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ORIGINAL RESEARCH

Physical Function and Subsequent Risk of Cardiovascular Events in Older Adults: The Atherosclerosis Risk in Communities Study

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BACKGROUND: Reduced physical function, a representative phenotype of aging, has been associated with cardiovascular disease (CVD). However, few studies have comprehensively investigated its association with composite and individual CVD outcomes in community-dwelling older adults and its predictive value for CVD beyond traditional risk factors.

METHODS AND RESULTS: We studied 5570 participants (mean age 75 [SD 5] years, female 58%, Black 22%) at visit 5 (2011–2013) of the ARIC (Atherosclerosis Risk in Communities) study. Physical function was evaluated with the Short Physical Performance Battery (SPPB), which incorporates a walk test, chair stands, and balance tests. The SPPB score was modeled categorically (low [0–6], intermediate [7–9], and high [10–12]) and continuously. We assessed the associations of SPPB score with subsequent composite (coronary heart disease, stroke, or heart failure) and individual CVD outcomes (components within composite outcome) using multivariable Cox models adjusting for major CVD risk factors and history of CVD. We also evaluated improvement in C-statistics by adding SPPB to traditional CVD risk factors in the Pooled Cohort Equation. Among the study participants, 13% had low, 30% intermediate, and 57% high SPPB scores. During a median follow-up of 7.0 (interquartile interval 5.3–7.8) years, there were 930 composite CVD events (386 coronary heart disease, 251 stroke, and 529 heart failure cases). The hazard ratios of composite CVD in low and intermediate versus high SPPB score were 1.47 (95% CI, 1.20–1.79) and 1.25 (95% CI, 1.07–1.46), respectively, after adjusting for potential confounders. Continuous SPPB score demonstrated independent associations with each CVD outcome. The associations were largely consistent across subgroups (including participants with prevalent CVD at baseline). The addition of SPPB to traditional CVD risk factors significantly improved the C-statistics of CVD outcomes (eg, ΔC-statistic 0.019 [95% CI, 0.011–0.027] for composite CVD).

CONCLUSIONS: Reduced physical function was independently associated with the risk of composite and individual CVD outcomes and improved their risk prediction beyond traditional risk factors in community-dwelling older adults. Although confirmatory studies are needed, our results suggest the potential usefulness of SPPB for classifying CVD risk in older adults.

Key Words: aged ■ cardiovascular diseases ■ humans ■ physical functional performance

Traditional cardiovascular disease (CVD) risk factors such as lipids are known to have limited prognostic ability among older adults.[1] A previous study found that, among older adults above 65 years, associations between traditional risk factors (total cholesterol, systolic blood pressure, and diabetes) and CVD "weakened as a function of age"; the study also demonstrated lower predictive performance of traditional risk factors among adults older than 75 years compared with that among adults 65 to 75 years.[1] Thus, there is an interest in identifying novel CVD predictors among older adults. Indeed, several circulating

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CLINICAL PERSPECTIVE

What Is New?

- Lower physical function, assessed by the Short Physical Performance Battery, was associated with higher risk of cardiovascular disease (CVD) such as coronary heart disease, stroke, and heart failure, among community-dwelling older adults.
- These associations were independent of traditional CVD risk factors such as age, hypertension, and diabetes.
- Short Physical Performance Battery scores significantly improved risk prediction of CVD outcomes beyond traditional CVD risk factors among older adults regardless of prior CVD history.

What Are the Clinical Implications?

- Our results suggest the potential usefulness of the Short Physical Performance Battery for classifying CVD risk in older adults.
- Clinicians should be mindful of patient physical function when managing CVD risk in older adults.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis Risk in Communities study
SPPB	Short Physical Performance Battery

biomarkers such as natriuretic peptide, cardiac troponin T, and C-reactive protein have been shown as potent predictors of CVD in older adults.[2–5] However, the cost associated with these novel blood biomarkers may be an issue, and additional blood assays may not be easily performed in resource-constrained settings.

In this context, reduced physical function, a representative phenotype of aging,[6] has promising properties as a predictor of CVD in older adults.[7–10] Several studies have shown that reduced physical function is independently associated with a higher risk of CVD.[11–18] Also, the assessment of physical function does not require blood draw or laboratory facilities.

The Short Physical Performance Battery (SPPB) is a valid multicomponent instrument developed by the National Institute on Aging to measure physical function among older adults.[19] It has 3 components: 5 repeated chair stands, 3 progressively harder standing balance poses, and usual gait speed over a short distance. Previous studies found independent associations between SPPB and CVD.[20,21] However, to our best knowledge, no studies formally assessed whether SPPB could improve CVD risk prediction beyond traditional risk factors. Moreover, no studies evaluated whether SPPB is similarly related to different CVD subtypes (eg, coronary heart disease [CHD], stroke, and heart failure [HF]) in a single population.

To address these knowledge gaps, we quantified the association of physical function, assessed with the SPPB, with subsequent risk of composite and individual CVD outcomes of CHD, stroke, and HF among a community-based sample of older adults. Then, we evaluated whether SPPB improved CVD risk prediction by adding it to traditional CVD risk factors. We hypothesized that individuals with lower SPPB score had higher risk of future cardiovascular events and that SPPB improved CVD risk prediction beyond traditional risk factors.

METHODS

Anonymized data from the ARIC (Atherosclerosis Risk in Communities) study are available through the National Heart, Lung, and Blood Institute Biologic Specimen and Data Repository Information Coordinating Center (https://biolincc.nhlbi.nih.gov/studies/aric/). Researchers may additionally contact the ARIC study coordinating center for data access.

Study Participants

We used data from the ARIC study, a community-based prospective cohort study originally designed to investigate the causes for atherosclerotic diseases.[22] A total of 15 792 participants, aged 45 to 64 years, were enrolled at the first visit (1987–1989) from 4 US communities: Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis suburbs, Minnesota; and Washington County, Maryland. Participants were followed up through annual phone interview (semiannual since 2012) and in-person clinic exams (visit 2 [1990–1992], visit 3 [1993–1995], visit 4 [1996–1998], visit 5 [2011–2013], visit 6 [2016–2017], and visit 7 [2018–2019]).

The present study used visit 5 as baseline, when the SPPB was first collected in ARIC. Among the 6538 participants who attended visit 5, we excluded participants who had missing information on the SPPB (n=731), those who were neither White nor Black because of their small numbers (n=13), and those who had missing information on the other covariates of interest (n=224), resulting in a final analytic sample of 5570 participants. The research protocol was approved by the institutional review boards and all participants gave informed consent.

Exposure: Short Physical Performance Battery

SPPB was implemented by trained and certified staff.[23] The chair stands test required participants to rise from a chair 5 times with arms folded across their chest.

Each individual received a score according to the time of completion: 0 (unable to finish in 60 seconds); 1 (≥16.7 to <60 seconds), 2 (≥13.7 to <16.7 seconds), 3 (≥11.2 to <13.7 seconds), and 4 (<11.2 seconds).

The standing balance for 10 seconds was first examined with the semitandem feet position. Once the semitandem position was completed, the tandem position was tested. The side-by-side position was assessed only when semitandem balance was not completed. For semitandem and side-by-side positions, a score of 1 was given if completed (0 if not). The score for the tandem position was based on the time able to hold standing position: 0 (≤3 seconds), 1 (>3 to <10 seconds), and 2 (≥10 seconds). Thus, the total score of standing balance ranged from 0 to 4.

In the gait speed test, participants walked 4 m at their usual pace twice, with the result of the faster trial recorded. The score was based on time needed to complete 4 m: 0 (unable to walk 4 m), 1 (>8.70 seconds), 2 (≥6.21 to ≤8.70 seconds), 3 (≥4.82 to <6.21 seconds), and 4 (<4.82 seconds).

The SPPB total score is the sum of the 3 test scores, ranging from 0 to 12, with higher score indicating better physical function.

CVD Outcomes

The outcomes of interest included the composite and individual outcomes of CHD, stroke, and HF. The identification and ascertainment of CVD events in the ARIC study have been described in detail elsewhere.[5] Briefly, CVD events were ascertained through phone interview and active surveillance of local hospitals. All individual CVD outcomes were adjudicated by a physician panel. CHD was defined as definite or probable myocardial infarction or fatal CHD. Stroke was defined as definite or probable ischemic or hemorrhagic stroke. HF was defined as definite or probable acute decompensated HF. Participants were followed until occurrence of the aforementioned CVD outcomes, loss to follow-up, or administrative censoring on December 31, 2019 (December 31, 2017, for participants from Jackson for administrative reasons), whichever came first.

Covariates

Sociodemographic characteristics, including age, sex, race, ARIC field centers, and education level were self-reported at visit 1 (age and center were updated at visit 5). Education level was classified as basic (≤11 years), intermediate (high school graduate or 1–3 years in vocational school), and advanced (≥1 year in colleges). All of the following covariates were measured at visit 5. Lifestyle information, including smoking status and physical activity levels, were self-reported. Smoking status was classified as never, former, and current. Physical activity included sport-related physical activity during leisure time (eg, jogging, bicycle racing, and boxing) and nonsport physical activity during leisure time (ie, TV viewing, walking, and bicycling); both were measured by the interviewer-administered Baecke Questionnaire.[24] This questionnaire integrates the intensity and frequency of reported activities, yielding a score ranging from 1 to 5 for each participant, with a higher score representing higher leisure-time physical activity levels.

Physical information was measured by trained staff following standard procedures. Body mass index was defined as the weight (kg) divided by the square of height (m^2). Blood pressure was measured 3 times, and the mean of the second and third readings was used for analysis. Total cholesterol was measured by the enzymatic method. High-density lipoprotein (HDL) cholesterol was determined by a homogenous method. Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation with cystatin C, to avoid misclassification of kidney function owing to lower serum creatinine resulting from lower muscle mass in older adults.[25] Cystatin C was assessed by a particle-enhanced immune-nephelometric assay by the Siemens Healthcare Diagnostics system.[26]

The use of medications was collected by trained personnel by inspecting medication containers participants brought to the field centers. Diabetes was defined as a hemoglobin A1c value of 6.5% or higher, use of antidiabetic medication, or self-reported physician-diagnosed diabetes. History of CVD was defined as prevalent CHD, stroke, or HF at baseline (visit 5). Prevalent CHD and stroke were defined as self-reported history at visit 1 or adjudicated cases between visit 1 and visit 5. Prevalent HF was defined as any of the following conditions at or before visit 5: adjudicated HF, hospitalized HF with first position *International Classification of Diseases* code of 428.x before the initiation of HF adjudication in ARIC in 2005, physician reported HF, self-reporting HF at least twice in the study, self-reporting HF once with N-terminal pro-B-type natriuretic peptide >125 pg/mL.[27]

Statistical Analysis

The SPPB score was categorized into low (0–6), intermediate (7–9), and high (10–12, reference) performance[28] and examined categorically and continuously (0–12 full range). Plots of Martingale residuals were used to confirm the linearity of full range SPPB score. Baseline characteristics were summarized as mean (SD) for continuous variables and percentages for categorical variables across SPPB categories. Baseline characteristics were also compared between participants with and without missing values on SPPB.

We then estimated the cumulative incidence of CVD outcomes according to the SPPB categories using the

Kaplan-Meier method. Subsequently, we quantified the independent associations of SPPB with the outcomes using multivariable Cox proportional hazards models. We constructed several models to acknowledge the impact of potential confounders. Model 1 adjusted for demographic variables: age, sex, race, center, and education level. Model 2 further adjusted for major CVD risk factors: systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication, body mass index, sport-related physical activity during leisure time score, nonsport physical activity during leisure time score, and estimated glomerular filtration rate. Model 3 additionally accounted for a clinical history of CVD.

As a sensitivity analysis, we repeated analyses (Model 3 with continuous SPPB only to obtain reliable estimates) in several subgroups by age (<75 versus ≥75 years), sex, race, diabetes status, hypertension treatment, cholesterol-lowering medication use, smoking status, and history of CVD. Statistical interaction was tested by likelihood ratio tests comparing models with and without interaction terms between SPPB and each of these factors. In addition, to account for possibility of reverse causation, we censored CVD events that occurred in the first 12 months. We also evaluated individual components

Table 1. Baseline Characteristics According to SPPB Categories

Characteristics	Total	SPPB		
		Low (0–6)	Intermediate (7–9)	High (10–12)
Total N	5570	705	1671	3194
Age, y	75.4 (5.1)	78.2 (5.5)	76.2 (5.1)	74.3 (4.6)
Black race, %	21.6	38.3	25.4	15.8
Female sex, %	57.7	67.9	62.0	53.2
Education level, %*				
Basic	13.2	25.1	15.5	9.4
Intermediate	42.2	40.7	45.5	40.8
Advanced	44.6	34.2	39.0	49.8
Field center, %				
Forsyth County, North Carolina;	20.9	17.3	25.0	19.5
Jackson, Mississippi	19.7	35.3	22.6	14.8
Minneapolis suburbs, Minnesota	31.3	23.4	26.0	35.8
Washington County, Maryland	28.1	24.0	26.4	29.9
Body mass index, kg/m^2	28.7 (5.6)	30.6 (7.4)	29.1 (5.6)	28.0 (4.9)
Systolic blood pressure, mm Hg	130.1 (17.9)	131.9 (20.5)	131.4 (18.4)	129.1 (17.0)
Hypertension treatment, %	74.8	85.8	80.6	69.3
Diabetes, %	33.1	48.7	37.8	27.1
Cholesterol-lowering medication use, %	56.1	60.0	58.1	54.2
Total cholesterol, mmol/L	4.7 (1.1)	4.5 (1.1)	4.7 (1.1)	4.7 (1.1)
High-density lipoprotein cholesterol, mmol/L	1.3 (0.4)	1.3 (0.4)	1.3 (0.4)	1.4 (0.4)
Smoking status, %				
Current smoker	7.0	7.9	8.5	6.0
Former smoker	51.3	48.1	50.8	52.3
Never smoker	41.7	44.0	40.7	41.7
Physical activity*,†				
Sports during leisure time	2.6 (0.8)	2.2 (0.7)	2.4 (0.7)	2.8 (0.8)
Leisure time activity excluding sport	2.3 (0.6)	2.0 (0.6)	2.2 (0.6)	2.4 (0.6)
Estimated glomerular filtration rate, mL/min per 1.73 m^2	61.7 (19.3)	50.5 (19.6)	58.7 (18.8)	65.7 (18.2)
History of cardiovascular disease, %	23.1	38.9	25.9	18.2
Prevalent coronary heart disease, %	14.5	19.1	15.7	12.9
Prevalent stroke, %	3.5	10.1	3.6	2.0
Prevalent heart failure, %	12.3	25.2	15.8	7.7

SPPB indicates Short Physical Performance Battery.
*Description in "Methods."
†Score ranging from 1 (least active) to 5 (most active). Description is in "Methods."

(as continuous variable) of the SPPB (ie, chair stands, standing balance, and gait speed) separately.

Finally, Harrell's C-statistics were assessed for models with and without SPPB. Calibration was evaluated by a calibration plot of predicted versus observed risk over 8 years (maximum follow-up time was 8.6 years). We included predictors in the Pooled Cohort Equation (ie, age, sex, race, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, and HDL cholesterol) in our base model and obtained coefficients of these predictors using Cox models from the current data.[29] All analyses were conducted with Stata, version 16 (StataCorp LP). A $P<0.05$ was considered statistically significant.

RESULTS

The mean age of the 5570 participants was 75.4 (SD 5.1) years old, with 57.7% female participants and 21.6% Black participants. The most prevalent SPPB category was high (57.3% [n=3194]), followed by intermediate (30.0% [n=1671]) and low (12.7% [n=705]). Compared with participants in the high SPPB category, those in the low and intermediate categories were more likely to be older, female, and Black and to have a lower education level and poorer CVD risk factor profile (eg, higher body mass index, higher systolic blood pressure, higher prevalence of diabetes, lower estimated glomerular filtration rate, and lower levels of physical activity) (Table 1). Moreover, the prevalence of CVD at baseline was highest in the low SPPB category (38.9%), followed by the intermediate (25.9%) and high (18.2%) categories. SPPB was modestly correlated with sport-related physical activity score and nonsport physical activity during leisure time score (r=0.29 and 0.24, respectively). Compared with participants with SPPB score, participants with missing values on SPPB had worse CVD risk factor profile (Tables S1).

During a median follow-up of 7.0 (interquartile interval 5.3–7.8) years, 930 participants developed the composite CVD outcome (386 CHD, 251 stroke, and 529 HF cases). Higher cumulative incidence of composite CVD was seen among participants with lower SPPB score (Figure 1). The 5-year cumulative incidence of the composite CVD outcome among participants in the low and intermediate SPPB categories were ≈3 times (23.4%) and ≈2 times (15.3%) higher than those in the high SPPB category (8.6%).

Continuous SPPB score demonstrated significant associations with composite and individual CVD outcomes in all models (Table 2). A 1-point lower SPPB score was associated with 6% to 10% higher risk of adverse CVD outcomes after adjusting for potential confounders (Table 2). The association of categorical SPPB with composite CVD was significant after adjusting for demographic variables, with a hazard ratio (HR) of 2.41 (95% CI, 1.99–2.91) in the low SPPB and 1.58 (95% CI, 1.36–1.84)

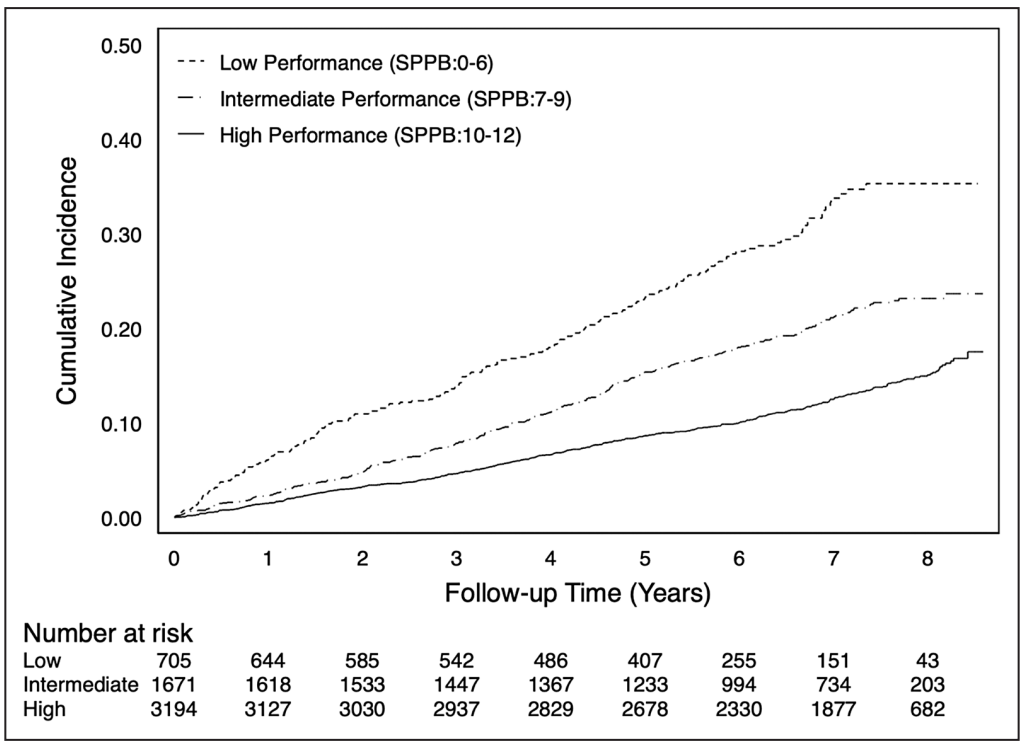

Figure 1. Cumulative incidence of composite CVD by SPPB categories estimated by the Kaplan-Meier method.
CVD indicates cardiovascular disease; and SPPB, Short Physical Performance Battery.

Table 2. Adjusted Hazard Ratios (95% CI) of CVD Outcomes Comparing SPPB Categories and Per 1-Unit Lower SPPB Score

Models	SPPB			
	Low (0–6) (N=705)	Intermediate (7–9) (N=1671)	High (10–12) (N=3194)	Per 1-unit lower SPPB score
Composite CVD*				
Cases	189	326	415	930
Model 1	2.41 (1.99–2.91)	1.58 (1.36–1.84)	Ref.	1.15 (1.12–1.18)
Model 2	1.70 (1.40–2.08)	1.29 (1.11–1.51)	Ref.	1.10 (1.07–1.13)
Model 3	1.47 (1.20–1.79)	1.25 (1.07–1.46)	Ref.	1.07 (1.04–1.10)
CHD				
Cases	74	135	177	386
Model 1	2.39 (1.78–3.22)	1.60 (1.27–2.02)	Ref.	1.16 (1.12–1.21)
Model 2	1.63 (1.19–2.23)	1.28 (1.01–1.62)	Ref.	1.10 (1.06–1.15)
Model 3	1.33 (0.97–1.82)	1.21 (0.96–1.54)	Ref.	1.07 (1.03–1.12)
Stroke				
Cases	55	82	114	251
Model 1	2.41 (1.69–3.43)	1.40 (1.04–1.88)	Ref.	1.15 (1.09–1.21)
Model 2	1.94 (1.33–2.82)	1.21 (0.89–1.63)	Ref.	1.12 (1.06–1.18)
Model 3	1.81 (1.24–2.64)	1.19 (0.88–1.60)	Ref.	1.10 (1.05–1.16)
HF				
Cases	113	191	225	529
Model 1	2.49 (1.94–3.20)	1.66 (1.36–2.02)	Ref.	1.16 (1.12–1.20)
Model 2	1.56 (1.20–2.03)	1.27 (1.04–1.56)	Ref.	1.08 (1.05–1.12)
Model 3	1.33 (1.02–1.73)	1.23 (1.00–1.50)	Ref.	1.06 (1.02–1.10)

Model 1: age, sex, race, ARIC field centers, education level. Model 2: model 1+systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, high-density lipoprotein cholesterol, cholesterol-lowering medication use, body mass index, sport-related physical activity during leisure time score, nonsport physical activity during leisure time score, and estimated glomerular filtration rate. Model 3: model 2+history of CVD. ARIC indicates Atherosclerosis Risk in Communities study; CHD, coronary heart disease; CVD, cardiovascular disease; HF, heart failure; and SPPB, Short Physical Performance Battery.

*Composite CVD included CHD, stroke, and HF.

in the intermediate SPPB categories versus the high SPPB category (Model 1 in Table 2). The association was slightly attenuated after further adjusting for major CVD risk factors (Model 2 in Table 2). Largely consistent results were observed even after additionally accounting for history of CVD (HRs of 1.47 [95% CI, 1.20–1.79] in low SPPB and 1.25 [1.07–1.46] in intermediate SPPB) (Model 3 in Table 2). Low SPPB category was associated with higher risk of stroke (HR, 1.81 [95% CI, 1.24–2.64]) and HF (HR, 1.33 [95% CI, 1.02–1.73]); the association for CHD was not significant in Model 3 (Table 2).

The results were largely consistent across subgroups (Figure S1). After censoring CVD events that occurred in the first 12 months, the associations were largely similar (Table S2). When we examined individual SPPB components, each was independently associated with composite CVD and HF (Figure S2). Standing balance and gait speed were significantly associated with CHD; chair stands and gait speed were significantly associated with stroke.

The addition of continuous SPPB to the traditional CVD predictors improved the risk prediction of composite CVD (ΔC-statistic 0.019 [95% CI, 0.011–0.027]) (Figure 2). The improvement of C-statistic was also seen for all individual CVD outcomes. The results were largely similar in participants with and without prevalent CVD at baseline, although, among participants with CVD history, the C-statistic improvement for stroke and CHD was not statistically significant. The calibration plot showed generally good calibration for CVD outcomes (Figures S3 through S5).

DISCUSSION

In community-dwelling older adults, we found that a lower SPPB score was associated with elevated risk of composite CVD outcomes, as well as with CHD, stroke, and HF. The associations were independent of cardiovascular risk factors and history of CVD and largely consistent across major subgroups. We also found that adding SPPB to traditional CVD risk factors significantly improved the C-statistic for CVD in older adults beyond traditional CVD risk factors, regardless of history of CVD at baseline.

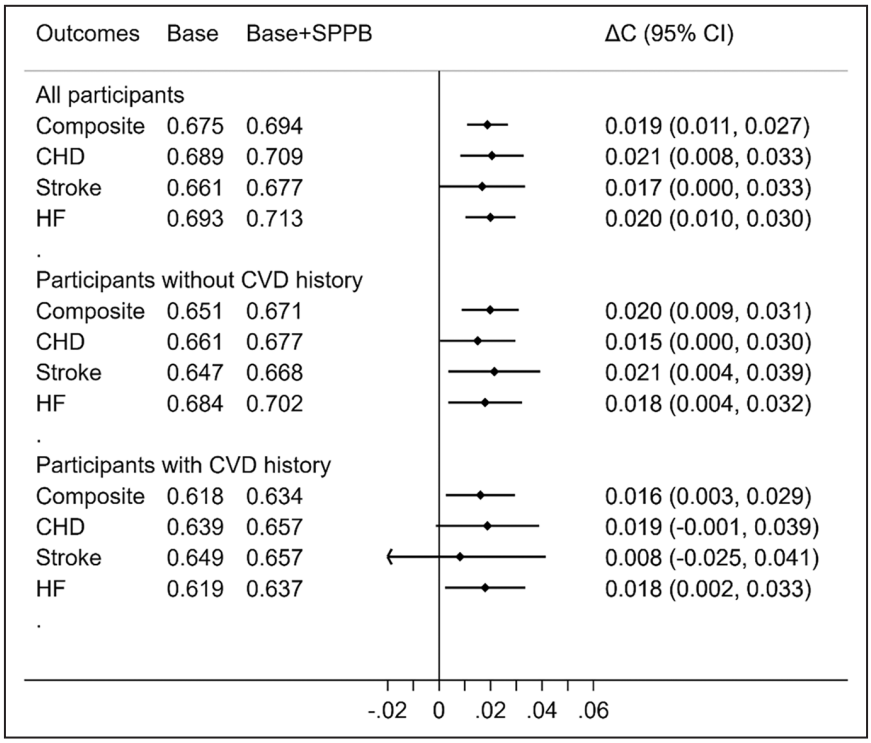

Figure 2. Improvements in C-statistics by adding continuous SPPB to traditional risk factors in base models with predictors from the Pooled Cohort Equation.
Base model included traditional risk factors in Pooled Cohort Equation (age, sex, race, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, diabetes, smoking status). SPPB was modeled continuously. Composite CVD included CHD, stroke, and HF. CHD indicates coronary heart disease; CVD, cardiovascular disease; HF, heart failure; and SPPB, Short Physical Performance Battery.

Our results are consistent with a few previous studies showing physical function, as measured by the SPPB, associated with CVD risk in older adults.[20,21] However, those studies either assessed only older women as a study population[20] or incident HF as an outcome.[21] Thus, the inclusion of both older men and women and the extension to 3 major CVD subtypes of CHD, stroke, and HF in a single population are important contributions of our study. Moreover, we uniquely observed an improvement in C-statistic by adding SPPB beyond traditional CVD risk factors.

The improvements in C-statistic (≈0.02) by adding SPPB in our study may look small. It is not straightforward to translate changes in C-statistic into the impact in clinical practice. Nonetheless, a traditional CVD risk factor in major CVD risk prediction models,[29,30] HDL cholesterol, improved C-statistic by <0.01, beyond other traditional risk factors.[31] Thus, it would not be optimal to simply regard the improvement in risk discrimination by SPPB incremental. Nonetheless, actual clinical utility of SPPB in terms of CVD risk prediction requires comprehensive evaluation, including confirmatory studies in other settings, cost-effectiveness, and acceptability among clinical staff and patients. A potential advantage of SPPB is that it does not require laboratory equipment or facility.

There are a few possible mechanisms that may link reduced physical function to future CVD risk. Physical function may represent age-related physiological and pathophysiological changes such as mitochondrial dysfunction, oxidative stress, chronic inflammation, neurodegeneration, and cellular senescence, all of which can contribute to the development of CVD.[32,33] Indeed, a few previous cross-sectional studies have shown an association between physical function and subclinical atherosclerosis among older adults.[23,34,35] Also, reduced physical function might reflect low physical activity level, which is a known risk factor for CVD.[36] However, the association between SPPB and CVD remained significant even after adjustment for both sport-related and non-sport physical activity scores in our study.

Our study has a few important clinical and research implications. Our results suggest that SPPB can be useful for classifying CVD risk in older adults. Although the best way to evaluate CVD risk in older adults (especially in those aged >79 years) is still under debate,[1,5,37] SPPB has a few unique properties in this regard. For example, SPPB needs only simple tools (eg, chair and stopwatch) and does not require laboratory test. Thus, it could be implemented in resource-limited settings. Also, SPPB may serve as a comprehensive prognostic

marker because it has been associated with a wide range of age-related adverse outcomes such as falls,[38] disability,[19,28] and all-cause mortality.[10] In addition, our study suggests that clinicians should pay attention to physical function when managing CVD risk in older adults. In terms of research implications, we should better understand exact mechanisms linking reduced physical function to elevated CVD risk to inform whether modifying physical function may reduce CVD risk. Importantly, some interventions like resistance training and/or physical therapy can improve physical function and thus may indirectly benefit CVD health.[39–41]

Our study has several limitations. Our findings may reflect reverse causation, namely worse physical function due to CVD. However, the results were comparable after censoring CVD events in the first 12 months, and we observed similar results in people without history of CVD at baseline. Also, this concern is not relevant for risk prediction.[42] Our study population consisted of White and Black older adults; thus, the results may not be generalizable to other race groups. Moreover, we had a fairly well-functioning population, which may underestimate the true association between SPPB and CVD risk. Also, we did not have standard data on muscle mass and thus could not compare prognostic value of physical function versus muscle mass. Nonetheless, a body of evidence indicates that muscle strength is more predictive of adverse outcomes than muscle mass.[43–46] Finally, as true in any observational study, we cannot exclude the possibility of residual confounding (eg, unmeasured comorbidities or no data on nutritional status).

Conclusions

Physical function, measured by SPPB, was independently associated with composite and individual CVD outcomes. SPPB also improved risk prediction of CVD beyond traditional risk factors. Our results suggest the potential usefulness of SPPB for classifying CVD risk in older adults.

ARTICLE INFORMATION

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Disclosures

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Supplemental Material

Tables S1–S2
Figures S1–S5

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics comparing participants with and without missing values on SPPB

Characteristics	Baseline characteristics summarized from non-missing values			% of participants with missingness on characteristics		
		Missing values on SPPB*			Missing values on SPPB*	
	Total	No	Yes	Total	No	Yes
Total N	6538	5807	731			
Age, years	75.8 (5.3)	75.4 (5.1)	78.8 (5.7)	0	0	0
Black, %	23.7	21.8	38.3	0.3	0.2	0.7
Female, %	58.8	57.7	67.3	0	0	0
Education level, %				0.2	0.2	0.3
Basic (≤11 years)	15.1	13.5	28.5			
Intermediate (12-16 years)	41.5	42	37.6			
Advanced (17-21 years)	43.2	44.4	33.7			
Field center				0	0	0
Forsyth County, North Carolina	22.1	21.5	26.7			
Jackson, Mississippi	21.7	19.9	35.8			
Minneapolis suburbs, Minnesota	29.2	30.6	17.6			
Washington County, Maryland	27.1	28.0	19.8			
BMI, kg/m^2	28.7 (5.8)	28.6 (5.6)	30.0 (7.8)	4.1	0.3	34.6
Systolic blood pressure, mmHg	130.7 (18.7)	130.2 (18.0)	134.9 (23.2)	0.5	0.3	2.5
Hypertension treatment, %	75.8	74.8	84.5	0.2	0.1	1.4
Diabetes, %	34.4	33.2	44	0	0	0
Cholesterol-lowering medication use, %	56	56	55.8	0.6	0.5	1.6
Total cholesterol, mmol/L	4.7 (1.1)	4.7 (1.1)	4.7 (1.1)	1.7	0.7	10.3
HDL cholesterol, mmol/L	1.3 (0.4)	1.3 (0.4)	1.3 (0.4)	1.7	0.7	10.3
Smoking status, %				0.1	0.1	0.1
Current smoker	7.5	7	11.8			
Former smoker	50.2	51.1	42.4			
Never smoker	42.2	41.8	45.7			
Physical activity†						
Sports during leisure time	2.6 (0.8)	2.6 (0.8)	2.3 (0.7)	8.3	0.9	66.9
Leisure time activity excluding sport	2.2 (0.6)	2.2 (0.6)	2.0 (0.6)	7.8	0.4	66.2
eGFR, $mL/min/1.73m^2$	60.6 (19.6)	61.6 (19.3)	51.5 (19.0)	1.5	0.6	9
History of CVD, %	24.9	23.3	37.9	0	0	0

Prevalent CHD, %	15	14.6	18.6	0	0	0
Prevalent stroke, %	4.2	3.7	8.5	0	0	0
Prevalent HF, %	13.9	12.4	25.6	0	0	0

Abbreviations: SPPB, Short Physical Performance Battery; BMI, body mass index; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration rate; CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.

*The reason for missingness on SPPB was “refused to participate”.

†Score ranging from 1 (least active) to 5 (most active). Description is in “Methods”.

Table S2. Adjusted hazard ratios (95% CI) of adverse outcomes comparing SPPB categories and per unit decrease of SPPB score after censoring events occurred within the first 12 months of follow-up

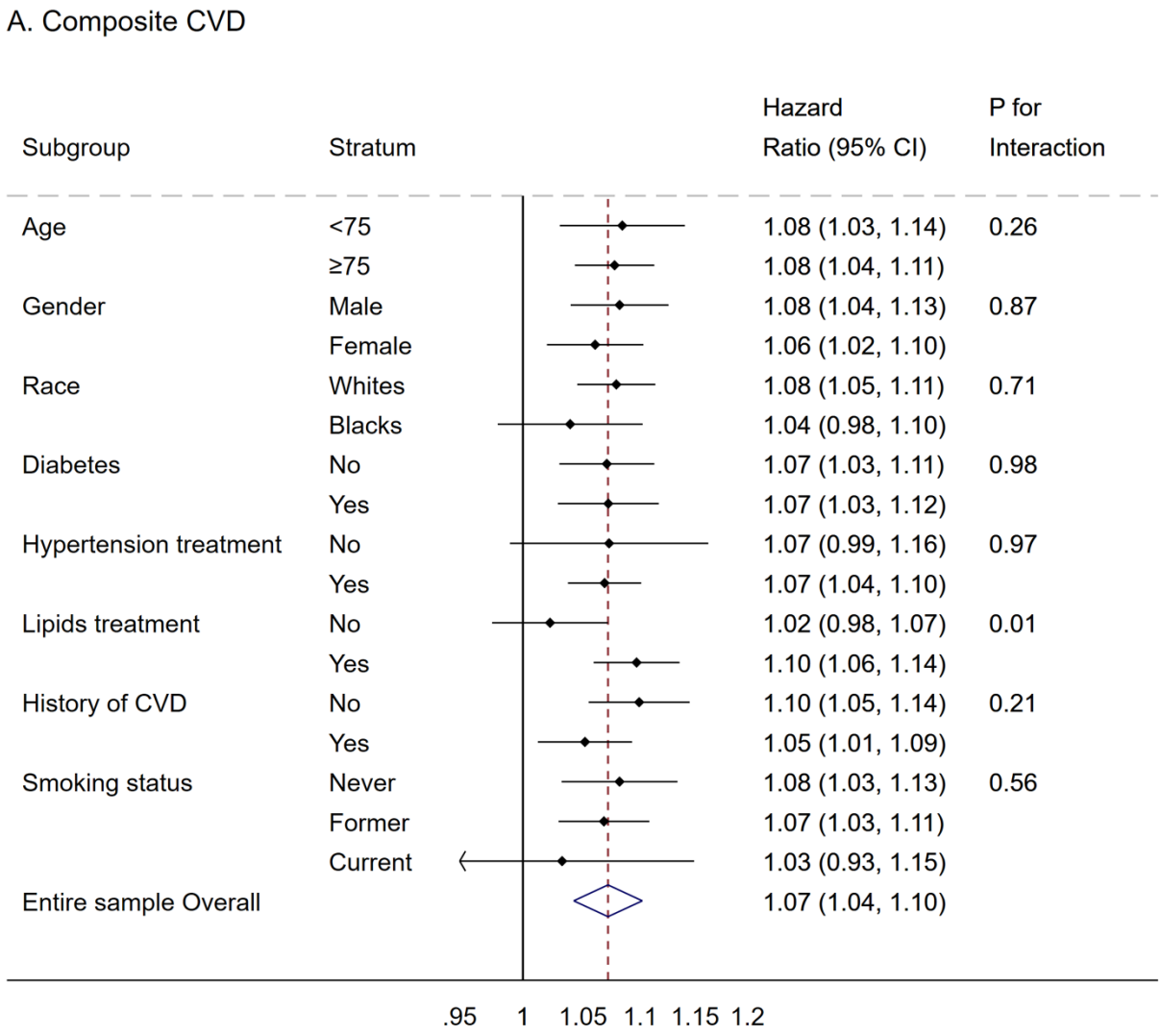
Outcomes	SPPB			
	Low (0-6)	Intermediate (7-9)	High (10-12)	Per one-unit lower SPPB score
All participants				
Composite*	1.41 (1.13, 1.76)	1.30 (1.10, 1.53)	Ref.	1.07 (1.04, 1.10)
CHD	1.21 (0.85, 1.71)	1.22 (0.95, 1.58)	Ref.	1.07 (1.02, 1.12)
Stroke	1.90 (1.27, 2.85)	1.34 (0.98, 1.83)	Ref.	1.11 (1.05, 1.17)
HF	1.18 (0.88, 1.59)	1.22 (0.98, 1.51)	Ref.	1.05 (1.00, 1.09)
Participants without CVD history				
Composite*	1.82 (1.35, 2.46)	1.26 (1.01, 1.56)	Ref.	1.10 (1.05, 1.15)
CHD	1.57 (0.93, 2.66)	1.06 (0.73, 1.54)	Ref.	1.07 (1.00, 1.16)
Stroke	1.65 (0.97, 2.83)	1.40 (0.97, 2.03)	Ref.	1.10 (1.02, 1.19)
HF	1.85 (1.23, 2.77)	1.21 (0.89, 1.64)	Ref.	1.08 (1.02, 1.15)
Participants with CVD history				
Composite*	1.13 (0.81, 1.57)	1.34 (1.04, 1.72)	Ref.	1.05 (1.00, 1.09)
CHD	1.12 (0.70, 1.79)	1.43 (1.00, 2.03)	Ref.	1.07 (1.01, 1.14)
Stroke	1.99 (1.04, 3.82)	1.10 (0.61, 1.97)	Ref.	1.10 (1.01, 1.20)
HF	0.84 (0.55, 1.27)	1.21 (0.89, 1.64)	Ref.	1.03 (0.97, 1.08)

Abbreviations: SPPB, Short Physical Performance Battery; CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.

Results were adjusted for covariates in model 3: age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity during leisure time score, non-sport physical activity during leisure time score, eGFR and history of CVD.

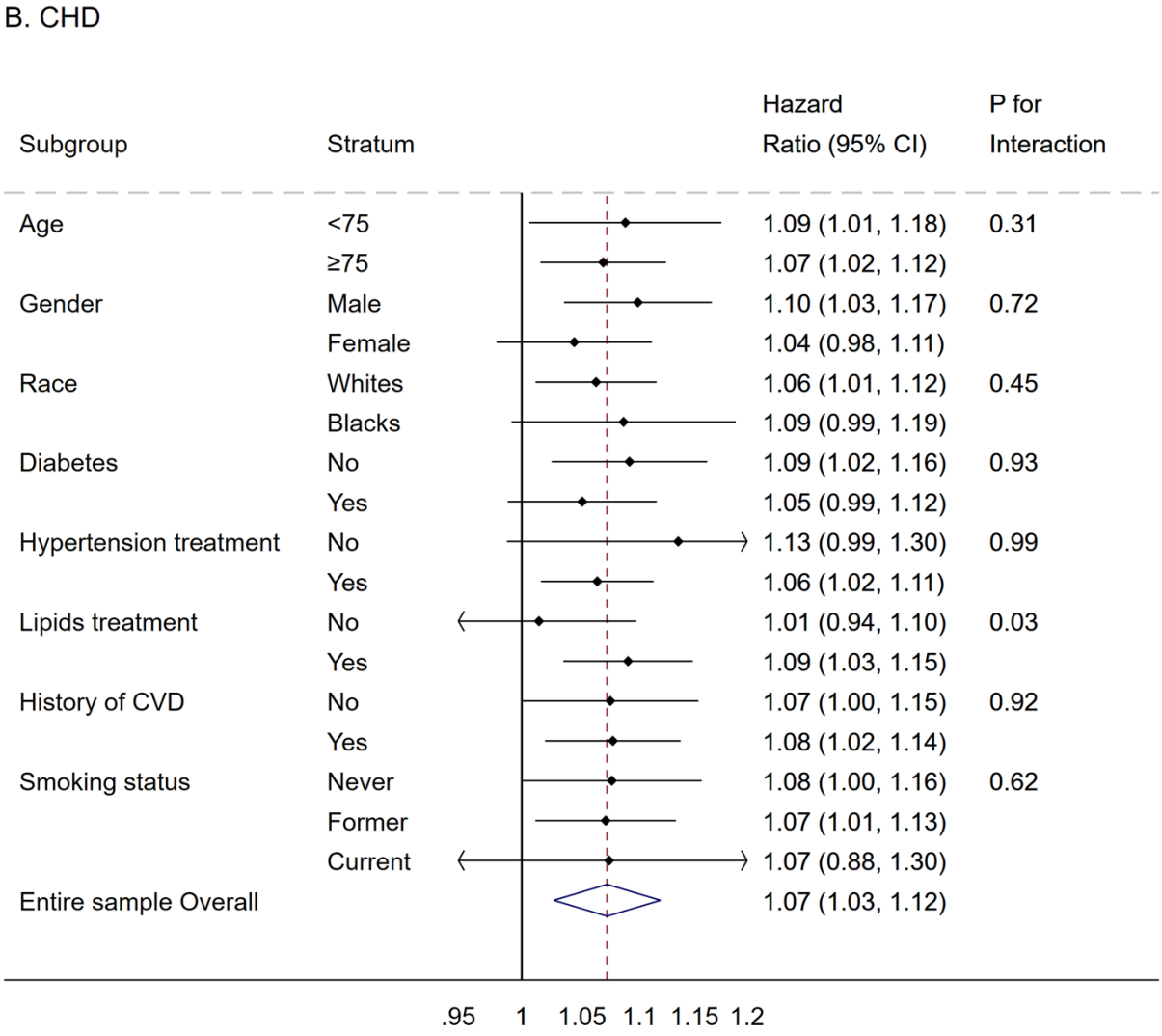
*Composite CVD included CHD, stroke and HF.

Figure S1A. Association of continuous Short Physical Performance Summary (SPPB) with composite CVD by demographic and clinical subgroups



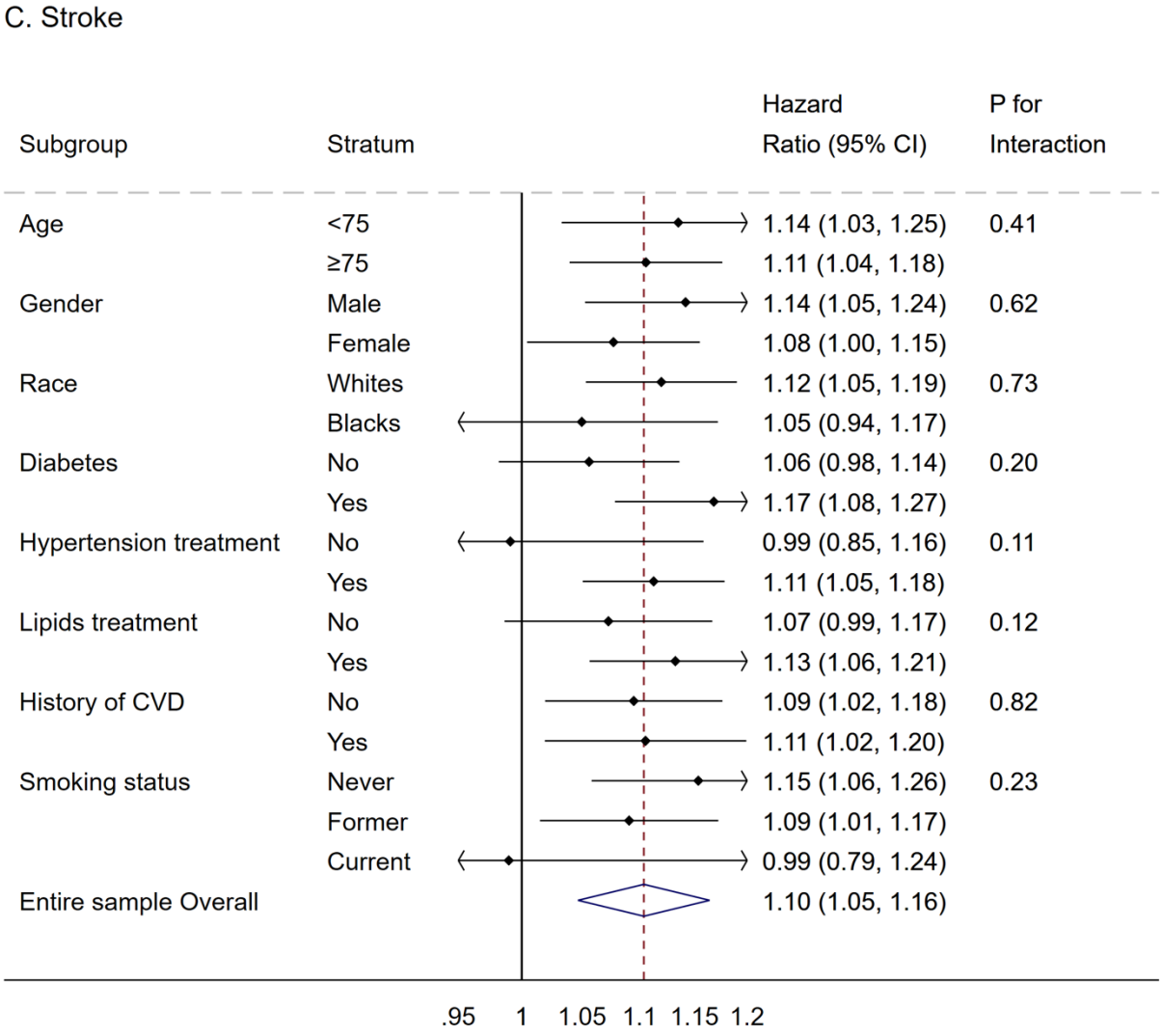
The overall results were adjusted for covariates in model 3: age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity during leisure time score, non-sport physical activity during leisure time score, eGFR and history of CVD.
The HR represents HR per unit decrease of SPPB score.

Figure S1B. Association of continuous Short Physical Performance Summary (SPPB) with coronary heart disease (CHD) by demographic and clinical subgroups



The overall results were adjusted for covariates in model 3: age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity score, non-sport physical activity during leisure time score, eGFR and history of CVD.
The HR represents HR per unit decrease of SPPB score.

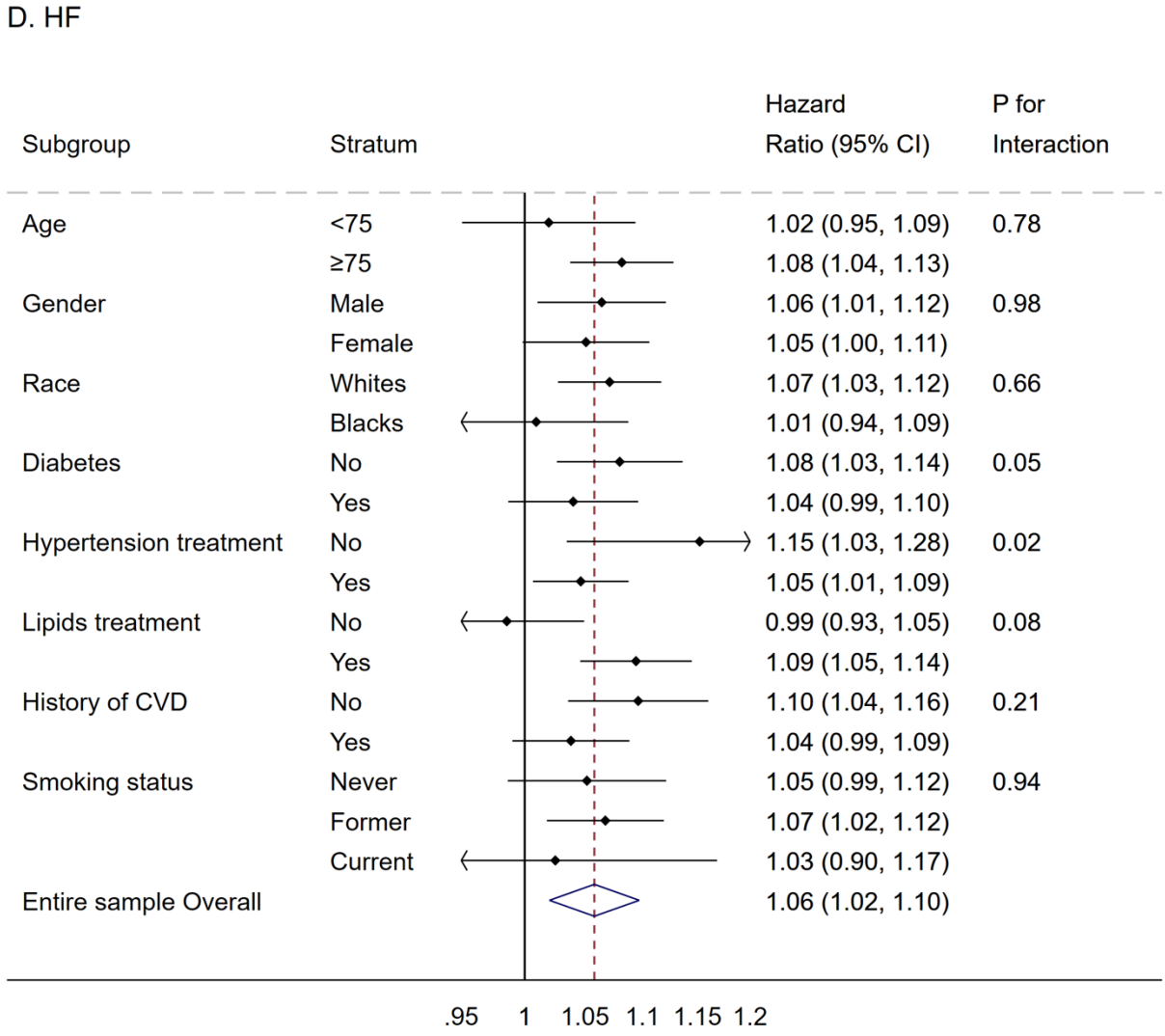
Figure S1C. Association of continuous Short Physical Performance Summary (SPPB) with stroke by demographic and clinical subgroups



The overall results were adjusted for covariates in model 3: age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity during leisure time score, non-sport physical activity during leisure time score, eGFR and history of CVD.

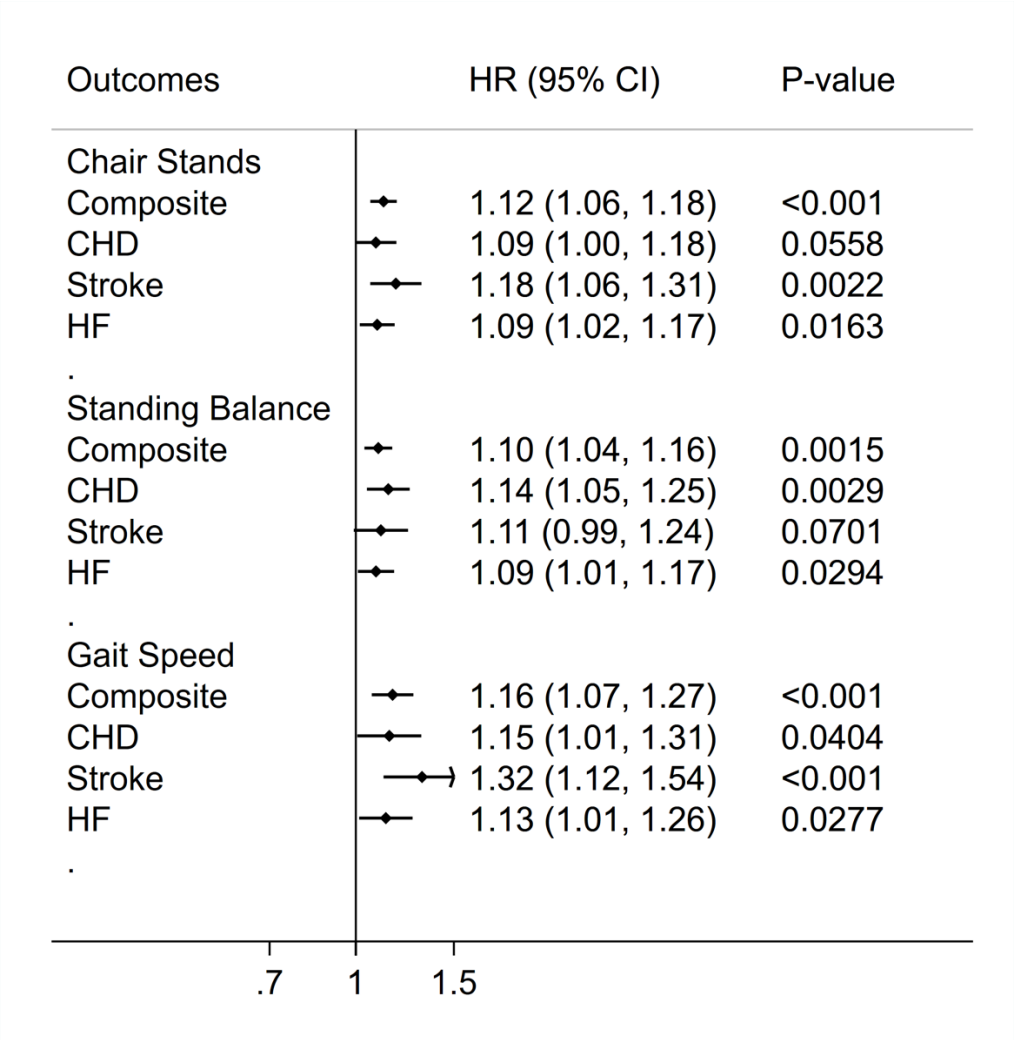
The HR represents HR per unit decrease of SPPB score.

Figure S1D. Association of continuous Short Physical Performance Summary (SPPB) with heart failure (HF) by demographic and clinical subgroups



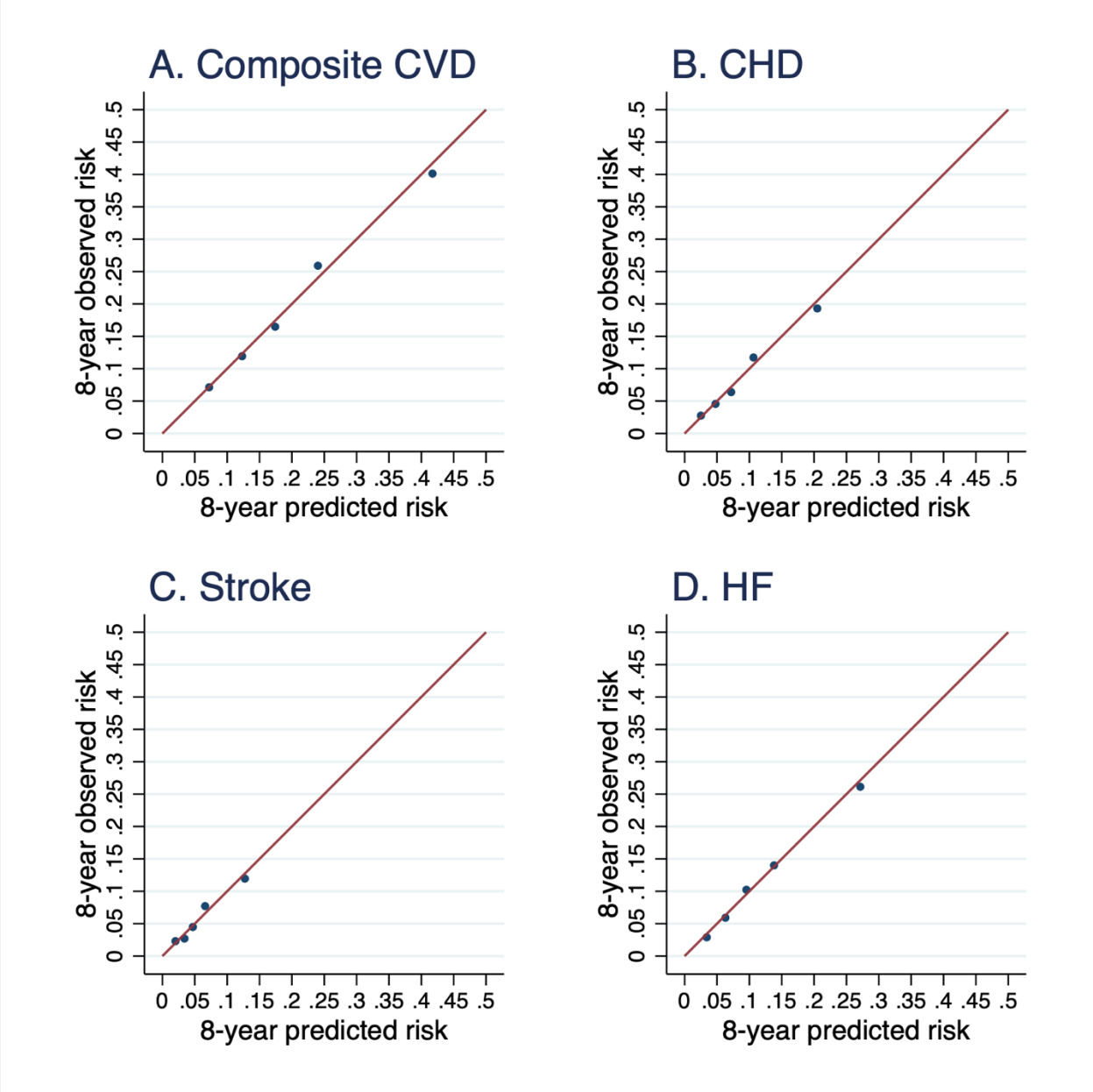
The overall results were adjusted for covariates in model 3: age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity during leisure time score, non-sport physical activity during leisure time score, eGFR and history of CVD.
The HR represents HR per unit decrease of SPPB score.

Figure S2. Adjusted hazard ratio of adverse outcomes per one unit lower of single test score



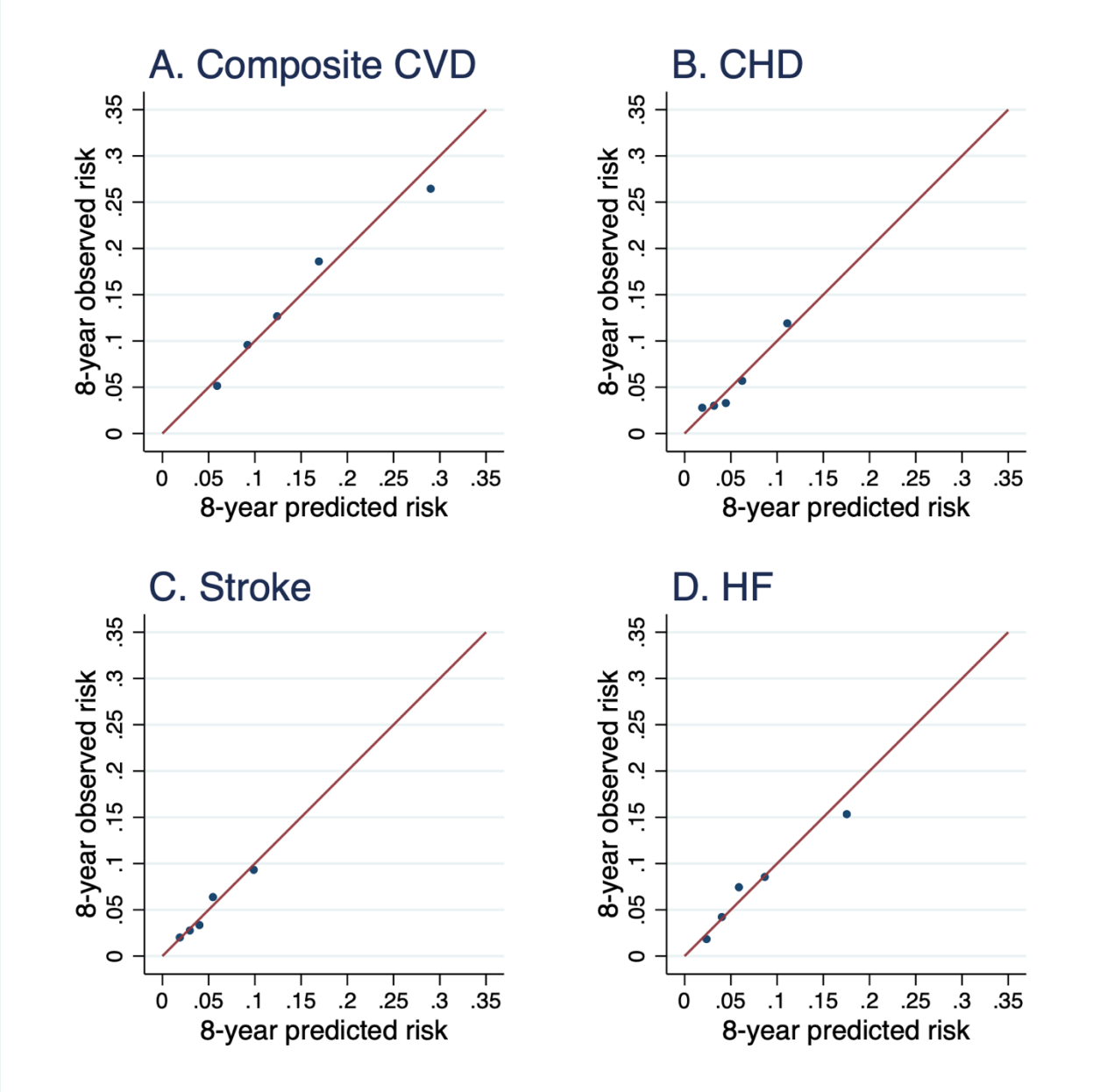
The results were adjusted for three SPPB components and covariates in model 3**:** age, sex, race, center, education level, systolic blood pressure, hypertension treatment, smoking status, diabetes, total cholesterol, HDL cholesterol, cholesterol-lowering medication use, BMI, sport-related physical activity during leisure time score, non-sport physical activity during leisure time score, eGFR and history of CVD.

Figure S3. Calibration plots of predicted risk based on SPPB and traditional risk factors in the Pooled Cohort Equation and observed risk among all participants



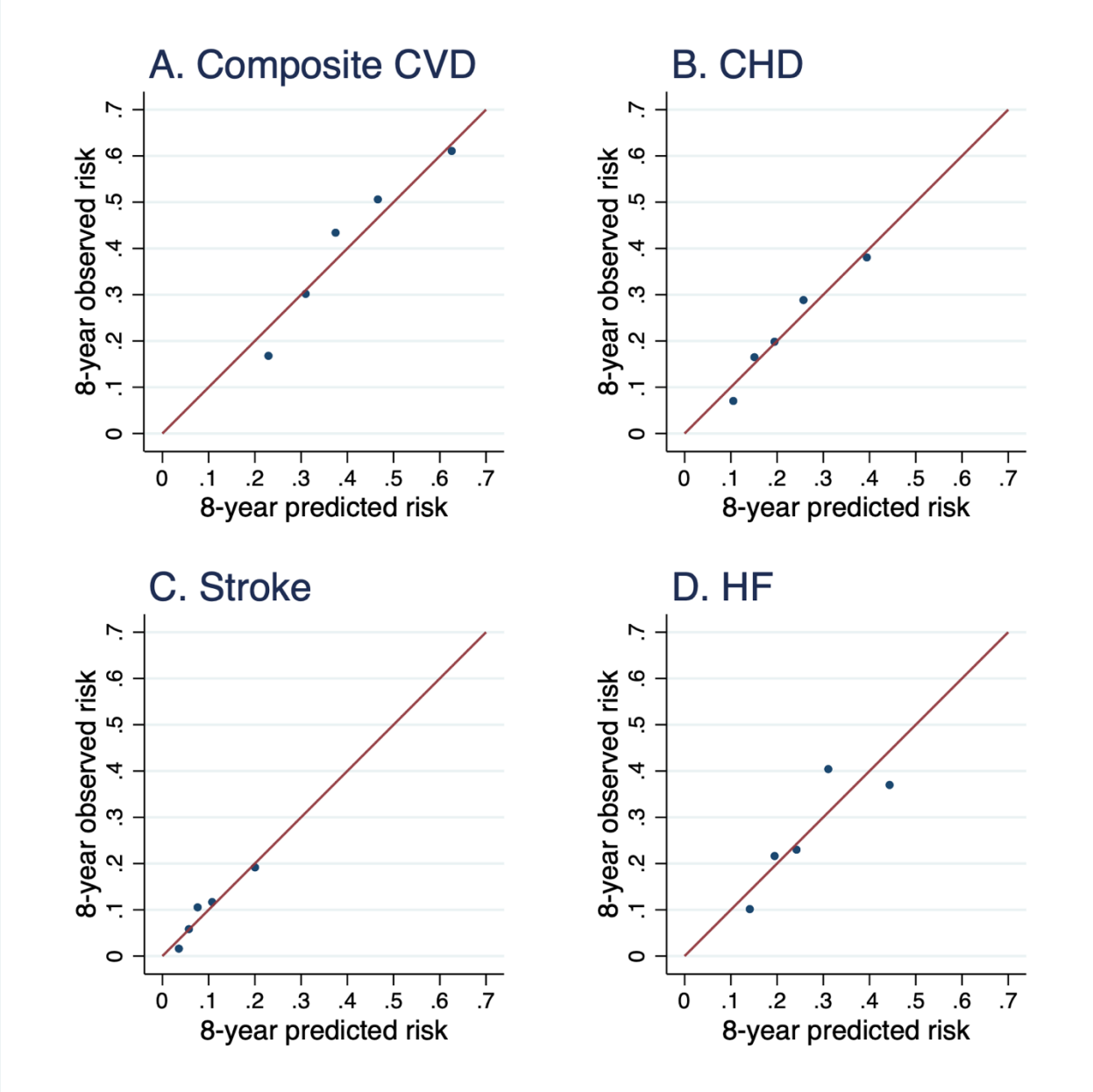
Abbreviations: SPPB, Short Physical Performance Battery; CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.
Base model included traditional risk factors in Pooled Cohort Equation (age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, diabetes, smoking status).
SPPB was modeled continuously.
Composite CVD included CHD, stroke and HF.

Figure S4. Calibration plots of predicted risk based on SPPB and traditional risk factors in the Pooled Cohort Equation and observed risk among participants without CVD history



Abbreviations: SPPB, Short Physical Performance Battery; CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.
Base model included traditional risk factors in Pooled Cohort Equation (age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, diabetes, smoking status).
SPPB was modeled continuously.
Composite CVD included CHD, stroke and HF.

Figure S5. Calibration plots of predicted risk based on SPPB and traditional risk factors in the Pooled Cohort Equation and observed risk among participants with CVD history



Abbreviations: SPPB, Short Physical Performance Battery; CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure.
Base model included traditional risk factors in Pooled Cohort Equation (age, sex, race, total cholesterol, HDL cholesterol, systolic blood pressure, diabetes, smoking status).
SPPB was modeled continuously.
Composite CVD included CHD, stroke and HF.