Do Moderate#Intensity and Vigorous#Intensity Physical Activities Reduce Mortality Rates to the Same Extent?

Do Moderate-Intensity and Vigorous-Intensity Physical Activities Reduce Mortality Rates to the Same Extent?

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***Background*—**Limited data exist directly comparing the relative benefits of moderate- and vigorous-intensity activities with all-cause and cardiovascular (CV) disease mortality rates when controlling for physical activity volume.

***Methods and Results*—**We followed 7979 men (Harvard Alumni Health Study, 1988–2008) and 38 671 women (Women's Health Study, 1992–2012), assessing their physical activity and health habits through repeated questionnaires. Over a mean follow-up of 17.3 years in men and 16.4 years in women, there were 3551 deaths (1077 from CV disease) among men and 3170 deaths (620 from CV disease) among women. Those who met or exceeded an equivalent of the federal guidelines recommendation of at least 150 minutes of moderate-intensity activity, 75 minutes of vigorous-intensity activity, or a combination of the 2 that expended similar energy experienced significantly lower all-cause and CV disease–related mortality rates (men, 28% to 36% and 31% to 34%, respectively; women: 38% to 55% and 22% to 44%, respectively). When comparing different combinations of moderate- and vigorous-intensity activity and all-cause mortality rates, we observed sex-related differences. Holding constant the volume of moderate- to vigorous-intensity physical activity, men experienced a modest additional benefit when expending a greater proportion of moderate- to vigorous-intensity physical activity in vigorous-intensity activities (P_{trend}=0.04), but women did not (P_{trend}<0.001). Moderate- to vigorous-intensity physical activity composition was not associated with further cardiovascular mortality rate reductions in either men or women.

***Conclusions*—**The present data support guidelines recommending 150 minutes of moderate-intensity activity per week, 75 minutes of vigorous-intensity activity per week, or an equivalent combination for mortality benefits. Among men, but not women, additional modest reductions in all-cause mortality rates are associated with a greater proportion of moderate- to vigorous-intensity physical activity performed at a vigorous intensity. **(*J Am Heart Assoc*. 2014;3:e000802 doi: 10.1161/JAHA.114.000802)**

Key Words: epidemiology • mortality • physical activity

The 2008 US federal physical activity guidelines recommend at least 150 minutes per week of moderate-intensity physical activity, 75 minutes per week of vigorous-intensity physical activity, or an equivalent combination for health benefits, including reduced mortality rates.[1] Because either 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity physical activity expends approximately the same energy, these guidelines imply that equal total energy expenditure of moderate-intensity or vigorous-intensity physical activity would confer similar health benefits.

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Data are limited regarding whether this assumption is correct. In examining the scientific evidence to guide current recommendations with regard to all-cause mortality, the US federal Physical Activity Guidelines Advisory Committee (www.health.gov/paguidelines) reviewed 11 studies that provided information regarding physical activity intensity, of which only 4 controlled for total volume of activity; the committee concluded that for the same volume, higher-intensity activities provide additional risk reduction.[2] More recent analyses, including a 2011 meta-analysis, have yielded less consistent findings, with studies showing no significant additional benefit from vigorous-intensity activity or even a slight added benefit in favor of moderate-intensity activity.[3–6] However, none of these studies directly compared an equal volume of activities of moderate intensity, vigorous intensity, or combinations of the 2 in relation to mortality.[4,7–9]

Holding physical activity volume constant, we examined whether the proportion of moderate- to vigorous-intensity physical activity (MVPA) affects mortality rate reduction.

Methods

Study Participants

We analyzed data from men in the Harvard Alumni Health Study (HAHS) and women in the Women's Health Study (WHS). The HAHS is a prospective cohort study of men matriculating at Harvard University between 1916 and 1950. Men completed periodic health questionnaires beginning in 1962 on health habits and medical history. For this analysis, 12 805 men who returned a questionnaire in 1988 were eligible. We chose 1988 as the baseline year so that the period of study for men would be similar to that of women described below. Men were excluded if they had missing information on physical activity at baseline (n=591) or a history of self-reported physician-diagnosed cardiovascular disease (CVD), cancer, or diabetes before 1988 (n=4235). This resulted in a final baseline population of 7979 men. Men provided written consent to participate, and the study was approved by the institutional review board of the Harvard School of Public Health.

The WHS is a completed randomized trial of aspirin and vitamin E in the prevention of CVD and cancer, conducted between 1992 and 2004 among 39 876 healthy women initially aged ≥45 years.[10–12] Women completed health questionnaires every 6 months during the first year and then annually thereafter. Following the scheduled end of the trial, women have been followed in an observational study. As with the men, we excluded 1205 women with missing information on physical activity at baseline or who had reported CVD, cancer, or diabetes diagnoses occurring before baseline, resulting in a final baseline population of 38 671 women. Women provided written consent to participate, and the study was approved by the institutional review board of Brigham and Women's Hospital.

Assessment of Physical Activity

In the HAHS, for the baseline (in 1988) and 2 subsequent physical activity questionnaires in 1993 and 1998, men reported the number of flights of stairs climbed daily and the number of blocks walked daily and listed the frequency and duration spent doing sports or recreational activities.[13] The HAHS questionnaire physical activity estimates had test-retest correlation over 1 month of 0.72, the correlation between questionnaire estimates and activity records was 0.65, and the correlation between questionnaires and doubly labeled water was 0.67.[14–16] Women reported their physical activity using a similar questionnaire (ie, the same questionnaire as the HAHS but modified so that the data could be coded more easily) at baseline, which was then updated every 2 to 3 years through 2008.[13] The WHS questionnaire physical activity estimates yielded a correlation of 0.79 when compared with activity recalls and 0.62 when compared with activity diaries over 4 past-week assessments. The WHS questionnaire test-retest correlation over 2 years was 0.59.[17] When compared with objective measures of physical activity, vigorous-intensity activities were somewhat better reported than moderate-intensity actvities.[18]

For each reported activity or group of activities, we assigned a metabolic equivalent (MET) score, which represents the energy cost of the activity (or group of activities).[19] Resting quietly requires 1 MET, and moderate-intensity activities are defined as activities requiring 3 to <6 METs, whereas vigorous-intensity activities are those requiring 6 METs or more.[20] Examples of moderate-intensity activities include brisk walking, casual bicycling, and gardening, whereas vigorous-intensity activities include jogging, lap swimming, and playing tennis.

The volume of each reported activity or group of activities was expressed as "MET-h/week," calculated by multiplying the MET score by the time spent per week (hours). We calculated 3 measures of physical activity volume for each subject: (1) total physical activity volume, the sum across all activities; (2) moderate-intensity volume, MET-h/week expended on activities of moderate intensity, which was estimated by summing across all activities in that intensity range; and (3) vigorous-intensity volume, MET-h/week expended on activities of vigorous intensity, which was estimated by summing across all activities in that intensity range.

We classified men and women into 5 categories based on the 2008 federal guidelines[1] to reflect total physical activity and to obtain reasonable distributions of subjects. The following categories were used: (1) less than half the recommended guideline (0 to <3.75 MET-h/week); (2) "some activity" (3.75 to <7.5 MET-h/week); (3) satisfying the guideline (7.5 to <15 MET-h/week); (4) 2 to <4 times the guideline (15 to <30 MET-h/week); and (5) at least 4 times the guideline (≥30 MET-h/week). The guidelines require that activities be performed in bouts of at least 10 minutes; however, we were unable to apply this requirement because we did not ask about bout length.

To examine the composition of MVPA, we classified participants into 5 categories of increasingly larger proportions of MVPA spent on vigorous-intensity activities: 10% or less, >10% to ≤25%, >25% to ≤50%, >50% to ≤75%, and >75%. In analyses that control for the total volume of physical activity, we compared participants with the same volume of activity but comprising different proportions of moderate and vigorous intensities.

Assessment of Baseline Covariates and Mortality

In men, baseline (1988) information was collected on age, height, weight, smoking habits, and physician-diagnosed hypertension and high cholesterol. Dietary habits (including alcohol consumption) were assessed using a semiquantitative food questionnaire. All information, except diet, was updated in 1993 and 1998. For women, baseline data included similar information plus postmenopausal status, postmenopausal hormone use, and parental history of myocardial infarction before age 60 years. All information, except for diet, was updated on the 36-, 72-, and 96-month questionnaires during the trial, at trial conclusion (120 months), and in cycle 2 (144 months) and in cycle 4 (168 months) of observational follow-up.

For men, mortality through 1997 was ascertained using information from the Harvard University alumni office to identify decedents and to obtain copies of death certificates; this follow-up is >99% complete.[8] Between 1998 and 2008, mortality was additionally ascertained using the National Death Index. For women, family members or postal authorities reported most deaths. Medical records and death certificates were obtained to confirm these deaths. Other deaths were ascertained using the National Death Index. Women were followed through March 2012, and mortality follow-up is >99% complete.

Statistical Analysis

Baseline characteristics of men and women were described by categories of total physical activity. To examine the association of mortality rates (all-cause and CVD) and increasing total physical activity volume, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated comparing participants with greater physical activity with those with the least, using time-varying Cox proportional hazard models because physical activity and covariates (except for diet) were updated over time.

We then compared categories of participants who expended increasingly larger proportions of their MVPA on vigorous-intensity activities with those in the referent category, who spent ≤10%, controlling for total MVPA volume. A statistically significant HR of less than 1.0 indicates that a larger proportion of MVPA at vigorous intensity is associated with additional rate reduction compared with the referent.

For all analyses, we used 3 nested analytical models:

1. A model adjusted for age and total MVPA per week;
2. A multivariable model adjusted for age plus smoking status; alcohol consumption; vegetable and fruit intake; saturated fat intake; total caloric intake; and, in women only, fiber intake, randomization arm of the clinical trial period, parental history of myocardial infarction, postmenopausal status, and hormone therapy; and
3. A multivariable model additionally adjusted for body mass index (kg/m^2), high cholesterol, and hypertension.

We also examined whether the association of MVPA composition and mortality differed by age (men, younger than 70 years or at least 70 years; women, less than 60 years or at least 60 years). Multivariable adjusted models used a complete case analysis. The proportional hazards assumption was tested and found not to be violated (P>0.05).

Results

Baseline characteristics of the men (mean age=66.1 years [SD=7.7 years]) and women (mean age=54.6 years [SD=7.0 years]) by total physical activity volume are in Table 1. Men expended a median of 18.6 MET-h/week (25th percentile: 6.3; 75th percentile: 37.4) in physical activity; the median for women was 8.4 MET-h/week (25th percentile: 2.7; 75th percentile: 20.5). Of the 7979 men at baseline (year 1988), 3551 died (1077 of CVD) during 17.3 mean years of follow-up. Of the 38 761 women at baseline (year 1992), 3170 died (620 of CVD) during 16.4 mean years of follow-up.

An inverse dose–response relationship of total physical activity volume with mortality was observed in both men and women after multivariable adjustment (P_{trend}<0.001 for both) (Figure 1). Men, who performed some activity, expending 3.75 to less than 7.5 MET-h/week in total physical activity, experienced a 19% reduction in mortality rate (HR=0.81; 95% CI: 0.69 to 0.94) compared with the least active men. In the most active men expending at least 30 MET-h/week in total physical activity (ie, ≥4 times the guideline), we observed a 36% mortality rate reduction (HR=0.64; 95% CI=0.57 to 0.72) compared with the least active men. Women expending 3.75 to less than 7.5 MET-h/week in total physical activity experienced a mortality rate reduction of 26% (HR=0.74; 95% CI=0.66 to 0.83) compared with the least active women. There was a 55% mortality rate reduction (HR=0.45; 95% CI=0.40 to 0.52) in the most active women compared with the least active women. Additionally adjusting for body mass index, hypertension, and high cholesterol (multivariable-adjusted model 2) resulted in similar findings. Consequently, we chose to report results from multivariable-adjusted model 1 because body mass index, hypertension, and high cholesterol mediate the inverse relationship between physical activity and mortality rate.

A similar inverse dose–response relationship of total physical activity volume and CVD mortality was observed in both men and women (Figure 2). Men with at least some activity experienced a 29% to 35% rate reduction compared with the least active men (P_{trend}=0.02), whereas corresponding women experienced a rate reduction between 27% and 44% compared with the least active women (P_{trend}<0.001) (Figure 2).

At baseline, 36.2% of men performed 10% or less of MVPA volume on vigorous-intensity activities, whereas 15.4%, 16.4%, 13.8%, and 18.2% respectively performed >10% to

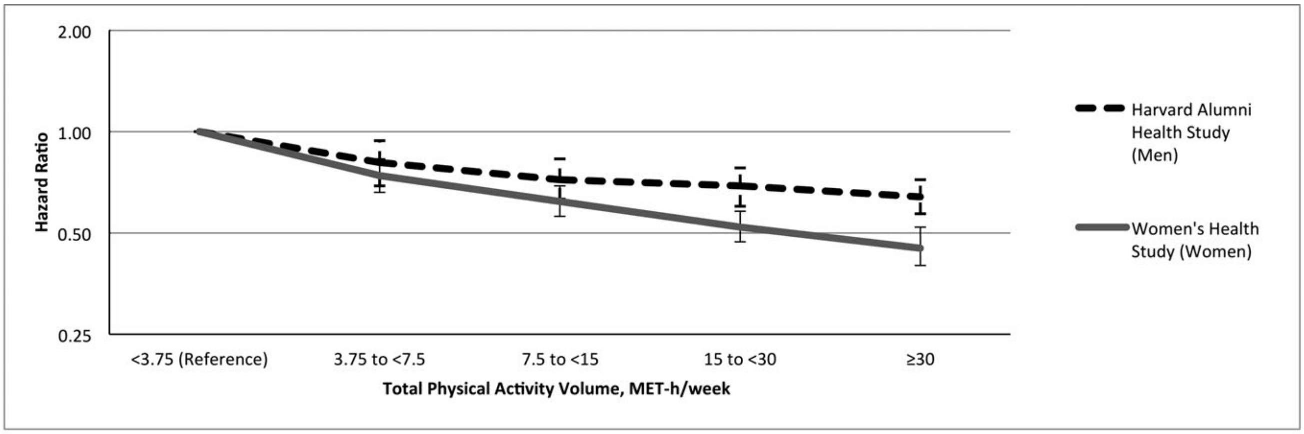
Table 1. Baseline Characteristics of Participants by Total Physical Activity Volume, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012)

Characteristic	Total Physical Activity Volume (MET-h/week)*				
	<3.75	3.75 to <7.5	7.5 to <15	15 to <30	≥30
	(n=1327)	(n=847)	(n=1247)	(n=1916)	(n=2642)
Harvard Alumni Health Study (men)					
Age, y, mean (SD)	68.5 (9.1)	66.5 (8.0)	65.6 (7.4)	65.2 (7.2)	66.0 (7.2)
BMI, kg/m^2, mean (SD)	25.2 (3.6)	24.8 (3.2)	24.7 (2.9)	24.6 (2.8)	24.4 (2.7)
Current smoking, no. (%)	171 (13.0)	111 (13.2)	97 (7.8)	116 (6.1)	178 (6.8)
Daily alcohol intake, no. (%)	489 (37.2)	338 (40.0)	526 (42.4)	798 (41.8)	1184 (45.0)
Highest quartile of energy intake, no. (%)	252 (25.3)	181 (26.7)	243 (24.0)	372 (23.3)	554 (25.3)
Highest quartile of saturated fat, no. (%)	301 (30.3)	194 (28.7)	242 (23.9)	366 (22.9)	543 (24.8)
≥3 Servings/d of vegetables, no. (%)	179 (13.6)	106 (12.6)	147 (11.8)	292 (15.3)	399 (15.2)
≥3 Servings/d of fruits, no. (%)	106 (9.7)	59 (8.1)	105 (9.8)	198 (11.8)	271 (11.7)
Hypertension, no. (%)	391 (30.0)	232 (27.6)	349 (28.1)	472 (24.7)	639 (24.4)
High cholesterol, no. (%)	221 (16.9)	159 (19.0)	242 (19.5)	363 (19.1)	488 (18.7)
Total physical activity, MET-h/week, median (IQR)	1.2 (0.7 to 2.3)	5.2 (4.4 to 6.1)	11.3 (9.3 to 13.1)	21.6 (18.0 to 25.3)	49.5 (37.6 to 70.5)
Vigorous physical activity, MET-h/week, median (IQR)	0.7 (0.2 to 1.3)	1.2 (0.2 to 2.4)	2.0 (0.7 to 7.7)	7.2 (1.3 to 15.5)	18.8 (1.6 to 38.4)
Women's Health Study (women)	(n=11 941)	(n=5763)	(n=7569)	(n=8291)	(n=5107)
Age, y, mean (SD)	54.5 (7.0)	54.3 (6.9)	54.5 (6.9)	55.0 (7.2)	54.4 (7.0)
BMI, kg/m^2, mean (SD)	27.3 (5.7)	26.0 (4.8)	25.7 (4.5)	25.0 (4.2)	24.4 (4.1)
Postmenopausal, no. (%)	6423 (16.6)	3035 (7.9)	4027 (10.4)	4591 (11.9)	2713 (7.0)
Current hormone replacement therapy, no. (%)	4615 (12.0)	2400 (6.2)	3211 (8.3)	3494 (9.1)	2203 (5.7)
Current smoking, no. (%)	2233 (5.8)	782 (2.0)	804 (2.1)	823 (2.1)	422 (1.1)
Parental history of MI, no. (%)	1774 (4.7)	755 (2.0)	1076 (2.8)	1147 (3.0)	724 (1.9)
Any alcohol intake, no. (%)	5756 (14.9)	3194 (8.3)	4384 (11.3)	4985 (12.9)	3194 (8.3)
Energy intake, kcal/d, mean (SD)	1690.1 (546.4)	1733.5 (531.6)	1730.8 (519.2)	1742.0 (522.6)	1767.7 (542.2)
Saturated fat, g/d, mean (SD)	20.6 (8.7)	20.1 (8.1)	19.5 (7.7)	19.1 (7.8)	18.2 (7.9)
Fiber intake, g/d, mean (SD)	16.7 (7.3)	18.5 (7.6)	19.3 (7.9)	20.1 (8.2)	22.0 (9.6)
Fruits and vegetables, servings/d, mean (SD)	5.2 (3.4)	5.9 (3.2)	6.2 (3.3)	6.6 (3.7)	7.5 (4.2)
Hypertension, no. (%)	3554 (9.2)	1472 (3.8)	1915 (5.0)	2005 (5.2)	1053 (2.7)
High cholesterol, no. (%)	3857 (10.0)	1732 (4.5)	2284 (5.9)	2415 (6.2)	1307 (3.4)
Total physical activity, MET-h/week, median (IQR)	1.3 (0.5 to 2.4)	5.4 (4.5 to 6.3)	10.3 (8.6 to 12.2)	20.9 (17.5 to 24.3)	42.5 (35.0 to 57.6)
Vigorous physical activity, MET-h/week, median (IQR)	0.2 (0.0 to 0.9)	0.9 (0.2 to 1.8)	1.5 (0.5 to 5.3)	5.1 (0.5 to 12.7)	23.0 (11.0 to 36.0)

BMI indicates body mass index; IQR, interquartile range; MET-h/week, metabolic equivalent score multiplied by the time spent per week (hours); MI, myocardial infarction.
*Total physical activity energy expenditure was calculated from walking, climbing stairs, and participating in leisure-time activities. Vigorous-intensity activities required at least 6 times the metabolic rate.

≤25%, >25% to ≤50%, >50% to ≤75%, and >75% of their MVPA on vigorous-intensity activities. The median MVPA volume varied across groups: Men with the lowest proportion of vigorous-intensity volume expended 26.6 MET-h/week, whereas those who performed >10% to ≤25%, >25% to ≤50%, >50% to ≤75%, and >75% of their MVPA on vigorous-intensity activities respectively expended 12.0, 21.1, 26.5, and 28.1 MET-h/week of MVPA.

A similar distribution was observed for the women: 30.6% of women performed 10% or less of their MVPA on vigorous-intensity activities, whereas 13.7%, 17.1%, 15.1%, and 23.6% respectively performed >10% to ≤25%, >25% to ≤50%, >50% to ≤75%, and >75% of their MVPA on vigorous-intensity activities. Women with the lowest proportion of vigorous-intensity volume expended 10.4 MET-h/week, whereas those in the higher categories respectively



	Total Physical Activity Volume (MET-h/week)[a]					*P* Value for Trend
	<3.75	3.75 to <7.5	7.5 to <15	15 to <30	≥30	
Harvard Alumni Health Study (Men)						
Cases, No. (person-years)	757 (20 625)	392 (14 244)	542 (21 833)	1170 (34 632)	1114 (46 888)	
Age Adjusted	Reference	0.79 (0.69, 0.90)	0.68 (0.60, 0.77)	0.65 (0.58, 0.72)	0.60 (0.54, 0.67)	<0.001
Multivariable Adjusted 1[b]	Reference	0.81 (0.69, 0.94)	0.72 (0.63, 0.83)	0.69 (0.60, 0.78)	0.64 (0.57, 0.72)	<0.001
Multivariable Adjusted 2[c]	Reference	0.79 (0.68, 0.92)	0.71 (0.62, 0.82)	0.68 (0.59, 0.77)	0.63 (0.55, 0.71)	<0.001
Women's Health Study (Women)						
Cases, No. (person-years)	1141 (194 422)	456 (94 749)	533 (125 337)	653 (136 513)	387 (84 055)	
Age Adjusted	Reference	0.67 (0.60, 0.75)	0.54 (0.49, 0.60)	0.46 (0.41, 0.51)	0.38 (0.34, 0.43)	<0.001
Multivariable Adjusted 1[d]	Reference	0.74 (0.66, 0.83)	0.62 (0.56, 0.69)	0.52 (0.47, 0.58)	0.45 (0.40, 0.52)	<0.001
Multivariable Adjusted 2[c]	Reference	0.72 (0.64, 0.81)	0.59 (0.53, 0.66)	0.49 (0.44, 0.54)	0.41 (0.36, 0.47)	<0.001

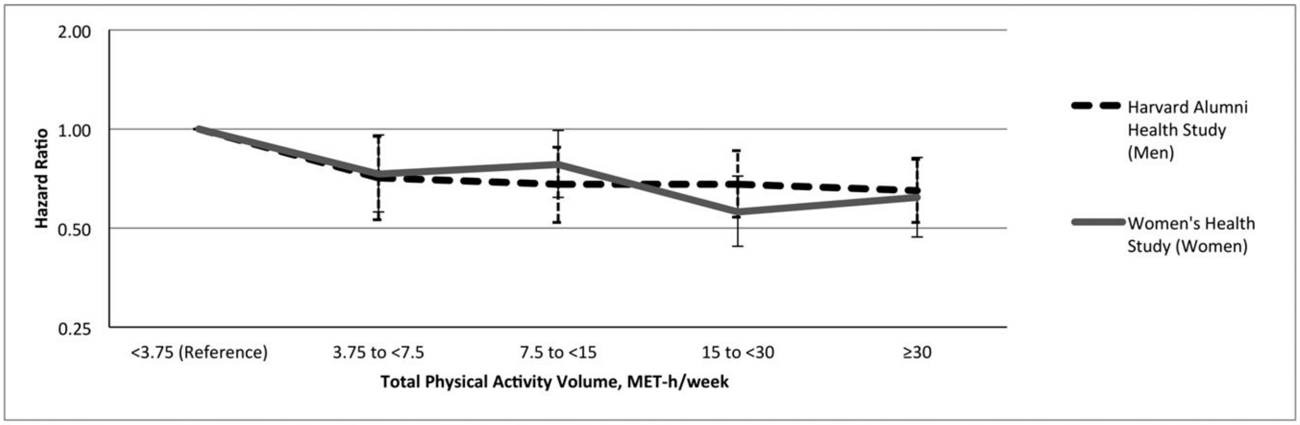
Figure 1. Hazard ratio of all-cause mortality according to total physical activity volume, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012). All values are hazard ratios (95% confidence intervals) unless otherwise specified. [a]Total physical activity volume was calculated from walking, climbing stairs, and participating in leisure-time activities. [b]Additionally adjusted for smoking status, dietary factors, and alcohol consumption. [c]Additionally adjusted for body mass index, high cholesterol, and hypertension. [d]Additionally adjusted for clinical trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction. Hazard ratios in figure were estimated using multivariable-adjusted model 1. MET indicates metabolic equivalent.

expended 7.2, 12.1, 16.4, and 1.6 MET-h/week of MVPA. Of note, women with the highest percentage of MVPA in vigorous-intensity activities actually had a low total volume of MVPA (1.6 MET-h/week); they likely represented women who did little activity but did climb stairs, a vigorous-intensity activity.

Men with higher proportions of MVPA in vigorous-intensity physical activity had modestly lower all-cause mortality rates compared with the referent group for the same volume of MVPA (P=0.04) (Figure 3). Compared with men who spent 10% or less of MVPA in vigorous-intensity activity, men with >10% to ≤25% vigorous activity had an 8% (HR=0.92 [95% CI: 0.81 to 1.05]) lower mortality rate. Men who spent >25% to ≤50%, >50% to ≤75%, and >75% of their MVPA on vigorous-intensity activities respectively had 10% (HR=0.90 [95% CI: 0.80 to 1.02]), 4% (HR=0.96 [95% CI: 0.83 to 1.09]), and 6% (HR=0.94 [95% CI: 0.82 to 1.09]) lower mortality rates after adjustment for total MVPA volume, smoking, and dietary factors.

In contrast, we did not observe this phenomenon in women (Figure 3). In adjusted models, compared with women with the lowest proportion of MVPA in vigorous-intensity activities (women with ≤10%), women with >10% to ≤25%, >25% to ≤50%, >50% to ≤75%, and >75% of their MVPA on vigorous-intensity activities had HRs of 0.94 (95% CI: 0.82 to 1.08), 1.04 (95% CI: 0.91 to 1.18), 0.94 (95% CI: 0.80 to 1.09), and 1.23 (95% CI: 1.11 to 1.36), respectively.

When examining CVD mortality, neither men nor women experienced any additional reduction in CVD mortality rate when a greater proportion of MVPA volume was in vigorous-intensity activity when total MVPA volume was held constant (P_{men}=0.19, P_{women}=0.29) (Figure 4). For both men and women, the association of varying MVPA composition with all-cause mortality rates did not differ by age (interaction: P_{men}=0.94, P_{women}=0.17) (Table 2). Similarly, no interaction of MVPA composition and cardiovascular mortality rates was observed by age (interaction: P_{men}=0.53, P_{women}=0.58) (Table 2).



	Total Physical Activity Volume (MET-h/week)[a]					P Value for
	<3.75	3.75 to <7.5	7.5 to <15	15 to <30	≥30	Trend
Harvard Alumni Health Study (Men)						
Cases, No. (person-years)	233 (20 625)	116 (14 244)	150 (21 833)	223 (34 632)	355 (46 888)	
Age Adjusted	Reference	0.72 (0.56, 0.92)	0.68 (0.54, 0.85)	0.73 (0.60, 0.90)	0.63 (0.55, 0.71)	0.06
Multivariable Adjusted 1[b]	Reference	0.71 (0.53, 0.95)	0.68 (0.52, 0.88)	0.68 (0.54, 0.86)	0.65 (0.52, 0.81)	0.02
Multivariable Adjusted 2[c]	Reference	0.69 (0.51, 0.93)	0.67 (0.52, 0.88)	0.69 (0.55, 0.87)	0.66 (0.53, 0.83)	0.04
Women's Health Study (Women)						
Cases, No. (person-years)	233 (194 422)	77 (94 749)	90 (125 337)	147 (136 513)	73 (84 055)	
Age Adjusted	Reference	0.62 (0.48, 0.80)	0.62 (0.50, 0.78)	0.45 (0.36, 0.57)	0.46 (0.35, 0.60)	<0.001
Multivariable Adjusted 1[d]	Reference	0.73 (0.56, 0.96)	0.78 (0.62, 0.99)	0.56 (0.44, 0.72)	0.62 (0.47, 0.82)	<0.001
Multivariable Adjusted 2[c]	Reference	0.74 (0.57, 0.97)	0.78 (0.62, 0.99)	0.58 (0.45, 0.74)	0.64 (0.49, 0.85)	<0.001

Figure 2. Hazard ratio of cardiovascular disease mortality according to total physical activity volume, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012). All values are hazard ratios (95% confidence intervals) unless otherwise specified. [a]Total physical activity volume was calculated from walking, climbing stairs, and participating in leisure-time activities. [b]Additionally adjusted for smoking status, dietary factors, and alcohol consumption. [c]Additionally adjusted for body mass index, high cholesterol, and hypertension. [d]Additionally adjusted for clinical trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction. Hazard ratios in figure were estimated using multivariable-adjusted model 1. MET indicates metabolic equivalent.

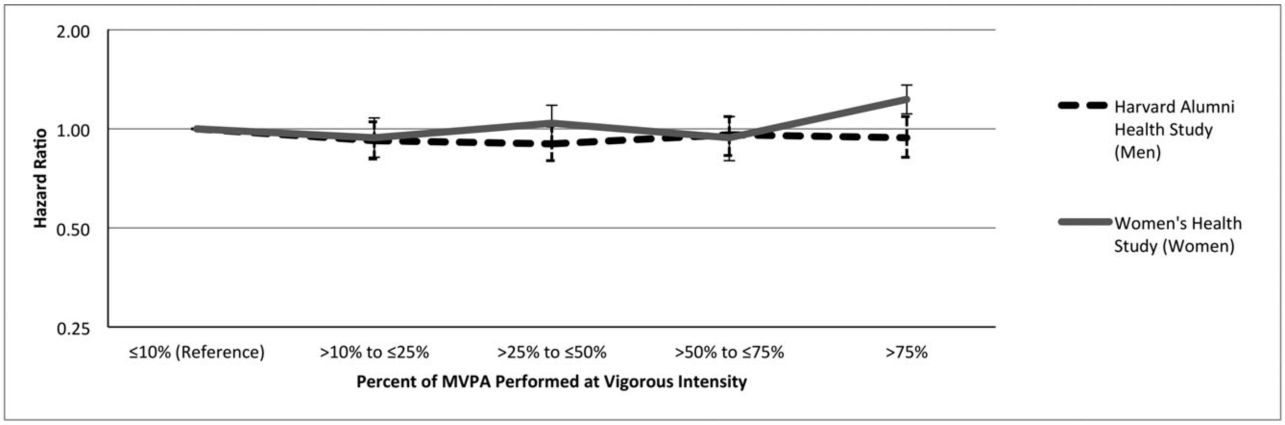
Discussion

In 2 parallel long-term prospective cohorts of older adults, we observed an inverse association between total physical activity volume and reductions in mortality among both men and women. The most active persons experienced mortality rates that were one third to one half lower compared with the least active. Even smaller amounts of physical activity were associated with lower mortality rates. These observations support current guidelines, which acknowledge, "Some physical activity is better than none," and recommending at least 150 minutes per week of at least moderate-intensity physical activity such as brisk walking.[1]

When comparing MVPA regimens of similar total volume but with varying proportions of moderate- and vigorous-intensity physical activities, we found sex-related differences. Men experienced a modest additional reduction of between 4% and 10% in all-cause mortality rates when their total MVPA volume comprised greater proportions of vigorous-intensity physical activities; however, women did not. In terms of CVD mortality, neither men nor women benefited further when a higher proportion of their MVPA volume was from vigorous-intensity physical activity.

Our findings in men support previous analyses of these same men at younger ages (mean baseline ages of 46[7] and 58 years[8]), which showed that vigorous-intensity physical activity further reduced the all-cause mortality rate but not the CVD mortality rate compared with moderate-intensity physical activity after controlling for total energy expenditure.[7,8] These analyses did not estimate the magnitude of further mortality rate reductions, which were found to be modest (4% to 10%) in the present study.

Among women, we found moderate-intensity physical activity to be at least as beneficial as vigorous-intensity physical activity when MVPA volume was the same. Two possible reasons might explain these findings in comparison with men. First, the distribution of physical activity volume differed between the 2 sexes, with men expending a larger



	Percent of MVPA Performed at Vigorous Intensity					*P* Value for
	≤10%	>10% to ≤25%	>25% to ≤50%	>50% to ≤75%	>75%	Trend
Harvard Alumni Health Study (Men)						
Cases, No. (person-years)	1407 (47 583)	542 (21 223)	543 (22 774)	408 (19 691)	561 (25 387)	
Age & MVPA Adjusted	Reference	0.96 (0.85, 1.07)	0.92 (0.83, 1.03)	0.91 (0.80, 1.02)	0.90 (0.79, 1.02)	0.08
Multivariable Adjusted 1[b]	Reference	0.92 (0.81, 1.05)	0.90 (0.80, 1.02)	0.96 (0.83, 1.09)	0.94 (0.82, 1.09)	0.04
Multivariable Adjusted 2[c]	Reference	0.92 (0.81, 1.06)	0.90 (0.80, 1.02)	0.96 (0.84, 1.09)	0.95 (0.82, 1.09)	0.06
Women's Health Study (Women)						
Cases, No. (person-years)	1014 (184 265)	362 (83 314)	435 (103 803)	374 (91 412)	703 (142 390)	
Age & MVPA Adjusted	Reference	0.92 (0.81, 1.06)	1.05 (0.93, 1.19)	0.92 (0.79, 1.07)	1.32 (1.20, 1.46)	<0.001
Multivariable Adjusted 1[d]	Reference	0.94 (0.82, 1.08)	1.04 (0.91, 1.18)	0.94 (0.80, 1.09)	1.23 (1.11, 1.36)	<0.001
Multivariable Adjusted 2[c]	Reference	0.93 (0.81, 1.07)	1.03 (0.90, 1.17)	0.94 (0.81, 1.10)	1.26 (1.14, 1.40)	<0.001

Figure 3. Hazard ratio of all-cause mortality according to percent of MVPA performed at vigorous intensity, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012). All values are hazard ratios (95% confidence intervals) unless otherwise specified. [a]Total physical activity volume was calculated from walking, climbing stairs, and participating in leisure-time activities. [b]Additionally adjusted for smoking status, dietary factors, and alcohol consumption. [c]Additionally adjusted for body mass index, high cholesterol, and hypertension. [d]Additionally adjusted for clinical trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction. Hazard ratios in figure were estimated using multivariable-adjusted model 1. MVPA indicates moderate- to vigorous-intensity physical activity.

volume of total and vigorous-intensity physical activity compared with women. Women with the largest proportion of MVPA volume spent on vigorous-intensity activities had a median MVPA volume of only 1.6 MET-h/week, which was substantially lower than the MVPA volume of women in the other categories of MVPA composition. These women may represent a higher risk group because overall physical activity was associated with lower mortality rates. Thus, potential residual confounding by diet and other healthy habits may have occurred, even though we tried to control for these statistically.

In addition, the results may reflect differences in dose–response for physical activity intensity, depending on the volume of physical activity expended. The present findings suggest that intensity has a larger effect in men, at the higher end of the physical activity spectrum, compared with women, at the lower end of the spectrum. A previous meta-analysis of physical fitness reported that the dose–response curve with all-cause morality was more marked at higher levels of fitness than at lower levels and that the dose response increased with higher levels of fitness.[21] This could plausibly explain why we observed no effect of intensity among women (at the lower end of the curve) but an added effect of intensity among the men (at the higher end of the curve).

Second, the findings in women may reflect lower precision in the reporting of physical activities of differing intensities compared with men. Walking accounted for the majority of moderate-intensity physical activity (mean: 72% of MVPA) in women, consistent with other studies. Walking is also more precisely reported compared with other activities[22,23]; therefore, this might also explain, in part, the observation that greater additional benefit was observed among women with the highest proportion of MVPA in moderate-intensity physical activity.

Limited data exist comparing the mortality benefits of moderate- and vigorous-intensity physical activity energy expenditure, particularly where total volume of physical activity is controlled. Of the 4 studies reviewed by the US Physical Activity Guidelines Advisory Committee,[2] including

Table 2. Hazard Ratio of All-Cause and Cardiovascular Disease Mortality According to Percentage of MVPA Performed at Vigorous Intensity by Age, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012)

	No. of Participants†	Percent of MVPA Performed at Vigorous Intensity*					*P* Value for Trend	*P* Value for Interaction
		≤10%	>10% to ≤25%	>25% to ≤50%	>50% to ≤75%	>75%		
Harvard Alumni Health Study (men)‡		All-cause mortality						
Age, y								
<70	5543	Reference	1.01 (0.84 to 1.21)	0.95 (0.80 to 1.12)	1.00 (0.83 to 1.19)	0.98 (0.80 to 1.19)	0.74	0.94
≥70	2436	Reference	0.85 (0.70 to 10.30)	0.86 (0.72 to 1.03)	0.90 (0.73 to 1.11)	0.94 (0.76 to 1.15)	0.008	
Women's Health Study (women)§								
Age, y								
<60	30 428	Reference	0.89 (0.69 to 1.14)	0.98 (0.83 to 1.16)	1.05 (0.82 to 1.34)	1.33 (1.16 to 1.54)	<0.001	0.17
≥60	8243	Reference	1.07 (0.82 to 1.41)	1.07 (0.89 to 1.29)	0.84 (0.63 to 1.11)	1.13 (0.98 to 1.31)	0.20	
Harvard Alumni Health Study (men)‡		Cardiovascular disease mortality						
Age, y								
<70	5543	Reference	1.29 (0.92 to 1.79)	0.73 (0.50 to 1.05)	0.85 (0.59 to 1.24)	0.93 (0.63 to 1.39)	0.87	0.53
≥70	2436	Reference	0.88 (0.64 to 1.21)	0.74 (0.54 to 1.02)	0.69 (0.47 to 1.01)	0.77 (0.53 to 1.12)	0.18	
Women's Health Study (women)§								
Age, y								
<60	30 428	Reference	0.52 (0.24 to 1.12)	0.97 (0.64 to 1.49)	1.00 (0.49 to 2.07)	0.90 (0.61 to 1.32)	0.86	0.58
≥60	8243	Reference	1.23 (0.68 to 2.20)	0.70 (0.44 to 1.10)	0.91 (0.50 to 1.66)	1.40 (1.04 to 1.87)	0.15	

All values are hazard ratios (95% confidence intervals) unless otherwise specified and represent additional associations, according to what percentage of MVPA is performed at vigorous intensity. MVPA indicates moderate- to vigorous-intensity physical activity.

*Percentage of MVPA performed at vigorous intensity was calculated as the vigorous-intensity physical activity energy expenditure divided by total moderate- and vigorous-intensity physical activity energy expenditure, estimated from walking, climbing stairs, and participating in leisure-time activities. Moderate-intensity activities required 3 to <6 times the metabolic rate; vigorous-intensity activities required a metabolic equivalent score ≥6.

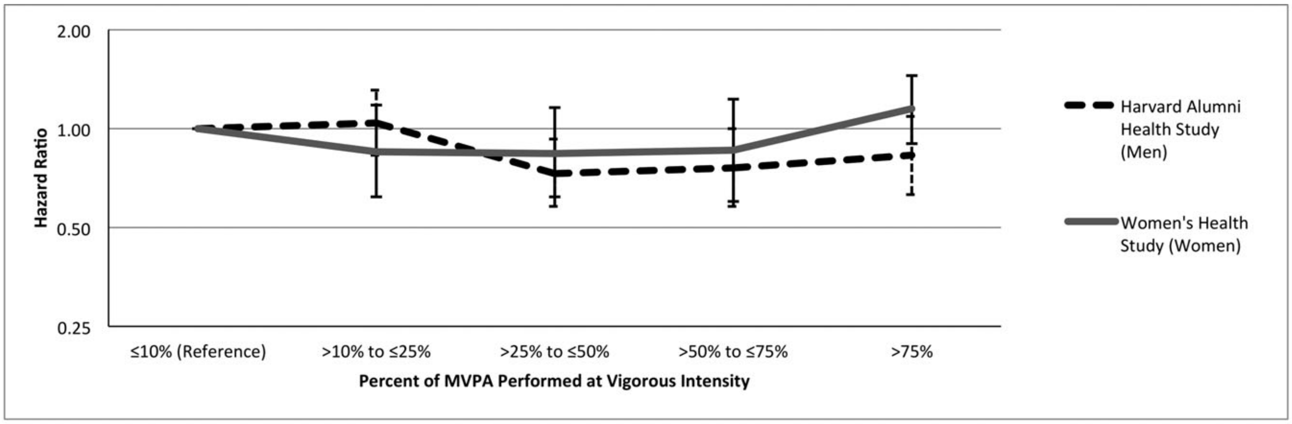
†Number of participants at baseline.

‡Hazard ratios are adjusted for age, MVPA, smoking status, dietary factors, and alcohol consumption.

§Hazard ratios are adjusted for age, MVPA, trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction.

the 2 previous analyses of the HAHS men described above and 1 in older men and women aged ≥65 years, all concluded that vigorous-intensity physical activity may further reduce mortality rates compared with moderate-intensity physical activity of equivalent energy expenditure.[7–9,24] More recent studies are less consistent. A 2011 meta-analysis observed that 75 minutes of vigorous-intensity activity and 150 minutes of moderate-intensity activities provided a similar mortality rate reduction (11% for vigorous intensity and 10% for moderate intensity), controlling for total physical activity volume.[4]

Strengths of this study include the large sample of older men and women in the HAHS and the WHS; multiple, detailed assessments of physical activity; and nearly complete mortality follow-up over >15 years, providing excellent statistical power. Several limitations are also worth noting. Although detailed, physical activity was self-reported. A recent study comparing self-reported physical activity with accelerometer-assessed physical activity found vigorous-intensity physical activities to be somewhat better reported than moderate-intensity activities (r=0.36 and 0.23, respectively).[18] In addition, these estimates of MVPA volume were



	Percent of MVPA Performed at Vigorous Intensity					*P* Value for
	≤10%	>10% to ≤25%	>25% to ≤50%	>50% to ≤75%	>75%	Trend
Harvard Alumni Health Study (Men)						
Cases, No. (person-years)	429 (47 583)	160 (21 223)	168 (22 774)	112 (19 691)	183 (25 387)	
Age & MVPA Adjusted	Reference	1.02 (0.83, 1.25)	0.90 (0.73, 1.09)	0.79 (0.63, 0.99)	0.77 (0.60, 0.97)	0.20
Multivariable Adjusted 1[b]	Reference	1.04 (0.83, 1.31)	0.73 (0.58, 0.93)	0.76 (0.58, 1.00)	0.83 (0.63, 1.09)	0.19
Multivariable Adjusted 2[c]	Reference	1.06 (0.85, 1.34)	0.74 (0.58, 0.93)	0.79 (0.60, 1.02)	0.83 (0.63, 1.10)	0.19
Women's Health Study (Women)						
Cases, No. (person-years)	225 (184 265)	69 (83 314)	64 (103 803)	50 (91 412)	142 (142 390)	
Age & MVPA Adjusted	Reference	0.83 (0.61, 1.15)	0.84 (0.62, 1.14)	0.84 (0.59, 1.18)	1.25 (0.99, 1.56)	0.07
Multivariable Adjusted 1[d]	Reference	0.85 (0.62, 1.18)	0.84 (0.62, 1.16)	0.86 (0.60, 1.23)	1.15 (0.90, 1.45)	0.29
Multivariable Adjusted 2[c]	Reference	0.86 (0.62, 1.19)	0.85 (0.62, 1.17)	0.87 (0.61, 1.24)	1.13 (0.89, 1.43)	0.36

Figure 4. Hazard ratio of cardiovascular disease mortality according to percent of MVPA performed at vigorous intensity, Harvard Alumni Health Study (1988–2008) and Women's Health Study (1992–2012). All values are hazard ratios (95% confidence intervals) unless otherwise specified. [a]Total physical activity volume was calculated from walking, climbing stairs, and participating in leisure-time activities. [b]Additionally adjusted for smoking status, dietary factors, and alcohol consumption. [c]Additionally adjusted for body mass index, high cholesterol, and hypertension. [d]Additionally adjusted for clinical trial randomization, smoking status, dietary factors, alcohol consumption, postmenopausal status, hormone therapy, and parental history of myocardial infarction. Hazard ratios in figure were estimated using multivariable-adjusted model 1. MVPA indicates moderate- to vigorous-intensity physical activity.

calculated using published MET values, which were established using primarily middle-aged subjects, and reflect an "absolute" intensity level, without taking into account "relative" intensity (ie, the same activity may require a higher relative intensity in an older person than in younger person because the older person's physical capacity has declined with age).[19] This may result in misclassification of moderate- and vigorous-intensity physical activity.

Current guidelines also require that physical activity be carried out in bouts of at least 10 minutes be to counted toward the guidelines; however, we did not collect information on bout length and so included all reported activities, regardless of bout length. Men in the HAHS and women in the WHS are older adults, primarily white, of high education and socioeconomic status—correlates of higher physical activity levels—which may limit the generalizability of our findings.

In conclusion, the present data support federal physical activity guidelines recommending at least 150 minutes of moderate-intensity physical activity per week, 75 minutes of vigorous-intensity physical activity per week, or a combination of the 2 for postponing premature mortality in older adults. In translating these guidelines into clinical practice, the focus is often on 150 minutes per week of moderate-intensity physical activity[25–28] because the US population is typically inactive, and it is easier to initially promote this lower intensity of activity, which would in turn lessen the risk of musculoskeletal injury.[2,29–32] Our findings indicate that a focus on moderate-intensity physical activity is appropriate in view of equivalent reductions in CVD mortality in men and women and in all-cause mortality among women.[2,29–32] In men, additional modest reductions in all-cause mortality rates were associated with a greater proportion of MVPA volume performed at a vigorous intensity. Future studies using objective measures of moderate- and vigorous-intensity physical activity will be helpful to add clarity.

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Author Responsibility

Shiroma and Lee had full access to the all of the data and take full responsibility for the integrity of the data and the accuracy of the data analysis.

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Shiroma, Sesso, Moorthy, Buring, and Lee report no conflicts of interest.

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