 (5.3)	62.4 (5.3)	62.3 (5.4)	62.2 (5.3)	62.1 (5.2)	62.5 (5.2)	62.3 (5.3)
High Deprivation Index*, %	15.8	14.4	16.2	18.3	22.1	28.4	22.6
High education†, %	57.8	70.7	62.8	54.4	44.3	17.5	39.3
Caucasian, %	93.5	95.5	95.2	94.7	94.5	93.6	94.3
Married, %	84.6	85.5	86.0	85.6	85.3	84.8	85.2
Obesity, %	16.9	16.7	19.6	21.8	23.5	24.8	22.6
Energy intake, calories	1951.8 (846.1)	1993.2 (812.6)	2000.8 (844.9)	2034.7 (890.9)	2063.2 (905.2)	2229.9 (1204.4)	2116.6 (1038.7)
HEI, score	67.8 (9.4)	68.6 (9.3)	68.2 (9.4)	67.9 (9.5)	67.5 (9.5)	65.7 (9.9)	67.0 (9.7)
Alcohol intake, g/day	17.3 (39.5)	18.9 (40.0)	18.5 (39.8)	18.9 (43.9)	18.1 (43.3)	19.1 (53.9)	18.8 (47.8)
Never smokers, %	33.8	33.3	28.3	27.7	25.2	23.8	26.2
Leisure time MVPA ≥4 hour/wk, %	47.1	50.3	50.2	51.1	52.4	51.8	51.4
Diabetes, %	9.3	8.0	8.7	9.2	9.8	11.0	9.9
Hypertension, %	40.8	36.5	39.4	40.0	40.9	41.7	40.5
Hypercholesterolaemia, %	41.6	43.4	42.0	41.9	42.1	42.0	42.1
Coronary heart disease, %	17.6	15.9	16.4	17.3	17.0	19.0	17.8
Stroke, %	2.0	1.6	1.6	2.0	2.3	2.7	2.2
Cancer‡, %	3.8	4.6	4.2	4.3	3.9	4.0	4.1
Osteoporosis, %	0.7	0.8	0.8	0.8	0.9	1.2	1.0
Pulmonary emphysema, %	2.2	2.1	2.6	2.9	3.5	4.2	3.4
Women, n (%)	113 552 (83.9)	1407 (1.0)	2131 (1.6)	3729 (2.8)	3122 (2.3)	11 313 (8.4)	21 702 (16.1)
Age, years	62.3 (5.3)	61.1 (5.6)	60.7 (5.5)	60.7 (5.4)	60.8 (5.4)	61.6 (5.4)	61.2 (5.4)
High deprivation index*, %	18.6	23.8	22.8	22.0	22.7	26.5	24.6
High education†, %	33.6	32.6	27.3	27.2	23.7	22.3	24.5
Caucasian, %	91.5	87.9	90.3	91.0	92.4	90.7	90.8
Married, %	45.1	39.1	42.8	42.8	44.6	39.8	41.0
Obesity, %	20.7	25.0	25.9	28.1	27.2	27.2	27.1
Energy intake, calories	1561.8 (734.0)	1745.2 (1065.3)	1645.5 (738.3)	1674.8 (809.1)	1717.3 (864.4)	1755.6 (971.6)	1724.7 (916.9)
HEI, score	69.2 (9.3)	68.5 (9.1)	68.4 (9.5)	67.9 (9.6)	68.0 (9.7)	67.9 (9.6)	68.0 (9.6)
Alcohol intake, g/day	6.2 (17.3)	6.2 (19.9)	5.5 (17.1)	6.0 (20.6)	6.1 (20.6)	6.1 (24.0)	6.0 (22.1)
Never smokers, %	44.8	40.7	39.0	37.5	38.4	40.3	39.4
Leisure time MVPA ≥4 hour/wk. %	47.2	46.9	50.6	52.2	54.3	58.5	55.3
Diabetes, %	6.8	7.4	7.5	8.1	7.3	8.3	8.0
Hypertension, %	37.2	36.0	37.1	38.7	36.7	39.3	38.4
Hypercholesterolaemia, %	46.9	45.8	45.6	45.5	46.6	45.6	45.7
Coronary heart disease, %	8.1	8.6	8.7	9.9	9.9	10.9	10.2
Stroke, %	1.6	2.2	2.2	2.2	2.1	2.4	2.3
Cancer‡, %	5.1	6.2	7.0	6.3	6.5	6.2	6.3
Osteoporosis, %	7.6	10.0	9.2	8.6	10.9	10.6	10.0
Pulmonary emphysema, %	2.2	4.0	3.1	3.0	3.3	3.6	3.4

*The highest sex-specific fifth.

†College or higher.

‡Excluding colorectal cancer, breast cancer and prostate cancer.

HEI, Healthy Eating Index; MVPA, moderate-to-vigorous physical activity.

educational level and smoking, the magnitude of these associations was substantially attenuated and, in most instances, associations became null in both genders. For example, compared with men who never had high OPA, mortality risk among those who worked in these jobs or worked in them for 10 years or more dropped from 14% to 2%, and from 29% to 6%, respectively, after adjusting for a variety of confounders. We found similar trends in risk when examining deaths from cancer, cardiovascular and other causes of death. Although some of the HRs attained statistical significance, the small magnitude of the HRs

observed in the multivariable models and the substantial attenuation of these associations by key confounders, and potential for unmeasured confounding, suggests that high OPA is not independently associated with increased mortality risk in these data.

After the earlies studies in 50s and 70s,[2 3] the next works have found mixed results regarding the potential effect of high OPA on mortality. For example, Chau *et al*[13] analysed data from 45 685 Norwegians adults, aged 20 years and older, from the Nord-Trøndelag Health Study 3 and after a 3.3-year follow-up they found that workers in high OPA did not have an increased
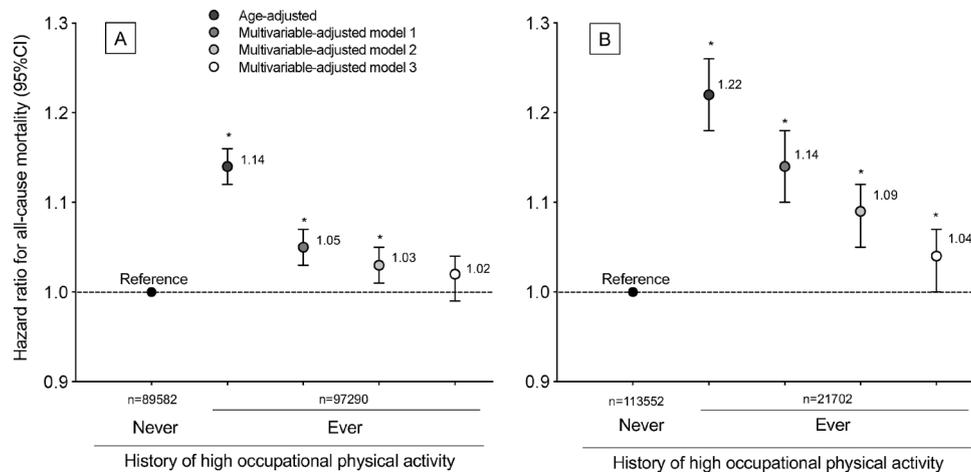
Figure 1 Association of history of high occupational physical activity with all-cause mortality, by sex. (A) Men. (B) Women. Multivariable-adjusted model 1 was adjusted for socioeconomic factors (age, deprivation index, educational level, race and marital status). Multivariable-adjusted model 2 was adjusted as multivariable-adjusted model 1 plus lifestyle behaviours (energy intake, Healthy Eating Index, smoking status, alcohol intake, leisure time moderate to vigorous physical activity and body mass index categories). Multivariable-adjusted model 3 was adjusted as multivariable-adjusted model 2 plus cardiometabolic risk factors (diabetes, hypertension, hypercholesterolaemia) and chronic health conditions (coronary heart disease, stroke, cancer excluding colorectal cancer, breast cancer and prostate cancer, osteoporosis, and pulmonary emphysema). *$P<0.05$.

risk of all-cause (HR 0.95, 95% CI 0.64 to 1.40) and cardiometabolic (HR 1.55, 95% CI 0.83 to 2.90) mortality, as compared with mainly sedentary workers and without evidence of moderating sex-specific effects. Etemadi et al[14] included 50 045 Iranian adults above the age of 40 who participated in the Golestan Cohort Study with 5.1 years of follow-up and found that high OPA reduced mortality risk in both men and women when compared with sedentary workers; similar results were found in a prospective cohort study with a large follow-up period (24 years) by Graff-Iversen[15] in 47 405 Norwegian participants. In contrast, some other studies with smaller sample sizes in other countries (eg, Denmark, China, Finland, Germany), and low number of events have found that men in high OPA had an increased mortality risk than those with lower OPA levels or in sedentary works.[16–21] For example, the study from Hu et al

reported a 3.4-fold increased risk of all-cause mortality among Taiwanese men in high OPA, however only 196 deaths occurred (30 deaths among the referent group). In this study, multivariable models did not adjust for SES and included a limited adjustment for education level, two confounders that were strongly associated with mortality in our study.[16]

Owing to the disparity of studies and results in the OPA research area from the first works, two key systematic reviews have tried to summarise the evidence to provide clearer conclusions on this issue. The first review by Samitz et al[22] in 2012 compared the highest vs the lowest OPA levels, according to intensity and/or duration, in the association with mortality, including 82 412 participants from 7 studies, and found that in men there was not a significant association with mortality (RR 0.94, 95% CI 0.75 to 1.19), whereas in women higher levels of
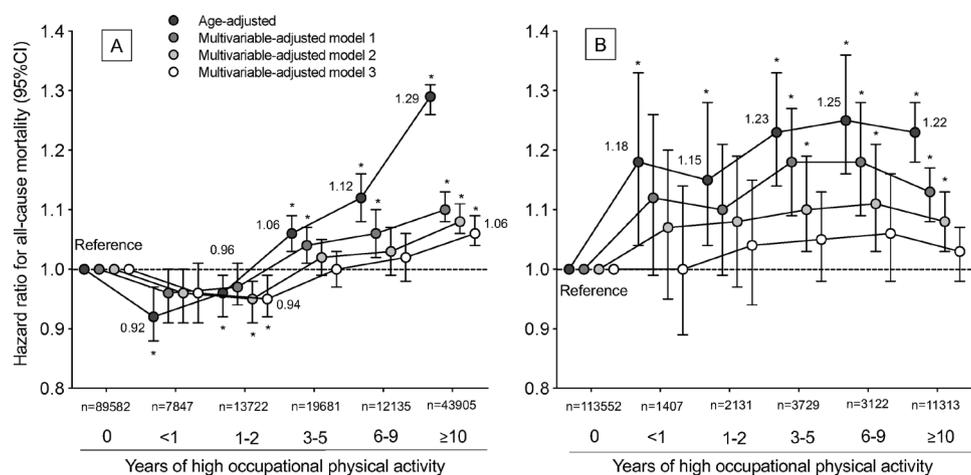

Figure 2 Association of duration of high occupational physical activity with all-cause mortality, by sex. (A) Men. (B) Women. Multivariable-adjusted model 1 was adjusted for socioeconomic factors (age, deprivation index, educational level, race and marital status). Multivariable-adjusted model 2 was adjusted as multivariable-adjusted model 1 plus lifestyle behaviours (energy intake, Healthy Eating Index, smoking status, alcohol intake, leisure time moderate to vigorous physical activity and body mass index categories). Multivariable-adjusted model 3 was adjusted as multivariable-adjusted model 2 plus cardiometabolic risk factors (diabetes, hypertension, hypercholesterolaemia) and chronic health conditions (coronary heart disease, stroke, cancer excluding colorectal cancer, breast cancer and prostate cancer, osteoporosis and pulmonary emphysema). For simplicity, only statistically significant HRs are presented numerically in the age-adjusted model and multivariable-adjusted model 3. *$P<0.05$.

Table 2 Association of history and duration of high occupational physical activity with cause-specific mortality, by sex

	Never	Ever					
	0 year	<1 year	1–2 years	3–5 years	6–9 years	≥10 years	Total (ever)
Men, n	89 582	7847	13 722	19 681	12 135	43 905	97 290
Deaths from cancer, cases	7688	628	1191	1772	1137	4496	9224
Age adjusted	1 (Reference)	0.95 (0.87 to 1.04)	1.03 (0.96 to 1.10)	1.10 (1.04 to 1.16)	1.16 (1.09 to 1.24)	1.27 (1.22 to 1.31)	1.16 (1.12 to 1.20)
Multivariable-adjusted model 1	1 (Reference)	0.98 (0.90 to 1.07)	1.04 (0.98 to 1.11)	1.08 (1.02 to 1.14)	1.10 (1.04 to 1.18)	1.11 (1.06 to 1.16)	1.08 (1.05 to 1.12)
Multivariable-adjusted model 2	1 (Reference)	0.97 (0.89 to 1.06)	1.01 (0.94 to 1.07)	1.04 (0.98 to 1.10)	1.05 (0.98 to 1.12)	1.06 (1.02 to 1.11)	1.04 (1.01 to 1.07)
Multivariable-adjusted model 3*	1 (Reference)	0.97 (0.89 to 1.05)	1.01 (0.95 to 1.07)	1.03 (0.98 to 1.09)	1.04 (0.98 to 1.11)	1.06 (1.01 to 1.10)	1.04 (1.00 to 1.07)
Deaths from CVD, cases	7366	569	986	1568	1038	4450	8611
Age-adjusted	1 (Reference)	0.91 (0.83 to 0.99)	0.90 (0.84 to 0.97)	1.03 (0.97 to 1.09)	1.12 (1.05 to 1.20)	1.33 (1.28 to 1.38)	1.15 (1.11 to 1.18)
Multivariable-adjusted model 1	1 (Reference)	0.94 (0.86 to 1.02)	0.92 (0.86 to 0.99)	1.01 (0.95 to 1.07)	1.07 (0.99 to 1.15)	1.13 (1.08 to 1.15)	1.05 (1.01 to 1.08)
Multivariable-adjusted model 2	1 (Reference)	0.95 (0.85 to 1.02)	0.90 (0.84 to 0.96)	0.99 (0.94 to 1.04)	1.04 (0.97 to 1.11)	1.11 (1.06 to 1.16)	1.03 (0.99 to 1.06)
Multivariable-adjusted model 3†	1 (Reference)	0.94 (0.87 to 1.03)	0.89 (0.83 to 0.95)	0.98 (0.93 to 1.04)	1.03 (0.96 to 1.10)	1.10 (1.06 to 1.15)	1.02 (0.98 to 1.05)
Deaths from non-cancer/CVD, cases	7208	562	997	1557	977	4154	8247
Age adjusted	1 (Reference)	0.91 (0.84 to 0.99)	0.93 (0.87 to 0.99)	1.05 (0.99 to 1.10)	1.08 (1.01 to 1.15)	1.27 (1.22 to 1.32)	1.12 (1.09 to 1.16)
Multivariable-adjusted model 1	1 (Reference)	0.95 (0.87 to 1.03)	0.95 (0.89 to 1.01)	1.02 (0.97 to 1.08)	1.02 (0.95 to 1.09)	1.07 (1.03 to 1.12)	1.03 (0.99 to 1.05)
Multivariable-adjusted model 2	1 (Reference)	0.95 (0.87 to 1.04)	0.93 (0.87 to 0.99)	1.02 (0.96 to 1.07)	1.01 (0.95 to 1.08)	1.07 (1.02 to 1.12)	1.02 (0.99 to 1.05)
Multivariable-adjusted model 3	1 (Reference)	0.95 (0.87 to 1.04)	0.93 (0.87 to 0.99)	0.99 (0.94 to 1.05)	0.98 (0.92 to 1.05)	1.04 (0.99 to 1.08)	0.99 (0.97 to 1.03)
Women, n	113 552	1407	2131	3729	3122	11 313	21 702
Deaths from cancer, cases	7771	105	144	261	258	839	1607
Age adjusted	1 (Reference)	1.21 (0.99 to 1.48)	1.11 (0.93 to 1.32)	1.18 (1.04 to 1.35)	1.37 (1.21 to 1.57)	1.14 (1.06 to 1.23)	1.18 (1.12 to 1.25)
Multivariable-adjusted model 1	1 (Reference)	1.18 (0.96 to 1.45)	1.08 (0.90 to 1.28)	1.15 (1.01 to 1.31)	1.33 (1.17 to 1.52)	1.08 (1.00 to 1.17)	1.13 (1.07 to 1.20)
Multivariable-adjusted model 2	1 (Reference)	1.12 (0.91 to 1.38)	1.02 (0.86 to 1.22)	1.06 (0.93 to 1.21)	1.22 (1.07 to 1.40)	1.03 (0.95 to 1.11)	1.07 (1.01 to 1.13)
Multivariable-adjusted model 3*	1 (Reference)	1.10 (0.90 to 1.33)	1.02 (0.87 to 1.21)	1.03 (0.91 to 1.16)	1.20 (1.06 to 1.36)	1.03 (0.96 to 1.11)	1.07 (1.00 to 1.15)
Deaths from CVD, cases	5783	74	101	207	172	658	1212
Age adjusted	1 (Reference)	1.20 (0.95 to 1.50)	1.11 (0.91 to 1.35)	1.32 (1.15 to 1.51)	1.30 (1.11 to 1.50)	1.26 (1.16 to 1.37)	1.26 (1.18 to 1.34)
Multivariable-adjusted model 1	1 (Reference)	1.11 (0.89 to 1.40)	1.05 (0.86 to 1.27)	1.24 (1.08 to 1.42)	1.19 (1.02 to 1.39)	1.12 (1.04 to 1.22)	1.14 (1.08 to 1.22)
Multivariable-adjusted model 2	1 (Reference)	1.07 (0.85 to 1.34)	1.03 (0.84 to 1.25)	1.17 (1.02 to 1.35)	1.14 (0.98 to 1.33)	1.08 (0.99 to 1.17)	1.10 (1.03 to 1.17)
Multivariable-adjusted model 3†	1 (Reference)	1.03 (0.82 to 1.29)	1.02 (0.83 to 1.24)	1.15 (1.00 to 1.33)	1.11 (0.95 to 1.29)	1.06 (0.97 to 1.15)	1.04 (0.97 to 1.10)
Deaths from non-cancer/CVD, cases	7310	89	146	256	192	853	1536
Age-adjusted	1 (Reference)	1.12 (0.91 to 1.39)	1.24 (1.05 to 1.46)	1.26 (1.11 to 1.43)	1.12 (0.97 to 1.29)	1.28 (1.19 to 1.37)	1.24 (1.17 to 1.31)
Multivariable-adjusted model 1	1 (Reference)	1.06 (0.86 to 1.31)	1.18 (0.99 to 1.39)	1.19 (1.05 to 1.35)	1.04 (0.90 to 1.19)	1.15 (1.07 to 1.24)	1.14 (1.07 to 1.21)
Multivariable-adjusted model 2	1 (Reference)	1.02 (0.82 to 1.25)	1.16 (0.98 to 1.37)	1.13 (0.99 to 1.28)	0.99 (0.84 to 1.15)	1.12 (1.04 to 1.20)	1.09 (1.03 to 1.16)
Multivariable-adjusted model 3	1 (Reference)	0.93 (0.75 to 1.14)	1.14 (0.97 to 1.34)	1.08 (0.95 to 1.22)	0.94 (0.82 to 1.09)	1.05 (0.98 to 1.13)	1.04 (0.98 to 1.10)

SValues are HRs (95% CI). Multivariable-adjusted model 1 was adjusted for socioeconomic factors (age, deprivation index, educational level, race and marital status). Multivariable-adjusted model 2 was adjusted as multivariable-adjusted model 1 plus lifestyle behaviours (energy intake, Healthy Eating Index, smoking status, alcohol intake, leisure time moderate to vigorous physical activity and body mass index categories). Multivariable-adjusted model 3 was adjusted as multivariable-adjusted model 2 plus cardiometabolic risk factors (diabetes, hypertension, hypercholesterolaemia) and chronic health conditions (coronary heart disease, stroke, cancer excluding colorectal cancer, breast cancer and prostate cancer, osteoporosis and pulmonary emphysema.

*The cancer variable was not included in this model, since they may be potential precursors (ie, mediators) of cancer mortality.

†The diabetes, hypertension, hypercholesterolaemia, coronary heart disease, stroke variables, potential were not included in this model, since they may be potential precursors (ie, mediators) of cardiovascular mortality.

CVD, cardiovascular disease.

activity were beneficial (RR 0.66, 95% CI 0.49 to 0.89). More recently, Coenen et al[5] included data from 193 696 participants from 17 studies and the pooled results showed that male workers with high levels of OPA had a statistically significant higher mortality risk when compared with men engaging in low levels of OPA (HR 1.18, 95% CI 1.05 to 1.34). In women, a non-significant but inverse association was found (HR 0.90, 95% CI 0.80 to 1.01). After these reviews, three very recent studies have also attempted to provide more robust evidence on the relationship between OPA and survival including large population-based cohorts.[23–25] Dalene et al[23] included 437 378 participants (aged 18–65 years) from Norway with a median follow-up of 28 years and they found that high OPA contributes to longevity in men but not in women. In a representative sample with 104 046 adults from the contemporary Copenhagen General Population Study, and a median 10-year follow-up, Holtermann et al[24] found that higher OPA associates with increased all-cause mortality risks in both genders. The most recent work by Pearce et al with 460 901 UK Biobank participants (aged 40–69 years), followed for a median 12 years, and within the working population, there was no evidence of differences in all-cause mortality by OPA group when comparing those reporting higher levels of OPA to the lowest OPA reference group for both women and men.[25] Taken together, the scientific evidence in this research area is therefore, to date, inconclusive.[26]

For this reason, a research agenda for generating more conclusive evidence regarding a potential 'physical activity paradox' was launched.[2] The present work helps filling this gap and includes lifetime data, a large sample of men and women, comprehensive list of potential confounders, and a long follow-up where ~70 000 events occurred. Our findings do not clearly support the 'physical activity paradox' and instead suggest that other related characteristics (eg, biological, socioeconomic, environmental, lifestyle, health) are likely to explain the excess mortality among workers in high physically active jobs. We also did not find clear sex-specific associations as shown in previous reports.[5 22–25] In our work, in age-adjusted models, there was a J-shape relationship between high OPA duration and mortality in men, whereas among women, we found a smooth inverted-U shape relationship with the same exposure; however, after multivariable adjustment, the associations were strongly attenuated or eliminated in both sexes, refuting some of the evidence supporting distinct effects in men and women.

As highlighted in a recent umbrella review[26] commissioned by WHO in preparation of the 2020 Physical Activity Guidelines, the health benefits that are associated with total physical activity and physical activity during leisure time may not always be generalisable to physical activity in other (ie, work) domains. In fact, our findings do not support that daily physical activity undertaken during work provides, at least, survival benefits. Therefore, workers in high OPA should be aware that they might not be getting all well-known health benefits of being physically active if they are only very active at work. Our results suggest that the public health message of 'every move counts' launched in the 2020 WHO guidelines needs to be interpreted with caution. However, given that a large part of the working-age population spends most of their daily physical activity at work,[26 27] in particular in low-income and middle-income countries, prospective studies with repeated measures and clinical trials, better assessments of physical activity and confounding and effect modifications analyses should be performed to provide a clearer understanding on the role of OPA on survival.[2]

Our study is one of the largest in sample size and number of deaths examining the physical activity paradox, with a regionally diverse population from the USA, and a long-term follow-up. In addition, all analyses were adjusted for numerous and key potential confounders.[7] Importantly, the study design allowed to examine lifetime high OPA in an older population, which adds new insights since an important number of previous studies were performed in young worker populations in earlier stages of their professional careers. Several limitations of our study should be noted. Given the observational nature of our study it is not possible to assess causality. However, the potential mechanisms by which a sustained high OPA might induce harmful consequences in health[6] are likely clinically small after considering the magnitude of the associations we found in our study before and after adjustment for potential confounders.[28–30] Some key unmeasured confounding factors in the association between job characteristics and mortality, such as job strain, physical and social environment and other work conditions were unfortunately lacking.[31–33] Information on lifetime high OPA was assessed by self-report and therefore provides a limited estimation of the exposure. This is a crude measure of OPA that does not include type, frequency and duration of OPA and therefore more comprehensive measures (eg, activity monitors) should be incorporated in prospective studies to advance our understanding of the health benefits of OPA. A great proportion of our participants were Caucasian and highly educated, hence our results might not be generalisable to other subgroups of the population. Although the study design and long-term exposure might attenuate concerns about reverse causation, the final sample included a 'surviving population' until the assessment; hence, people who worked in high OPA who died before enrolment in this cohort, by definition, could not be assessed. Similarly, we cannot rule out the possibility that some participants could not participate in physically active jobs because they were in poor health during their life and before baseline assessments took place. Finally, the role of musculoskeletal diseases others than osteoporosis on the association between high OPA and survival needs further research[26]; unfortunately, the assessment of musculoskeletal health variables is limited in the NIH-AARP cohort.

CONCLUSION

This large prospective cohort study showed some weak but statistically significant positive associations of a lifetime high OPA with deaths from any cause and other specific causes. However, these associations were strongly attenuated and, in most instances, disappeared after considering key confounder variables, mainly socioeconomic status and smoking. This study does not clearly support neither earlier studies showing negative health effects of OPA nor the good practice statement from the current physical activity guidelines suggesting that physical activity in all domains (eg, every move counts) provide the same health benefits. This work adds relevant information about the health effects of work-related activity that can inform future physical activity guidelines.

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SUPPLEMENTARY FILE.

Martinez-Gomez et al. Lifetime High Occupational Physical Activity and Total and Cause-Specific Mortality Among 320,000 Adults in the NIH-AARP Study: A Cohort Study

Table S1. Association of history and duration of high occupational physical activity with all-cause mortality with individual adjustments in men.

	Never	Ever					
	0 years	<1 year	1-2 years	3-5 years	6-9 years	10+ years	Total (ever)
n	89582	7847	13722	19681	12135	43905	97290
cases	7688	628	1191	1772	1137	4496	9224
Age-adjusted	1 (Reference)	0.92 (0.87-0.97)	0.96 (0.92-0.99)	1.06 (1.08-1.16)	1.12 (1.08-1.17)	1.29 (1.26-1.31)	1.14 (1.12-1.16)
Socioeconomic factors							
Age-adjusted + deprivation index	1 (Reference)	0.93 (0.88-0.98)	0.95 (0.91-0.98)	1.04 (1.00-1.07)	1.08 (1.04-1.13)	1.20 (1.17-1.22)	1.10 (1.08-1.12)
Age-adjusted + educational level	1 (Reference)	0.95 (0.90-1.00)	0.98 (0.93-1.01)	1.05 (1.01-1.08)	1.08 (1.04-1.13)	1.13 (1.10-1.15)	1.07 (1.05-1.09)
Age-adjusted + race/ethnicity	1 (Reference)	0.92 (0.87-0.96)	0.96 (0.91-0.98)	1.06 (1.02-1.09)	1.12 (1.08-1.17)	1.28 (1.25-1.31)	1.14 (1.12-1.15)
Age-adjusted + marital status	1 (Reference)	0.92 (0.89-0.98)	0.96 (0.93-1.00)	1.06 (1.03-1.10)	1.13 (1.09-1.17)	1.29 (1.26-1.29)	1.15 (1.13-1.17)
Lifestyle behaviors							
Age-adjusted + calorie intake	1 (Reference)	0.92 (0.89-0.98)	0.96 (0.93-0.99)	1.06 (1.02-1.09)	1.12 (1.07-1.16)	1.27 (1.24-1.29)	1.13 (1.11-1.15)
Age-adjusted + HEI	1 (Reference)	0.94 (0.88-0.98)	0.96 (0.92-1.00)	1.06 (1.03-1.10)	1.12 (1.08-1.17)	1.24 (1.21-1.26)	1.13 (1.11-1.15)
Age-adjusted + alcohol intake	1 (Reference)	0.92 (0.87-0.96)	0.96 (0.91-0.99)	1.06 (1.02-1.09)	1.12 (1.08-1.17)	1.28 (1.25-1.31)	1.14 (1.12-1.16)
Age-adjusted + smoking	1 (Reference)	0.92 (0.87-0.97)	0.92 (0.88-0.95)	1.00 (0.99-1.08)	1.04 (0.99-1.08)	1.18 (1.15-1.20)	1.07 (1.05-1.09)
Age-adjusted + MVPA	1 (Reference)	0.95 (0.90-0.99)	0.99 (0.95-1.02)	1.10 (1.06-1.13)	1.17 (1.12-1.22)	1.31 (1.28-1.34)	1.17 (1.15-1.20)
Age-adjusted + body mass index	1 (Reference)	0.92 (0.87-0.97)	0.95 (0.92-0.98)	1.04 (1.01-1.07)	1.10 (1.06-1.14)	1.25 (1.22-1.28)	1.12 (1.10-1.14)
Cardiometabolic risk factors							
Age-adjusted + diabetes	1 (Reference)	0.93 (0.88-0.98)	0.96 (0.92-0.99)	1.06 (1.02-1.09)	1.12 (1.07-1.16)	1.27 (1.24-1.30)	1.14 (1.12-1.16)
Age-adjusted + hypertension	1 (Reference)	0.93 (0.88-0.98)	0.96 (0.93-0.99)	1.06 (1.02-1.09)	1.12 (1.08-1.17)	1.28 (1.25-1.31)	1.14 (1.12-1.16)
Age-adjusted + hypercholesterolemia	1 (Reference)	0.92 (0.87-0.97)	0.95 (0.91-0.99)	1.06 (1.02-1.09)	1.12 (1.08-1.17)	1.28 (1.25-1.31)	1.14 (1.12-1.16)
Chronic health conditions							
Age-adjusted + coronary heart disease	1 (Reference)	0.93 (0.88-0.98)	0.96 (0.93-0.99)	1.05 (1.02-1.09)	1.12 (1.08-1.16)	1.28 (1.25-1.31)	1.14 (1.12-1.16)
Age-adjusted + stroke	1 (Reference)	0.92 (0.87-0.97)	0.96 (0.93-0.99)	1.06 (1.03-1.09)	1.11 (1.07-1.16)	1.28 (1.25-1.30)	1.14 (1.12-1.16)
Age-adjusted + osteoporosis	1 (Reference)	0.92 (0.87-0.97)	0.96 (0.92-0.99)	1.06 (1.03-1.09)	1.12 (1.08-1.17)	1.28 (1.25-1.31)	1.14 (1.12-1.16)
Age-adjusted + cancer*	1 (Reference)	0.92 (0.86-0.96)	0.95 (0.91-0.98)	1.05 (1.01-1.08)	1.12 (1.08-1.17)	1.29 (1.25-1.31)	1.14 (1.12-1.16)
Age-adjusted + pulmonary emphysema	1 (Reference)	0.92 (0.87-0.96)	0.95 (0.91-0.98)	1.04 (1.01-1.08)	1.09 (1.05-1.14)	1.24 (1.21-1.27)	1.12 (1.10-1.14)

HEI: Healthy Eating Index. MVPA: moderate-to-vigorous physical activity. Values are hazard ratios (95% confidence interval). *Others than colorectal cancer, breast cancer, and prostate cancer.

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Table S2. Association of history and duration of high occupational physical activity with all-cause mortality with individual adjustments in women.

	Never	Ever					
	0 years	<1 year	1-2 years	3-5 years	6-9 years	10+ years	Total (ever)
n	113552	1407	2131	3729	3122	11313	21702
cases	7771	105	144	261	258	839	1607
Age-adjusted	1 (Reference)	1.18 (1.04-1.33)	1.15 (1.04-1.28)	1.23 (1.14-1.33)	1.25 (1.16-1.36)	1.23 (1.17-1.28)	1.22 (1.18-1.26)
Socioeconomic factors							
Age-adjusted + deprivation index	1 (Reference)	1.15 (1.02-1.30)	1.13 (1.02-1.25)	1.20 (1.12-1.30)	1.22 (1.12-1.32)	1.18 (1.13-1.23)	1.18 (1.14-1.23)
Age-adjusted + educational level	1 (Reference)	1.16 (1.02-1.30)	1.13 (1.02-1.24)	1.21 (1.12-1.31)	1.21 (1.12-1.31)	1.17 (1.12-1.22)	1.18 (1.14-1.22)
Age-adjusted + race/ethnicity	1 (Reference)	1.17 (1.04-1.32)	1.15 (1.04-1.28)	1.23 (1.14-1.32)	1.26 (1.16-1.36)	1.22 (1.17-1.28)	1.22 (1.18-1.26)
Age-adjusted + marital status	1 (Reference)	1.15 (1.02-1.30)	1.14 (1.03-1.26)	1.22 (1.13-1.31)	1.24 (1.15-1.35)	1.20 (1.16-1.26)	1.20 (1.17-1.24)
Lifestyle behaviors							
Age-adjusted + calorie intake	1 (Reference)	1.16 (1.03-1.31)	1.15 (1.04-1.27)	1.22 (1.14-1.32)	1.24 (1.14-1.35)	1.21 (1.15-1.26)	1.20 (1.17-1.25)
Age-adjusted + HEI	1 (Reference)	1.16 (1.03-1.31)	1.14 (1.03-1.26)	1.21 (1.12-1.30)	1.23 (1.13-1.33)	1.23 (1.13-1.33)	1.19 (1.14-1.24)
Age-adjusted + alcohol intake	1 (Reference)	1.18 (1.04-1.32)	1.16 (1.04-1.27)	1.23 (1.15-1.32)	1.26 (1.16-1.36)	1.22 (1.17-1.28)	1.22 (1.18-1.27)
Age-adjusted + smoking	1 (Reference)	1.12 (0.99-1.26)	1.10 (0.99-1.26)	1.14 (1.06-1.24)	1.16 (1.07-1.26)	1.15 (1.10-1.20)	1.14 (1.10-1.18)
Age-adjusted + MVPA	1 (Reference)	1.18 (1.05-1.33)	1.19 (1.07-1.31)	1.27 (1.17-1.37)	1.30 (1.20-1.41)	1.29 (1.23-1.34)	1.27 (1.23-1.31)
Age-adjusted + body mass index	1 (Reference)	1.15 (1.02-1.30)	1.13 (1.03-1.25)	1.20 (1.11-1.29)	1.23 (1.13-1.33)	1.18 (1.13-1.23)	1.18 (1.15-1.22)
Cardiometabolic risk factors							
Age-adjusted + diabetes	1 (Reference)	1.16 (1.03-1.31)	1.15 (1.04-1.27)	1.21 (1.12-1.30)	1.25 (1.15-1.35)	1.21 (1.16-1.26)	1.20 (1.17-1.24)
Age-adjusted + hypertension	1 (Reference)	1.18 (1.05-1.33)	1.19 (1.07-1.31)	1.27 (1.12-1.31)	1.25 (1.16-1.36)	1.22 (1.16-1.27)	1.21 (1.17-1.26)
Age-adjusted + hypercholesterolemia	1 (Reference)	1.17 (1.04-1.32)	1.15 (1.04-1.27)	1.23 (1.14-1.32)	1.25 (1.15-1.36)	1.22 (1.17-1.28)	1.22 (1.18-1.26)
Chronic health conditions							
Age-adjusted + coronary heart disease	1 (Reference)	1.17 (1.04-1.32)	1.14 (1.03-1.26)	1.20 (1.11-1.30)	1.22 (1.13-1.32)	1.19 (1.13-1.24)	1.19 (1.15-1.23)
Age-adjusted + stroke	1 (Reference)	1.17 (1.03-1.32)	1.14 (1.03-1.26)	1.22 (1.13-1.32)	1.24 (1.15-1.35)	1.21 (1.16-1.27)	1.21 (1.17-1.25)
Age-adjusted + osteoporosis	1 (Reference)	1.16 (1.02-1.30)	1.14 (1.03-1.28)	1.22 (1.14-1.32)	1.23 (1.14-1.34)	1.21 (1.16-1.26)	1.21 (1.17-1.25)
Age-adjusted + cancer*	1 (Reference)	1.16 (1.01-1.31)	1.14 (1.04-1.29)	1.22 (1.13-1.32)	1.24 (1.16-1.37)	1.22 (1.16-1.27)	1.21 (1.17-1.25)
Age-adjusted + pulmonary emphysema	1 (Reference)	1.13 (1.00-1.27)	1.14 (1.03-1.26)	1.21 (1.12-1.30)	1.23 (1.13-1.33)	1.19 (1.14-1.24)	1.19 (1.15-1.23)

HEI: Healthy Eating Index. MVPA: moderate-to-vigorous physical activity. Values are hazard ratios (95% confidence interval). *Others than colorectal cancer, breast cancer, and prostate cancer.

Table S3. Association of history and duration of high occupational physical activity with all-cause mortality in men, stratified by socioeconomic factors, lifestyle behaviors, cardiometabolic risk factors and chronic health conditions.

		Never	Ever						P for interaction	
	n/deaths	0 years	<1 year	1-2 years	3-5 years	6-9 years	10+ years	Total (ever)	History	Duration
Age < 62 years*	84746/13351	1 (Reference)	0.92 (0.84-1.01)	0.98 (0.91-1.05)	0.99 (0.94-1.05)	1.03 (0.96-1.09)	1.09 (1.04-1.14)	1.03 (0.99-1.07)		
Age ≥ 62 years*	102126/34993	1 (Reference)	0.97 (0.92-1.03)	0.94 (0.90-0.98)	1.01 (0.97-1.05)	1.02 (0.97-1.06)	1.05 (1.02-1.08)	1.01 (0.99-1.03)	0.005	<0.001
Low deprivation*	94368/21367	1 (Reference)	0.95 (0.89-1.02)	0.98 (0.93-1.03)	1.02 (0.97-1.06)	1.04 (0.98-1.10)	1.09 (1.05-1.13)	1.03 (1.00-1.06)		
High deprivation*	92504/26977	1 (Reference)	0.97 (0.90-1.04)	0.93 (0.88-0.98)	0.99 (0.95-1.04)	1.00 (0.95-1.05)	1.05 (1.02-1.08)	1.01 (0.98-1.04)	0.379	0.046
Low education*	94027/27713	1 (Reference)	1.03 (0.95-1.11)	0.98 (0.93-1.04)	1.00 (0.95-1.04)	1.03 (0.98-1.08)	1.06 (1.03-1.09)	1.04 (1.01-1.06)		
High education*	88587/19146	1 (Reference)	0.94 (0.88-1.00)	0.93 (0.88-0.98)	1.02 (0.97-1.06)	1.01 (0.95-1.07)	1.09 (1.04-1.16)	0.99 (0.97-1.03)	0.039	0.333
Married	158621/39156	1 (Reference)	0.96 (0.90-1.01)	0.95 (0.91-0.99)	0.99 (0.96-1.03)	1.02 (0.98-1.06)	1.06 (1.03-1.09)	1.02 (0.99-1.04)		
Single/widowed	27249/8857	1 (Reference)	0.97 (0.87-1.09)	0.96 (0.88-1.05)	1.03 (0.95-1.10)	1.02 (0.93-1.11)	1.06 (1.00-1.11)	1.02 (0.98-1.07)	0.995	0.671
Never smoker	55167/9416	1 (Reference)	0.97 (0.88-1.08)	0.86 (0.78-0.94)	0.99 (0.92-1.06)	1.04 (0.95-1.14)	1.10 (1.04-1.16)	1.01 (0.97-1.06)		
Ever smoker	125162/37001	1 (Reference)	0.96 (0.91-1.02)	0.99 (0.95-1.03)	1.03 (0.99-1.06)	1.05 (1.01-1.09)	1.08 (1.05-1.11)	1.04 (1.02-1.06)	0.260	0.819
Leisure time MVPA < 4 hours/day*	92670/26741	1 (Reference)	0.95 (0.89-1.02)	0.93 (0.88-0.97)	0.96 (0.92-1.01)	1.00 (0.95-1.05)	1.04 (1.00-1.07)	0.99 (0.97-1.02)		
Leisure time MVPA ≥ 4 hours/day*	92147/20823	1 (Reference)	0.97 (0.90-1.04)	0.98 (0.93-1.04)	1.04 (0.99-1.08)	1.02 (0.97-1.08)	1.07 (1.03-1.11)	1.03 (1.00-1.06)	0.983	0.665
Low HEI*	92356/26049	1 (Reference)	0.92 (0.85-0.98)	0.96 (0.91-1.01)	0.98 (0.94-1.02)	0.99 (0.93-1.04)	1.04 (1.01-1.07)	1.00 (0.98-1.03)		
High HEI*	94510/22293	1 (Reference)	1.00 (0.94-1.07)	0.94 (0.89-0.99)	1.03 (0.98-1.07)	1.05 (0.99-1.11)	1.09 (1.05-1.13)	1.04 (1.01-1.07)	<0.001	<0.001
Non-alcohol drinker	10762/3633	1 (Reference)	0.82 (0.66-1.02)	1.00 (0.87-1.16)	0.99 (0.87-1.11)	1.02 (0.89-1.17)	1.05 (0.97-1.14)	1.01 (0.95-1.08)		
Alcohol drinker	176110/44711	1 (Reference)	0.97 (0.92-1.02)	0.95 (0.91-0.99)	1.00 (0.97-1.03)	1.02 (0.99-1.05)	1.06 (1.03-1.08)	1.05 (0.99-1.04)	0.844	0.546
Non-obesity	146849/36190	1 (Reference)	0.96 (0.91-1.01)	0.94 (0.90-0.98)	1.00 (0.96-1.04)	1.01 (0.97-1.06)	1.05 (1.02-1.08)	1.01 (0.99-1.03)		
Obesity	37197/11291	1 (Reference)	0.95 (0.85-1.05)	0.97 (0.90-1.05)	0.99 (0.93-1.06)	1.02 (0.95-1.10)	1.09 (1.04-1.14)	1.04 (0.99-1.08)	0.574	0.881
Without diabetes	168613/39986	1 (Reference)	0.97 (0.92-1.02)	0.96 (0.92-0.99)	1.00 (0.97-1.04)	1.02 (0.98-1.06)	1.06 (1.03-1.09)	1.02 (0.99-1.04)		
With diabetes	18259/8358	1 (Reference)	0.92 (0.81-1.04)	0.92 (0.84-1.01)	0.99 (0.92-1.07)	1.01 (0.92-1.10)	1.07 (1.01-1.13)	1.01 (0.97-1.06)	0.324	0.492
Without hypertension	88881/18905	1 (Reference)	1.02 (0.94-1.09)	0.93 (0.88-0.99)	1.00 (0.95-1.05)	1.03 (0.97-1.09)	1.02 (0.98-1.06)	1.00 (0.97-1.03)		
With hypertension	76154/23971	1 (Reference)	0.93 (0.86-0.99)	0.96 (0.92-1.01)	1.00 (0.96-1.05)	1.02 (0.97-1.08)	1.09 (1.05-1.13)	1.03 (1.00-1.06)	0.724	0.908
Without hypercholesterolemia	80966/21155	1 (Reference)	0.97 (0.89-1.04)	0.99 (0.94-1.05)	1.03 (0.98-1.07)	1.07 (1.01-1.14)	1.08 (1.04-1.12)	1.04 (1.01-1.07)		
With hypercholesterolemia	77897/19211	1 (Reference)	0.97 (0.89-1.04)	0.94 (0.88-0.99)	0.98 (0.93-1.03)	0.97 (0.91-1.03)	1.04 (0.99-1.08)	0.99 (0.97-1.02)	0.099	0.255
Without coronary heart disease	153513/34466	1 (Reference)	0.96 (0.91-1.02)	0.95 (0.91-0.98)	1.00 (0.97-1.04)	1.02 (0.97-1.06)	1.05(1.02-1.08)	1.01 (0.99-1.04)		
With coronary heart disease	33359/13878	1 (Reference)	0.96 (0.87-1.05)	0.96 (0.90-1.03)	1.01 (0.95-1.07)	1.02 (0.95-1.09)	1.09 (1.04-1.13)	1.03 (0.99-1.06)	0.765	0.637
Without stroke	182870/46225	1 (Reference)	0.96 (0.92-1.01)	0.96 (0.92-0.99)	1.01 (0.98-1.04)	1.04 (0.99-1.08)	1.06 (1.04-1.09)	1.02 (1.00-1.04)		
With stroke	4002/2119	1 (Reference)	0.83 (0.64-1.07)	0.86 (0.70-1.05)	0.87 (0.75-1.02)	0.73 (0.60-0.88)	1.04 (0.93-1.16)	0.93 (0.84-1.01)	<0.001	0.001
Without osteoporosis	185334/47734	1 (Reference)	0.95 (0.91-1.00)	0.95 (0.91-0.98)	1.00 (0.97-1.03)	1.02 (0.98-1.06)	1.06 (1.03-1.08)	1.01 (0.99-1.04)		
With osteoporosis	1538/610	1 (Reference)	1.36 (0.88-2.07)	1.32 (0.96-1.82)	1.02 (0.75-1.40)	0.96 (0.68-1.37)	1.35 (1.09-1.66)	1.23 (1.03-1.48)	0.351	0.731
Without cancer	170823/42698	1 (Reference)	0.98 (0.93-1.03)	0.96 (0.92-0.99)	1.02 (0.98-1.05)	1.03 (0.99-1.07)	1.06 (1.03-1.09)	1.02 (1.00-1.04)		
With cancer	7346/3160	1 (Reference)	0.85 (0.71-1.02)	1.03 (0.90-1.18)	0.92 (0.82-1.04)	1.00 (0.87-1.16)	1.04 (0.95-1.15)	0.99 (0.92-1.06)	0.137	0.227
Without pulmonary emphysema	181526/45047	1 (Reference)	0.96 (0.91-1.01)	0.95 (0.92-0.99)	1.01 (0.98-1.04)	1.02 (0.98-1.06)	1.07 (1.04-1.09)	1.02 (1.00-1.04)		
With pulmonary emphysema	5346/3297	1 (Reference)	0.95 (0.77-1.17)	0.93 (0.80-1.07)	0.91 (0.80-1.02)	0.97 (0.84-1.11)	1.01 (0.93-1.10)	0.97 (0.90-1.04)	<0.001	<0.001

HEI: Healthy Eating Index. MVPA: moderate-to-vigorous physical activity. HR: hazard ratios. CI: confidence interval. * According to the median in this cohort. Analyses were adjusted for age, deprivation index, educational level, race, marital status, energy intake, HEI, smoking status, alcohol intake, leisure time MVPA, body mass index categories, diabetes, hypertension, hypercholesterolemia, coronary heart disease, stroke, cancer (excluding colorectal cancer, breast cancer, and prostate cancer), osteoporosis, and pulmonary emphysema

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Table S4. Association of history and duration of high occupational physical activity with all-cause mortality in women, stratified by socioeconomic factors, lifestyle behaviors, cardiometabolic risk factors and chronic health conditions.

		Never	Ever						P for interaction	
	n/deaths	0 years	<1 year	1-2 years	3-5 years	6-9 years	10+ years	Total (ever)	History	Duration
Age < 62 years*	66107/7574	1 (Reference)	0.95 (0.77-1.16)	1.06 (0.91-1.24)	1.11 (0.99-1.25)	1.18 (1.05-1.33)	1.02 (0.94-1.10)	1.06 (1.00-1.12)		
Age ≥ 62 years*	69147/17645	1 (Reference)	1.05 (0.90-1.21)	1.02 (0.89-1.17)	1.01 (0.92-1.11)	0.98 (0.88-1.10)	1.03 (0.97-1.08)	1.02 (0.98-1.06)	0.046	0.039
Low deprivation*	68146/11140	1 (Reference)	0.87 (0.68-1.11)	1.10 (0.91-1.33)	1.05 (0.91-1.20)	1.10 (0.94-1.29)	1.02 (0.94-1.12)	1.04 (0.99-1.10)		
High deprivation*	67108/14079	1 (Reference)	1.16 (0.97-1.38)	1.02 (0.87-1.19)	1.11 (0.99-1.24)	1.17 (1.04-1.31)	1.09 (1.02-1.16)	1.04 (0.99-1.08)	0.677	0.556
Low education*	88375/17951	1 (Reference)	1.05 (0.91-1.22)	1.03 (0.91-1.15)	1.06 (0.97-1.16)	1.09 (1.00-1.19)	1.00 (0.95-1.05)	1.03 (0.99-1.15)		
High education*	43050/6346	1 (Reference)	0.93 (0.72-1.19)	1.17 (0.96-1.44)	1.00 (0.85-1.16)	1.02 (0.84-1.24)	1.11 (1.00-1.23)	1.07 (0.98-1.17)	0.477	0.253
Married	59882/8930	1 (Reference)	1.08 (0.88-1.32)	0.90 (0.75-1.07)	0.92 (0.80-1.05)	1.12 (0.98-1.28)	0.99 (0.92-1.07)	0.99 (0.94-1.05)		
Single/widowed	74306/16033	1 (Reference)	0.99 (0.85-1.15)	1.11 (0.98-1.26)	1.11 (1.01-1.21)	1.04 (0.94-1.15)	1.04 (0.98-1.10)	1.06 (1.01-1.10)	0.083	0.155
Never smoker	59437/7937	1 (Reference)	1.11 (0.89-1.39)	0.96 (0.79-1.17)	1.05 (0.91-1.22)	1.06 (0.91-1.24)	1.05 (0.97-1.14)	1.05 (0.98-1.11)		
Ever smoker	71605/16421	1 (Reference)	0.99 (0.85-1.15)	1.09 (0.96-1.22)	1.12 (1.03-1.23)	1.10 (1.00-1.22)	1.05 (0.99-1.11)	1.07 (1.03-1.11)	0.675	0.761
Leisure time MVPA < 4 hours/day*	67441/13925	1 (Reference)	1.00 (0.85-1.17)	0.98 (0.85-1.12)	1.03 (0.93-1.14)	1.03 (0.92-1.16)	1.02 (0.96-1.09)	1.02 (0.97-1.07)		
Leisure time MVPA ≥ 4 hours/day*	65575/10710	1 (Reference)	1.02 (0.85-1.23)	1.10 (0.95-1.27)	1.09 (0.98-1.22)	1.11 (0.99-1.24)	1.02 (0.96-1.08)	1.05 (0.99-1.10)	0.340	0.555
Low HEI*	56184/12013	1 (Reference)	0.89 (0.74-1.08)	1.06 (0.92-1.22)	1.01 (0.91-1.12)	1.09 (0.98-1.22)	1.03 (0.97-1.09)	1.03 (0.98-1.08)		
High HEI*	79066/13205	1 (Reference)	1.12 (0.95-1.31)	1.03 (0.89-1.19)	1.09 (0.99-1.21)	1.03 (0.92-1.16)	1.03 (0.97-1.10)	1.05 (0.99-1.10)	0.006	0.541
Non-alcohol drinker	12806/3192	1 (Reference)	1.05 (0.75-1.47)	1.02 (0.78-1.33)	1.13 (0.93-1.36)	1.06 (0.86-1.31)	1.01 (0.90-1.13)	1.04 (0.95-1.13)		
Alcohol drinker	122428/22027	1 (Reference)	1.00 (0.88-1.14)	1.04 (0.94-1.16)	1.04 (0.96-1.12)	1.07 (0.98-1.16)	1.03 (0.98-1.08)	1.03 (0.99-1.07)	0.940	0.776
Non-obesity	102125/17604	1 (Reference)	0.97 (0.83-1.13)	1.03 (0.91-1.17)	1.04 (0.95-1.14)	1.03 (0.93-1.14)	1.04 (0.99-1.10)	1.04 (0.99-1.08)		
Obesity	29423/6646	1 (Reference)	1.10 (0.88-1.36)	1.03 (0.86-1.23)	1.06 (0.93-1.20)	1.18 (1.03-1.35)	1.00 (0.92-1.08)	1.04 (0.98-1.10)	0.944	0.720
Without diabetes	125859/21546	1 (Reference)	1.04 (0.91-1.19)	1.04 (0.93-1.16)	1.05 (0.97-1.14)	1.06 (0.97-1.16)	1.02 (0.97-1.07)	1.03 (0.99-1.07)		
With diabetes	9395/3673	1 (Reference)	0.92 (0.67-1.27)	1.03 (0.80-1.33)	1.08 (0.90-1.30)	1.09 (0.89-1.34)	1.07 (0.96-1.19)	1.06 (0.98-1.15)	0.666	0.462
Without hypertension	75941/11288	1 (Reference)	0.92 (0.76-1.11)	1.03 (0.89-1.21)	1.12 (1.00-1.25)	1.06 (0.94-1.19)	0.99 (0.93-1.06)	1.02 (0.97-1.08)		
With hypertension	50574/12519	1 (Reference)	1.03 (0.87-1.22)	1.04 (0.91-1.20)	1.03 (0.93-1.15)	1.07 (0.96-1.21)	1.04 (0.98-1.10)	1.04 (0.99-1.09)	0.745	0.824
Without hypercholesterolemia	61929/11823	1 (Reference)	1.06 (0.89-1.27)	1.06 (0.92-1.22)	1.00 (0.90-1.11)	1.11 (0.99-1.25)	1.01 (0.95-1.08)	1.03 (0.98-1.08)		
With hypercholesterolemia	63232/10897	1 (Reference)	0.99 (0.82-1.19)	1.01 (0.87-1.19)	1.18 (1.05-1.32)	1.03 (0.91-1.17)	1.04 (0.98-1.12)	1.06 (1.00-1.11)	0.345	0.294
Without coronary heart disease	123869/21005	1 (Reference)	0.99 (0.87-1.13)	1.03 (0.92-1.15)	1.09 (1.00-1.18)	1.10 (1.01-1.20)	1.03 (0.98-1.08)	1.05 (1.00-1.09)		
With coronary heart disease	11385/4214	1 (Reference)	1.07 (0.81-1.43)	1.10 (0.87-1.38)	0.95 (0.79-1.13)	0.96 (0.80-1.16)	1.03 (0.94-1.14)	1.02 (0.94-1.10)	0.093	0.099
Without stroke	132921/24255	1 (Reference)	1.01 (0.90-1.15)	1.07 (0.96-1.18)	1.06 (0.98-1.15)	1.09 (1.00-1.18)	1.03 (0.99-1.08)	1.05 (1.01-1.08)		
With stroke	2333/964	1 (Reference)	0.78 (0.40-1.53)	0.61 (0.36-1.05)	0.94 (0.66-1.33)	0.71 (0.44-1.12)	0.86 (0.70-1.06)	0.83 (0.70-0.98)	0.001	0.004
Without osteoporosis	124428/22227	1 (Reference)	1.04 (0.92-1.19)	1.04 (0.94-1.16)	1.07 (0.99-1.16)	1.09 (1.00-1.19)	1.05 (1.00-1.10)	1.06 (1.02-1.10)		
With osteoporosis	10826/2992	1 (Reference)	0.83 (0.59-1.16)	1.03 (0.78-1.35)	0.96 (0.77-1.20)	0.96 (0.79-1.18)	0.90 (0.80-1.02)	0.93 (0.85-1.01)	<0.001	<0.001
Without cancer	122461/21844	1 (Reference)	0.99 (0.87-1.13)	1.04 (0.93-1.16)	1.05 (0.97-1.14)	1.08 (0.99-1.18)	1.03 (0.98-1.08)	1.04 (1.00-1.07)		
With cancer	7106/2222	1 (Reference)	1.17 (0.83-1.66)	1.01 (0.75-1.36)	1.01 (0.80-1.28)	1.07 (0.84-1.36)	0.94 (0.81-1.09)	0.99 (0.89-1.11)	0.072	0.029
Without pulmonary emphysema	132015/23414	1 (Reference)	1.02 (0.90-1.15)	1.01 (0.91-1.12)	1.05 (0.97-1.13)	1.06 (0.98-1.16)	1.03 (0.99-1.08)	1.04 (1.00-1.07)		
With pulmonary emphysema	3239/1805	1 (Reference)	0.94 (0.65-1.36)	1.37 (0.99-1.90)	1.25 (0.97-1.61)	1.18 (0.90-1.54)	0.97 (0.84-1.13)	1.06 (0.95-1.20)	0.122	0.045

HEI: Healthy Eating Index. MVPA: moderate-to-vigorous physical activity. HR: hazard ratios. CI: confidence interval. * According to the median in this cohort. Analyses were adjusted for age, deprivation index, educational level, race, marital status, energy intake, HEI, smoking status, alcohol intake, leisure time MVPA, body mass index categories, diabetes, hypertension, hypercholesterolemia, coronary heart disease, stroke, cancer (excluding colorectal cancer, breast cancer, and prostate cancer), osteoporosis, and pulmonary emphysema

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Table S5. Joint associations of high occupational physical activity and leisure-time physical activity with all-cause mortality, stratified by sex

Leisure time physical activity	History of high occupational physical activity		Duration of high occupational physical activity					
	Never	Ever	0 years	<1 years	1-2 years	3-5 years	6-9 years	10+ years
Men								
MVPA <4 h/week	1 (Ref)	0.99 (0.96-1.01)	1 (Ref)	0.95 (0.89-1.01)	0.92 (0.88-0.97)	0.96 (0.92-1.00)	1.00 (0.95-1.05)	1.03 (1.00-1.06)
MVPA ≥4 h/week	0.81 (0.78-0.83)	0.84 (0.82-0.86)	0.80 (0.78-0.82)	0.78 (0.72-0.84)	0.79 (0.75-0.83)	0.84 (0.80-0.87)	0.83 (0.78-0.87)	0.87 (0.84-0.90)
Women								
MVPA <4 h/week	1 (Ref)	1.02 (0.97-1.07)	1 (Ref)	1.00 (0.85-1.17)	0.97 (0.84-1.12)	1.03 (0.92-1.14)	1.03 (0.92-1.15)	1.02 (0.96-1.09)
MVPA ≥4 h/week	0.85 (0.82-0.85)	0.89 (0.85-0.93)	0.85 (0.82-0.87)	0.87 (0.72-1.05)	0.94 (0.81-1.08)	0.94 (0.84-1.04)	0.94 (0.84-1.05)	0.87 (0.82-0.92)

HR: hazard ratios. CI: confidence interval. MVPA: moderate to vigorous physical activity. Analyses were adjusted for age, deprivation index, educational level, race, marital status, energy intake, Healthy Eating Index, smoking status, alcohol intake, body mass index categories, diabetes, hypertension, hypercholesterolemia, coronary heart disease, stroke, cancer (excluding colorectal cancer, breast cancer, and prostate cancer), osteoporosis, and pulmonary emphysema
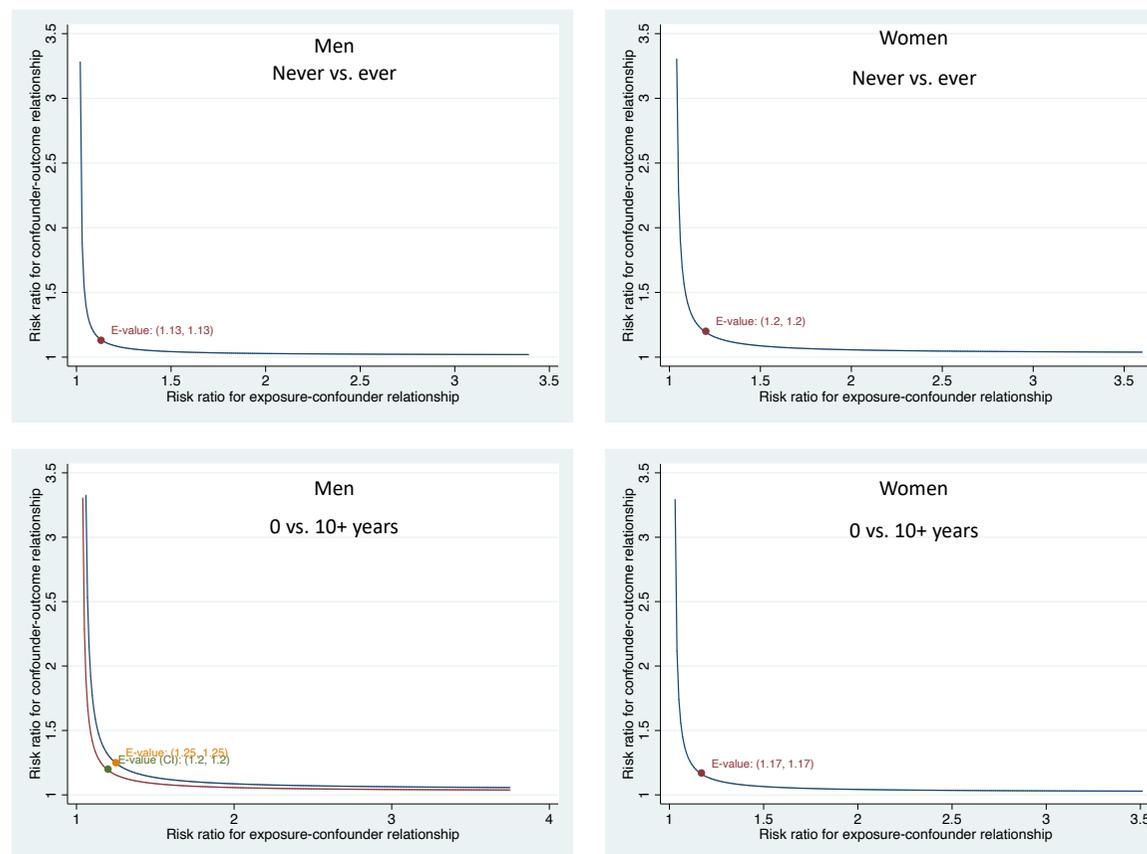
Figure S1. Robustness to unmeasured confounding with reported e-values for the association of history and duration of high occupational physical activity with all-cause mortality. Analyses were adjusted for age, deprivation index, educational level, race, marital status, energy intake, Healthy Eating Index, smoking status, alcohol intake, leisure time moderate to vigorous physical activity, body mass index categories, diabetes, hypertension, hypercholesterolemia, coronary heart disease, stroke, cancer (excluding colorectal cancer, breast cancer, and prostate cancer), osteoporosis, and pulmonary emphysema. E-values (CI) =1.00 if not shown.