Systolic Blood Pressure Levels Among Adults With Hypertension and Incident Cardiovascular Events
The Atherosclerosis Risk in Communities Study

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**IMPORTANCE** Studies document a progressive increase in heart disease risk as systolic blood pressure (SBP) rises above 115 mm Hg, but it is unknown whether an SBP lower than 120 mm Hg among adults with hypertension (HTN) lowers heart failure, stroke, and myocardial infarction risk.

**OBJECTIVE** To examine the risk of incident cardiovascular (CV) events among adults with HTN according to 3 SBP levels: 140 mm Hg or higher; 120 to 139 mm Hg; and a reference level of lower than 120 mm Hg.

**DESIGN, SETTING, AND PARTICIPANTS** A total of 4480 participants with HTN but without prevalent CV disease at baseline (years 1987-1989) from the Atherosclerosis Risk in Communities Study were included. Measurements of SBP were taken at baseline and at 3 triennial visits; SBP was treated as a time-dependent variable and categorized as elevated (≥140 mm Hg), standard (120-139 mm Hg), and low (<120 mm Hg). Multivariable Cox regression models included baseline age, sex, diabetes status, BMI, high cholesterol level, smoking status, and alcohol intake.

**MAIN OUTCOMES AND MEASURES** Incident composite CV events (heart failure, ischemic stroke, myocardial infarction, or death related to coronary heart disease).

**RESULTS** After a median follow-up of 21.8 years, a total of 1622 incident CV events had occurred. Participants with elevated SBP developed incident CV events at a significantly higher rate than those in the low BP group (adjusted hazard ratio [HR], 1.46; 95% CI, 1.26-1.69). However, there was no difference in incident CV event-free survival among those in the standard vs low SBP group (adjusted HR, 1.00; 95% CI, 0.85-1.17). Further adjustment for BP medication use or diastolic BP did not significantly affect the results.

**CONCLUSIONS AND RELEVANCE** Among patients with HTN, having an elevated SBP carries the highest risk for cardiovascular events, but in this categorical analysis, once SBP was below 140 mm Hg, an SBP lower than 120 mm Hg did not appear to lessen the risk of incident CV events.
Elevated blood pressure (BP) is an important public health concern. It is highly prevalent and leads to several adverse cardiovascular outcomes, especially coronary heart disease (CHD), stroke, and heart failure (HF). Thus it is believed that even small improvements in the treatment of elevated BP would result in widespread cardiovascular benefit. The report to the Eighth Joint National Committee for Detection, Evaluation, and Treatment of High Blood Pressure (JNC-8) recommends that individuals achieve a target systolic BP (SBP) <140 mm Hg and diastolic BP (DBP) lower than 90 mm Hg. The benefit of lowering SBP to around 140 mm Hg is well accepted, but patients treated to this level of BP may still be at increased risk of adverse cardiovascular outcomes. Observational studies document a progressive increase in heart disease risk as BP rises above 115/75 mm Hg. Such evidence suggests that there may be substantial benefit to targeting treatment to an SBP lower than 120 mm Hg instead of lower than 140 mm Hg, but whether an SBP lower than 120 mm Hg lowers cardiovascular event risk (such as HF, ischemic stroke, and CHD) is unknown.

The Atherosclerosis Risk in Communities (ARIC) Study prospectively collected data on incident cardiovascular events in a predominantly biracial cohort. In this context, we evaluate the relationship between SBP and the development of incident cardiovascular events in participants with hypertension (HTN). We hypothesized that among participants with HTN (treated or untreated), cardiovascular event incidence would differ according to SBP levels, with an SBP of 140 mm Hg or higher or 120 to 139 mm Hg having an increased risk of incident cardiovascular events compared with an SBP lower than 120 mm Hg. And because African Americans are at greater risk of HTN and HTN-related cardiovascular outcomes, we hypothesized that the this relationship would be more pronounced among African Americans.

Methods

The ARIC Study is an ongoing longitudinal cohort study designed to investigate the causes of atherosclerosis and cardiovascular disease. Detailed study rationale, design, and procedures have been previously published. The institutional review board at each participating institution approved the ARIC study, and all participants provided informed consent before each examination. At baseline (years 1987-1989), 15,792 men and women aged 45 to 64 years were enrolled in the study from 4 US communities: Forsyth County, North Carolina; Jackson, Mississippi; suburban Minneapolis, Minnesota; and Washington County, Maryland. Subsequently, 3 follow-up examinations occurred at 3-year intervals after the baseline visit until the 1996-1998 follow-up. Telephone calls were made annually after enrollment to ascertain participant health status and any hospitalizations.

Trained study personnel and research technicians took all physical measurements and administered all questionnaires following a standardized protocol that included quality control measures. Technicians measured 3 seated BP readings after a 5-minute rest using random 0 sphygmomanometers. The average of the last 2 measures was used for analysis. Participants were requested to bring all their current medications during the field center visits. Interviewers inquired about whether the participants used medications for hypertension or diabetes, and the names of medications used in the past 2 weeks were transcribed from participants’ medication bottles. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Diabetes mellitus was defined as having a fasting blood glucose level higher than 126 mg/dL, use of hypoglycemic medication, or a self-reported physician’s diagnosis. High cholesterol was defined as a total serum cholesterol higher than 240 mg/dL. Current smoking status (ever or never smoker) and alcohol drinking status (ever or never drinker) were self-reported. (To convert glucose to millimoles per liter, multiply by 0.0555; to convert cholesterol to millimoles per liter, multiply by 0.0259.)

Of the original ARIC cohort study members, because of a small sample size, non-African Americans and nonwhites were excluded from this analysis (n = 35), as were African Americans who resided in Minneapolis or Washington County (n = 55). Only participants with HTN (defined as having an SBP >140 mm Hg and a DBP >90 mm Hg at baseline; having a self-reported history of physician-diagnosed HTN; or taking antihypertensive medication) were included in this analysis. Participants with missing baseline BP data were excluded from this analysis. Included participants were further categorized into 3 groups based on SBP level: Elevated SBP (≥140 mm Hg), Standard SBP (120-139 mm Hg), and Low SBP (<120 mm Hg) groups. Measurements of BP from the first screening visit (baseline) plus all 3 subsequent clinic visits spanning a period of 9 years were used to derive a time-dependent BP exposure variable for this study. Reclassification of participants into different BP categories based on subsequent clinic visits is detailed in eTable 1 in the Supplement.

Study Outcome Events

Our primary outcome was a composite of incident MI, CHD death, HF, and ischemic stroke. Each of these outcomes was also analyzed separately in secondary analysis. Incident MI or a CHD-related death was treated as a singular outcome (MI/CHD) throughout. Cardiovascular events were ascertained via annual telephone contacts with participants (or proxies) to identify all deaths and hospitalizations and by surveying discharge lists from local hospitals and death certificates from state vital statistics offices for potential cardiovascular events and recording of International Classification of Diseases, Ninth Revision (ICD-9) and/or International Classification of Diseases, Tenth Revision (ICD-10) codes from all hospital records occurring from baseline (1987-1989) through December 31, 2010.

Heart failure was defined as the first occurrence of either (1) an HF hospitalization that included an ICD-9 discharge code of 428 (428.0 to 428.9) in any position or (2) a death certificate with an ICD-9 code of 428 (HF) or an ICD-10 code of 150...
or unknown history of prevalent stroke and/or transient ischae-
mined by the presence of at least 1 of the following at the base-
ti hypotensive treatment as a time-varying covariate; (2) ad-
cision for key covariates (baseline age, race, sex, diabetes, BMI,

even at the baseline visit: Q-waves on the electrocardiogram, self-reported his-

event was modeled in the presence of censor-

ting for DBP as a time-varying covariate; (3) censoring

ted log-rank test.

The validity of this end point in ARIC has been documented. For ischemic stroke and MI/CHD, hospital-

cratic factors and key covariates across baseline SBP level cat-
coverages of hypertension.8 In the current primary analysis, the ef-

disease and physician review.9 Prazosin and Val-

cohort baseline characteristics according to SBP level categories. Among this cohort of individu-

HF, ischemic stroke, or MI/CHD death) using the unad-

tability of this endpoint in ARIC has been
documented.7 For ischemic stroke and MI/CHD, hospital-

tal records were obtained and abstracted. All MI/CHD events

Statistical Analysis
To assess statistically significant differences of baseline demo-

graphic factors and key covariates at baseline SBP level cat-

tistical tests for categorical measures and Wilcoxon rank sum tests for continuous measures. Inci-
dent rates (IRRs) of hospitalized cardiovascular events were cal-

culated by dividing the number of new HF, ischemic stroke,
or MI/CHD cases in each SBP level category by the corre-

cidence ratios (IRRs) were derived using the low BP group as the reference group. Poisson regres-

test for categorical measures and Wilcoxon rank sum tests for continuous measures. Inci-
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dent rates (IRRs) were derived using the low BP group as the reference group. Poisson regres-

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Results
At baseline, the cohort of 4408 participants with HTN was relatively young, had a high prevalence of being overweight, and almost three-quarters were taking antihypertensive medi-

teNH had diabetes, and two-

After a median follow-up of 21.8 years, a total of 1622 in-

cidence composite cardiovascular events had occurred. The age-

adjusted IR (AAIR) was lowest among adults with HTN in the low SBP group and progressively higher in the higher SBP cat-

ded that African Americans had the highest absolute AAIR differential when comparing the highest SBP group (38.6 per 1000 person-

years) vs the lowest (28.6 per 1000 person-years), which sug-

Table 1 summarizes participant baseline characteristics according to SBP level categories. Among this cohort of individuals with HTN, 43.7% had elevated SBP (≥140 mm Hg); 33.6% had standard SBP (120-139 mm Hg); and 22.7% had low SBP (<120 mm Hg). Within each category, and across both races, the proportions of par-

cicipants taking antihypertensive medication at baseline were lowest among those with elevated SBP. Participants in the el-


elevated SBP group had a significantly higher IRR than the low SBP group, for HF events, the elevated SBP group had a significantly higher IRR than the low SBP group, but the IRR in the standard SBP group was not significantly dif-

The unadjusted HRs of incident composite cardiovascular events were

cardiovascular event follow-up at the year 2000, since the BP

to significantly by SBP category. This pattern was similar across race and sex groups. Is-

The unadjusted IRRs of incident composite cardiovascular events were

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BP and CV Events in Patients With Hypertension

Original Investigation  Research

BP and CV Events in Patients With Hypertension

1.65) compared with those in the low SBP group. The standard SBP group was not significantly different from the low SBP group in risk for incident cardiovascular events. This relationship remained unchanged after adjustments for age, sex, BMI, high cholesterol level, smoking status, alcohol intake, and diabetes. Cox proportional hazards models showed a 46% increased risk for incident composite events (HF, ischemic stroke, or MI/CHD) in the elevated SBP vs the low SBP group (HR, 1.46; 95% CI, 1.26-1.69). There was no difference in incident cardiovascular-free survival among those in the standard vs the low SBP groups (HR, 1.00; 95% CI, 0.85-1.17). Among participants with HTN, having elevated BP carries the highest risk for cardiovascular events, but in this categorical analysis we observed no overall risk difference between the whites (HR, 1.26; 95% CI, 1.04-1.54) (Figure 1). Further adjustment for BP medication use, DBP, or censoring cardiovascular event follow-up at year 2000 did not significantly affect the results (data not shown). Crude rates of MI/CHD, HF, or ischemic stroke stratified by SBP at 140 to 159 mm Hg and 160 mm Hg or higher suggested an increase in incident cardiovascular events mostly in the 160 mm Hg or higher group (Figure 2 in the Supplement). This pattern was not supported in multivariate models with SBP as a time-varying covariate, where significantly more composite events were seen in both the SBP 140 to 159 mm Hg and 160 mm Hg or higher groups compared with the low SBP and the standard SBP groups (eFigure A, in the Supplement).

Discussion

In this large, biracial, community-based cohort of men and women with HTN and long-term follow-up that addresses the time-varying nature of BP, we show that elevated BP among adults with HTN is an important risk factor for cardiovascular events (HF, stroke, and MI/CHD) regardless of race and sex. We expected to see a significantly higher cardiovascular event-free survival among participants with HTN with progressively lower BP levels, but the relationship seen was not graded. Among participants with HTN, having elevated BP carries the highest risk for cardiovascular events, but in this categorical analysis we observed no overall risk difference between the

Table 1. Baseline Characteristics of ARIC Participants With Hypertension Stratified by SBP Category

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n = 5466)</th>
<th>Low (n = 1239)</th>
<th>Standard (n = 1837)</th>
<th>Elevated (n = 2390)</th>
<th>P Value, Standard vs Low</th>
<th>P Value, Elevated vs Low</th>
<th>Overall P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3054 (55.9)</td>
<td>740 (59.7)</td>
<td>1003 (54.6)</td>
<td>.005</td>
<td>1311 (54.9)</td>
<td>.005</td>
<td>.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1121 (20.8)</td>
<td>227 (18.6)</td>
<td>391 (21.5)</td>
<td>.05</td>
<td>503 (21.4)</td>
<td>.05</td>
<td>.08</td>
</tr>
<tr>
<td>Cigarette use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>1326 (24.3)</td>
<td>338 (27.8)</td>
<td>399 (21.7)</td>
<td>.002</td>
<td>589 (24.7)</td>
<td>.07</td>
<td>.09</td>
</tr>
<tr>
<td>Former</td>
<td>1752 (32.1)</td>
<td>389 (31.4)</td>
<td>641 (34.9)</td>
<td></td>
<td>722 (30.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>2599 (47.9)</td>
<td>563 (45.7)</td>
<td>889 (48.6)</td>
<td>.23</td>
<td>1147 (48.5)</td>
<td>.02</td>
<td>.02</td>
</tr>
<tr>
<td>Former</td>
<td>1146 (21.1)</td>
<td>291 (23.6)</td>
<td>393 (21.5)</td>
<td></td>
<td>492 (19.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihypertensive medication use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>3975 (73.0)</td>
<td>1232 (99.4)</td>
<td>1648 (89.8)</td>
<td>&lt;.001</td>
<td>1095 (46.1)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Former</td>
<td>2491 (46.0)</td>
<td>750 (60.5)</td>
<td>941 (50.5)</td>
<td></td>
<td>305 (13.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>2348 (43.0)</td>
<td>489 (39.5)</td>
<td>774 (42.1)</td>
<td>.14</td>
<td>1085 (45.4)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>White</td>
<td>3118 (57.0)</td>
<td>750 (60.5)</td>
<td>1063 (57.9)</td>
<td></td>
<td>1305 (54.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>55.5 (5.7)</td>
<td>54.5 (5.7)</td>
<td>55.2 (5.7)</td>
<td>&lt;.001</td>
<td>56.3 (5.5)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>29.6 (5.7)</td>
<td>29.4 (5.7)</td>
<td>30.0 (5.9)</td>
<td>.01</td>
<td>29.2 (6.0)</td>
<td>.51</td>
<td>.09</td>
</tr>
<tr>
<td>SBP, mean (SD)</td>
<td>135.7 (20.7)</td>
<td>110.2 (7.5)</td>
<td>129.0 (5.6)</td>
<td>NA</td>
<td>154.1 (14.8)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: ARIC, Atherosclerosis Risk in Communities Study; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NA, not applicable; SBP, systolic blood pressure.

a Unless otherwise noted, data are reported as number (percentage) of participants.

b Low SBP is defined as lower than 120 mm Hg; standard SBP, 120 to 139 mm Hg; and elevated SBP, 140 mm Hg or higher.

c P values comparing standard and elevated with low SBP groups were obtained by the x² test for categorical measures and the Wilcoxon rank-sum test for continuous measures.

d By Cochran-Armitage trend test.

e By Kruskal-Wallis test for trend.

f By Spearman ρ test.
standard (SBP, 120-139 mm Hg) and low (SBP, <120 mm Hg) SBP groups. Although our results reinforce that control of elevated BP is beneficial to prevent incident cardiovascular events, our results suggest that once SBP is controlled below 140 mm Hg, an SBP below 120 mm Hg does not appear to provide additional benefit in terms of preventing incident cardiovascular events. Furthermore, to our knowledge, this study provides the most information of this kind for African Americans, a population that manifests a heavy burden of HTN as associated morbidity and mortality. Accessory result shows that African Americans achieve a greater absolute benefit than whites in reduced incident cardiovascular events when elevated SBP is controlled.

According to a study of the NHANES population (National Health and Nutrition Examination Survey), nearly 20% of all hypertensive individuals in the United States are unaware of their condition, and more than 30% are not being treated. In addition, 49.9% of adults with high BP did not have their HTN controlled at the target of lower than <140 mm Hg as set out by JNC-7. This is due to many factors, including possible reluctance of physicians to achieve such goals, defined as clinical inertia, or perhaps lack of acceptance of aggressive therapy by patients as well.13-15

It should be noted that for the present study, the concept of control among adults with HTN was based solely on the participant’s BP, not on how much or what particular treatment they were undergoing. For example, the BP of some participants might have been controlled with lifestyle modifications alone or with only 1 medication, while others taking multiple medications or none at all might have had uncontrolled BP. Similarly, a person with an SBP of 140 mm Hg or higher is at increased cardiovascular risk whether taking antihypertensive medications or not, based simply on the BP. Nevertheless, our results do not support the notion that SBP control to lower than 120 mm Hg is better. Elevated BP is undoubtedly a risk factor for cardiovascular events, but standard BP control appears to be just as good as lower BP control in preventing HF, ischemic stroke, and MI/CHD. These results are potentially important, since treatment to a lower BP may have adverse consequences such as orthostatic hypotension, medication adverse effects, and increased healthcare costs.15,16

A large meta-analysis of 61 cohort studies targeting 1 million participants including those with and without HTN demonstrated that cardiovascular morbidity and mortality decreased as the SBP decreased from 180 mm Hg to 115 mm Hg. Since then, the principle “the lower, the better” has been widely accepted. The contribution of elevated BP to the risk for developing cardiovascular events such as HF, MI, and stroke is substantial. Several clinical trials have demonstrated that treatment of an elevated SBP of 140 mm Hg or higher de-

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Low SBP</th>
<th>Standard SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>All Events</td>
</tr>
<tr>
<td>Composite</td>
<td>Total</td>
<td>911</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>354</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>557</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>373</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>538</td>
</tr>
<tr>
<td>HF</td>
<td>Total</td>
<td>1028</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>433</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>595</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>398</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>630</td>
</tr>
<tr>
<td>Stroke</td>
<td>Total</td>
<td>1201</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>482</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>719</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>473</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>728</td>
</tr>
<tr>
<td>MI/CHD</td>
<td>Total</td>
<td>1109</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>408</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>701</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td>461</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>648</td>
</tr>
</tbody>
</table>

Abbreviations: AAIR, age-adjusted incidence rate; HF, heart failure; IRR, incidence rate ratio; MI/CHD, combination measure myocardial infarction/coronary heart disease death; Ref, referent; SBP, systolic blood pressure.

A low SBP is defined as lower than 120 mm Hg; standard SBP, 120 to 139 mm Hg.
creases the risk for cardiovascular events. However, although this evidence is very consistent for SBPs lower than 150 mmHg, the benefit in preventing cardiovascular events among patients with HTN with SBPs lower than 120 mm Hg is unknown. Adequate control of elevated BP provides the earliest opportunity to prevent cardiovascular events. This notion is emphasized by the results of our study. However, the belief that intensifying antihypertensive treatment in patients with an SBP of 130 to 140 mmHg offers any extracardiovascular benefit has come into question.

Table 3. Age-Adjusted Cardiovascular Event Incidence Rates and Incidence Rate Ratios by SBP Category,* 1987-2010

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Elevated SBP 1*</th>
<th>Elevated SBP 2*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. All Events Person-years AAIR IRR (95% CIs)</td>
<td>No. All Events Person-years AAIR IRR (95% CIs)</td>
</tr>
<tr>
<td>Composite</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1538 579 25 140 28.6 1.16 (1.01-1.34)</td>
<td>490 242 671 42.7 1.73 (1.46-2.05)</td>
</tr>
<tr>
<td>Male</td>
<td>681 300 10 253 34.1 1.19 (0.97-1.47)</td>
<td>203 104 256 52.8 1.85 (1.43-2.40)</td>
</tr>
<tr>
<td>Female</td>
<td>867 279 14 887 31.4 1.10 (0.91-1.34)</td>
<td>287 138 414 36.8 1.61 (1.28-2.02)</td>
</tr>
<tr>
<td>African American</td>
<td>639 272 9 875 35.0 1.23 (1.00-1.51)</td>
<td>282 136 364 43.3 1.52 (1.20-1.93)</td>
</tr>
<tr>
<td>White</td>
<td>899 305 15 266 25.7 1.18 (0.97-1.43)</td>
<td>208 106 307 41.8 1.92 (1.50-2.46)</td>
</tr>
<tr>
<td>HF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1637 447 28 493 22.4 1.14 (0.97-1.34)</td>
<td>541 182 796 29.5 1.49 (1.23-1.81)</td>
</tr>
<tr>
<td>Male</td>
<td>755 239 12 990 26.9 1.08 (0.86-1.35)</td>
<td>234 83 318 35.7 1.44 (1.08-1.92)</td>
</tr>
<tr>
<td>Female</td>
<td>882 208 16 183 18.9 1.15 (0.92-1.45)</td>
<td>307 99 477 25.4 1.54 (1.18-2.02)</td>
</tr>
<tr>
<td>African American</td>
<td>669 199 10 1085 26.4 1.43 (1.12-1.83)</td>
<td>311 101 430 28.9 1.57 (1.18-2.08)</td>
</tr>
<tr>
<td>White</td>
<td>968 248 17 509 21.0 1.01 (0.82-1.25)</td>
<td>230 81 365 30.0 1.44 (1.09-1.90)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1752 201 31 134 7.17 1.05 (0.83-1.23)</td>
<td>574 106 867 12.7 1.87 (1.43-2.44)</td>
</tr>
<tr>
<td>Male</td>
<td>801 104 13 404 7.69 1.02 (0.73-1.43)</td>
<td>245 44 342 14.3 1.90 (1.27-2.85)</td>
</tr>
<tr>
<td>Female</td>
<td>951 97 17 727 6.9 1.08 (0.78-1.49)</td>
<td>329 62 524 11.4 1.83 (1.28-2.61)</td>
</tr>
<tr>
<td>African American</td>
<td>717 107 11 879 9.54 1.10 (0.80-1.52)</td>
<td>336 70 476 14.2 1.61 (1.15-2.32)</td>
</tr>
<tr>
<td>White</td>
<td>1035 94 19 253 6.18 1.09 (0.78-1.52)</td>
<td>238 36 390 11.4 2.01 (1.33-3.09)</td>
</tr>
<tr>
<td>MI/CHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1698 292 29 419 11.6 0.99 (0.82-1.20)</td>
<td>557 119 831 16.5 1.41 (1.12-1.78)</td>
</tr>
<tr>
<td>Male</td>
<td>753 165 12 169 14.8 0.88 (0.68-1.14)</td>
<td>227 58 321 25.6 1.53 (1.10-2.13)</td>
</tr>
<tr>
<td>Female</td>
<td>945 127 17 250 9.5 1.03 (0.78-1.36)</td>
<td>330 61 510 10.9 1.18 (0.85-1.65)</td>
</tr>
<tr>
<td>African American</td>
<td>700 121 11 690 12.8 1.00 (0.74-1.34)</td>
<td>229 67 469 17.2 1.35 (0.97-1.88)</td>
</tr>
<tr>
<td>White</td>
<td>998 171 17 728 10.9 1.00 (0.78-1.29)</td>
<td>228 52 362 15.8 1.45 (1.03-2.04)</td>
</tr>
</tbody>
</table>

Abbreviations: AAIR, age-adjusted incidence rate; HF, heart failure; IRR, incidence rate ratio; MI/CHD, myocardial infarction/coronary heart disease death; SBP, systolic blood pressure.

* Elevated SBP 1 is defined as 140 to 159 mm Hg; Elevated SBP 2, 160 mm Hg or higher.

† Compared with low SBP (see Table 2).

Recent randomized controlled trial, the Action to Control Cardiovascular Risk in Diabetes, showed no significant difference in cardiovascular events between the intensive BP-lowering group, with a target SBP below 120 mm Hg, and the standard treatment group, with a target SBP below 140 mm Hg. The recent JNC-8 report reinforces the 140/90 mmHg or higher threshold for individuals younger than 60 years, citing a lack of evidence for increased cardiovascular risk at lower BP thresholds. Our results show that patients with HTN and SBPs below 120 mm Hg do not appear to have a lower risk of incident cardiovascular events than those with SBPs of 120 to 139 mm Hg. Furthermore, some have suggested that mild hypertension (SBP, 140-159 mmHg) does not confer significantly higher risk of cardiovascular events. However, our results show an increased risk for cardiovascular event for mild hypertension as well as for moderate to severe hypertension (SBP >160 mm Hg). This also supports the JNC-8 treatment threshold of an SBP of 140 mm Hg or higher.

One possible reason for our observed results is the so-called J-curve phenomenon, which describes a relationship between treatment to low BP levels and increased cardiovascular complications. Secondary analysis from recent large clinical outcomes trials have observed a J-curve effect between a DBP of 70 to 80 mm Hg as well as an SBP
lower than 130 mm Hg.\textsuperscript{34,35} This effect does not seem to appear in the absence of known obstructive CHD,\textsuperscript{33} presumably because the coronary arteries are perfused during diastole, but may be more pronounced in patients with HTN. However, the J-curve phenomenon remains controversial and has not been consistently shown. Examples are the Systolic Hypertension in the Elderly Program study\textsuperscript{36} and the Syst-Eur study,\textsuperscript{37} where no increase in myocardial ischemia or cardiovascular disease risk was shown at a DBP of 55 to 60 mm Hg. According to the Cardiovascular Health Study\textsuperscript{38} the BP level and cardiovascular risk showed a linear relationship, and a J-curve was not observed. The Physicians’ Health Study and Women’s Health Study\textsuperscript{39} observed 22,071 men and 39,876 women for a median of 13.0 years and 6.2 years, respectively, and found a linear association of SBP and DBP with the risk of MI, stroke, coronary artery bypass graft, angioplasty, and cardiovascular death without any evidence of a J-curve relationship.

The Atherosclerosis Risk in Communities Study\textsuperscript{5} (1987-2010) stratified by composite event (heart failure, ischemic stroke, or combination measure myocardial infarction/incidence of coronary heart disease death [MI/CHD]) (A), heart failure (B), ischemic stroke (C), and MI/CHD (D). Elevated BP is defined as an SBP of 140 mm Hg or higher; standard BP, an SBP of 120 to 139 mm Hg; and low BP, an SBP of lower than 120 mm Hg. The vertical lines through the HRs represent 95% CIs.
Our study has some limitations. First, HF was based on hospital discharge ICD codes and not validated by physician review of medical records. Although HF diagnosis codes have been demonstrated to have high validity in ARIC, the true incidence of HF may be underestimated. Second, our study was observational, so despite a consistent statistical association, we cannot establish causality or account for unmeasured confounders not modeled in this study. We therefore await results from ongoing randomized clinical trials, such as the Systolic Blood Pressure Intervention Trial (SPRINT) sponsored by the National Heart, Lung, and Blood Institute (NHLBI), to help determine whether lowering SBP levels among patients with HTN has the potential to reduce cardiovascular events. Finally, the BP control period for which we had data was 9 years following baseline, whereas follow-up was for 20 years. It is likely that BP control for the final 11 years changed, and therefore some participants were misclassified prior to cardiovascular event diagnosis. However, our sensitivity analysis, ending follow-up at year 2000, showed similar results.

Conclusions

We show in a large, biracial, community-based cohort of unselected individuals with HTN that those with an SBP lower than 120 mm Hg do not have reduced longitudinal risk of developing incident HF, ischemic stroke, or MI/CHD compared with individuals with HTN who have an SBP of 120 to 139 mm Hg. Thus, for controlling cardiovascular risk, a treatment goal of 120 to 139 mm Hg may be acceptable among most patients with HTN. Further studies are needed to support this conclusion, including the eventual results of the NHLBI SPRINT trial.
Drafting of the manuscript: Rodriguez, Swett, Agarwal, Loehr, Fox, Loehr, N. Raw content: Rodriguez, Agarwal, Folsom, Fox, Loehr, N. Raw content: Rosamond, Chang.

Statistical analysis: Swett, Agarwal, Loehr.

Obtained funding: Folsom, N.

Administrative, technical, or material support: N.

Study supervision: Rodriguez, Fox, Loehr, Rosamond.

Conflict of Interest Disclosures: None reported.

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Previous Presentation: This research was presented in part at the American Heart Association’s Epidemiology and Prevention/Physical Activity, Nutrition and Metabolism 2013 Scientific Sessions; March 26, 2013; New Orleans, Louisiana.

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Let’s Prioritize the Right Care for the Right Patients With Hypertension

Paul Arthur James, MD

High-quality health care is often summarized as delivering the right care to the right patient every time. In this issue of JAMA Internal Medicine, Rodriguez and colleagues1 publish an important study using data from the Atherosclerosis Risk in Communities (ARIC) Study to further inform the debate about which patients should receive antihypertensive medicines every time to achieve goal blood pressure (BP) targets— but it also informs us about much more in the treatment of hypertension (HTN). This observational study among patients with HTN finds no additional risk among the participants in the standard systolic BP (SBP) cohort (120-139 mm Hg) compared with those in the low SBP cohort (<120 mm Hg). This finding differs from epidemiologic data that consistently suggests a linear relationship between rising SBP in a population and increasing rates of poor outcomes (eg, stroke, myocardial infarction [MI], heart failure [HF], and mortality). Based on this strong epidemiologic association, conventional wisdom has held that using medication to achieve lower BPs in patients with HTN should result in lower rates of stroke, MI, and HF, similar to those seen among persons who take no antihypertensive medications.

However, Rodriguez et al2 appear to provide observational evidence that lower BP is not always better. Recent randomized controlled trials (RCTs)3-5 have also raised the concern that no additional benefit is gained by lowering SBPs below the recently established new treatment goals.6 These RCTs were influential in justifying an increased SBP goal for those 60 years or older in the 2014 Guidelines set forth by the panel appointed to the Eighth Joint National Committee (JNC-8),7 especially because the methodology of the evidence review required RCT evidence as opposed to observational data. While Rodriguez and colleagues5 do not provide a definitive answer to those troubled by raising the SBP goal for those older than 60 years without diabetes or chronic kidney disease, they do illustrate the marginal benefits of adding more medications to achieve lower BPs in the general population.

Both observational studies and RCTs can provide important information about HTN, but they often have different purposes. The methodology used by the panel members appointed to JNC-88 for answering their specific critical questions focused on the evidence supporting medication management in patients with high BP. All members of the panel agreed that RCTs were the appropriate source to answer these questions prior to the external methodology team’s literature review and synthesis of the evidence. However, the evidence from RCTs caused discomfort for a minority of panel members because the RCT evidence did not comport with the findings from observational studies.9

All research methodologies have limitations, and this is true of the study by Rodriguez et al.1 The authors created longitudinal cohorts segregated by time-dependent BP measures of low, standard and elevated for patients with HTN over 9 years and then observed these patients for a median of 21.8 years and increasing rates of poor outcomes (eg, stroke, myocardial infarction [MI], heart failure [HF], and mortality). Based on this strong epidemiologic association, conventional wisdom has held that using medication to achieve lower BPs in patients with HTN should result in lower rates of stroke, MI, and HF, similar to those seen among persons who take no antihypertensive medications.

However, Rodriguez et al1 appear to provide observational evidence that lower BP is not always better. Recent randomized controlled trials (RCTs)2-4 have also raised the concern that no additional benefit is gained by lowering SBPs below the recently established new treatment goals.5 These RCTs were influential in justifying an increased SBP goal for those 60 years or older in the 2014 Guidelines set forth by the panel appointed to the Eighth Joint National Committee (JNC-8),6 especially because the methodology of the evidence review required RCT evidence as opposed to observational data. While Rodriguez and colleagues5 do not provide a definitive answer

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