

## Associations Between Blood Pressure and Outcomes Among Blacks in the Jackson Heart Study

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**Background**—In 2014, new hypertension guidelines liberalized blood pressure goals for persons 60 years and older. Little is known about the implications for blacks.

**Methods and Results**—Using data from 2000 through 2011 for 5280 participants in the Jackson Heart Study, a community-based black cohort in Jackson, Mississippi, we examined whether higher blood pressure was associated with greater risk of mortality and heart failure hospitalization, and whether the risk was the same across age groups. We investigated associations between baseline blood pressure and both mortality and heart failure hospitalization. We also tested for interactions between age and blood pressure in the mortality model. Median systolic and diastolic blood pressures at baseline were 125 mm Hg (25th–75th percentile, 114–137 mm Hg) and 79 mm Hg (72–86 mm Hg), respectively. Median follow-up was 9 years for mortality and 7 years for heart failure hospitalization. After multivariable adjustment, every 10 mm Hg increase in systolic blood pressure was associated with greater risks of mortality (hazard ratio, 1.12; 95% CI, 1.06–1.17) and heart failure hospitalization (1.07; 95% CI, 1.00–1.14). The mortality risk per 10 mm Hg increase in systolic blood pressure was greater in participants younger than 60 years (1.26; 95% CI, 1.13–1.42) than among participants 60 years and older (1.09; 95% CI, 1.03–1.15).

**Conclusions**—Adults in all age groups were at greater risk of mortality as systolic blood pressure increased. In the context of the 2014 hypertension guidelines, these findings should be considered when determining treatment goals in black patients. (*J Am Heart Assoc.* 2016;5:e003928 doi: 10.1161/JAHA.116.003928)

**Key Words:** Blacks • heart failure • hospitalization • hypertension • mortality

Hypertension is an important modifiable risk factor for adverse clinical outcomes including heart failure (HF), stroke, chronic kidney disease (CKD), and death.<sup>1–4</sup> For the past 25 years, 140/90 mm Hg has been the blood pressure (BP) associated with diagnoses of hypertension, and goals for blood pressure control have focused on achieving blood pressure <140/90 mm Hg, except in patients with CKD or diabetes mellitus, for whom the target was <130/80 to 85 mm Hg.<sup>5–7</sup> In 2014, the panel members selected for the eighth Joint National

Committee published recommendations for the management of hypertension in adults.<sup>8</sup> These recommendations were published after the National Heart, Lung and Blood Institute elected to stop issuing clinical practice guidelines. The hypertension guidelines have been controversial,<sup>9–11</sup> because they liberalized BP goals for persons 60 years and older without CKD or diabetes to <150/90 mm Hg, citing the paucity of randomized evidence to support lower goals. The new recommendations also raised the goal BP for those with diabetes or CKD to <140/90 mm Hg, regardless of age.

Given that tighter BP control has been associated with lower mortality and lower likelihood of developing progressive disease,<sup>12,13</sup> many have questioned the potential health impact of liberalizing hypertension goals that previously were achieved in only 50% of patients in clinical practice.<sup>14</sup> The Association of Black Cardiologists and the Working Group on Women's Cardiovascular Health published a statement of concern regarding these new guidelines, citing the disproportionate burden of hypertension among black patients<sup>15</sup> and its role as a risk factor for mortality and incident cardiovascular disease with differential effects on black patients, such as stroke,<sup>16</sup> HF,<sup>17</sup> and CKD.<sup>18</sup> These groups also expressed concern that the liberalized guidelines will have a differential

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effect on women, as older women are also disproportionately affected by hypertension and its downstream sequelae.<sup>19</sup>

We used data from the Jackson Heart Study (JHS) to explore the potential impact of the 2014 guidelines for hypertension management on heart failure hospitalization (HFH) and mortality across a spectrum of systolic blood pressure (SBP) and diastolic blood pressure (DBP) values in an black cohort. We also examined interactions between age and BP on the risk of mortality.

## Methods

### Data Sources

The JHS is a prospective, community-based, observational study designed to investigate risk factors for cardiovascular disease in blacks.<sup>20,21</sup> Participants completed 3 study visits: examination 1 between 2000 and 2004, examination 2 between 2005 and 2008, and examination 3 between 2009 and 2013. The details of data collected and visit procedures have been described previously.<sup>22,23</sup> Information collected during in-person visits included medical history, BP, medications, laboratory values, anthropometrics, physical activity, dietary data, and social and environmental risk factors. The JHS surveillance system collected follow-up data on all participants, including deaths from 2000 through 2011 and HFH from 2005 through 2011.<sup>24</sup> All participants provided written informed consent, and study protocols were approved by local institutional review boards.

We linked data for Medicare-eligible participants to Medicare denominator, inpatient, outpatient, and carrier files directly using Social Security numbers, dates of birth, and sex.<sup>25</sup> The institutional review board of the Duke University Health System approved the study.

### Study Population

For all outcomes, we included participants who completed examination 1 with documentation of SBP and DBP. For the analysis of HFH using JHS surveillance data, we limited the cohort to participants who survived to January 1, 2005, when HFH surveillance began. For the sensitivity analysis of HF incidence using Medicare data, we included participants who were linked to Medicare claims, were 65 years or older, had fee-for-service Medicare for at least 12 months before examination 1, and had no diagnosis of HF before the examination 1 visit date.

### Blood Pressure

The main exposures of interest were baseline visit SBP and DBP. Blood pressure was measured by arm cuff and

calculated as the average of 2 readings. We assessed SBP and DBP on a continuous scale per 10 mm Hg and according to the following clinically relevant categories on the basis of the 2003 and 2014 hypertension management guidelines from the seventh and eighth Joint National Committee panels<sup>6,19</sup>: for SBP, <130, 130 to 139, 140 to 149, and  $\geq$ 150 mm Hg; for DBP: <80, 80 to 89, and  $\geq$ 90 mm Hg.

### Outcomes

The primary outcomes were all-cause mortality and hospital admission for HF. As previously described,<sup>24</sup> the JHS surveillance system identifies all cohort illnesses and deaths via annual follow-up and medical record abstraction. We assessed all-cause mortality within 9 years after the examination 1 visit date based on a median follow-up time of 9 years and 75th percentile of 10 years. We also assessed the cumulative incidence of HFH between 2005 and 2011 (median and 75th percentile follow-up was 7 years).

As a sensitivity analysis, we assessed HF incidence among Medicare enrollees on the basis of a diagnosis of HF (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* 428.x, 402.x1, 404.x1, 404.x3) on either a single inpatient claim or at least 3 carrier or outpatient claims provided on different days within 20 consecutive months.<sup>26</sup> To specify disease onset, we used the earlier of the date of the earliest inpatient HF diagnosis or the date of the third outpatient or carrier HF diagnosis. Due to a high rate of switching to Medicare managed care in this population (61%) during the study period (2000–2012), we assessed incident HF within 8 years after the examination 1 visit date.

### Covariates

Medical history was based on either direct clinical examination (for diabetes and atrial fibrillation) or self-reported disease history (for myocardial infarction, stroke, chronic lung disease, and smoking). Since HF history was not collected at clinical examinations, we derived prevalent HF at examination 1 using the modified Gothenburg criteria developed and validated in the Atherosclerosis Risk in Communities Study data set and as recently applied to the JHS cohort.<sup>27,28</sup> To ascertain left ventricular (LV) hypertrophy, we used quantitative LV mass measurement from 2-dimensional or M-mode echocardiography when available (missing for 5% of participants); otherwise, LV hypertrophy was based on a qualitative assessment of mild, moderate, or severe hypertrophy, as described previously.<sup>22</sup> We derived medication variables by searching for therapeutic classification codes that were recorded based on medications taken within 2 weeks of examination 1. We defined a variable for CKD based on baseline estimated glomerular filtration rate

less than 60 mL/min per 1.73 m<sup>2</sup>.<sup>29</sup> Most variables had very low rates of missingness (ie, less than 5%). For variables with less than 5% missingness, we imputed continuous variables to the overall median value, dichotomous variables to “no,” and multichotomous variables to the most frequent categorical value.

## Statistical Analysis

We describe examination 1 baseline characteristics of the study population by SBP and DBP categories using frequencies with percentages for categorical variables and medians with 25th to 75th percentiles for continuous variables. We tested for differences between groups using  $\chi^2$  tests for categorical variables and Kruskal–Wallis tests for continuous variables.

We calculated the cumulative incidence of all-cause mortality and HFH by BP categories using Kaplan–Meier estimates and tested for differences between the groups using log-rank tests. For all survival analyses, we censored data at the time of participant loss to follow-up, or the end of study event surveillance follow-up (December 31, 2011). For HF hospitalization, we also censored data for participants at the time of death.

We estimated associations between BP and mortality and between BP and HFH in 4 separate Cox proportional hazards models: (1) unadjusted SBP, (2) unadjusted DBP, (3) SBP and DBP, and (4) SBP and DBP adjusted for other covariates. We chose the adjustment list on the basis of previous research<sup>28,30</sup> and clinical judgment. Covariates were prespecified by the minimum events per variable method and included the following: age, sex, medical history (ie, prior myocardial infarction, HF, prior stroke, hyperlipidemia, diabetes, lung disease, current smoking, prior smoking, alcoholic drinks per week), clinical features (ie, body mass index, heart rate, sodium, estimated glomerular filtration rate, hemoglobin, ejection fraction, QRS duration, LV hypertrophy, LV dimension), socioeconomic characteristics (ie, high school education or greater, annual family income less than \$50 000, and a variable for missing income data), and medications (any antihypertensive,  $\beta$ -blocker, calcium channel blocker, diuretic, statin, antiplatelet, and a variable for missing medication data). In addition, we tested for interactions between age and both SBP and DBP in the mortality model and performed subgroup analyses (<60 years versus  $\geq$ 60 years) for significant interactions. Given that the new hypertension guidelines recommended treatment goals of <140/90 mm Hg for individuals with CKD or diabetes, we performed subgroup analyses for significant interactions by presence of CKD or diabetes at baseline.

In a sensitivity analysis, we estimated unadjusted and adjusted associations between continuous BP per 10 mm Hg

and incident HF identified in Medicare claims using Cox proportional hazards models as described above. Due to an anticipated lower event count, we reduced the total number of model variables to 18 (ie, 2 BP variables plus 16 covariates) for this analysis. The covariates included age, sex, prior myocardial infarction, HF, prior stroke, diabetes, lung disease, current or prior smoking, body mass index, heart rate, sodium, estimated glomerular filtration rate, ejection fraction, LV hypertrophy, BP medication (antihypertensive,  $\beta$ -blocker, calcium channel blocker, or diuretic), and a variable for missing medication data. For all analyses, we used a 2-tailed  $\alpha=0.05$  to establish statistical significance and report 95% CIs.

## Results

Tables 1 and 2 show the baseline characteristics of the study population. Among the 5280 participants who met the study criteria, 36.5% were men and the median age was 56 years (25th–75th percentile, 46–65 years). Sixty percent had a diagnosis of hypertension at baseline and 50% of the overall population reported that they were prescribed at least 1 BP medication. Median SBP was 125 mm Hg (25th–75th percentile, 114–137 mm Hg), and DBP was 79 mm Hg (25th–75th percentile, 72–86 mm Hg). Most participants had SBP <130 mm Hg (61%) and DBP <80 mm Hg (53%). Participants with SBP of  $\geq$ 150 mm Hg were more likely to have prior myocardial infarction, stroke, or CKD.

There were 520 deaths within 9 years of the baseline examination. Unadjusted mortality increased linearly with SBP, with the highest mortality rates among participants with SBP  $\geq$ 150 mm Hg (22.9%), followed by 140 to 149 mm Hg (15.9%), 130 to 139 mm Hg (11.4%), and >130 mm Hg (7.0%) ( $P<0.001$ ; Figure 1). After adjustment for age, differences in the cumulative incidence of mortality across categories of SBP persisted ( $P<0.001$ ; Figure 2). The cumulative incidence of mortality was highest among patients with DBP <80 mm Hg (11.8%), compared with 80 to 89 mm Hg (8.6%) and  $\geq$ 90 mm Hg (9.9%) ( $P=0.004$ ). However, after adjustment for age, there was no difference in mortality by DBP category ( $P=0.33$ ) (Figures 1 and 2).

The HFH analysis included 5172 participants (98%) who survived until 2005. There were 340 HFHs recorded. Rates were highest among participants with SBP  $\geq$ 150 mm Hg (14.1%), followed by 140 to 149 mm Hg (10.3%), 130 to 139 mm Hg (8.3%), and <130 mm Hg (4.8%) ( $P<0.001$ ; Table 3). This relationship persisted after adjustment for age ( $P<0.001$ ). Prior to age adjustment, HFH was more common in participants with DBP <80 mm Hg than those with higher DBP ( $P=0.007$ ) (Figure 1). After age adjustment, there was no difference (Figure 2). Among the 928 (17.6%) participants who met the inclusion criteria for the

**Table 1.** Baseline Characteristics of the Study Population by SBP Category\*

Characteristic	SBP <130 mm Hg (n=3215)	SBP 130 to 139 mm Hg (n=941)	SBP 140 to 149 mm Hg (n=557)	SBP ≥150 mm Hg (n=567)	P Value
Age, median (25th–75th percentile)	51.4 (42.7–62.2)	59.6 (50.2–66.8)	61.0 (52.1–67.8)	64.0 (55.3–71.1)	<0.001
Men, N (%)	1169 (36.4)	328 (34.9)	207 (37.2)	225 (39.7)	0.30
Medical history, N (%)					
Chronic lung disease	223 (6.9)	63 (6.7)	48 (8.6)	43 (7.6)	0.48
Current smoker	400 (12.4)	107 (11.4)	87 (15.6)	92 (16.2)	0.009
Diabetes mellitus	583 (18.1)	247 (26.2)	154 (27.6)	164 (28.9)	<0.001
HF	220 (6.8)	75 (8.0)	51 (9.2)	50 (8.8)	0.12
Hyperlipidemia	837 (26.0)	279 (29.6)	162 (29.1)	175 (30.9)	0.02
Hypertension <sup>†</sup>	1401 (43.6)	652 (69.3)	557 (100.0)	567 (100.0)	<0.001
Myocardial infarction	146 (4.5)	49 (5.2)	44 (7.9)	50 (8.8)	<0.001
Stroke	108 (3.4)	47 (5.0)	36 (6.5)	43 (7.6)	<0.001
Physical examination, median (25th–75th percentile)					
BMI, kg/m <sup>2</sup>	30.3 (26.7–35.1)	31.2 (27.3–36.4)	30.6 (26.8–35.8)	30.5 (26.9–35.1)	<0.001
Systolic blood pressure, mm Hg	117.0 (109.0–123.0)	134.0 (132.0–136.0)	144.0 (142.0–147.0)	159.0 (153.0–169.0)	<0.001
Diastolic blood pressure, mm Hg	76.0 (70.0–82.0)	82.0 (74.0–88.0)	85.0 (77.0–91.0)	87.0 (79.0–97.0)	<0.001
Pulse, bpm	63.0 (57.0–71.0)	64.0 (57.0–71.0)	65.0 (58.0–72.0)	63.0 (57.0–72.0)	0.03
Laboratory test results, median (25th–75th percentile)					
LDL cholesterol, mg/dL	123.0 (100.0–145.0)	124.0 (103.0–150.0)	126.0 (104.0–152.0)	124.0 (105.0–152.0)	<0.001
eGFR, mL/min per 1.73 m <sup>2</sup>	87.5 (77.3–98.9)	85.7 (75.3–95.6)	83.6 (73.4–94.8)	80.8 (68.8–90.9)	<0.001
Glucose, mg/dL	90.0 (84.0–98.0)	93.0 (87.0–103.0)	95.0 (88.0–107.0)	95.0 (88.0–107.0)	<0.001
Echocardiography and electrocardiography					
LVEF, median (25th–75th percentile), %	65.0 (55.0–65.0)	65.0 (55.0–65.0)	65.0 (55.0–65.0)	65.0 (55.0–65.0)	0.002
Left ventricular hypertrophy, N (%)	158 (4.9)	89 (9.5)	68 (12.2)	105 (18.5)	<0.001
Medications, N (%)					
Any blood pressure medication <sup>‡</sup>	1362 (42.4)	565 (60.0)	350 (62.8)	372 (65.6)	<0.001
Antihypertensive agent	855 (26.6)	353 (37.5)	221 (39.7)	259 (45.7)	<0.001
ACE inhibitor or ARB	434 (13.5)	179 (19.0)	113 (20.3)	153 (27.0)	<0.001
Adrenolytic antihypertensive agent <sup>§</sup>	139 (4.3)	65 (6.9)	36 (6.5)	73 (12.9)	<0.001
Antihypertensive combination	346 (10.8)	137 (14.6)	88 (15.8)	72 (12.7)	<0.001
β-Blocker	260 (8.1)	111 (11.8)	65 (11.7)	96 (16.9)	<0.001
Calcium channel blocker	382 (11.9)	197 (20.9)	137 (24.6)	138 (24.3)	<0.001
Diuretic	656 (20.4)	242 (25.7)	151 (27.1)	170 (30.0)	<0.001
Thiazide	301 (9.4)	113 (12.0)	72 (12.9)	79 (13.9)	<0.001
Loop diuretic	136 (4.2)	65 (6.9)	41 (7.4)	66 (11.6)	<0.001
Antiplatelet agent	36 (1.1)	17 (1.8)	10 (1.8)	18 (3.2)	0.002
Nitrate	70 (2.2)	18 (1.9)	22 (3.9)	15 (2.6)	0.06
Statin	334 (10.4)	127 (13.5)	70 (12.6)	69 (12.2)	0.04

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BMI, body mass index; eGFR, estimated glomerular filtration rate; HF, heart failure; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure.

\*Cohort A has 5280 participants after 21 were excluded for missing blood pressure data. Cohort B has 5172 participants who survived to 2005.

<sup>†</sup>Based on the Jackson Heart Study coordinating center definition of hypertension (blood pressure ≥140/90 or taking blood pressure-lowering medication).

<sup>‡</sup>Any blood pressure medication includes antihypertensive agent (ie, ACE inhibitor, ARB, α-blocker, adrenolytic vasodilator, antihypertensive combination), β-blocker, calcium channel blocker, or diuretic (ie, thiazide diuretic, loop diuretic, potassium-sparing diuretic, or combination diuretic).

<sup>§</sup>Adrenolytic antihypertensive agent includes central or peripheral adrenolytic or reserpine.

**Table 2.** Baseline Characteristics of the Study Population by DBP Category (Cohort A: All Participants)\*

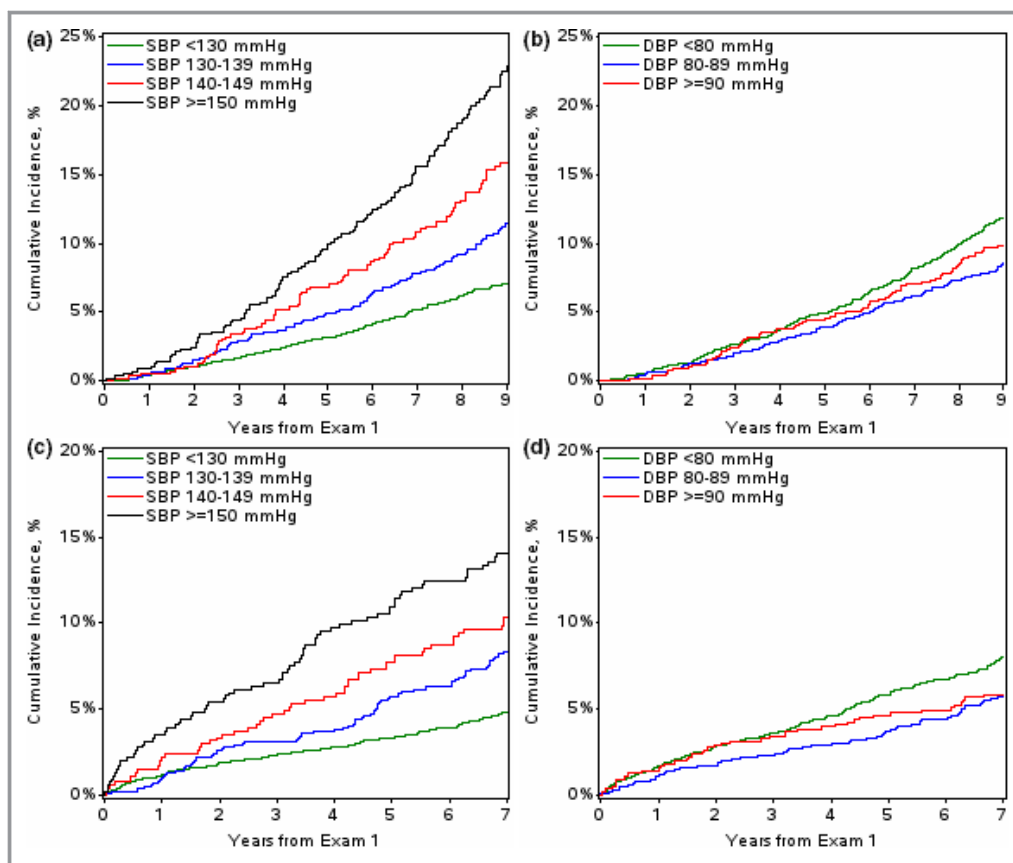
	DBP <80 mm Hg	DBP 80 to 89 mm Hg	DBP ≥90 mm Hg	P Value
<b>N</b>	2821	1669	790	
<b>Demographics</b>				
Age, median (25th–75th percentile)	58.6 (45.6–67.1)	54.1 (45.6–62.8)	52.8 (45.1–61.2)	<0.001
Male sex, N (%)	834 (29.6)	687 (41.2)	408 (51.6)	<0.001
<b>Medical history, N (%)</b>				
Myocardial infarction	176 (6.2)	66 (4.0)	47 (5.9)	0.004
Heart failure	246 (8.7)	100 (6.0)	50 (6.3)	0.001
Hypertension <sup>†</sup>	1433 (50.8)	954 (57.2)	790 (100.0)	<0.001
Stroke	135 (4.8)	70 (4.2)	29 (3.7)	0.34
Diabetes	700 (24.8)	317 (19.0)	131 (16.6)	<0.001
Chronic lung disease	210 (7.4)	106 (6.4)	61 (7.7)	0.31
Hyperlipidemia	806 (28.6)	462 (27.7)	185 (23.4)	0.02
Current smoker	330 (11.7)	231 (13.8)	125 (15.8)	0.004
<b>Physical examination, median (25th–75th percentile)</b>				
BMI, kg/m <sup>2</sup>	30.4 (26.7–35.4)	30.7 (27.0–35.3)	30.8 (26.9–36.0)	0.39
Systolic blood pressure, mm Hg	118.0 (109.0–130.0)	127.0 (120.0–137.0)	142.0 (132.0–153.0)	<0.001
Diastolic blood pressure, mm Hg	72.0 (67.0–76.0)	84.0 (82.0–86.0)	94.0 (91.0–98.0)	<0.001
Pulse, beats per minute	63.0 (56.0–71.0)	63.0 (57.0–71.0)	65.0 (58.0–72.0)	<0.001
<b>Laboratories, median (25th–75th percentile)</b>				
eGFR, mL/min per 1.73 m <sup>2</sup>	85.9 (75.2–97.6)	85.9 (76.5–95.9)	86.0 (76.5–96.3)	0.88
Glucose, mg/dL	92.0 (85.0–102.0)	92.0 (86.0–100.0)	92.0 (86.0–100.0)	0.91
LDL cholesterol, mg/dL	124.0 (99.0–145.0)	124.0 (102.0–150.0)	125.0 (105.0–150.0)	<0.001
<b>Echocardiography and ECG</b>				
Left ventricular EF, %, median (25th–75th percentile)	65.0 (55.0–65.0)	65.0 (55.0–65.0)	65.0 (55.0–65.0)	<0.001
Left ventricular hypertrophy, N (%)	230 (8.2)	105 (6.3)	85 (10.8)	<0.001
<b>Medications, N (%)</b>				
Any blood pressure medication <sup>‡</sup>	1402 (49.7)	843 (50.5)	404 (51.1)	0.73
Anti-hypertensive	915 (32.4)	503 (30.1)	270 (34.2)	0.10
ACE-inhibitor/ARB	492 (17.4)	243 (14.6)	144 (18.2)	0.02
Antihypertensive combination	335 (11.9)	208 (12.5)	100 (12.7)	0.76
β-Blocker	287 (10.2)	152 (9.1)	93 (11.8)	0.12
Calcium channel blocker	447 (15.8)	275 (16.5)	132 (16.7)	0.78
Diuretic	715 (25.3)	350 (21.0)	154 (19.5)	<0.001
Thiazide	316 (11.2)	174 (10.4)	75 (9.5)	0.35
Loop diuretic	197 (7.0)	73 (4.4)	38 (4.8)	<0.001
Nitrate	88 (3.1)	28 (1.7)	9 (1.1)	<0.001
Statin	371 (13.2)	175 (10.5)	54 (6.8)	<0.001
Antiplatelet	48 (1.7)	26 (1.6)	7 (0.9)	0.26

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein.

\*Cohort A has n=5280 participants after 21 excluded for missing BP data. Cohort B has n=5172 participants who survived to 2005.

<sup>†</sup>Based on the JHS coordinating center definition of hypertension (BP ≥140/90 or taking BP-lowering medication).

<sup>‡</sup>Any BP medication includes antihypertensives (ACE-inhibitor, ARB, α-blocker, adrenergic vasodilator, antihypertensive combination), β-blocker, calcium channel blocker, or diuretic (thiazide diuretic, loop diuretic, potassium-sparing diuretic, or combination diuretic).



**Figure 1.** Unadjusted cumulative incidence of outcomes. Unadjusted cumulative incidence of (A) mortality by SBP group, (B) mortality by DBP group, (C) heart failure hospitalization by SBP group, and (D) heart failure hospitalization by DBP group. DBP indicates diastolic blood pressure; SBP, systolic blood pressure.

sensitivity analysis of associations between HF incidence and age, there was no statistically significant difference in HF incidence across the range of SBP ( $P=0.17$ ) or DBP ( $P=0.62$ ).

After multivariable adjustment, each 10 mm Hg increase in SBP was associated with a 12% increase in risk of mortality and each 10 mm Hg increase in DBP was associated with a 15% reduction in mortality (Table 4). Box-Tidwell and Supremum tests indicated linear functional form for both. There were no significant associations between SBP or DBP and HF hospitalization. In the HF incidence analysis, each 10 mm Hg increase in SBP was associated with a 10% increase in unadjusted risk of HF incidence (hazard ratio, 1.10; 95% CI, 1.01–1.19). However, there was no association between DBP and HF incidence before multivariable adjustment. After adjustment, BP was not associated with HF incidence.

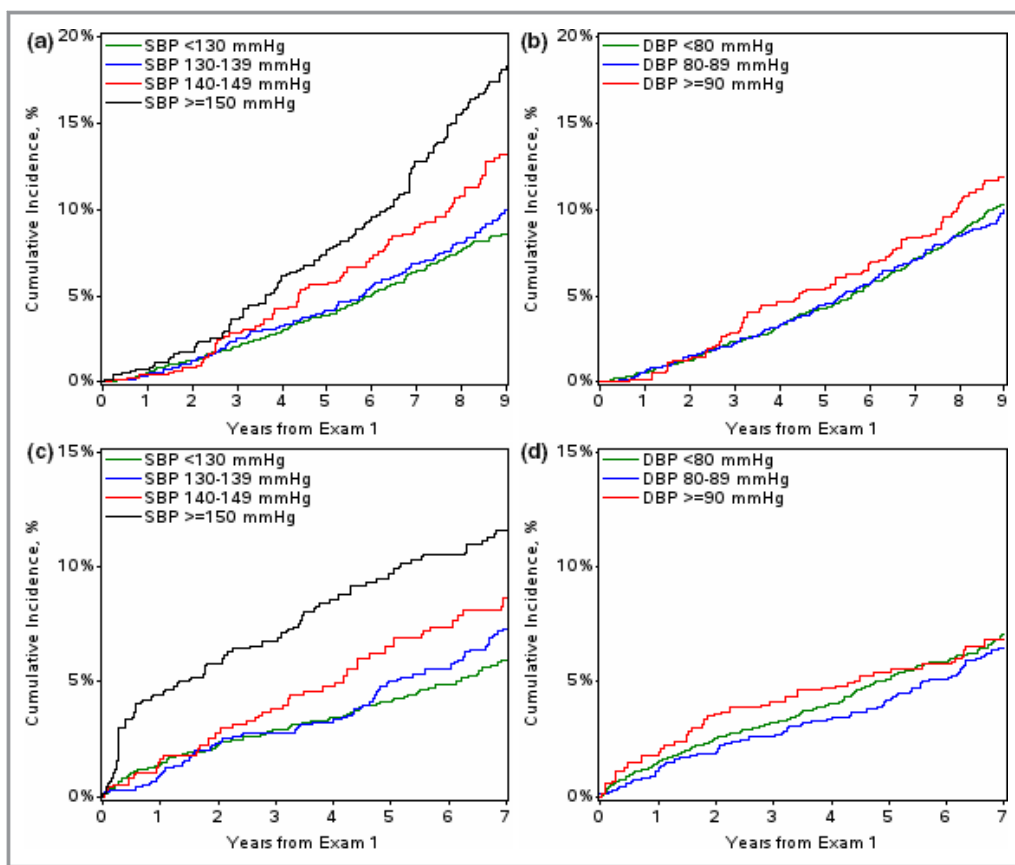
We found a statistically significant interaction between age and SBP in the mortality model ( $P=0.004$ ). After multivariable adjustment, a 10 mm Hg increase in SBP was associated with a 26% increase in mortality among participants younger than

60 years and a 9% increase in participants 60 years and older (Table 5). The adjusted relationship between DBP and mortality was not significant in the younger group. However, among participants 60 years and older, there was a 15% lower mortality risk for each 10 mm Hg increase in DBP.

After multivariable adjustment, HFH did not differ by age in either the SBP or DBP models (Table 6). Similarly, there were no differences in associations between BP and either mortality or HFH by the presence of CKD or diabetes mellitus.

## Discussion

Our finding of greater mortality risk with increasing SBP is consistent with previous studies.<sup>31,32</sup> A meta-analysis of 61 observational studies found a direct relationship between elevated baseline BP and both vascular and all-cause mortality.<sup>31</sup> In a cohort of 316 009 white men, there was a continuous relationship between increasing SBP and coronary artery disease mortality.<sup>32</sup> Our study adds to existing data by showing a direct relationship between SBP and mortality in blacks, a population underrepresented in observational



**Figure 2.** Age-adjusted cumulative incidence of outcomes. Age-adjusted cumulative incidence of (A) mortality by SBP group, (B) mortality by DBP group, (C) heart failure hospitalization by SBP group, and (D) heart failure hospitalization by DBP group. DBP indicates diastolic blood pressure; SBP, systolic blood pressure.

studies and randomized trials despite greater burden of hypertension and risk of adverse outcomes.

We also observed an association between low DBP and greater mortality risk, consistent with cohort studies involving older patients,<sup>33</sup> men,<sup>34</sup> and young adults.<sup>35</sup> Similar to our findings, Tuomilehto et al found an association between lower

DBP and mortality among older patients.<sup>36</sup> One proposed mechanism for this association is increased arterial stiffness among older patients, which lowers DBP, is a marker of vascular disease, and is an independent predictor of mortality.<sup>37–39</sup>

The strength of the association between SBP and mortality was attenuated in older participants compared with younger

**Table 3.** Age-Adjusted Cumulative Incidence of Outcomes by Blood Pressure Category

Systolic Blood Pressure					
	<130 mm Hg N=3215	130 to 139 mm Hg N=941	140 to 149 mm Hg N=557	≥150 mm Hg N=567	P Value
Mortality	7.0 (6.2–8.0)	11.4 (9.5–13.8)	15.9 (13.0–19.3)	22.9 (19.5–26.8)	<0.001
HF hospitalization	4.8 (4.1–5.7)	8.3 (6.7–10.4)	10.3 (8.0–13.4)	14.1 (11.3–17.5)	<0.001
Diastolic Blood Pressure					
	<80 mm Hg	80 to 89 mm Hg	≥90 mm Hg	P Value	
Mortality	10.3 (9.2–11.6)	9.9 (8.5–11.6)	11.9 (9.6–14.6)	0.33	
HF hospitalization	7.1 (6.2–8.2)	6.4 (5.3–7.8)	6.9 (5.2–9.1)		

Values presented as cumulative incidence (95% CI). HF indicates heart failure.

**Table 4.** Associations Between Blood Pressure Measurements Per 10 mm Hg Increase and Outcomes\*

Model	Mortality Hazard Ratio (95% CI)	P Value	HF Hospitalization Hazard Ratio (95% CI)	P Value
Model 1. Unadjusted SBP per 10 mm Hg	1.26 (1.22–1.31)	<0.001	1.25 (1.19–1.31)	<0.001
Model 2. Unadjusted DBP per 10 mm Hg	0.84 (0.77–0.91)	<0.001	0.82 (0.74–0.91)	<0.001
Model 3. SBP plus DBP				
SBP per 10 mm Hg	1.38 (1.33–1.44)	<0.001	1.38 (1.31–1.44)	<0.001
DBP per 10 mm Hg	0.65 (0.59–0.70)	<0.001	0.64 (0.57–0.71)	<0.001
Model 4. Multivariable adjustment <sup>†</sup>				
SBP per 10 mm Hg	1.12 (1.06–1.17)	<0.001	1.07 (1.00–1.14)	0.05
DBP per 10 mm Hg	0.85 (0.77–0.94)	0.002	0.92 (0.81–1.04)	0.20

DBP indicates diastolic blood pressure; HF, heart failure; SBP, systolic blood pressure.

\*Box-Tidwell and Supremum tests indicated linear functional form for both SBP and DBP.

<sup>†</sup>Multivariable adjustment variables are included in the Methods section under Statistical Analysis.

participants. This finding is consistent with findings from the Lewington et al meta-analysis,<sup>31</sup> which showed that each 20 mm Hg increase above 115 mm Hg among participants aged 40 to 69 years was associated with a 2-fold increase in cardiovascular end points, including death. However, in participants aged 80 to 89 years, this risk increased by only one third.<sup>31</sup> In our findings and the Lewington et al analysis, it is important to note that although the potential relative risk reduction associated with reducing BP is greatest in the younger population, the absolute reduction in mortality risk is likely to be highest in the older population, as they have a higher baseline risk of disease.

The 2014 hypertension guidelines increased the point of initiation of antihypertensive therapy and goal SBP from 140 to 150 mm Hg for patients older than 60 years without CKD or diabetes. This decision was based on data from randomized trials showing lower risks of stroke, HF, and mortality among

older patients when SBP was lowered to <150 mm Hg and no benefit below 140 mm Hg among older Japanese patients.<sup>12,13,40–43</sup> Several Joint National Committee 8 panelists, the Association of Black Cardiologists, and a working group on women's cardiovascular health expressed concerns about the generalizability of the populations in these randomized trials to older, black, and female patients in the United States. The concerns centered on the potential increase in adverse events due to lowering SBP treatment goals in populations most at risk for sequelae of poorly controlled hypertension.<sup>11,19</sup> Recent data presented at the International Stroke Conference corroborate these concerns. Among 1706 patients, mostly black or Hispanic and 60 years or older, stroke rates were highest among patients with SBP  $\geq$ 150 mm Hg.<sup>44</sup>

Recently, the Systolic Blood Pressure Intervention Trial (SPRINT) enrolled 30% black study participants and reported

**Table 5.** Age Subgroup Analyses of Associations Between Blood Pressure Per 10 mm Hg and Mortality

Model	Age <60 Years*		Age $\geq$ 60 Years <sup>†</sup>	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Model 1. Unadjusted SBP per 10 mm Hg	1.38 (1.27–1.49)	<0.001	1.11 (1.06–1.16)	<0.001
Model 2. Unadjusted DBP per 10 mm Hg	1.22 (1.03–1.44)	0.02	0.88 (0.80–0.96)	0.007
Model 3. SBP plus DBP				
SBP per 10 mm Hg	1.48 (1.36–1.62)	<0.001	1.18 (1.12–1.25)	<0.001
DBP per 10 mm Hg	0.77 (0.64–0.93)	0.007	0.76 (0.68–0.84)	<0.001
Model 4. Multivariable adjustment <sup>†</sup>				
SBP per 10 mm Hg	1.26 (1.13–1.42)	<0.001	1.09 (1.03–1.15)	0.004
DBP per 10 mm Hg	0.83 (0.67–1.03)	0.09	0.85 (0.76–0.95)	0.005

DBP indicates diastolic blood pressure; SBP, systolic blood pressure.

\*The cohort included 3194 participants and 126 events.

<sup>†</sup>The cohort included 2086 participants and 394 events.



**Table 6.** Age Subgroup Analyses: Associations Between Blood Pressure Measurements Per 10 mm Hg and JHS-Based HF Hospitalization

Model	Age <60 Years (n=3194 Participants, n=86 Events)		Age ≥60 Years (n=2086, n=254 Events)	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Model 1. Unadjusted SBP, per 10 mm Hg	1.34 (1.22–1.48)	<0.001	1.09 (1.03–1.16)	0.004
Model 2. Unadjusted DBP, per 10 mm Hg	1.22 (1.00–1.50)	0.05	0.85 (0.75–0.95)	0.006
Model 3. SBP+DBP				
SBP, per 10 mm Hg	1.43 (1.28–1.61)	<0.001	1.18 (1.10–1.26)	<0.001
DBP, per 10 mm Hg	0.81 (0.64–1.03)	0.08	0.74 (0.65–0.84)	<0.001
Model 4. Multivariable adjustment				
SBP, per 10 mm Hg	1.12 (0.96–1.31)	0.14	1.04 (0.97–1.12)	0.26
DBP, per 10 mm Hg	0.85 (0.66–1.11)	0.23	0.93 (0.80–1.08)	0.33

DBP indicates diastolic blood pressure; HF, heart failure; JHS, Jackson Heart Study; SBP, systolic blood pressure.

fewer cardiovascular deaths, strokes, and myocardial infarctions among patients 50 years and older who were treated to a target of 120 mm Hg compared with 140 mm Hg.<sup>45</sup> This is consistent with our finding that higher SBP is associated with greater risk of mortality across all age ranges. Interestingly, SPRINT did not show a difference in mortality among black participants who were treated with standard versus intensive BP control, though they were underpowered for this subgroup analysis. SPRINT and the ongoing Optimal Blood Pressure and Cholesterol Targets for Preventing Recurrent Stroke Trial (NCT01563731) will provide randomized trial evidence on appropriate BP targets in older adults.

We found no interaction between BP and the presence of CKD or diabetes for mortality or HFH. Citing a paucity of evidence that a goal of 130/80 mm Hg in patients with CKD is associated with improved outcomes,<sup>46–48</sup> the Joint National Committee 8 panel recommended that all patients 18 years and older with CKD or diabetes should have a BP goal of <140/90 mm Hg,<sup>19</sup> rather than the prior target of 130/80 mm Hg.<sup>6</sup> Our finding of no interaction between CKD or diabetes mellitus and BP and the limited availability of randomized controlled trial data highlights the importance of future randomized trials addressing the optimal BP target in individuals with multiple comorbid conditions.

Our analysis has limitations. First, the primary outcomes included only mortality and HFH. The JHS database had insufficient events to assess associations between BP and stroke, or myocardial infarction, and the incidence of CKD was not measured. Second, given the small number of events in several subgroup analyses, our analysis may have lacked statistical power to detect associations in clinically relevant strata. For example, there was no difference in the incidence of HFH in participants with SBP of 130 to 139 mm Hg, compared with 140 to 149 mm Hg. This finding may reflect low HFH rates in these groups rather than a true lack of

difference. Additionally, our analysis used a single baseline BP and could not measure the association between variability of BP and outcomes. This limits the comparability of this study to modern BP trials such as SPRINT, where ambulatory BP was recorded. Finally, the JHS is a voluntary program, and the study population may differ from the general black population. Nevertheless, to our knowledge, ours is the only study to assess associations between BP and cardiovascular outcomes in a well-characterized, contemporary black population.

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## **Associations Between Blood Pressure and Outcomes Among Blacks in the Jackson Heart Study**

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