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Blood Pressure and Cognitive Decline over 8 Years in Middle-Aged and Older Black and White Americans

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Abstract

Although the association between high blood pressure (BP), particularly in midlife, and late-life dementia is known, less is known about variations by race and sex. In a prospective national study of 22,164 blacks and whites ≥45 years without baseline cognitive impairment or stroke from the Reasons for Geographic and Racial Differences in Stroke cohort enrolled 2003–2007 and followed through September 2015, we measured changes in cognition associated with baseline systolic and diastolic BP (SBP, DBP), as well as pulse pressure (PP) and mean arterial pressure (MAP), and we tested whether age, race, and sex modified the effects. Outcomes were global cognition (Six-Item Screener)(primary outcome)), new learning (Word List Learning), verbal memory (Word List

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Delayed Recall), and executive function (Animal Fluency Test). Median follow-up was 8.1 years. Significantly faster declines in global cognition were associated with higher SBP, lower DBP, and higher PP with increasing age (P<0.001 for age*SBP* follow-up-time, age*DBP*follow-up-time, and age*PP*follow-up-time interaction). Declines in global cognition were not associated with MAP after adjusting for PP. Blacks, compared to whites, had faster declines in global cognition associated with SBP (P=0.02) and MAP (P=0.04). Men, compared to women, had faster declines in new learning associated with SBP (P=0.04). BP was not associated with decline of verbal memory and executive function, after controlling for the effect of age on cognitive trajectories. Significantly faster declines in global cognition over 8 years were associated with higher SBP, lower DBP, and higher PP with increasing age. SBP-related cognitive declines were greater in Blacks and men.

Keywords

hypertension; high blood pressure; cognition; ethnicity; gender

INTRODUCTION

Cognitive impairment and dementia (CID) increases the risk of disability, burden of illness, and costs.[1] CID affects about 8.6 million Americans[2], a number expected to triple by 2050 as the Baby Boomer generation ages[3], with higher prevalence in Blacks compared with Whites and in women compared with men.[4] The identification of modifiable risk factors that reduce disparities and prevent CID are top public health priorities.[5] Exciting preliminary results from the SPRINT MIND trial show that high blood pressure (BP) is a modifiable risk factor to reduce CID risk.[6]

Although it is known that high BP, particularly in midlife, is associated with late-life CID[7], less is known about variations by race and sex. Blacks are more likely to develop high BP and to have greater severity of high BP than Whites.[8] Not only are Blacks more likely to have worse BP control than Whites[9], but they also appear more likely to have detrimental brain effects from high BP[10–13]. A recent study[14] suggests that Blacks have greater BP-related cognitive declines; whereas, another study[15] suggests that Whites do.

Gender differences in the association between BP and cognitive decline are less clear. Men are more likely than women to have high BP before age 50 but this disparity narrows and reverses at older ages. A recent study[16] suggests that mid-life high BP increases late-life CID risk in women but not in men. It is uncertain whether the effect of high BP on late-life CID risk is greater in Blacks than in Whites or in women than in men, after accounting for the effect of age on the BP-cognition relationship[17].

We assessed the association between systolic and diastolic BP (SBP and DBP) levels as well as levels of mean arterial pressure (MAP) and pulse pressure (PP) and cognitive trajectories over 8 years in a large, nationally representative cohort of middle-aged and older black and white adults, and tested whether race and sex modified the associations. We hypothesized that 1) higher SBP, lower DBP, and higher PP at baseline each are associated with faster

cognitive decline, and 2) that the effects of SBP and DBP on the slope of cognitive decline are greater in Blacks compared with Whites and in women compared with men.

METHODS

Study Design, Participants, and Measurements

Study protocol is available at http://www.regardsstudy.org/. Statistical code is available through written agreement with authors from Dr. Levine (e-mail: deblevin@umich.edu). Data set is available through a data use agreement with University of Alabama at Birmingham (e-mail: regardsadmin@uab.edu).The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study is a prospective cohort study of 30,239 non-Hispanic black and white individuals examining regional and racial influences on stroke mortality.[18] Details are described elsewhere.[18]

Participants or their proxies were followed every 6 months by telephone with retrieval of medical records for reported hospitalizations. For this study, we followed participants through September 30, 2015. We required participants to have the first measurement of cognition by study design. We excluded participants with baseline cognitive impairment, defined as a Six-item Screener (SIS) score <5.[19] We also excluded participants who self-reported a baseline history of stroke or with an incident stroke before the first measurement of each cognitive outcome. The institutional review boards of all participating institutions approved the study and all participants provided written informed consent.

Cognitive Function Assessments

Trained REGARDS interviewers administered cognitive function tests longitudinally by telephone including: 1) the SIS (primary outcome; scores range 0–6) assessed global cognition annually beginning in 2003; and 2) a battery of 3 cognitive tests (secondary outcomes) measured biennially starting in 2006 that included the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Word List Learning (WLL; new learning; scores range, 0–30), Word List Delayed Recall (WLD; verbal memory; scores range 0–10), and Animal Fluency Test (AFT); executive function; scores range >0).[20, 21] These tests can be measured reliably and precisely over the telephone,[22–24] are used in Vascular Cognitive Impairment Harmonization Standards,[25] and have been validated in Blacks and Whites.[19, 26]

Measurement of Blood Pressure

At baseline, following a 5-minute rest, BP was measured twice in the left arm with a standard aneroid sphygmomanometer and the participant seated in a chair with 30 seconds between measurements.[27] REGARDS uses the average of the two BP measurements. We centered BP at 120/80 mmHg because this was close to the mean BP for the study cohort and is considered normal BP.[28] We excluded 1 participant with an extreme value of BP (diastolic BP ≤20; BP was 122/20) because this value is likely to be a result of incorrect measurement.

Statistical Analysis

Each outcome measure was treated as a continuous variable and analyzed separately. Linear mixed-effects models measured changes in cognitive function over time by BP and included random effects for intercept and slopes as well as the covariates in Table 1. Time was expressed as the years from the date of the first measurement of each cognitive outcome. We rescaled the outcomes by dividing the cognitive scores by the standard deviation (SD) of the distribution of the baseline cognitive measurement of each test to facilitate interpretation. For each outcome, all available cognitive observations were used in the analysis except observations after the time of first expert-adjudicated incident stroke during follow-up because we have previously shown that incident stroke alters the intercept and trajectory of cognition.[29] To examine assumptions of linear mixed effects models, e.g. linearity of the studied relationships and normality of residual errors we inspected residual plots. There was no evidence of non-linear effects of SBP or DBP on cognitive slopes.

To test the effect of baseline BP on the slopes of cognitive trajectories (first hypothesis), Model A included SBP*follow up time and DBP*follow up time interaction terms as well as SBP, DBP, follow up time, and covariates (Table 1 and online-only Data Supplement). We examined whether age[17] and hypertension treatment status[30] modified the effect of BP level on the slopes of cognitive trajectories (e.g., by investigating age*SBP*follow up time and age*DBP*follow up time interaction terms). To test whether race and sex modified the effect of BP level on the slopes of cognitive trajectories (second hypothesis), Model B added race*BP*follow up time and sex*BP*follow up time interaction terms to Model A. We stratified the data by age at baseline (45–64 versus ≥65 years) and fitted Model B for the primary outcome, Six-Item Screener. The parameter estimates from the age-stratified analyses were similar to the parameter estimates from the analysis of all ages (data not shown) so we present the results from the total sample.

We also performed analyses replacing SBP and DBP with mean arterial pressure (MAP) [((DBP x 2) + SBP)/3] and pulse pressure (PP) [SBP – DBP]. We calculated participant-specific predicted values for each cognitive score over time for an exemplar subject, i.e., a 75 year-old residing in the Stroke Belt with typical values of all covariates Slopes of cognitive decline were estimated for 20-mmHg differences in SBP and 10-mmHg differences in DBP.[31] We also estimated the difference in predicted cognitive scores for different BPs (SBP: 160 mmHg vs 120 mmHg; DBP 60 mmHg vs 80 mmHg) at different intervals (study time 0 vs year 8, the median follow-up time) for the exemplar subject.

Statistical significance for all analyses was set as $P<0.05$ (two-sided). We performed all analyses using STATA version 14.2 (Stata Corporation, College Station, TX).

RESULTS

The study sample included 22,164 participants. Median follow-up was 8.1 years (interquartile range, 5.0–10.1 years). Follow-up time was 7.4 years in the 13,670 white participants and 6.8 years in the 8,494 black participants (absolute difference, 0.63 years [95% CI, 0.54 years to 0.72 years]; P<0.001). Follow-up time was 7.2 years in the 12,436

female participants and 7.1 years in the 9,728 male participants (absolute difference, 0.05 years [95% CI, −0.04 years to 0.13 years]; P=0.3).

Figure I in the online-only Data Supplement presents derivation of cohort. Table I in the online-only Data Supplement presents baseline characteristics of study participants. Mean age was 64.2 (SD, 9.2) years, mean SBP was 127 (SD, 16) mmHg, and mean DBP was 76 (SD, 10) mmHg. Of the 22,164 participants, 849 had incident stroke (727 ischemic, 78 hemorrhagic, and 44 of undeterminable type) during follow-up. The frequency of incident stroke did not differ by race (521 strokes [3.8%] in whites and 328 [3.9%] strokes in blacks [absolute difference, 0.05%;95% CI, −0.4% to 0.5%; P = 0.85]) but was greater in men compared with women (428 [4.4%] strokes in men and 421 [3.4%] strokes in women [absolute difference, 1.0%; 95% CI, 0.5% to 1.5%; P<0.001]).

Participants had a median of 7 SIS tests (IQR, 4–10 tests) and a median of two 3-test batteries (IQR, 2–4 tests). Because the secondary outcome measures were introduced during follow-up and performed less frequently, the WLL analysis included 12,178 participants, the WLD analysis included 11,984 participants, and the AFT analysis included 12,902 participants.

Change in Global Cognition associated with BP, Race, and Sex

Age significantly modified the effect of SBP, DBP, and PP levels, but not MAP, on the slope of global cognition trajectories (P<0.001 for age*SBP*follow up time interaction, P<0.001 for age*DBP*follow up time interaction, P<0.001 for age*PP*follow up time interaction, and P=0.26 for age*MAP*follow up time interaction)(Model A for SBP/DBP and PP/MAP, Table 1). With increasing age, higher SBP, lower DBP, and higher PP were each associated with faster declines in global cognition. The effect of SBP and DBP on the slope of global cognition trajectories was not significantly different by hypertension treatment status (P=0.53 for hypertension treatment*SBP*follow up time interaction and P=0.26 for hypertension treatment*DBP*follow up time interaction).

In models replacing SBP and DBP with PP and MAP, PP (*P*<0.001), but not MAP (*P*=0.23), was significantly associated with changes in global cognition (Model A for PP and MAP, Table 1). Independent of MAP, higher PP was associated with significantly faster declines in global cognition controlling for age.

Blacks had significantly faster declines in global cognition associated with SBP compared to Whites (P=0.02 for race*SBP*follow up time interaction); but, race did not modify the effect of DBP on the slope of global cognition (P=0.79 for race*DBP*follow up time interaction) (Model B for SBP and DBP, Table 1). Black race also modified the effect of MAP on the slope of global cognition (P=0.04 for race*MAP*follow up time interaction) but not the effect of PP (P=0.22 for RACE*PP*follow up time interaction) (Model B for PP and MAP, Table 1). Blacks, compared to Whites, had significantly faster declines in global cognition associated with higher MAP. The effect of BP on the slope of global cognition trajectories was not significantly different by sex (P=0.23 for sex*SBP* follow up time interaction, P=0.57 for sex*DBP* follow up time interaction, P=0.31 for sex*PP* follow up

time interaction and P=0.86 for sex*MAP*follow up time interaction) (Model B for SBP/DBP and PP/MAP, Table 1).

We illustrate results of Models B using slope estimates of global cognition changes by age, race, sex, and the 4 BP measures (SBP, DBP, PP, and MAP) and by calculating participant-specific predicted values of cognition (Table 2). Black women age 75 with common values of all covariates, compared with white women, had faster declines in global cognition associated with higher SBPs by 0.012 SD points-per-year-per 20 mmHg-increase (95% CI, 0.002 to 0.022; p=0.02). Declines in global cognition associated with lower DBPs were similar in black women (decrease in slope: 0.015 SD points-per-year-per-10 mmHg-decrease [95% CI, 0.005 to 0.024; *P*=0.002]) and white women (decrease in slope: 0.016 SD points-per-year-per-10 mmHg-decrease [95% CI, 0.008 to 0.024; *P*<0.001]) (Table 2). Figure 1 shows slopes of global cognition by SBP, race, and sex (DBP fixed at 80 mmHg). Figure 2 shows slopes of global cognition by DBP, race, and sex (SBP fixed at 120 mmHg). At age 75, the difference in global cognition at year 8 was significantly greater than that at year 0 for baseline SBP 160 vs. 120 mmHg (difference of difference for white women: −0.12 points [95% CI, −0.05 to −0.19]; P<0.001) and non-significantly greater for baseline DBP 60 vs. 80 mmHg (difference of difference: −0.05 points [95% CI, −0.11 to 0.01]; P=0.08).

Changes in New Learning, Verbal Memory, and Executive Function associated with BP, Race, and Sex

Higher SBP, lower DBP, and higher PP were significantly associated with faster declines in new learning, verbal memory, and executive function in partially adjusted models that did not include the effect of age on cognitive slopes (age*follow up time interaction) (Tables II and III in online-only Data Supplement). However, the effects of SBP, DBP, and PP on the slopes of these cognitive functions did not remain significant after further adjustment for the age-by-time interaction effect except men, compared to women, had faster declines in new learning associated with SBP (P=0.04)(Tables IV and V in online-only Data Supplement).

Sensitivity Analyses

Results were similar in analyses imputing missing values of baseline covariates, adjusting for death, adding history of myocardial infarction and GFR to models, and in analyses limited to participants with ≥2 follow-up cognitive measures (Tables VI and IX in online-only Data Supplement).

DISCUSSION

In this national cohort of black and white Americans 45 years or older, faster declines in global cognition were associated with higher SBP, lower DBP, and higher PP in older adults. Faster declines in global cognition were associated with higher SBP and lower DBP as well as higher PP but not MAP. Blacks, compared to whites, had faster declines in global cognition associated with SBP and MAP. Men, compared to women, had faster declines in new learning associated with SBP. BP was not associated with slopes of verbal memory and executive function, after controlling for the effect of age on cognitive trajectories.

Our data suggest that BP-related cognitive declines are greater in Blacks compared with Whites and in men compared with women. Our results are consistent with a recent study[14] of older adults showing that Blacks, compared with Whites, have faster cognitive declines associated with high BP. Some studies have suggested that the effect of high BP on CID risk is greater in Whites compared with Blacks[15] and in women compared with men[16, 32, 33]. Our results may differ because we used different cognitive measures, we studied older adults, and we controlled for the age-dependent effect of BP on cognition[17]. The results of the analysis of secondary outcomes may differ from those of the SIS because the former have fewer observations, longer measurement intervals, and reduced statistical power.

The declines in global cognition associated with high SBP and low DBP in older adults are likely clinically meaningful. Declines of ≥0.5 standard deviations (SD) from baseline have been defined as clinically meaningful decline[34] and are correlated with clinically meaningful decline in adults with normal cognition and dementia.[35, 36] A 0.5-SD decrease from the baseline score is approximately 0.2 points for the SIS. The 95% confidence intervals for the 8-year differences in global cognition for baseline SBP of 160 compared with that of 120 mmHg for exemplar individuals aged 75 or older include declines of this magnitude or approach them for white women (95% CI, 0.05 to 0.19). Declines in global cognition significantly increase the risk of death, dementia, and functional decline.[19, 37–39]

High or low BP may cause cognitive decline through several mechanisms. Hypertension may cause ongoing inflammation, oxidative stress, and cerebrovascular injury.[40] Although we excluded cognitive measures occurring after the time of clinically apparent stroke, hypertension may cause subclinical vascular brain injury and damage to white matter integrity that contribute to subsequent cognitive decline.[41, 42] Hypertension may also induce or exacerbate neurodegenerative disease.[43, 44] Low BP may cause cognitive decline due to cerebral hypoperfusion. Blacks and men may be more likely to have detrimental brain effects from high BP because of early age of onset of high BP and worse BP control over the life course leading to greater arterial stiffness and more severe atherosclerosis[10–13]. Our data suggest a scientific need to determine how the timing, duration, and intensity of BP lowering interventions over the life course as well as race and sex influence the risk of cognitive decline.

Our study has several strengths. We had longitudinal cognitive assessments in a cohort of sufficient size to estimate BP-related changes in cognitive decline and to examine potential effect modification by race, sex, age, and hypertension treatment. REGARDS systematically measured cognitive domains commonly affected by vascular factors like hypertension: global cognition, learning, memory, and executive function.[25] We had repeated measures over time up to 14 years of follow-up.

Our study has limitations. Results are generalizable only to community-dwelling adults not requiring a proxy respondent. Although excluded participants had higher prevalence of dementia risk factors than included participants, these differences would reduce the ability to detect the cognitive effects of BP. BP was measured only at baseline. Although selective attrition may lead to underestimation of cognitive decline because participants with worse cognition at baseline or during follow-up die, drop out, or require a proxy, analyses that

accounted for loss to follow-up or death did not change our results, consistent with prior research.[45] Fewer cognitive observations potentially limited statistical power to detect associations between BP and the secondary outcomes. The slight increases in global cognition, new learning, and verbal memory over time may be due to selective attrition of cognitively impaired participants and practice effects associated with repeated testing.[46, 47] We did not have data on functional impairments, brain imaging, daily medication use or incident dementia.

Our study has clinical and policy implications. Preliminary results of the SPRINT MIND trial suggest that aggressive lowering of SBP reduces CID risk in older adults at high cardiovascular risk.[6] Our results extend this work by suggesting that treatment of high SBP will reduce CID risk in a broader population of older adults, particularly Blacks and men. Our results also suggest that avoidance of low DBP is important to prevent cognitive decline in older adults. This is clinically important because SBP tends to increase and DBP tends to decrease as adults age. Blacks are more likely to have worse BP control than Whites. Our results suggest that eliminating the Black-White disparity in BP control has the potential to reduce racial disparities in CID risk. Our data also show that failure to account for the effect of age on cognitive slopes can overestimate the effect of BP on cognitive slopes and even cause a spurious association between BP and cognitive decline. Moreover, our results suggest that PP rather than MAP is a potential target for preventing CID.

PERSPECTIVES

Faster declines in global cognition over 8 years were associated with higher SBP, lower DBP, and higher PP in older adults. SBP-related cognitive declines were greater in Blacks and men. Our results suggest that blood pressure may contribute to Black-White disparities in CID risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Novelty and Significance:

What Is New?

- It is unclear whether hypertension contributes to racial/ethnic and sex differences in dementia risk.
- We assessed the association between blood pressure (BP) levels and cognitive trajectories over 8 years and tested whether race and sex modified the associations, in a large, nationally representative cohort of middle-aged and older black and white adults.
- Our results suggest that lowering systolic BP in older adults, particularly Blacks and men, will reduce dementia risk. This is critical because Blacks have double the risk of dementia as Whites.

What Is Relevant?

- Hypertension is a modifiable risk factor associated with late-life dementia.

Summary: Higher systolic BP, lower diastolic BP, and higher pulse pressure were associated with faster declines in global cognition over 8 years in older adults. Systolic BP-related cognitive declines were greater in Blacks and men.

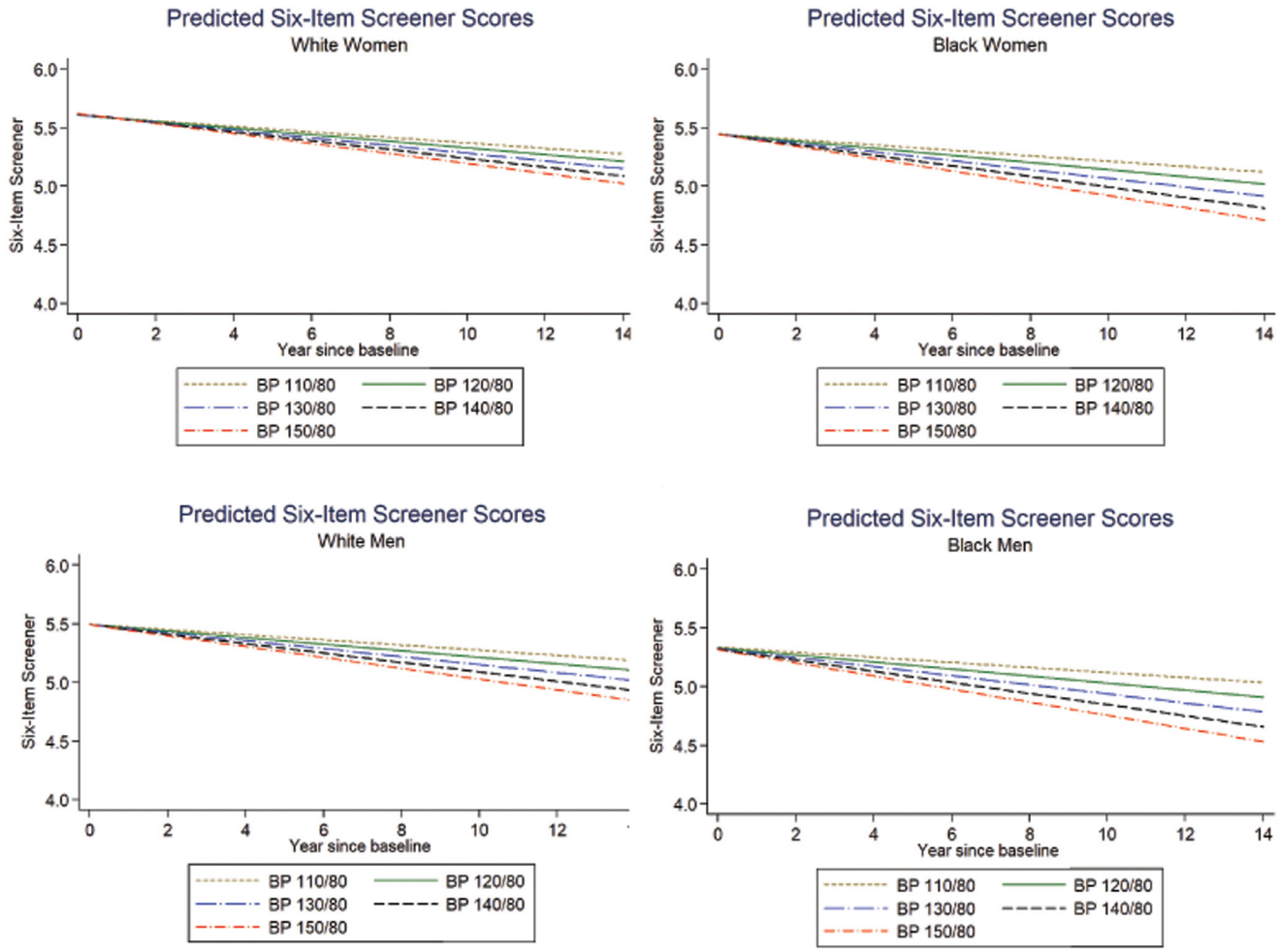

Figure 1: Conditional Predicted Values of Global Cognition over Time by Baseline Systolic Blood Pressure, Race, and Sex: REGARDS Study, 2003–2013

Participant-specific predicted values of global cognition were calculated for 75 year-old adults with the common values of all covariates at baseline (college education, stroke belt residence, income $20,000-$34,999, never smoker, no alcohol use, no diabetes, no hypertension treatment, waist circumference 95 cm, overweight BMI, 4-item CES-D score of 0.9 points, and fair health status) and Model B. Global cognition was measured by Six-Item Screener. Six-Item Screener scores range 0 to 6 with higher scores indicating better performance. Diastolic blood pressure (BP) is fixed at 80 mmHg. The brown line indicates the slopes for participants with systolic BP of 110 mmHg. The green line indicates the slopes for participants with systolic BP of 120 mmHg. The blue line indicates the slopes for participants with systolic BP of 130 mmHg. The black line indicates the slopes for participants with systolic BP of 140 mmHg. The red line indicates the slopes for participants with systolic BP of 150 mmHg.

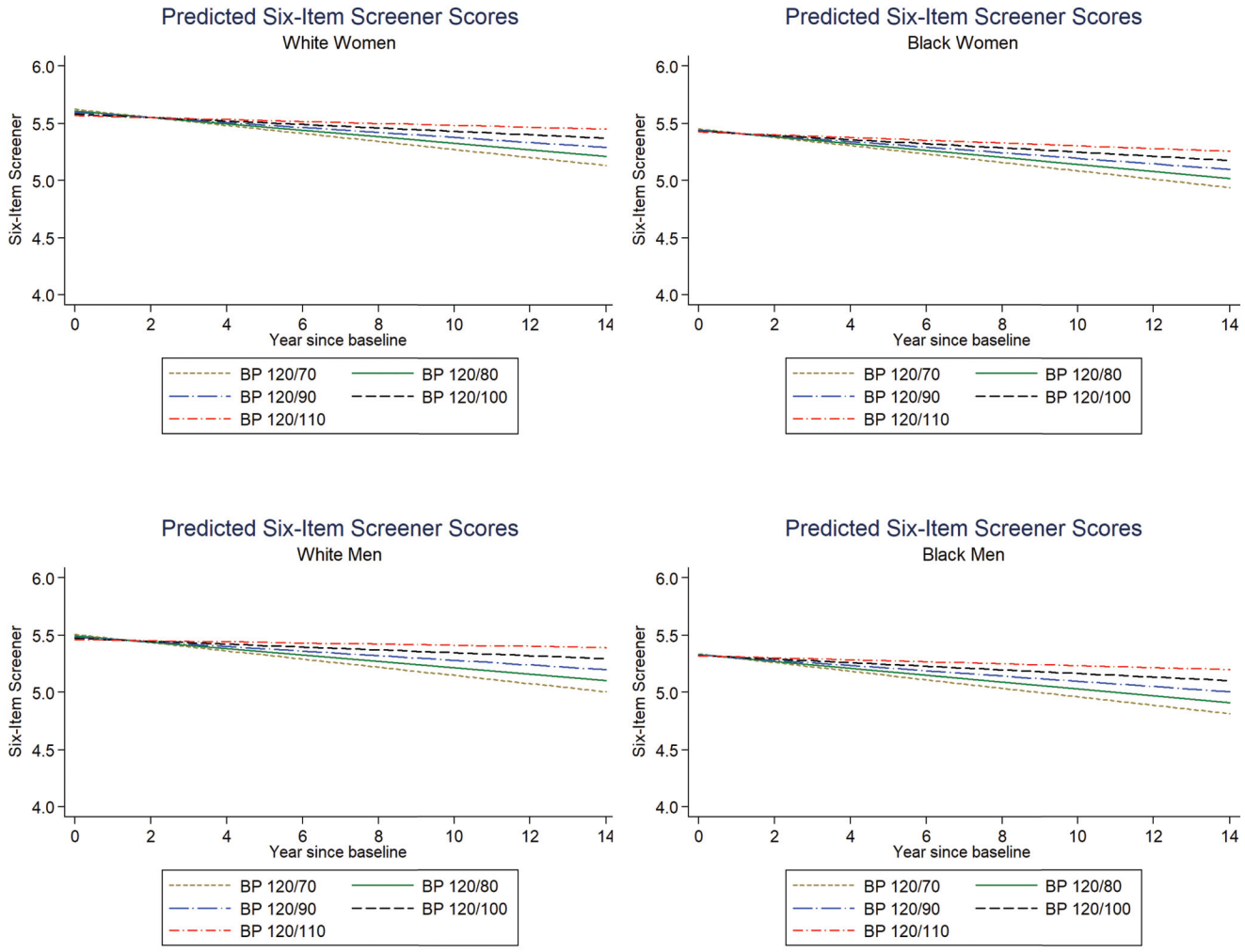

Figure 2: Conditional Predicted Values of Global Cognition over Time by Baseline Diastolic Blood Pressure, Race, and Sex: REGARDS Study, 2003–2013

Participant-specific predicted values of global cognition were calculated for 75 year-old adults with the common values of all covariates at baseline (college education, stroke belt residence, income $20,000-$34,999, never smoker, no alcohol use, no diabetes, no hypertension treatment, waist circumference 95 cm, overweight BMI, 4-item CES-D score of 0.9 points, and fair health status) and Model B. Global cognition was measured by Six-Item Screener. Six-Item Screener scores range 0 to 6 with higher scores indicating better performance. Systolic blood pressure (BP) is fixed at 120 mmHg. The brown line indicates the slopes for participants with diastolic BP of 70 mmHg. The green line indicates the slopes for participants with diastolic BP of 80 mmHg. The blue line indicated the slopes for participants with diastolic BP of 90 mmHg. The black line indicates the slopes for participants with diastolic BP of 100 mmHg. The red line indicates the slopes for participants with diastolic BP of 110 mmHg.

Table 1:

Adjusted Changes of Global Cognitive Function associated with BP Levels and Age over Time: REGARDS Study, 2003 to 2015

Six-Item Screener Score (n=22,164)									
SBP and DBP					MAP and PP				
	Model A		Model B			Model A		Model B	
Coefficient	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*	Coefficient	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*
Slope per year of follow-up	0.26 (0.23 to 0.29)	<.001	0.26 (0.23 to 0.29)	<.001	Slope per year	0.32 (0.30 to 0.35)	<.001	0.32 (0.30 to 0.35)	<.001
Effect of age at baseline on slope per 10 year increase	−0.04 (−0.05 to −0.04)	<.001	−0.04 (−0.05 to −0.04)	<.01	Effect of age on slope per 10 year increase	−0.05 (−0.06 to −0.05)	<.001	−0.05 (−0.06 to −0.05)	<.001
Change in slope associated with 20 mm Hg increase in SBP, per year	0.12 (0.08 to 0.16)	<.001	0.12 (0.09 to 0.16)	<.001	Change in slope associated with 10 mm Hg increase in MAP, per year	−0.01 (−0.04 to 0.01)	.23	−0.01 (−0.04 to 0.01)	.36
Change in slope associated with 10 mm Hg increase in DBP, per year	−0.08 (−0.11 to −0.04)	<.001	−0.07 (−0.11 to −0.04)	<.001	Change in slope associated with 10 mm Hg in PP, per year	0.07 (0.05 to 0.09)	<.001	0.07 (0.05 to 0.09)	<.001
Effect of age on slope associated with SBP (age per 10 year increase; SBP per 20 mm Hg increase)	−0.02 (−0.03 to −0.01)	<.001	−0.02 (−0.03 to −0.01)	<.001	Effect of age on slope associated with MAP (age per 10 year increase; MAP per 10 mm Hg increase)	0.002 (−0.002 to 0.01)	.26	0.002 (−0.002 to 0.01)	.29
Effect of age on slope associated with DBP (age per 10 year increase; DBP per 10 mm Hg increase)	0.012 (0.01 to 0.02)	<.001	0.012 (0.01 to 0.02)	<.001	Effect of age on slope associated with PP (age per 10 year increase; PP per 10 mm Hg increase)	−0.011 (−0.014 to −0.008)	<.001	−0.011 (−0.014 to −0.008)	<.001
Effect of Black race on slope	NA	NA	−0.005 (−0.01 to 0.004)	.26		NA	NA	−0.008 (−0.02 to −0.002)	.01
Effect of Black race on slope associated with SBP (SBP per 20 mm Hg increase)	NA	NA	−0.01 (−0.02 to −0.002)	.02	Effect of Black race on slope associated with MAP (MAP per 10 mm Hg increase)	NA	NA	−0.007 (−0.01 to 0.00)	.04

Six-Item Screener Score (n=22,164)									
SBP and DBP					MAP and PP				
	Model A		Model B			Model A		Model B	
Coefficient	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*	Coefficient	Estimate (95% CI)	*P*	Estimate (95% CI)	*P*
Effect of Black race on slope associated with DBP (DBP per 10 mm Hg increase)	NA	NA	−0.001 (−0.01 to 0.01)	.79	Effect of Black race on slope associated with PP (PP per 10 mm Hg increase)	NA	NA	−0.004 (−0.01 to 0.002)	.22
Effect of female sex on Slope	NA	NA	−0.001 (−0.009 to 0.008)	.89				0.002 (−0.004 to 0.009)	.49
Effect of female sex on slope associated with SBP (SBP per 20 mm Hg increase)	NA	NA	0.006 (−0.004 to 0.02)	.23	Effect of female sex on slope associated with MAP (MAP per 10 mm Hg increase)	NA	NA	0.001 (−0.01 to 0.01)	.86
Effect of female sex on slope associated with DBP (DBP per 10 mm Hg increase)	NA	NA	−0.002 (−0.01 to 0.01)	.57	Effect of female sex on slope associated with PP (PP per 10 mm Hg increase)	NA	NA	0.003 (−0.003 to 0.01)	.31
Interpretative Key: The Six-Item Screener (SIS) measures global cognition (scores range 0–6). Higher scores indicate better performance. SBP=systolic blood pressure. DBP=diastolic blood pressure. PP=pulse pressure. MAP=mean arterial pressure. The SIS was rescaled by dividing the SIS scores by the standard deviation of the distribution of the baseline SIS measurement. Consequently estimates of the effects (i.e., coefficients from our models) are expressed relative to the standard deviation of the outcome at baseline.									
Linear mixed-effects models for a continuous included time since baseline, and baseline values of SBP, DBP, SBP*time, DBP*time, age, race, sex, age*SBP, age*DBP, race*SBP, race*DBP, current hypertension treatment, education, region, income, cigarette smoking, waist circumference, diabetes, alcohol use, depressive symptoms, self-reported health status, body mass index, age*time, race*time, age*SBP*time, age*DBP*time, and a subject-specific random intercept and slope. SBP and DBP were centered at 120 and 80 mm Hg, respectively. MAP and PP were centered at 93 and 50 mm Hg, respectively. Model A tested the hypothesis that higher SBP and lower DBP at baseline are associated with faster cognitive decline in older adults by including age*SBP and age*DBP interaction effects on the slope of global cognition. Model B tested the hypothesis that the effects of SBP and DBP on cognitive decline are greater in Blacks compared with Whites and in women compared with men by including race*SBP, race*DBP, sex*SBP, and sex*DBP interaction effects on the slope of global cognition. Model A for SBP and DBP is equivalent to Model A for PP and MAP. Model B for SBP and DBP is equivalent to Model B for PP and MAP.									

Table 2:

Estimated Changes in Slopes of Global Cognition associated with Baseline Blood Pressure, Age, and Race-Sex: REGARDS Study, 2003 to 2015

Age at baseline, years	Change in slope for each 20 mm Hg increase in SBP per year (DBP fixed at 80 mmHg), points per year (95% CI)	*P*	Change in slope for each 10 mmHg decrease in DBP per year (SBP fixed at 120 mmHg), points per year (95% CI)	*P*	Change in slope for each 10 mm Hg increase in MAP per year (pulse pressure fixed at 40 mmHg), points per year (95% CI)	*P*	Change in slope for each 15 mm Hg increase in pulse pressure per year (MAP fixed at 93.3 mmHg), points per year (95% CI)	*P*
White Women								
55	0.019 (0.008 to 0.028)	<.001	0.009 (0.0002 to 0.017)	.04	0.0003 (−0.007 to 0.008)	.93	0.013 (0.005 to 0.022)	.003
65	−0.002 (−0.01 to 0.006)	.57	−0.004 (−0.01 to 0.003)	.31	0.002 (−0.005 to 0.01)	.51	−0.003 (−0.01 to 0.004)	.43
75	−0.023 (−0.032 to −0.013)	<.001	−0.016 (−0.024 to −0.008)	<.001	0.004 (−0.004 to 0.013)	.30	−0.019 (−0.028 to −0.011)	<.001
White Men								
55	0.012 (0.001 to 0.023)	.03	0.006 (−0.002 to 0.015)	.16	−0.0003 (−0.009 to 0.008)	.94	0.009 (0 to 0.02)	.05
65	−0.009 (−0.017 to 0)	.05	−0.006 (−0.013 to 0.001)	.09	0.002 (−0.005 to 0.009)	.63	−0.007 (−0.015 to 0.0002)	.05
75	−0.029 (−0.038 to −0.019)	<.001	−0.018 (−0.026 to −0.01)	<.001	0.004 (−0.005 to 0.012)	.37	−0.024 (−0.032 to −0.015)	<.001
Black Women								
55	0.006 (−0.004 to 0.016)	.26	0.01 (0.001 to 0.019)	.03	−0.007 (−0.015 to 0.001)	.08	−0.008 (−0.001 to 0.017)	.08
65	−0.014 (−0.023 to −0.005)	.002	−0.002 (−0.01 to 0.005)	.55	−0.005 (−0.013 to 0.003)	.22	−0.008 (−0.016 to −0.0004)	.04
75	−0.035 (−0.045 to −0.024)	<.001	−0.015 (−0.024 to −0.005)	.002	−0.003 (−0.012 to 0.006)	.56	−0.025 (−0.034 to −0.015)	<.001
Black Men								
55	−0.002 (−0.012 to 0.012)	.98	0.007 (−0.002 to 0.017)	.14	−0.008 (−0.016 to 0.001)	.09	0.004 (−0.007 to 0.014)	.49
65	−0.021 (−0.031 to −0.01)	<.001	−0.005 (−0.014 to 0.004)	.29	−0.005 (−0.014 to 0.003)	.20	−0.013 (−0.022 to −0.004)	.007
75	−0.041 (−0.053 to −0.029)	<.001	−0.017 (−0.027 to −0.007)	.001	−0.003 (−0.013 to 0.006)	.50	−0.029 (−0.039 to −0.019)	<.001

These results are from Model B shown in Table 2. Participant-specific estimated changes in slopes for participants with the common values of all covariates at baseline (some college education, stroke belt residence, income $20,000-$34,999, never smoker, no alcohol use, no diabetes, no hypertension treatment, waist circumference 95 cm, overweight BMI, 4-item CES-D score of 0.9 points, and fair health status). Global cognition was measured by Six-Item Screener. Six-Item Screener scores range 0 to 6. Systolic blood pressure and diastolic blood pressure were centered at 120 and 80 mm Hg, respectively.

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Similarly, pulse pressure and mean arterial pressure were centered at 40 and 93.33 mm Hg. The SIS was rescaled by dividing the SIS scores by the standard deviation of the distribution of the initial SIS measurement. The changes in slopes (i.e., coefficients from our models) are expressed relative to the standard deviation of the outcome at baseline.