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Longitudinal Physical Performance and Blood Pressure Changes in Older Women: Findings form the Women's Health Initiative

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abstract

Background: This study evaluated the association between changes in physical performance and blood pressure (BP) (e.g., systolic [SBP], diastolic [DBP], pulse pressure) in older women.

Methods: 5627 women (mean age 69.8 ± 3.7 y) with grip strength, chair stand, gait speed performance and clinic-measured BP at baseline and at least one follow-up (years 1, 3 or 6) were included. Generalized estimating equation analysis of multivariable models with standardized point estimates described the longitudinal association between physical performance and BP changes in the overall cohort, and in models stratified by baseline cardiovascular disease (CVD), time-varying antihypertensive medication use (none, ≥1) and enrollment age (65–69 y; 70–79 y).

Results: Overall, each z-score unit increment in grip strength was associated with 0.59 mmHg (95% CI 0.10, 1.08) higher SBP, and 0.39 mmHg (95% CI 0.11, 0.67) higher DBP. In stratified models, a standardized increment in grip strength was associated with higher SBP in women without CVD (0.81; 95% CI 0.23–1.39), among antihypertensive medication users (0.93; 95% CI 0.44, 1.41) and non-users (0.37; 95% CI 0.03, 0.71), and in those aged 65–69 y (0.64; 95% CI 0.04, 1.24). Similarly, a standardized increment in any of the three performance measures was associated with modestly higher DBP in antihypertensive medication users, and those aged 70–79 y. Associations between any performance measure and pulse pressure change were not significant.

Conclusion: These results suggest a positive, and statistically significant relationship between physical performance and BP that appears to be influenced by CVD history, antihypertensive medication use, and age.

Keywords

physical functioning; grip strength; gait speed; chair stand; blood pressure; trajectories; aging; older women

1.0 Introduction

The United States is projected to experience rapid growth in its older population, with the number of Americans aged ≥ 65 y expected to be 88.5 million (56% women) by 2030.[1] This increased life-expectancy is foretelling of an old-age population in whom the growing burden of high blood pressure (BP) and hypertension is high (77%), particularly in older

women (~76%).[2] Although the prevalence of hypertension increases with age, changes in systolic and diastolic BP with advancing age do not occur universally, nor are increases in BP inevitable during old age.[3] Aging is also associated with widening of pulse pressure, a reflection of vascular function and accelerated arterial stiffening that may perpetuate reductions in BP in old age.[4] While changes in BP during aging may partly be explained by underlying or imminent pathology (e.g., cardiovascular disease [CVD], heart failure) or intensive medication, it cannot be ruled out that other heterogenic markers of biological age may have an effect on vascular function.

Over the past several decades, there has been growing awareness regarding measures of muscle function (e.g., grip strength) and physical performance (e.g., chair stand, or gait speed), as signs of health, independence and survival in older adults.[5–7] Although mechanisms are not completely discernable, skeletal muscle function and performance appear to be closely connected to vascular function.[8–12] Previous epidemiological literature has provided good evidence of an inverse relationship between high systolic BP or pulse pressure and grip strength[13] or physical performance (e.g., chair stand, gait speed)[14–17] in well-functioning older populations. However, little is known about how muscle function or physical performance might affect BP during old age, and whether this relationship differs by prevalent CVD or hypertension status or age in postmenopausal women. Observing women with multiple repeated measures of muscle function and physical performance and BP over time could help clarify these questions.

The purpose of the present study was to better understand the simultaneous relationship between change in function and physical performance and change in BP over time in a large well-characterized cohort, the Women's Health Initiative (WHI). The primary objectives were to 1) describe trends in grip strength, chair stand, and gait speed, herein described collectively as physical performance, and BP outcomes (e.g., systolic BP, diastolic BP, and pulse pressure), and 2) evaluate the longitudinal association between change in performance measures and BP outcome over time. Additional analyses examined whether the associations between performance and BP differed by clinical factors (CVD and antihypertensive medication usage) or age. We hypothesized that lower performance would be associated with higher systolic BP and widening of pulse pressure. We further hypothesized that the performance relationship with diastolic BP will vary by age group, given prior evidence indicating that declining diastolic BP is commonly observed in late life years in part due to greater burden from comorbidities, such as CVD.[18, 19]

2.0 Materials and Methods

2.1 Study Population

The WHI enrolled 161,808 postmenopausal women (aged 50–79 y, mean age 63 y) at 40 U.S, clinical centers between 1993 and 1998. The WHI protocol, including study design, eligibility criteria, data collection, and outcomes ascertainment and adjudication, has been published previously.[20, 21] Briefly, eligible participants were free from serious medical conditions (e.g., severe chronic heart, liver, kidney, or lung disease) associated with a predicted survival of less than 3 years and were likely to continue to reside in the vicinity of a WHI clinical center for at least 3 years. The WHI Clinical Trials (WHI-CT, n=68,133)

consisted of 3 concurrent, randomized controlled evaluation of three distinct interventions: Hormone Therapy trials, the Dietary Modification trial (low-fat eating pattern), and the Calcium and Vitamin D supplementation trial. For the WHI Hormone Therapy Trials, women with intact uterus were randomized to receive placebo or conjugated equine estrogen with medroxyprogesterone acetate, and women with a prior hysterectomy were randomized to receive placebo or conjugated equine estrogen alone. Women were initially enrolled in the Hormone Trials and/or Dietary Modification Trial at baseline. One year later, women were asked to join the Calcium/ Vitamin D Trial.[20, 21] Women ineligible or not interested in the WHI-CT components were given an opportunity to enroll in the observational study (OS; n= 93,676). Additionally, other women were specifically invited to participate in the OS. The OS was designed to explore the predictors and natural history of important causes of morbidity and mortality in postmenopausal women of diverse ethnicities.[22]

The study population for the current analysis was limited to a random sample of 6,025 (25%) WHI-CT participants, who at enrollment were aged 65–79 y and completed strength and performance-based physical function tests (i.e., timed walk speed, repeated chair stand, and hand grip strength). Of this sample, 5,882 had complete data for at least one of the three performance measures in addition to clinic-measured systolic or diastolic BP at baseline. Of these, 255 were excluded for not having at least 1 follow-up measure of each performance measure in addition to a BP report at year 1, 3, or 6, resulting in a final analytic sample size of 5,627 women (Figure 1). Study protocols were approved by appropriate institutional review boards and participant informed consent was obtained at WHI centers.

2.2 Physical Performance Measures

Standard physical performance measures were assessed at baseline and at years 1, 3, and 6 by trained, certified study staff using standard protocols.[20, 21] The reliability, sensitivity to change, and predictive validity of timed gait speed (m/s), chair stand (number) and grip strength (kg) have been published.[23, 24] Gait speed was assessed by measuring the time in seconds that it took to complete a 6-meter walk, performed at usual pace, using ambulatory aids as needed. The test was repeated, and the faster of the two measured times was used to calculate speed in this analysis. Chair stands were conducted if the participant was able to stand at least once, without using hands or arms, from a straight-backed, non-padded, flat-seated, armless chair. The number of chair stands able to be performed in 15 seconds was measured to assess lower extremity muscle strength and balance. Two 15-second trials of repeated chair stand were performed with arms folded across the chest, with a 1–2 minutes rest between trials, and the score with the greater number of chair stands of the two trials was included in this analysis. Grip strength, tested on the dominant hand, measured voluntary muscle strength using a hydraulic hand grip dynamometer (Jamar hand dynamometer; Lafayette Instruments, Lafayette, IN). The participant performed the test in the seated position with the elbow bent to 90° and was instructed to squeeze the handle of the dynamometer as hard as she could during two trials, with staff coaching. The higher score was used in this analysis.

2.3 Blood pressure

Blood pressure (BP) was measured at baseline and at follow up years 1, 3, and 6 by certified staff using standard protocols and instruments. Appropriate cuff bladder size was determined based on arm circumference at each visit. BP was measured in the right arm with a mercury sphygmomanometer, with the participant in seated position, legs not crossed, after 5 minutes of rest. The average of two measurements, taken 30 seconds apart, were used in the analyses. Pulse pressure was calculated as systolic BP minus diastolic BP.

2.4 Antihypertensive Medication Ascertainment

WHI participants were asked to bring all medications taken on a regular basis in the past two weeks to their first screening interview. Trained clinic interviewers entered each medication name and strength from the containers directly into a database that assigned drug codes using Medi-Span software that was updated quarterly (First DataBank, Inc., San Bruno, CA). In the present analyses, women were classified as a user or non-user of antihypertensive medication coded according to their therapeutic classes (e.g., ACE inhibitors, Angiotensin II Receptor Antagonist, and Angiotensin II Receptor Antagonists and thiazides, β-blockers, calcium channel blockers) based on the medication inventory at screening and at follow up clinic visits 1, 3, and 6. These medications were specifically chosen based on plausible physiological mechanisms shared between skeletal muscle and the vascular system.[25–29] Women reported duration of use prior to baseline for each current medication. Information was available on tablet strength but not on the prescribed dose. Number of medications was calculated as the sum score of included prescription medication. Maximum duration of use which takes into account medication class and strength to make plausible assumptions about medication dosage was calculated as calculated for each visit year as the maximum duration of use among all taken antihypertensive medications through follow up year 6.

2.5 Covariate Assessment

Information on socio-demographics (age, race and ethnicity, education), medical history, physical activity habits, alcohol intake, and smoking was obtained using self-administered questionnaires at baseline.

Anthropometrics were assessed at each clinic visit. BMI was calculated as weight (kg) / height (m^2). Physical functioning was assessed by SF-36 subscale of the Rand-36 (SF-36).[30] Diabetes was coded positive if participants reported oral medication or insulin intake. Presence of arthritis at baseline was based on self-report. Hypertension status was based on antihypertensive medication use and/or blood pressure > 140/90 mmHg at baseline visit as this was the clinical guideline[31] used at the time of WHI enrollment. History of CVD was based on self-reported physician diagnosis of myocardial infarction, stroke or heart failure.

2.6 Statistical Analysis

Baseline demographic and health characteristics were summarized for the overall analytical cohort. The primary exposure variables of interest were grip strength, chair stands, and gait speed. The primary outcomes were systolic BP, diastolic BP, and pulse pressure, evaluated separately.

Pearson's correlation (r) was used to examine bivariate correlations between physical performance exposures and each BP outcome at baseline and follow-up years 1, 3, and 6. Generalized Estimating Equations (GEE) with an identify link function was conducted to determine the association between each performance measure and BP outcome over time. This modeling approach accounts for within subject correlation of the repeated measures using working correlation structure to obtain the population averaged estimates of coefficients. The main interest is the estimated correlation coefficient between performance measures and BP outcomes. Each performance exposure was standardized into a z-score to correlate with BP outcomes to allow for direct comparisons of the regression coefficients (β) across the three different units of physical performance measures. Adjustment for model covariates were considered using four modeling approaches based on previous literature:[8–10, 14] Model 1 (base model): adjusted for age, race and ethnicity, WHI clinical trial arm; Model 2: additionally adjusted for education, BMI, menopausal hormone therapy use, smoking status, alcohol intake, baseline recreational physical activity levels, diabetes; Model 3 was based on Model 2 plus self-reported CVD diagnosis at baseline; finally, Model 4 used Model 3 plus the number of antihypertensive medications and duration of antihypertensive medication usage (as a proxy of dosage and severity of hypertension), expressed as time-varying covariates calculated as the average of baseline, and year 1, 3 and 6 follow-up time points. Multicollinearity was assessed using variance inflation factors (<1.5) and by tolerance (>0.2)[32] in multivariable model 4, which were not large, suggesting meaningful collinearity was unlikely.

Given that CVD could also lead to worsening physical function as well as increases in BP, for which the antihypertensive medication is used to treat, we conducted additional sensitivity analyses using GEE of multivariable models to examine the association between each exposure and BP outcome over time by separating out women with and without CVD diagnosis at baseline, and separately, among those using and not using antihypertensive medications at any follow-up. The latter approach accounts for within subject changes in medication usage over time. Additional analyses were carried out to investigate differences in the performance-BP relationship by median age at enrollment.

Statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC); all reported P-values are two-sided under significance level 0.05.

3.0 Results

3.1 Study Population Characteristics

Baseline characteristics of the analytic cohort of 5,627 women (mean age 69.9 years) who were followed for an average of 7.6 y (± 1.65) through the planned main WHI study close out in 2005 are presented in Table 1. The majority of participants were White and not of Hispanic origin, and on average were overweight (mean BMI 28.5 kg/m^2). Participants self-rated health to be very good or good and overall had moderately high physical functioning (mean RAND-36 score, 77.0). Prevalence of current smoking (5.3%), and cancer (5.0%) was relatively low. More than half of the participants reported a history of arthritis at baseline, 14% reported diabetes, and 21% reported CVD at baseline. Nearly a third of the cohort reported receiving treatment for hypertension. Mean BP (systolic BP/diastolic BP:

132.2 / 74.8 mmHg) met the criteria for prehypertension under JNC 7 guidelines used at WHI enrollment,[31] and pulse pressure, on average was high at baseline.[33] Expectedly, the proportion of participants receiving one or more medications to control BP, and the duration of medication (maximum and mean usage) incrementally increased over time (P<.0001; Supplement Table 1).

3.2 Blood Pressure trends over time

There was a decline over time in systolic BP and diastolic BP and an increase in pulse pressure, with mean annual changes of −0.59 mmHg, −0.75 mmHg, 0.16 mmHg, respectively (all slopes P<.0001). Similar trends in systolic BP and diastolic BP were observed across groups based on baseline CVD status, antihypertensive medication use, and median age groups (Supplemental Figures 1–3). Of note, pulse pressure decreased over time among antihypertensive medication users whereas increasing pulse pressure patterns were observed in non-users (interaction P<.0001).

3.3 Cross-sectional Associations of Physical Performance and Blood Pressure at each Visit

Overall, the correlation between physical performance and BP outcomes at baseline and at follow-up visits 1,3 and 6 were weak (Supplemental Table 2). Among significant bivariate findings, chair stand and gait speed performance were negatively correlated with systolic BP at baseline. For diastolic BP outcome, positive correlations with grip strength, and negative correlations with gait speed were observed. All three performance measures demonstrated significant negative correlations with pulse pressure. Direction and general magnitude of correlation of performance measures with BP outcomes were consistent at each observed follow-up visit.

3.4 Longitudinal Associations and Effect Modification of Physical Performance and Blood Pressure Over time

Results of the sequential covariate adjustment and beta coefficients (β; 95% CI) using one z-score increment in performance measures in multivariable models of BP outcomes are described in Table 2. Overall, several patterns were observed. First, each z-score increment in grip strength was associated with 0.59 mmHg (95% CI 0.10, 1.08) higher systolic BP, and 0.39 mmHg (0.11, 0.67) higher diastolic BP, with minimal attenuation seen between the base model and multivariable models. Second, each standardized z-score unit increment in the number of chair stands performed was associated with higher diastolic BP after adjustment for cardiometabolic risk factors (Model 2), however, the effects were no longer significant after further adjustment for CVD and antihypertensive medications. Third, a one z-score increase in gait speed, indicating faster speed, was associated with higher diastolic BP (0.29; 95% CI 0.02, 0.56) only after full covariate adjustment in multivariable models (Model 4). For pulse pressure, only associations with gait speed performance remained significant between base and multivariable model 3 (−0.30; 95% CI −0.52, −0.08); however, was no longer significant after full covariate adjustment (Model 4).

Overall, there was little evidence that the association between physical performance and BP change over time was modified by presence of CVD at baseline. Among women without

CVD, a standardized unit increase in grip strength was associated with 0.81 mmHg (95% CI 0.23, 1.39) higher systolic BP and a 0.50 mmHg (95% CI 0.18, 0.83) higher DBP over time; however, there were no other significant differences in the associations observed across the two defined groups based on baseline CVD status (Table 3). In contrast, effect modification by time-varying antihypertensive medication use was observed for two of the three BP outcomes, with interactions between physical performance measures and systolic BP or diastolic BP (but not pulse pressure) being either significant or borderline significant (Table 4). For the systolic BP outcome, in antihypertensive medication users, each standardized unit increase in grip strength was associated with a 0.93 mmHg (95% CI 0.44, 1.41) higher systolic BP over time, and smaller but significantly higher systolic BP by 0.37 mmHg (95% CI 0.03, 0.71) among non-medication users. No significant association between chair stand performance and systolic BP over time was found across the two medication groups. However, in non-medication users only, each unit increase in gait speed was associated with lower systolic BP over time by 0.52 mmHg (95% CI −0.83, −0.22). Significant effect modification by time-varying antihypertensive medication use was most apparent for the diastolic BP outcome where, in antihypertensive medication users, better grip strength, greater chair stand performance, and faster gait speed was significantly associated with a 0.48 mmHg, 0.35 mmHg, and 0.45 mmHg higher diastolic BP, respectively over time. In models with pulse pressure as the outcome, per unit increases in grip strength was associated with higher pulse pressure (0.43; 95% CI 0.03, 0.84) in women using antihypertensive medications, whereas in those not using medication, faster gait speed was associated with lower pulse pressure over time (−0.42; 95% CI −0.67, −0.17).

Although the test for interaction between physical performance and age was not statistically significant, the results of stratified analyses by age suggested the presence of a significant association between grip strength and systolic BP by 0.64 mmHg (95% CI 0.04, 1.24) only in women aged 65–69 y (Supplement Table 3). Evidence of effect modification by age was more clearly observed for the diastolic BP outcome and all three exposures. Specifically, in women aged 70–79 y, each incremental unit increase in grip strength, number of chair stands performed and gait speed were associated with higher levels of diastolic BP by 0.50 mm Hg, 0.52 mm Hg and 0.52 mm Hg, respectively, over time (all interaction $P<.05$). No significant association between performance and pulse pressure was observed in age stratified models.

Additional sensitivity analyses were performed evaluating the potential role of age as the time variable and as a covariate in the multivariable fully adjusted model (Model 4). Results were materially similar to the primary results for all performance-BP associations.

4.0 Discussion

In this large cohort of postmenopausal women, after covariate adjustment, positive associations for grip strength with systolic and diastolic BP over time were observed. These findings remained robust in models stratified by CVD, antihypertensive medication use, and age. Additionally, positive associations were found between chair stand performance and gait speed and diastolic BP over time, which was consistently observed in women aged 70–79 y and those using antihypertensive medication during follow-up. The relationship between change in physical performance and change in pulse pressure was overall

inconsistent, and particularly in stratified models of antihypertensive medication use. Taken together, our findings suggest that changes in physical performance and BP are associated with one another over time, and it appears that these associations might differ according to CVD history, antihypertensive medication use, and age. Further research is needed to better understand the longer-term clinical impact of physical performance on BP during aging.

To our knowledge, this is the first study to evaluate longitudinal changes in BP parameters in relation to change in physical functioning measures over a defined time interval wherein both BP and physical performance was assessed contemporaneously. Uniquely, the performance tests captured different aspects of muscular strength and physical functioning over time. Evidence from previous observational studies,[13, 34] which reported more anticipatory findings may not have controlled for relevant factors as was done here. In contrast to our hypothesis, the results from our multivariable analyses suggested a positive association between performance and BP over time. Results for grip strength were particularly interesting given its positive association with systolic BP and diastolic BP remained robust to covariate adjustment and was observed in all stratified models. Conceivably, lower grip strength and declines in BP, may both reflect an epiphenomenon to coexisting or underlying poor health, which is related to increasing CVD outcomes, morbidity and mortality.[18, 35, 36] Accordingly, grip strength is recognized as the most reliable measure of muscle function and surrogate for whole body muscle strength. There is clear evidence showing that low grip strength, a common phenomenon of advanced age due to skeletal muscle weakness and disuse atrophy,[37] is a sensitive discriminator of adverse health outcomes, including mobility disability, falls, and all-cause and cause-specific mortality.[37–42] Aging-related declines in muscular strength, as measured by the dominant hand grip strength test, might precede declines in other domains of physical functioning such as gait speed and balance.[37] This would increase vulnerability to poor lower-extremity performance (e.g., chair stand performance, gait speed)[37] which in turn could reduce circulating vasoactive metabolites of skeletal muscle contraction, such as adenosine, and also impair endothelial-dependent vasoconstriction, each of which contribute to poor vascular compliance.[8–12] This may explain why associations of BP with grip strength were more consistently observed compared to associations with other performance measures. Importantly, these findings suggest that change in grip strength may be an aging biomarker that is associated with vascular changes impacting usual BP in older adults.

Another unexpected finding was that increments in chair stand performance or gait speed were independently associated with higher diastolic BP over time, and these findings remained robust in models specific to antihypertensive medication users and women aged 70–79 y. Although our effect sizes were modest, it is not implausible that incrementally higher levels of diastolic BP we observed could have important implications on future disease or health outcomes.[43] How improvements in gait speed and chair stand performance might untowardly affect diastolic BP requires further investigation. Pathophysiological mechanisms have been proposed including the plausibility that higher performance elicits a compensatory hemodynamic response to increase or rather attenuate further declines in diastolic BP, and maintain adequate organ perfusion to the heart which is perfused during diastole.[35] Synonymous with ageing, increases in peripheral resistance due to impaired functional sympatholysis resulting in skeletal muscle malperfusion and elevated sympathetic

tone, or endothelial dysfunction contributing to decreased vasodilator capacity have also been suggested mechanisms linking higher performance with increased BP in older adults.[44] Collectively, these findings raise the intriguing possibility that physical performance, important indicators of whole-body resiliency,[45] may be inextricably linked to BP, pulse pressure and hence vascular function during aging. There is a need for further evaluation regarding the long-term influence of physical performance on BP regulation in older women.

4.1 Strengths and Limitations

Strengths of this study include the longitudinal study design, the large sample size, and the collection of clinic-measured physical performance measures and BP over prolonged follow up. The results observed in the present study accounted for several confounding factors on BP control, cardiometabolic disease and aging. However, this study is not without limitations. First, the study population comprised of older, predominantly White women or Non-Hispanic origin, thereby limiting generalizability of our results to men and to other race and ethnic groups. Second, dose of medication, and the primary indication for medication or reason for medication change (e.g., to manage high/low BP) was not available, and medication adherence was unknown. Lack of dose or adherence information is particularly relevant when understanding its individual effects on BP or performance, where higher doses would conceivably lead to greater reductions in BP, and potentially better performance.[25] Despite the measures we took to control for confounding such as time-varying adjustment for the number of antihypertensive medications and maximum duration of use, and stratification by medication use, we cannot dismiss the likelihood of issues related to confounding by indication, or structural confounding, which may otherwise explain the statistically significant but not clinically significant performance-BP associations observed in this study. This underscores the need for future investigations that account, more precisely, for the influence of antihypertensive medications, and other factors related to aging and hemodynamic resiliency on BP trajectories over time.

5.0 Conclusion

Findings from this study suggest that longitudinally over repeated measurements higher grip strength is positively associated with higher systolic BP and diastolic BP over time, an effect that is present in women without a CVD history. This effect, however, appears to be influenced by antihypertensive medication use and age. Additionally, better physical performance over time, reflected by greater chair stand performance or faster gait speed, was positively associated with diastolic BP over time in women using antihypertensive therapy at any time and in those aged 70 y and older. Future research clarifying mechanistically, how changes in physical performance influences BP regulation during aging appears warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Availability of data and materials:

The Women's Health Initiative Study data supporting the conclusions of this article are available via the BioLINCC website of the National Heart, Lung, and Blood Institute at https://biolincc.nhlbi.nih.gov/home/.

Glossary

BP	blood pressure
CI	Confidence interval
CVD	cardiovascular disease
WHI	Women's Health Initiative
GEE	Generalized Estimating Equations

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Highlights

- Factors contributing to changes in blood pressure (BP) during old age are not well understood.
- Higher grip strength was associated with higher systolic and diastolic BP.
- Greater chair stand or gait speed performance was positively associated with diastolic BP
- CVD history, antihypertensive medication use, and age may influence the longitudinal relationship between physical performance and BP
- More research is needed to better understand clinical impact of physical performance on BP during aging.

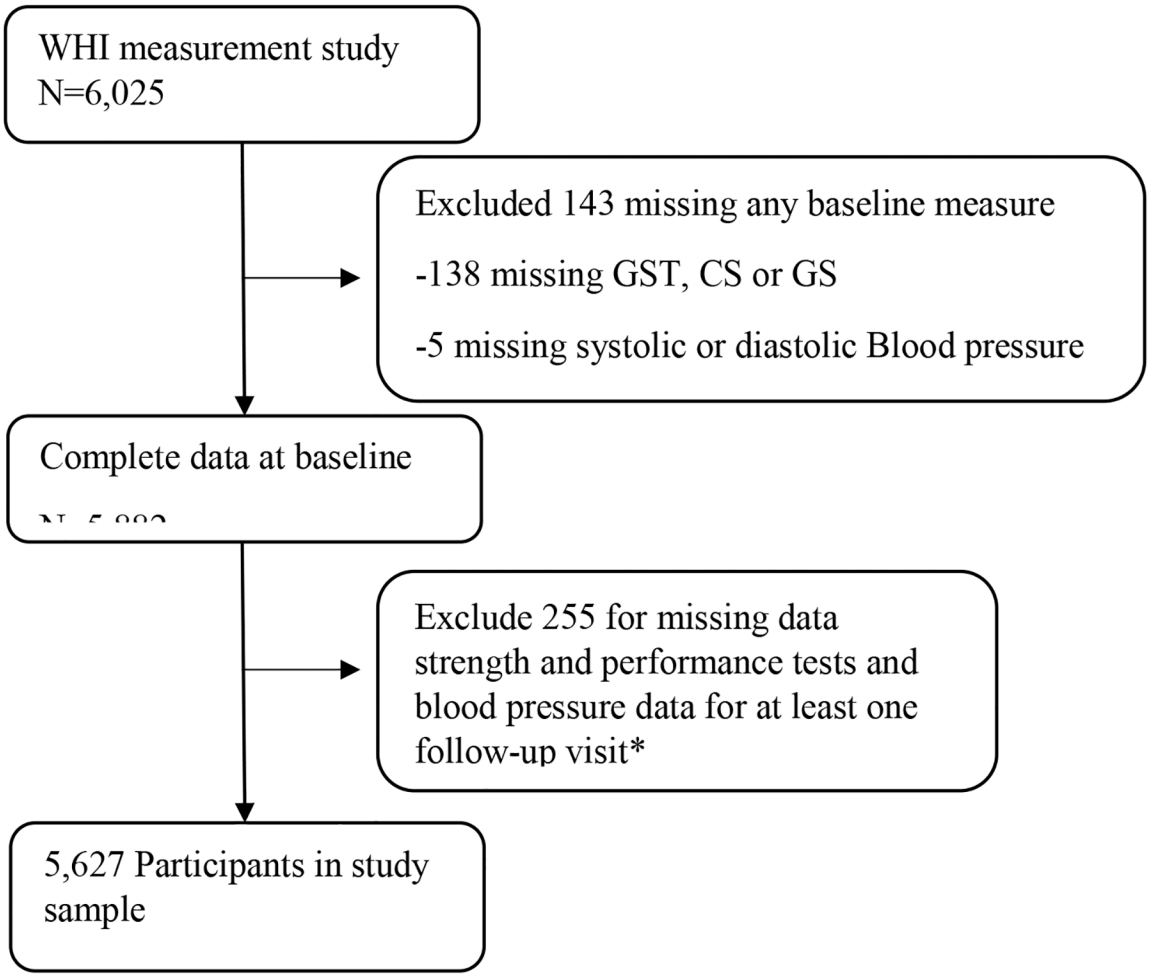

Figure 1.

GST, grip strength; CS, chair stand; GS, gait speed

Note: Flow chart describing WHI sample subject characteristics for the final N=5,627 in the final multivariate model with complete data on grip strength, chair stand and gait speed measures and blood pressure data at baseline and at least one follow-up visit, year 1, 3, or 6.

Table 1:

WHI participant characteristics by age at baseline

Variables	Whole cohort (n=5627)
Mean age (y)	69.85 ± 3.68
Race and ethnicity--n(%)	
White (not of Hispanic origin)	4849 (86.31)
Black or African American	432 (7.69)
Hispanic or Latina	142 (2.53)
American Indian or Alaskan Native	10 (0.18)
Asian or Pacific Islander	130 (2.31)
Other race or ethnicity	55 (0.98)
Employed (yes)	962 (17.20)
Living alone	1786 (35.59)
Education	
high school or vocational or below	2114 (37.82)
some college (includes associate degree)	1596 (28.56)
college degree BA/BS or beyond	1879 (33.62)
BMI kg/m ^{2}	28.50 ± 5.60
Underweight (≤18.5)	29 (0.52)
Normal (18.5–24.9)	1570 (28.12)
Overweight (25.0–29.9)	2069 (37.05)
Obese (≥30)	1916 (34.31)
Alcohol use-n (%)	
None and past	1784 (31.92)
<1 drink/month	708 (12.67)
<1 drink/wk	1195 (21.38)
1 to <7 drinks/wk	1299 (23.24)
≥7 drinks/wk	603 (10.79)
Smoking	
never smoked -n (%)	3065 (55.28)
past smoked -n (%)	2187 (39.45)
current smoker (n, %)	292 (5.27)
Physical Activity; Met-hr/week	11.34 ± 12.89
SF-36 score (0–100)	77.31 ± 20.18
Self-reported General Health	
Excellent -n (%)	808 (14.45)
Very good -n (%)	2297 (41.08)
Good -n (%)	2018 (36.09)
Fair/Poor -n (%)	468 (8.37)
Hormone therapy use	

Variables	Whole cohort (n=5627)
Never	2364 (42.12)
Past	1668 (29.72)
Current	1581 (28.17)
Falls in past 12 mo	
None	3812 (68.13)
1 time	1096 (19.59)
2 times	492 (8.79)
≥ 3 times	195 (3.49)
Depression (CES-D > 0.06)	0.03 ± 0.10
Activities of daily living score	4.03 ± 0.23
Treated Diabetes (pills or shots)	801 (14.23)
History of Arthritis	3129 (56.10)
History of cancer	281 (5.03)
History of hypertension	
Never hypertensive	3314 (59.72)
Untreated hypertension	456 (8.22)
Treated Hypertension	1779 (32.05)
History of CVD or CHD *	1180 (20.97)
No. of antihypertensive medications †	
0	4085 (72.59)
1	1199 (21.31)
2	294 (5.22)
3	42 (0.75)
>3	6 (0.11)
Systolic BP, mmHg	132.18 ± 17.49
Diastolic BP, mmHg	74.78 ± 9.2
Pulse pressure, mmHg	57.39 ± 14.93

Notes: Mean ± SD or N (%), as appropriate.

*History of cardiovascular disease or coronary heart disease defined as reported history of either myocardial infarction, stroke, or congestive heart failure

†Use of antihypertensive medication coded according to therapeutic classes based on the medication inventory at screening: ACE inhibitors, Angiotensin II Receptor Antagonist, ACE Inhibitors; and Angiotensin II Receptor Antagonists and thiazides, β-blockers, calcium channel blockers

Missing covariates: race and ethnicity, n=9; employment status, n=33; living alone, n=609; education, n=38; BMI, n=43; alcohol, n=38; smoking status, n=83; physical activity, n=20; SF-36, n=126; self-reported general health, n=36; hormone therapy use, n=14; prior fall history, n=32; depression, n= 168; activities of daily living, n=55; history of arthritis, n=49, history of cancer, n=44; history of hypertension, n=77; systolic bp, n=4; diastolic bp, n=5; pulse pressure, n=5

Table 2.

Associations between the change in performance measures and blood pressure after sequential covariate adjustment (N=5627) *

		Outcomes		
		Systolic Blood Pressure β (95% CI)	**Diastolic Blood Pressure β (95% CI)**	**Pulse Pressure β (95% CI)**
Model 1				
	Grip strength	**0.52 (0.25, 0.80)** ‡	**0.38 (0.23, 0.52)** #	0.14 (−0.09, 0.38)
	Chair Stand	**−0.43 (−0.70, −0.15)**‡	0.08 (−0.07, 0.23)	**−0.51 (−0.73, −0.28)**#
	Gait speed	**−0.47 (−0.71, −0.23)**‡	−0.02 (−0.15, 0.12)	**−0.46 (−0.66, −0.25)**#
Model 2				
	Grip strength	**0.56 (0.27, 0.85)** ‡	**0.37 (0.21, 0.52)** #	0.18 (−0.06, 0.43)
	Chair Stand	−0.09 (−0.39, 0.21)	**0.16 (0.00, 0.33)** †	**−0.25 (−0.49, −0.01)**†
	Gait speed	−0.21 (−0.47, 0.05)	0.09 (−0.05, 0.24)	**−0.31 (−0.53, −0.09)**‡
Model 3				
	Grip strength	**0.56 (0.27, 0.85)** ‡	**0.36 (0.21, 0.52)** #	0.19 (−0.05, 0.44)
	Chair Stand	−0.09 (−0.39, 0.21)	0.15 (−0.01, 0.31)	−0.23 (−0.48, 0.01)
	Gait speed	−0.21 (−0.47, 0.05)	0.08 (−0.06, 0.23)	**−0.30 (−0.52, −0.08)**‡
Model 4				
	Grip strength	**0.59 (0.10, 1.08)** †	**0.39 (0.11, 0.67)** ‡	0.19 (−0.23, 0.61)
	Chair Stand	−0.11 (−0.62, 0.40)	0.24 (−0.04, 0.52)	−0.37 (−0.79, 0.05)
	Gait speed	0.09 (−0.39, 0.57)	**0.29 (0.02, 0.56)** †	−0.19 (−0.60, 0.22)

Notes:

* point estimates express the association between one standardized unit change in each performance measure and the associated BP change

Bold print indicates Statistical significance

† p<0.05;

‡ p<0.01;

# p<0.0001

Model 1: age, race/ethnicity, CT arm

Model 2: Model 1+ education, BMI, current hormone status, smoking status, alcohol intake, physical activity, diabetes

Model 3 Model 1+ CVD diagnosis

Model 4: Model 3 + number of antihypertensive medications and duration of antihypertensive medication usage (expressed as time-varying covariates calculated as the average of baseline, and 1, 3 and 6 follow up time points)

Table 3.

Associations between strength and performance and blood pressure change over time by baseline CVD status [*,‡]

Exposure by CVD status[†]	Systolic BP β (95% CI)	Diastolic BP β (95% CI)	Pulse Pressure β (95% CI)	p-interaction
Grip Strength				0.13, 0.17, 0.45
No CVD	**0.81 (0.23, 1.39)** [#]	**0.50 (0.18, 0.83)** [#]	0.29 (−0.19, 0.76)	
Yes CVD	0.01 (−0.87, 0.89)	0.09 (−0.42 0.59)	−0.08 (−0.92, 0.76)	
Chair Stand				
No CVD	−0.13 (−0.72, 0.46)	0.21 (−0.12, 0.54)	−0.38 (−0.85, 0.09)	0.88, 0.72, 0.95
Yes CVD	−0.05 (−1.00, 0.91)	0.32 (−0.19, 0.84)	−0.35 (−1.17, 0.47)	
Gait Speed				
No CVD	0.21 (−0.35, 0.76)	0.26 (−0.05, 0.57)	−0.04 (−0.51, 0.42)	
Yes CVD	−0.21 (−1.13, 0.70)	0.37 (−0.15, 0.89)	−0.56 (−1.35, 0.22)	0.43, 0.72, 0.25

Notes: BP, blood pressure; CVD, cardiovascular disease; CI, confidence interval

[*] point estimates express the association between one standardized unit change in each performance measure and the associated BP change

[†] History of cardiovascular disease defined as reported history of either myocardial infarction, stroke, or congestive heart failure

p-interaction represents the overall effect of the performance*CVD interaction in the model, by GEE

Bold print indicates Statistical significance

[#] $p<0.05$

[‡] Model 2 + antihypertensive medications was used to estimate all effect magnitude (β): age, ethnicity, CT arm, education, BMI, current hormone status, smoking status, alcohol intake, baseline physical activity, diabetes, time-varying number of antihypertensive medications and duration of antihypertensive medication usage

Table 4.

Associations between strength and performance and blood pressure change over time by time-varying antihypertensive medication usage[*,‡]

Exposure by BP medication status[†]	Systolic BP β (95% CI)	Diastolic BP β (95% CI)	Pulse Pressure β (95% CI)	p-interaction
Grip Strength				
No $BP_{medication}$	**0.37 (0.03, 0.71)** [#]	**0.29 (0.12, 0.47)** [§]	0.07 (−0.20, 0.35)	0.05, 0.23, 0.13
Yes $BP_{medication}$	**0.93 (0.44, 1.41)** [≠]	**0.48 (0.21, 0.74)** [#]	**0.43 (0.03, 0.84)** [#]	
Chair Stand				
No $BP_{medication}$	−0.20 (−0.54, 0.15)	0.03 (−0.16, 0.22)	−0.22 (−0.51, 0.06)	0.21, **0.05**, 0.88
Yes $BP_{medication}$	0.16 (−0.32, 0.65)	**0.35 (0.08, 0.62)** [§]	−0.19 (−0.58, 0.21)	
Gait Speed				
No $BP_{medication}$	**−0.52 (−0.83, −0.22)** [≠]	−0.10 (−0.27, 0.06)	**−0.42 (−0.67, −0.17)** [≠]	**0.0005, 0.0002**, 0.08
Yes $BP_{medication}$	0.44 (−0.03, 0.91)	**0.45 (0.20, 0.71)** [≠]	−0.02 (−0.40, 0.37)	

Notes: BP, blood pressure, CVD, cardiovascular disease, CI = confidence interval

[*] point estimates express the association between one standardized unit change in each performance measure and the associated BP change

[†] **Yes $BP_{medication}$** defined as the time-varying usage of antihypertensive medication at baseline or any follow-up period to account for within subject changes in medication use over time.

p-interaction represents the overall effect of the performance*Antihypertensive medication use interaction in the model, by GEE

Bold print indicates Statistical significance

[#] $p<0.05$;

[§] $p<0.01$;

[≠] $p<0.001$

[‡] Model 3 was used to estimate all effect magnitude (β): age, ethnicity, CT arm, education, BMI, current hormone status, smoking status, alcohol intake, baseline physical activity, diabetes, CVD