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ORIGINAL RESEARCH

Short Physical Performance Battery and Incident Cardiovascular Events Among Older Women

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BACKGROUND: The Short Physical Performance Battery (SPPB) is an inexpensive, reliable, and easy-to-implement measure of lower-extremity physical function. Strong evidence links SPPB scores with all-cause mortality, but little is known about its relationship with incident cardiovascular disease (CVD).

METHODS AND RESULTS: Women (n=5043, mean age=79±7) with no history of myocardial infarction or stroke completed 3 timed assessments—standing balance, strength (5 chair stands), and usual gait speed (4 m walk)—yielding an SPPB score from 0 (worst) to 12 (best). Women were followed for CVD events (myocardial infarction, stroke, or CVD death) up to 6 years. Hazard ratios were estimated for women with *Very Low* (0–3), *Low* (4–6), *Moderate* (7–9), and *High* (10–12) SPPB scores using Cox proportional hazard models adjusted for demographic, behavioral, and health-related variables including objective measurements of physical activity, blood pressure, lipids, and glucose levels. Restricted cubic splines tested linearity of associations. With 361 CVD cases, crude incidence rates/1000 person-years were 41.0, 24.3, 16.1, and 8.6 for *Very Low*, *Low*, *Moderate,* and *High* SPPB categories, respectively. Corresponding fully adjusted hazard ratios (95% CIs) were 2.28 (1.50–3.48), 1.70 (1.23–2.36) 1.49 (1.12–1.98), and 1.00 (referent); *P*-trend <0.001. The dose-response relationship was linear (linear *P*<0.001; nonlinear *P*>0.38).

CONCLUSIONS: Results suggest SPPB may provide a measure of cardiovascular health in older adults beyond that captured by traditional risk factors. Because of its high test-retest reliability and low administrative burden, the SPPB should be a routine part of office-based CVD risk assessment.

Key Words: balance ■ frailty ■ gait speed ■ geriatric cardiology ■ healthy cardiovascular aging ■ physical functioning

Cardiovascular disease (CVD) is the leading cause of death worldwide and in the United States.[1,2] CVD occurs most often among older adults,[3–5] who comprise an increasing proportion of the world's population.[6] For women over 85, rates of myocardial infarction (MI) and death from MI are higher (12%) than they are for men (8.5%),[7] making CVD risk prediction and prevention in older women especially important for improving public health.

The Short Physical Performance Battery (SPPB) was designed by National Institute on Aging researchers[8] to measure lower extremity physical function.[9] The SPPB is an objective performance-based measure composed of 3 timed tests that are easily and quickly administered without special equipment—standing balance, walking speed, and chair stands.[10,11] In a systematic review of 12 functional assessment instruments for older adults, reviewers gave the SPPB the most positive overall rating and the highest scores on reliability, validity, and responsiveness to change.[12]

The SPPB has been proposed, and used, as a marker of biological aging among older adults primarily

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CLINICAL PERSPECTIVE

What Is New?

- The Short Physical Performance Battery has long been used to objectively quantify physical functioning and identify mobility disability.
- However, its relationship to cardiovascular disease and its prognostic utility are less understood.

What Are the Clinical Implications?

- Among women 63 to 99 years of age, the absolute risk difference in incident primary cardiovascular events between the lowest and highest Short Physical Performance Battery category was 32.4 events per 1000 women annually.
- The relative risk for cardiovascular events remained significantly elevated by more than 2-fold following control for measures of baseline health status, lifestyle factors including accelerometer-measured physical activity, and traditional cardiovascular risk factors.
- Low physical functioning has cardiovascular disease prognostic relevance in later life; because of its high reliability and low administrative burden, the Short Physical Performance Battery should be a routine part of office-based cardiovascular disease risk assessment in older adults.

Nonstandard Abbreviations and Acronyms

BMI	body mass index
CVD	cardiovascular disease
HR	hazard ratio
MVPA	moderate-to-vigorous physical activity
MI	myocardial infarction
OPACH	Objective Physical Activity and Cardiovascular Health
SPPB	Short Physical Performance Battery
WHI	Women's Health Initiative

because it is highly predictive of all-cause mortality[13] and incident disability.[10,14] SPPB scores are strongly correlated with measures of physical fitness in older adults,[15] and physical fitness is associated with CVD incidence and mortality in middle- and older-aged adults.[16] Although inclusion of a physical performance measure in conventional approaches to CVD risk assessment has been proposed,[17] it has not been widely implemented due to administrative burden of traditional exercise testing methods, especially in older adults. If SPPB score is related to incident CVD after accounting for traditional risk factors monitored by clinicians, it could potentially be used to enhance conventional office-based methods for CVD risk assessment, as well as to study and promote healthy cardiovascular aging by researchers, gerontologists, and cardiologists who work with older people.[18] To our knowledge, the only evidence to date relating SPPB to CVD outcomes is a study showing SPPB improved prediction of incident heart failure.[19] Our study directly addresses this gap in the literature by assessing associations of SPPB with the full range of incident CVD end points among 5043 older women.

METHODS

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to Women's Health Initiative (WHI) P&P Committee at p&p@whi.org.

Study Design and Population

Postmenopausal women from 40 sites across the United States (n=161 809; ages of 50 and 79 years) enrolled in the WHI between 1993 and 1998.[20] In 2012 to 2013, 7875 community-living women from the second WHI Extension Study participated in the Long Life Study, which included an in-home assessment of height, weight, blood pressure, pulse, physical function, and, in most participants, phlebotomy. Of the study participants, 7058 participants ages 63 to 99 years who were ambulatory and without significant cognitive decline were invited to participate in the OPACH (Objective Physical Activity and Cardiovascular Health) study.[21] OPACH participants were given an accelerometer to measure physical activity and sedentary behavior. Accelerometers were returned by 6489 women and 6382 of them had data for at least 1 adherent day (using the common definition of ≥10 hours of accelerometer wear while awake[22]). A consort diagram for the OPACH accelerometer sample is published here.[21] For this study, we excluded 903 women who did not have SPPB measured and 436 who had an MI or stroke before SPPB measurement. The remaining 5043 women composed our primary analytic sample. These participants were followed for up to 6 years (through March 31, 2018) for cardiovascular events. The Fred Hutchinson Cancer Research Center Institutional Review Board approved this study protocol and all women provided informed consent.

Short Physical Performance Battery Assessment

The SPPB is a series of 3 tests to assess lower extremity physical function: a 4-meter walk at usual pace,

time to complete 5 unassisted chair stands, and 3 standing balance tests, each held for 10 seconds and the stances are progressively more difficult. Each test is scored on a 0 to 4 scale using previously validated norms and summed for an overall score range of 0 to 12, with 0 indicating the lowest physical performance, and scores of 12 indicating the highest performance.[8] To facilitate interpretation, SPPB scores were split into the following previously defined[13] categories: *Very Low* (SPPB score range=0–3), *Low* (4–6), *Moderate* (7–9), and *High* (10–12).

CVD Ascertainment

Ascertainment methods have been previously described.[21] Briefly, annual medical updates with information related to new CVD events (MI, coronary revascularization, hospitalized angina, heart failure, and stroke) were collected from each participant. The first reported occurrence of each event was adjudicated by study physicians through a medical record review.[23] Hospitalized angina was not adjudicated. The primary outcome for this study was incidence of a major CVD event, defined as MI, stroke, or death from CVD. We also examined total CVD (defined as the first occurrence of a major CVD event or revascularization, hospitalized angina, or heart failure) and CVD mortality as separate end points.

Assessment of Physical Activity

A triaxial accelerometer (ActiGraph GT3X+, Pensacola, FL) was worn around the participant's waist 24 hours per day for 7 days, removed only when showering or swimming. Accelerometer data were processed using the most common methods for older adults,[22] as described in detail elsewhere,[24] and were calibrated in a separate laboratory study to measure moderate-to-vigorous physical activity (MVPA) and sedentary behavior in older women.[25] MVPA was measured as the average minutes with vector magnitude counts/15-second ≥574 and sedentary behavior was measured as the average minutes with vector magnitude counts/15-second ≤18.[25] The residuals method was used to adjust MVPA and sedentary time for awake accelerometer wear time.

Other Covariates

Age, race/ethnicity, and education were obtained by questionnaire at WHI baseline. Alcohol consumption was categorized as nondrinker, <1 drink/week, ≥1 drink/week, and unspecified; current smoking status was categorized as smoker or nonsmoker (446 missing values were coded as nonsmokers); and prevalent diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, and depression were measured using available information collected in WHI through OPACH baseline. Height was measured with a tape measure and weight with a calibrated scale at OPACH baseline. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. An aneroid sphygmomanometer measured systolic and diastolic blood pressure after the participant was sitting for 5 minutes with feet uncrossed and on the ground; the average of 2 measures was used in analyses. Among the subset of participants who had phlebotomy (n=4101), fasting blood samples were obtained and serum levels of glucose, high-density lipoprotein, and triglycerides were measured at the University of Minnesota with respective coefficients of variation equal to 1.8%, 2.9%, and 2.1%.[26] The Reynolds Risk Score was computed to summarize participants' predicted probability of having a major CVD event in the subsequent 10 years, as used previously in OPACH[26,27] and WHI.[28]

Statistical Analysis

Covariates were described across *Very Low*, *Low*, *Moderate*, and *High* SPPB groups. F-tests (for continuous variables) and Pearson's chi-square tests (for categorical variables) assessed associations between covariates and SPPB.

Multivariable Cox proportional hazards regression models were used to assess whether SPPB (in categories defined previously) was related to future CVD events. Time to event was computed as the number of days from OPACH baseline to an incident event—participants were censored because of death unrelated to a CVD event or at their last available medical update. Five successively adjusted models were used. Model 1 adjusted for age and race-ethnicity; model 2 adjusted for model 1 covariates along with education, smoking status, alcohol use, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, and depression; model 3 additionally adjusted for BMI; model 4 was adjusted for model 3 covariates along with sedentary time and MVPA; and model 5 was adjusted for model 4 covariates along with CVD-risk biomarkers systolic blood pressure, high-density lipoprotein cholesterol, log (triglycerides), and fasting glucose. The *P*-for-trend was computed by including SPPB in continuous form (ie, 0–12) in each respective model. To address missing blood biomarker data for 942 women who did not receive phlebotomy (18.7%), we used multivariable chained equations implemented using the MICE package in R by including all relevant variables (eg, incident CVD, time to event, all covariates) with 100 iterations. Results from the complete-case analysis for model 5 are presented in Table S1 for comparison.

The dose-response relationship of SPPB (as a continuous variable; using model 3) with incident

CVD events was assessed using the methods of Desquilbet and Mariotti, implemented using restricted cubic spline functions[29] in the Regression Modeling Strategies (rms) package in R. Associations were tested for nonlinearity by placing 3, 4, and 5 knots at default locations along the SPPB distribution and computing a Wald test for the nonlinear components of the model; statistical results were confirmed by visually inspecting plots of the dose-response trajectories.

To assess whether associations differed among subgroups defined by age (<80 and ≥80), BMI (<30, and ≥30 kg/m^2), Reynolds Risk Score (10-year risk <9.7% and ≥9.7%; median split), MVPA (<43 and ≥43 min/day; median split), and race-ethnicity (White, Black, Hispanic), model 5 was repeated in each subgroup. Effect modification was assessed both by visual inspection of hazard ratios across strata and by interpreting *P* values from multiplicative interactions of each stratification variable in continuous form with continuous SPPB using Cox proportional hazard model 5. Statistical significance for tests of effect modification was set to $P<0.10$, for all other test, statistical significance was set to $P<0.05$.

Sensitivity Analyses

Because symptoms preceding new CVD events could affect SPPB test results, we repeated model 3 analyses after removing CVD cases that occurred within the first 6 months of follow-up. Symptoms of heart failure and angina could also affect SPPB and increase chances for subsequent CVD events. To address this, we repeated all models after removing women with a history of angina or heart failure at or before OPACH baseline. We also repeated all models with and without adjustment for antihypertension and anti-hypercholesterolemia medication use. To investigate whether 1 of the 3 physical function tests within the SPPB (chair stand, gait speed, and balance) were driving associations with major CVD, we examined Pearson's correlation coefficients among the 3 test scores then repeated model 5 to examine the following 5 scenarios, modeling the scores from each individual physical function test in continuous functional form using the previously validated norms that result in scores ranging from 0 to 4: model 5 covariates+chair-stand score; model 5 covariates+gait speed score; model 5 covariates+balance score; model 5 covariates+chair-stand score+gait speed score+balance score (ie, a mutually adjusted model); and model 5 covariates+total SPPB score (range 0–12).

RESULTS

SPPB scores averaged 8.3±2.5 (out of 12) and the highest proportion of OPACH women (42.4%) had *Moderate* SPPB scores. Women with *High* SPPB (compared with those with *Low* SPPB) were younger, a higher proportion were Hispanic, and they had better self-rated health and the lowest prevalence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, and depression (Table 1). Predicted 10-year CVD risk based on the Reynolds Risk Score was 19.2% for the *Very Low* SPPB group, and decreased in dose-response fashion over categories of *Low* SPPB (16.9%), *Moderate* SPPB (13.1%), and *High* SPPB (10.8%). Women with the highest SPPB scores had the lowest sedentary time and the highest light physical activity and MVPA. Age-adjusted Spearman correlations for SPPB score were $r=0.15$ with light physical activity, $r=0.26$ with MVPA, and $r=-0.21$ with sedentary behavior.

The crude incidence rate of major CVD for women with *Very Low* SPPB scores was 41.0 per 1000 person-years, a rate that was 4.8 times higher than the crude incidence rate among women with *High* SPPB (8.6 per 1000-person years; Table 2). Following adjustment for age and race-ethnicity, HRs for women with *Moderate*, *Low*, and *Very Low* SPPB were 1.64 (95% CI, 1.23–2.18), 2.08 (1.52–2.84), and 3.02 (2.02–4.52), respectively (P-trend <0.001), when compared with women with *High* SPPB. After adjustment for Model 5 covariates that included health behavior and health status indicators along with measures of physical behavior and CVD risk biomarkers, women with the *Very Low* SPPB compared with women with *High* SPPB had 2.28 times higher risk for major CVD (HR, 2.28; 95% CI, 1.50–3.48; P-trend <0.001). It is noteworthy that in all models, having *Moderate* compared with *High* SPPB scores was associated with significantly higher risk for major CVD. Associations for total CVD and CVD mortality followed similar patterns.

The dose-response association of SPPB (using the continuous form of the variable) and all 3 CVD end points was linear (all P-nonlinear >0.38; as depicted in Figure 1). The fully adjusted hazard ratio (HR) (95% CI) for major CVD associated with each 3-unit decrease in SPPB (equivalent to comparing the 25th percentile with the 75th percentile) was 1.25 (1.10–1.42); 1.25 (1.14–1.38) for total CVD; and 1.49 (1.24–1.79) for CVD mortality (Figure 2). In stratified analyses, point estimates for all subgroups indicated that lower SPPB scores were associated with higher risk for all CVD end points. There was statistical evidence (indicated by $P<0.10$) of effect modification by Reynolds Risk Score for all 3 CVD end points, with suggestion that SPPB was slightly more strongly associated with CVD risk among those with higher (versus lower) Reynolds Risk Score. For example, for major CVD, among women with below-median Reynolds Risk Score, each 3-unit decrement in SPPB was associated with 1.21 times higher risk for

Table 1. Baseline Sociodemographic and Health-Related Characteristics, by SPPB Score Rank (n=5043); OPACH (2012–2014)

	Categories of SPPB				
	Very Low (SPPB: 0–3)	Low (SPPB: 4–6)	Moderate (SPPB: 7–9)	High (SPPB: 10–12)	
	n=237	n=900	n=2139	n=1767	*P* Value*
Age, y, mean (SD)	82.9 (6.3)	81.0 (6.2)	78.5 (6.5)	76.7 (6.4)	<0.001
Race-ethnicity, n (%)					<0.001
White	139 (58.6)	479 (53.2)	1011 (47.3)	827 (46.8)	
Black	75 (31.6)	303 (33.7)	798 (37.3)	512 (29.0)	
Hispanic/Latina	23 (9.7)	118 (13.1)	330 (15.4)	428 (24.2)	
Highest education level, n (%)					0.002
High school or less	51 (21.8)	215 (24.1)	421 (19.8)	323 (18.4)	
Some college	100 (42.7)	353 (39.5)	805 (37.9)	673 (38.3)	
College graduate	83 (35.5)	325 (36.4)	900 (42.3)	761 (43.3)	
Health behavior/status					
Current smoker, n (%)	4 (1.7)	24 (2.7)	61 (2.9)	33 (1.9)	0.192
Alcohol intake past 3 mo, n (%)					<0.001
Non-drinker	104 (43.9)	378 (42.0)	733 (34.3)	480 (27.2)	
Less than 1 drink per week	58 (24.5)	260 (28.9)	687 (32.1)	580 (32.8)	
1 or more drinks per week	42 (17.7)	166 (18.4)	547 (25.6)	570 (32.3)	
Unknown	33 (13.9)	96 (10.7)	172 (8.0)	137 (7.8)	
Body mass index, kg/m^2, mean (SD)	29.8 (7.0)	28.9 (6.2)	28.2 (5.6)	27.3 (5.3)	<0.001
Self-rated health					<0.001
Excellent or very good	68 (29.2)	324 (36.2)	1059 (49.7)	1167 (66.2)	
Good	109 (46.8)	418 (46.7)	900 (42.3)	531 (30.1)	
Fair or poor	56 (24.0)	153 (17.1)	171 (8.0)	65 (3.7)	
History of diabetes mellitus, n (%)	62 (26.2)	234 (26.0)	449 (21.0)	252 (14.3)	<0.001
History of hypertension, n (%)	196 (82.7)	700 (77.8)	1532 (71.6)	1125 (63.7)	<0.001
History of COPD, n (%)	13 (5.5)	29 (3.2)	63 (2.9)	35 (2.0)	0.009
History of osteoarthritis, n (%)	151 (63.7)	559 (62.1)	1177 (55.0)	878 (49.7)	<0.001
History of depression, n (%)	35 (14.8)	92 (10.2)	160 (7.5)	119 (6.7)	<0.001
Use lipid-lowering medication, n (%)	103 (50.2)	347 (43.5)	882 (44.9)	685 (41.3)	0.035
CVD biomarkers and risk score					
Reynolds Risk Score, %, mean (SD)	19.2 (13.6)	16.9 (12.6)	13.1 (10.6)	10.8 (10.3)	<0.001
Systolic blood pressure, mean (SD)	127.3 (15.9)	127.0 (14.0)	125.7 (14.1)	124.4 (13.7)	<0.001
Diastolic blood pressure, mean (SD)	71.9 (11.0)	72.8 (8.7)	72.3 (8.7)	72.4 (8.2)	0.483
Glucose, mean (SD)	101.0 (27.4)	100.7 (28.9)	97.7 (28.2)	95.8 (21.4)	<0.001
Total cholesterol, mean (SD)	188.7 (37.3)	195.0 (39.5)	197.8 (38.4)	203.6 (39.1)	<0.001
High-density lipoprotein cholesterol, mean (SD)	58.1 (14.0)	59.8 (14.6)	60.5 (14.8)	62.0 (15.1)	<0.001
Low-density lipoprotein cholesterol, mean (SD)	108.8 (30.3)	113.4 (34.4)	115.9 (33.7)	120.4 (34.0)	<0.001
Log triglycerides, mean (SD)	4.58 (0.47)	4.59 (0.43)	4.57 (0.45)	4.57 (0.45)	0.603
PA intensity and behaviors†					
Sedentary time; h/d, mean (SD)	10.2 (1.4)	9.6 (1.4)	9.1 (1.4)	8.8 (1.5)	<0.001
Light PA time; h/d, mean (SD)	4.1 (1.2)	4.5 (1.2)	4.8 (1.2)	5.0 (1.2)	<0.001
MVPA; h/d, mean (SD)	0.51 (0.42)	0.64 (0.46)	0.83 (0.52)	1.06 (0.60)	<0.001

COPD indicates chronic obstructive pulmonary disease; CVD, cardiovascular disease; MVPA, moderate-to-vigorous PA; PA, physical activity; and SPPB, Short Physical Performance Battery.

*_P_ value is from chi-square test for categorical variables and from trend test for continuous variables.

†All activity-related variables are adjusted for accelerometer awake wear time using the residuals method.

Table 2. Associations of Physical Function Measured by the SPPB With Incident CVD and CVD Mortality: OPACH (2012–2018)

	Categories of SPPB				
	Very Low (SPPB: 0–3)	Low (SPPB: 4–6)	Moderate (SPPB: 7–9)	High (SPPB: 10–12)	
	n=237	n=900	n=2139	n=1767	*P*-Trend
Major CVD					
No. events [rate†]	39 [41.0]	96 [24.3]	155 [16.1]	71 [8.6]	
Model 1‡	3.02 (2.02–4.52)	2.08 (1.52–2.84)	1.64 (1.23–2.18)	1 (ref)	<0.001
Model 2‡	2.75 (1.82–4.15)	1.94 (1.41–2.68)	1.61 (1.21–2.15)	1 (ref)	<0.001
Model 3‡	2.74 (1.81–4.16)	1.94 (1.41–2.69)	1.63 (1.22–2.18)	1 (ref)	<0.001
Model 4‡	2.39 (1.56–3.66)	1.79 (1.29–2.48)	1.57 (1.17–2.10)	1 (ref)	<0.001
Model 5‡,§	2.28 (1.50–3.48)	1.70 (1.23–2.36)	1.49 (1.12–1.98)	1 (ref)	<0.001
Total CVD					
No. events [rate†]	56 [60.7]	162 [42.6]	267 [28.4]	139 [17.3]	
Model 1‡	2.53 (1.84–3.48)	1.98 (1.57–2.50)	1.50 (1.22–1.84)	1 (ref)	<0.001
Model 2‡	2.26 (1.63–3.12)	1.83 (1.44–2.32)	1.44 (1.17–1.78)	1 (ref)	<0.001
Model 3‡	2.21 (1.59–3.08)	1.82 (1.43–2.31)	1.45 (1.17–1.79)	1 (ref)	<0.001
Model 4‡	2.05 (1.46–2.86)	1.73 (1.36–2.20)	1.41 (1.14–1.75)	1 (ref)	<0.001
Model 5‡,§	1.96 (1.40–2.73)	1.67 (1.32–2.13)	1.37 (1.11–1.69)	1 (ref)	<0.001
CVD mortality					
Mortality [rate†]	27 [27.4]	56 [13.8]	56 [5.7]	28 [3.4]	
Model 1‡	4.34 (2.51–7.48)	2.64 (1.66–4.20)	1.39 (0.88–2.19)	1 (ref)	<0.001
Model 2‡	3.74 (2.13–6.55)	2.42 (1.50–3.90)	1.37 (0.86–2.19)	1 (ref)	<0.001
Model 3‡	3.66 (2.07–6.45)	2.39 (1.48–3.86)	1.37 (0.86–2.18)	1 (ref)	<0.001
Model 4‡	2.90 (1.62–5.18)	2.08 (1.28–3.40)	1.28 (0.80–2.05)	1 (ref)	<0.001
Model 5‡,§	2.66 (1.50–4.73)	1.93 (1.20–3.12)	1.19 (0.75–1.88)	1 (ref)	<0.001

Major CVD includes incident myocardial infarction, stroke, or death from CVD. Total CVD includes major CVD+coronary revascularization, hospitalized angina, and heart failure. BMI indicates body mass index; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; OPACH, Objective Physical Activity and Cardiovascular Health; and SPPB, Short Physical Performance Battery.

†Crude incidence rate per 1000 person-years.

‡Data are hazard ratio (95% CI). Model 1 is age and ethnicity adjusted (n=5043); Model 2=Model 1+education+smoking status+alcohol use+diabetes+hypertension+COPD+osteoarthritis+depression [n=5010]; Model 3=Model 2+BMI [n=4976]; Model 4=Model 3+sedentary time and moderate-to-vigorous physical activity [n=4976]; Model 5=Model 4+systolic blood pressure+HDL-cholesterol+log(triglycerides) +glucose [n=5043].

§Model 5 results were estimated using multiple imputation; results from the complete cases analysis are presented in Table S1.

CVD (HR, 1.21; 95% CI, 0.92–1.58) whereas among women with above-median Reynolds Risk Score, each 3-unit decrement in SPPB was associated with a 1.26 times higher risk for CVD (HR, 1.26; 95% CI, 1.08–1.46; *P*-interaction=0.064). For major and total CVD only, there was also statistical evidence of effect modification for BMI, with higher HRs observed among those with BMI ≥30 kg/m^2.

Removal of women with CVD in the first 6 months of follow-up did not appreciably change the results (Table S2). Results also remained unchanged after excluding women who had symptomatic conditions (angina and/or heart failure [n=303]) at the time SPPB was measured (Table S3) and after adjustment for antihypertension and anti-hypercholesterolemia medication use. Correlations between the physical function test scores were chair stand and balance r=0.21, chair stand and gait speed r=0.34, and balance and gait speed r=0.25. There was no evidence that any one physical function test within the SPPB was more strongly associated with incident major CVD than the other tests—the HR (95% CI) for a 1-unit increase in each physical function test score using model 5 was chair-stand score only 0.89 (0.81–0.97); gait speed score only 0.89 (0.82–0.98); balance score only 0.91 (0.83–0.99); the mutually adjusted model including chair-stand score + gait speed score + balance score 0.92 (0.83–1.01) +0.93 (0.85–1.02)+0.93 (0.85–1.02), respectively; and total SPPB score 0.93 (0.89–0.97).

DISCUSSION

Good physical function is a hallmark of physiologic resilience.[30] Although strong evidence indicates higher physical function is associated with lower risks

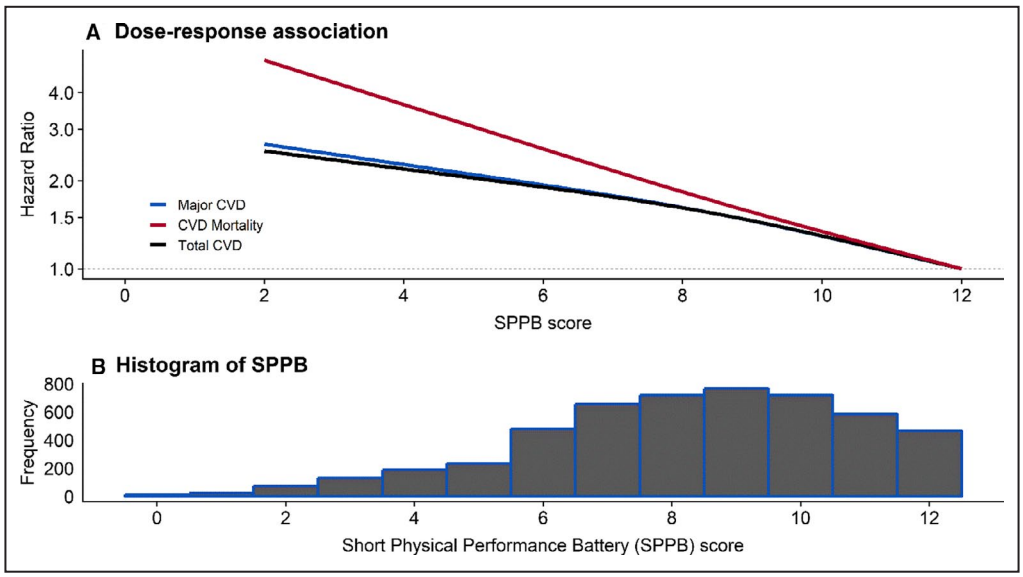

Figure 1. Baseline SPPB distribution and hazard ratios for incident major CVD, total CVD, and CVD mortality.

A, The continuous dose-response relation of SPPB score with major cardiovascular disease (blue line), total CVD (black line), and CVD mortality (red line) estimated using Cox regression models adjusted for age, race/ethnicity, education, smoking status, alcohol use, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, osteoarthritis, depression, and body mass index. Results are from restricted cubic splines allowing for 3 knots placed at default locations. The reference category was SPPB=12. Results were trimmed at an SPPB score of 2 because of sparse data in the tail. **B**, A histogram of SPPB score. CVD indicates cardiovascular disease; and SPPB, Short Physical Performance Battery.

of disability, falls, fracture,[31] and all-cause mortality,[13] the role that SPPB has in CVD research and prevention is less clear. Our results demonstrated a strong, inverse linear dose-response association between SPPB scores and CVD in older women. Having a *Moderate* SPPB score was associated with significantly higher major (↑49%) and total CVD (↑37%) risk compared with having a *High* SPPB score, and associations were even stronger for women with *Low* and *Very Low* SPPB scores. Importantly, all associations persisted after adjustment for several covariates and common CVD risk factors (including CVD-risk biomarkers and accelerometer-measured physical activity).

Pavasini et al performed a harmonized meta-analysis of 16 534 adults aged 76±3 (78% women) from 17 studies, 11 of which were conducted among the general population. When comparing adults with the best functioning (ie, SPPB scores between 10 and 12) to those with SPPB scores of 0 to 3, 4 to 6, and 7 to 9, the odds ratios of mortality were 3.25, 2.14, and 1.50, respectively.[13] The results from the present study were remarkably similar in magnitude and exhibited the same dose-response pattern. For example, our respective HR for CVD mortality were 2.66, 1.93, and 1.19.

We know of just one other published study of SPPB and a cardiovascular-related outcome. Khan et al[19] administered the battery, modified by additional balance tests, to a sample of 2825 septuagenarians without heart failure (52% women, 41% non-White) and reported that each standard deviation decrease in physical performance was associated with a 24% higher risk for heart failure (HR, 1.24). Results for CVD outcomes in our study (using model 5) were similar, with each standard deviation (SD_{SPPB}=2.5) lower SPPB score associated with a 21% higher risk of major CVD (HR, 1.21), a 21% higher risk for total CVD (HR, 1.21), and a 39% higher risk for CVD mortality (HR, 1.39), demonstrating consistency in the association of SPPB and cardiovascular health. The study by Khan and colleagues, like ours, included participants with very low SPPB scores, a subgroup with very high disability in activities of daily living and therefore higher risk of CHD.[32] In a sensitivity analysis, we repeated our models after excluding participants with SPPB scores between 0 and 3, and the results were unchanged (data not shown), indicating that results were not being driven by this high-risk group.

This study was not intended to make a causal argument about the relation of SPPB to CVD; rather, it was designed to assess whether low SPPB is also an early marker for risk of future CVD events. The SPPB is an integrated measure of physical function that reflects a constellation of aging-related processes at the cellular level (eg, capillary density and perfusion), organ-specific level (eg, cardiac output), and physiologic level (eg, mitochondrial respiratory capacity), that affect

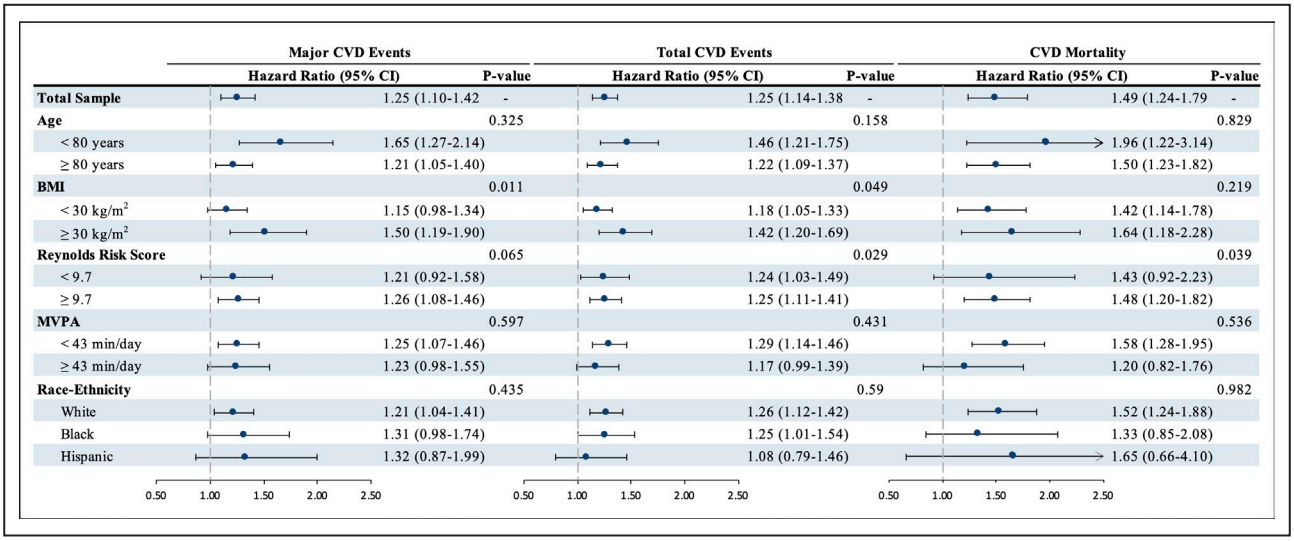

Figure 2. Hazard ratios (HRs) and 95% CI for associations of the Short Physical Performance Battery (SPPB) score (comparing the 75th percentile to the 25th percentile [SPPB score interquartile range=3]) and major cardiovascular disease (CVD), total CVD, and CVD mortality by selected participant characteristics; Objective Physical Activity and Cardiovascular Health Study (2012–2018).

Associations were adjusted for age, race-ethnicity, education, smoking status, alcohol use, diabetes mellitus, hypertension, COPD, osteoarthritis, depression, BMI, accelerometer-measured sedentary time, accelerometer-measured moderate-to-vigorous physical activity, systolic blood pressure, high-density lipoprotein cholesterol, log(triglycerides), and glucose. Major CVD includes incident myocardial infarction, stroke, and death from CVD. Total CVD includes major CVD+coronary revascularization, hospitalized angina, and heart failure. BMI indicates body mass index; and MVPA, moderate-to-vigorous physical activity.

the overall lived experience (eg, health and disease states).[30] Moreover, SPPB score is a measure of physical fitness,[15] which is a known determinant of CVD outcomes independent of major CVD risk factors.[16] In the present study, SPPB score was moderately correlated with accelerometer-measured physical activity, and was related to CVD independent of physical activity and sedentary behavior, which suggests SPPB is not merely a proxy measure of physical behavior. Thus, there is biologic plausibility that poor physical function might be related to CVD through mechanisms beyond low physical activity and traditional CVD risk factors. These additional mechanisms could include increased oxidative stress[33] and DNA damage,[34] inflammation,[35] endocrine dysregulation,[36] and potentially, genetic variation.[37] For example, the SPPB may be analogous to a cardiac exercise stress test in that poor performance indicates poor physiologic reserve and inability of the cardiovascular system to match cardiac demand leading to critical levels of ischemia and a subsequent clinical CVD event. Widespread use of the SPPB in studies of cardiovascular health in older adults would help investigate these and other potential mechanisms.

Strengths and Limitations

Strengths of this study include the large, racially/ethnically diverse cohort of older women, which is a rapidly increasing proportion of the US population that historically has been understudied in CVD epidemiology. It is the first study of SPPB and incident CVD that we are aware of. The SPPB was administered in the home by trained staff. We also had objective measures of sedentary behavior and physical activity. By including both MVPA and sedentary behavior in the same model we effectively controlled for all ambulatory movement including light physical activity. Furthermore, our sequential modeling approach controlled for several known CVD risk factors and comorbidities, some of which are possible mediators on the causal pathway between SPPB and CVD. The possibility that reverse causation was a primary explanation for our results was minimized by measuring SPPB first and then subsequently ascertaining the outcome during up to 6 years of follow-up. Sensitivity analyses provided further evidence against reverse causation bias by showing that results persisted after removing women in whom incident CVD events occurred within the first 6 months of follow-up, and after excluding women with histories of angina and heart failure at the time of the SPPB measure. We also statistically controlled for several comorbidities and self-rated health status, which is a conservative analytic approach that might, in fact, attenuate the true strength of association between SPPB and CVD risk. Finally, use of the SPPB itself is a major strength of the study. The SPPB score combines 3 essential dimensions of lower extremity physical

function: functional mobility (gait speed), lower extremity strength (chair stands), and balance. In our study, tests scores among these 3 dimensions were not strongly correlated and each physical function test contributed, and with equal magnitude, to associations between SPPB and major CVD risk. It is common to combine several measures of an underlying construct (eg, lower extremity physical function) into a single composite score to improve measurement properties such as reliability.[10,11,38–40] In the case of the SPPB, combining scores from the 3 separate tests has the additional benefit of ensuring that deficiencies or declines in any 1 of the 3 essential physical function dimensions are captured in the composite metric.

This study was limited in that it focused only on older women, so the results require replication in men and in adults younger than this study population. Repeated measures of SPPB were not available, and thus, longitudinal changes in physical function in association with incident CVD or CVD mortality could not be assessed. Longitudinal SPPB measures could also answer questions such as how long after an initial decline in SPPB might clinical CVD manifest, which should be the subject of future studies. The SPPB has a known ceiling effect where the majority of younger adults, and some older adults, have an SPPB score of 12.[15] However, as demonstrated in our cohort of women ages 63 to 97, there is a wide range of SPPB scores, with the majority of women (65%) having scores below 10, and 4577 women (91%) having scores below 12. With a rapidly increasing older adult population, and the fastest increases occurring among those over age 80, the absolute number of people for whom low SPPB predisposes to higher risk of a major CVD event will be substantial. Thus, the attributable fraction of CVD within the population that could potentially be averted through identifying and intervening on low physical performance is large and underscores the importance of measuring physical performance in clinical settings as part of conventional office-based CVD risk assessment. The SPPB test can be implemented with relatively low administrative burden (it takes between 5 and 10 minutes to administer) and offers an opportunity for routine measurement of physical performance in clinical settings.

Implications/Future Studies

Because SPPB is predictive of key components of aging—all-cause mortality[13] and mobility disability[14,41–43]—low scores, or early detection of decline, can provide useful prognostic information to gerontologists and their patients.[18,44] Our findings that SPPB scores are also associated with CVD incidence and CVD mortality suggest that the prognostic benefits of administering the SPPB extend to geriatric cardiology as well. Furthermore, many of the current cardiovascular risk indicators (eg, Reynolds Risk Score, Framingham Risk Score, and the atherosclerotic cardiovascular disease risk score) rely heavily on chronological age, which plays less of a role in determining overall health for people aged 70 to 90 than in younger populations.[45] Future studies assessing whether adding objective and reliable measures of physical function like the SPPB can improve existing CVD risk prediction models such as the Reynolds Risk Score, particularly in older adult populations, are now needed.

Physical activity interventions have achieved clinically meaningful[46] improvements in SPPB-measured physical function.[47] For older adults with SPPB scores below 10, increases in physical activity over a 2-year period were related to dose-dependent improvements in both SPPB and onset of major mobility disability.[43] The finding in our study of a robust independent association of SPPB with incident CVD, if replicated in other cohorts, sets the stage for determining whether interventions to enhance physical function can improve CVD-related outcomes in population or clinical contexts.

CONCLUSIONS

SPPB is a reliable measure of physical function and a marker of biological aging providing a good "vital sign" in older people. Strong linear inverse associations were observed between SPPB and incident CVD, independent of traditional CVD risk factors. SPPB holds promise for aiding with risk stratification among older adults and informing research designed to understand CVD etiology. Because SPPB can be improved through increased physical activity and reduced sedentary behavior, it may prove to be a treatable risk factor that can help reduce the public health burden of CVD.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Materials

Tables S1–S3

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SUPPLEMENTAL MATERIAL

Table S1. Regression Model 5 with and without multiple imputation: Associations of incident cardiovascular disease (CVD) and CVD mortality with physical functioning measured by the Short Physical Performance Battery (SPPB); OPACH (2012-2018)

	Categories of SPPB				P-Trend*
	Very Low (SPPB: 0-3)	Low (SPPB: 4-6)	Moderate (SPPB: 7-9)	High (SPPB: 10-12)	
	n=237	n=900	n=2139	n=1767	
Major CVD					
Model 5 (imputed)† ‡	2.28 (1.50-3.48)	1.70 (1.23-2.36)	1.49 (1.12-1.98)	1 (ref)	**<0.001**
Model 5 (complete cases)† §	2.46 (1.53-3.94)	1.98 (1.39-2.84)	1.73 (1.26-2.38)	1 (ref)	**<0.001**
Total CVD					
Model 5 (imputed)† ‡	1.96 (1.40-2.73)	1.67 (1.32-2.13)	1.37 (1.11-1.69)	1 (ref)	**<0.001**
Model 5 (complete cases)† §	2.02 (1.40-2.93)	1.73 (1.33-2.25)	1.49 (1.18-1.87)	1 (ref)	**<0.001**
CVD Mortality					
Model 5 (imputed)† ‡	2.66 (1.50-4.73)	1.93 (1.20-3.12)	1.19 (0.75-1.88)	1 (ref)	**<0.001**
Model 5 (complete cases)† §	2.83 (1.48-5.41)	2.31 (1.36-3.91)	1.30 (0.77-2.17)	1 (ref)	**<0.001**

* P-values from Cox multivariable linear regression models including total sedentary time in models in continuous form .

† Data are hazard ratio (95% confidence interval)

Model 5 = age + race-ethnicity + education + smoking status + alcohol use + diabetes + hypertension + COPD + osteoarthritis + depression + sedentary time + moderate-to-vigorous physical activity + systolic blood pressure + HDL-cholesterol + log(triglycerides) + glucose [$n_{complete\ cases}$=4054; $n_{imputed}$=5043].

‡ Model 5 results estimated using multiple imputation

§ Model 5 results estimated using complete cases analysis

Table S2. After excluding women with CVD in the first 6 months of follow-up: Associations of incident cardiovascular disease (CVD) and CVD mortality with the Short Physical Performance Battery; OPACH (2012-2018)

	Categories of SPPB				P-Trend*
	Very Low (SPPB: 0-3)	Low (SPPB: 4-6)	Moderate (SPPB: 7-9)	High (SPPB: 10-12)	
	n=203	n=814	n=2019	n=1704	
Major CVD					
Major CVD events [rate†]	36 [37.9]	90 [22.7]	139 [14.4]	66 [8.0]	
Model 1‡	3.09 (2.03-4.70)	2.13 (1.54-2.95)	1.6 (1.19-2.15)	1 (ref)	**<0.001**
Model 2‡	2.88 (1.88-4.42)	2.04 (1.46-2.84)	1.6 (1.18-2.16)	1 (ref)	**<0.001**
Model 3‡	2.89 (1.87-4.46)	2.05 (1.46-2.87)	1.62 (1.19-2.19)	1 (ref)	**<0.001**
Model 4‡	2.53 (1.63-3.94)	1.89 (1.34-2.66)	1.56 (1.15-2.11)	1 (ref)	**<0.001**
Model 5‡ §	2.41 (1.55-3.73)	1.80 (1.28-2.51)	1.47 (1.09-1.98)	1 (ref)	**<0.001**
Total CVD					
Total CVD events [rate†]	51 [37.9]	147 [22.7]	239 [14.4]	126 [8.0]	
Model 1‡	2.58 (1.85-3.61)	2.00 (1.57-2.56)	1.49 (1.20-1.85)	1 (ref)	**<0.001**
Model 2‡	2.38 (1.69-3.35)	1.89 (1.47-2.42)	1.45 (1.16-1.81)	1 (ref)	**<0.001**
Model 3‡	2.33 (1.65-3.30)	1.87 (1.46-2.41)	1.46 (1.17-1.83)	1 (ref)	**<0.001**
Model 4‡	2.14 (1.51-3.04)	1.77 (1.37-2.29)	1.42 (1.14-1.78)	1 (ref)	**<0.001**
Model 5‡ §	2.00 (1.42-2.82)	1.72 (1.35-2.20)	1.36 (1.09-1.68)	1 (ref)	**<0.001**
CVD Mortality					
Mortality [rate†]	26 [26.4]	55 [13.6]	51 [5.2]	27 [3.2]	
Model 1‡	4.30 (2.47-7.49)	2.67 (1.67-4.28)	1.30 (0.82-2.09)	1 (ref)	**<0.001**
Model 2‡	3.74 (2.11-6.63)	2.46 (1.52-4.00)	1.30 (0.80-2.10)	1 (ref)	**<0.001**
Model 3‡	3.71 (2.08-6.62)	2.45 (1.51-3.99)	1.30 (0.80-2.10)	1 (ref)	**<0.001**
Model 4‡	2.91 (1.61-5.27)	2.12 (1.29-3.48)	1.21 (0.74-1.96)	1 (ref)	**<0.001**
Model 5‡ §	2.83 (1.56-5.14)	2.08 (1.27-3.41)	1.14 (0.71-1.86)	1 (ref)	**<0.001**

* P-values from Cox multivariable linear regression models including total sedentary time in models in continuous form .

† Crude incidence rate per 1000 person-years

‡ Data are hazard ratio (95% confidence interval)

Model 1 is age and ethnicity adjusted [n=5013]; Model 2 = Model 1 + education + smoking status + alcohol use + diabetes + hypertension + COPD + osteoarthritis + depression [n=4980]; Model 3 = Model 2 + BMI [n=4946]; Model 4 = Model 3 + sedentary time and moderate-to-vigorous physical activity [n=4946]; Model 5 = Model 4 + systolic blood pressure + HDL-cholesterol + log(triglycerides) + glucose [n=5013].

§ Model 5 results estimated using multiple imputation

Table S3. After excluding women who had symptomatic conditions (angina or heart failure) at the time SPPB was measured: Associations of incident cardiovascular disease (CVD) and CVD mortality with the Short Physical Performance Battery (SPPB); OPACH (2012-2018)

	Categories of SPPB				P-Trend*
	Very Low (SPPB: 0-3)	Low (SPPB: 4-6)	Moderate (SPPB: 7-9)	High (SPPB: 10-12)	
	n=203	n=814	n=2019	n=1704	
Major CVD					
Major CVD events [rate†]	29 [35.0]	73 [20.0]	131 [14.3]	67 [8.4]	
Model 1‡	2.51 (1.60-3.93)	1.71 (1.22-2.40)	1.48 (1.10-1.99)	1 (ref)	**<0.001**
Model 2‡	2.38 (1.51-3.77)	1.63 (1.16-2.31)	1.47 (1.08-1.98)	1 (ref)	**0.001**
Model 3‡	2.37 (1.49-3.77)	1.63 (1.15-2.32)	1.48 (1.09-2.01)	1 (ref)	**0.001**
Model 4‡	2.10 (1.31-3.36)	1.53 (1.07-2.18)	1.43 (1.06-1.95)	1 (ref)	**0.008**
Model 5‡ §	2.05 (1.28-3.27)	1.49 (1.05-2.11)	1.38 (1.02-1.87)	1 (ref)	**0.01**
Total CVD					
Total CVD events [rate†]	44 [35.0]	135 [20.0]	234 [14.3]	129 [8.4]	
Model 1‡	2.32 (1.63-3.31)	1.85 (1.44-2.37)	1.43 (1.15-1.78)	1 (ref)	**<0.001**
Model 2‡	2.16 (1.51-3.09)	1.73 (1.35-2.23)	1.39 (1.11-1.73)	1 (ref)	**<0.001**
Model 3‡	2.13 (1.48-3.06)	1.72 (1.33-2.22)	1.39 (1.12-1.74)	1 (ref)	**<0.001**
Model 4‡	1.98 (1.37-2.87)	1.66 (1.28-2.14)	1.36 (1.09-1.70)	1 (ref)	**<0.001**
Model 5‡ §	1.91 (1.32-2.76)	1.62 (1.25-2.09)	1.33 (1.07-1.66)	1 (ref)	**<0.001**
CVD Mortality					
Mortality [rate†]	19 [22.3]	41 [11.0]	46 [4.9]	27 [3.4]	
Model 1‡	3.15 (1.72-5.77)	1.99 (1.21-3.27)	1.17 (0.72-1.89)	1 (ref)	**<0.001**
Model 2‡	2.83 (1.53-5.26)	1.83 (1.10-3.03)	1.13 (0.69-1.83)	1 (ref)	**<0.001**
Model 3‡	2.73 (1.46-5.11)	1.79 (1.08-2.97)	1.12 (0.69-1.82)	1 (ref)	**<0.001**
Model 4‡	2.16 (1.14-4.09)	1.57 (0.94-2.64)	1.05 (0.64-1.71)	1 (ref)	**0.002**
Model 5‡ §	2.07 (1.10-3.92)	1.54 (0.92-2.57)	1.02 (0.63-1.65)	1 (ref)	**0.002**

* P-values from Cox multivariable linear regression models including total sedentary time in models in continuous form .

† Crude incidence rate per 1000 person-years

‡ Data are hazard ratio (95% confidence interval)

Model 1 is age and ethnicity adjusted [n=4740]; Model 2 = Model 1 + education + smoking status + alcohol use + diabetes + hypertension + COPD + osteoarthritis + depression [n=4710]; Model 3 = Model 2 + BMI [n=4676]; Model 4 = Model 3 + sedentary time and moderate-to-vigorous physical activity [n=4676]; Model 5 = Model 4 + systolic blood pressure + HDL-cholesterol + log(triglycerides) + glucose [n=4710].

§ Model 5 results estimated using multiple imputation