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Incidence of Cardiovascular Disease in Individuals Affected by Recent Changes to US Blood Pressure Treatment Guidelines

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Abstract

Objective—We evaluated the incidence of cardiovascular disease (CVD) in individuals whose blood pressure (BP) management strategy would change with adoption of recent US hypertension guidelines in two large, community-based cohorts with different racial and geographic compositions: the Framingham and Jackson Heart Studies (FHS and JHS).

Methods—We assigned 11,237 FHS (mean age 46, 53% women) and 2948 JHS (mean age 55, 69% women) participants free of chronic kidney disease to one of five categories representing different treatment recommendations between JNC 8 and JNC 7 guidelines. Absolute incidence rates (IR; per 1000 person-years) and multivariable-adjusted hazard ratios (HR) were calculated for each group; cohort-specific results were combined using fixed effect meta-analysis.

Results—CVD events occurred in 1047 FHS and 230 JHS participants during mean follow-up times of 11 and 8.9 years, respectively. Compared to individuals without hypertension, those with BP 140-149/<90 mm Hg had increased risk for CVD regardless of treatment status (HR for untreated BP 140-149/<90 mm Hg 1.96, 95% confidence interval [CI] 1.40-2.75; HR for treated BP 140-149/<90 mm Hg 3.37, 95% CI 2.37-4.78). The risk for those with treated BP 140-149/<90 mm Hg was consistent in those aged ≥60 years (HR: 2.61, 95% CI 1.75-3.90). Statistical power was limited to evaluate the effect of diabetes.

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Conclusions—Individuals with treated BP 140-149/<90 mm Hg have increased risk of CVD compared with those without hypertension including in participants ≥60 years. The JNC 8 recommendations to treat BP levels less aggressively may be associated with substantial residual CVD risk.

Keywords

hypertension; cardiac risk factors and prevention; epidemiology

INTRODUCTION

The “2014 Evidence-Based Guidelines for the Management of High Blood Pressure in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee” (JNC 8) [1] recommended several important changes to blood pressure (BP) management from the previous guidelines (“The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure” [JNC 7]) [2]. Specifically, the JNC 8 guidelines endorsed a more conservative target systolic BP (SBP) of <150 mm Hg for individuals aged ≥60 years, and raised the BP target from <130/<80 mm Hg to <140/<90 mm Hg for those with diabetes mellitus or chronic kidney disease (CKD). The guideline committee determined that there was insufficient evidence to support the previous, more aggressive, treatment thresholds [1]. Hypertension guidelines have great potential impact on population health and have been suggested to be partly responsible for improvements in SBP in the US over the past 20 years [3]. If fully implemented, the JNC 8 guidelines are predicted to affect the treatment recommendations of up to 20 million Americans [4], and as a result, the guidelines have been the subject of considerable debate [5,6].

In order to further understand the impact of recent changes to the BP treatment guidelines, we compared the ‘real-world’ incidence of cardiovascular disease (CVD) among individuals whose BP management matched the less aggressive targets advocated by JNC 8, with those whose management was consistent with JNC 7 recommendations. We hypothesized that less aggressive BP treatment would be associated with a higher risk of CVD regardless of age group. We tested this hypothesis in two large, community-based cohorts with different racial and geographic backgrounds: the predominantly white Framingham Heart Study (FHS) and the all-black Jackson Heart Study (JHS).

METHODS

Study Sample

The design and enrollment of the JHS cohort and FHS Offspring cohort have been described previously [7–9]. Of the 5301 JHS participants who attended the baseline examination (performed in 2000–2004), we excluded those with missing blood pressure measurements or antihypertensive treatment status (n=990), prevalent CVD (n=959), prevalent chronic kidney disease (CKD, defined as creatinine >2 mg/dL; n=11), missing covariates (n=376), or follow-up time <1 year (n=17), yielding a sample of 2948 individuals.

In the FHS, participants attending the first (1971-1975), third (1983-1987), or sixth (1995-1998) Offspring examination cycles were eligible for inclusion. From 12,529 participant-visits, we excluded those with missing blood pressure measurements or unknown hypertension treatment status (n=56), prevalent CVD (n=746), CKD (n=19), no follow-up (n=47), and missing covariates (n=424). These resulted in a final sample of 11,237 individual observations (4715, 3467 and 3055 from examination cycle one, three and six). All participants in both cohorts provided written informed consent, and the study protocols were approved by each study's institutional review board.

Classification of Blood Pressure Categories

In both studies, seated BP measurements were obtained using a mercury column sphygmomanometer and the average of two measurements obtained using a standardized protocol was recorded. In the JHS, hypertension treatment status was determined by medication review or self-report. In the FHS, hypertension treatment status was ascertained by a questionnaire. Each participant was assigned to one of five mutually exclusive BP categories based on their BP reading and their hypertension treatment status (Supplemental Table 1). *Category 1* ("no hypertension by JNC 7 or JNC 8") included untreated participants with SBP <140 mm Hg and diastolic blood pressure (DBP) <90 mm Hg. *Category 2* ("need BP medications by JNC 7, no medications by JNC 8") consisted of untreated participants with SBP 140-149 mm Hg and DBP <90 mm Hg. *Category three* ("successfully treated by JNC 7, unnecessarily treated by JNC 8") included participants with treated SBP <140 mm Hg and DBP <90 mm Hg. *Category 4* ("inadequately treated by JNC 7, successfully treated by JNC 8") contained participants with treated SBP 140-149 mm Hg and DBP <90 mm Hg. *Category 5* ("hypertension by JNC 7 and JNC 8") consisted of all other participants (SBP ≥150 mm Hg and/or DBP ≥90 mm Hg regardless of hypertension treatment status).

Outcome Ascertainment

The outcome was a first CVD event, defined as a composite of: fatal and nonfatal myocardial infarction, coronary insufficiency, angina, stroke or transient ischemic attack, intermittent claudication or heart failure.[10] FHS participants are under continuous surveillance for the occurrence of CVD events, which are adjudicated by a committee of three experienced physicians after a detailed review of all pertinent medical records, examination visits, and health history updates. Events in JHS were ascertained by a combination of active and passive surveillance through annual health updates and review of discharge lists and death certificates from local hospitals [11].

Covariates

A cardiovascular-focused physical examination, anthropometry, and phlebotomy (for assessment of CVD risk factors) were performed at each examination cycle of the FHS and at the baseline visit of the JHS. Participants were defined as having diabetes if they had non-fasting blood glucose ≥200 mg/dL, fasting blood glucose of ≥126 mg/dL, had hemoglobin A1c concentrations ≥6.5% (for JHS only) or were taking medication for diabetes [12]. Smoking history was self-reported, and we defined current smoking as regular cigarette smoking within the prior year.

Statistical Analysis

The assigned BP category was the exposure of interest for all analyses, and follow-up was censored at 12 years after each examination. By using pooled repeated observations [13], FHS participants were eligible to reenter the analyses if they did not have a prevalent CVD event in the follow-up window. We calculated incidence rates (IR) of CVD for each cohort overall, and stratified by age group (<60 years, ≥60 years). Kaplan-Meier plots were produced for each cohort, not accounting for competing risk of non-CVD mortality. To evaluate the associations of each BP category with incident CVD, we used Cox proportional hazards regression models treating category one (“no hypertension by JNC 7 or JNC 8”) as referent. The assumption of proportionality of hazards was tested by assessing the interaction between time to CVD (log-transformed) and BP category, which held for the FHS and for the JHS (after excluding individuals with <1 year of follow-up), $p > 0.05$ for both cohorts. We stratified by baseline examination, and used robust sandwich covariance estimators to account for correlated observations within participants (in FHS only). In multivariable models, we adjusted for age ≥60 years (yes/no), sex, the ratio of total to high-density lipoprotein cholesterol, diabetes (yes/no), and current smoking. In secondary analyses, we adjusted for age as a continuous variable. Effect modification by age group, sex, and diabetes status was tested using multiplicative interaction terms. We then re-tested associations within subgroups of statistically significant effect modifiers.

We performed all analyses separately in FHS and JHS, and then we conducted a meta-analysis to combine results. We used fixed effect models for the meta-analyses to avoid excess leverage from the smaller sample (JHS). As a sensitivity analysis, a random-effects meta-analysis was performed.

To account for four different comparisons with each referent group, a Bonferroni correction was used to adjust our p-values (calculated p-values were multiplied by four) and confidence intervals. Therefore, a 2-sided adjusted p-value of <0.05 (after Bonferroni correction) was used to assess statistical significance for all analyses. All analyses were performed with SAS version 9.3 (Cary, NC).

RESULTS

Characteristics of the study samples are displayed for each cohort (Table 1). Overall, individuals included in this investigation were middle-aged to older, and over half were women. There are several notable differences in baseline characteristics between the FHS and JHS samples, likely representing both demographic differences in the two cohorts and secular trends in cardiovascular risk factors (the baseline JHS examination occurred subsequent to all FHS examination cycles included in this investigation). JHS participants had higher mean body mass index, and were more likely to be women, to have diabetes, and to be receiving medications for treatment of high BP, while smoking was more common in FHS participants. The proportion of participants placed into each of the BP categories also varied substantially between the two cohorts with JHS participants less likely to be free of hypertension (category 1), but substantially more likely to have treated BP of <140/<90 (category 3), likely reflecting observations made in different time periods as noted above.

Incidence of CVD by BP category

CVD events were observed in 1047 of 11,237 individuals (9.3%) in the FHS, and 230 of 2948 participants (7.8%) in the JHS, over mean follow-up times of 11.0 years (range 0-12 years) in FHS and 8.9 years (range 1.1-11.2 years) in JHS. We observed an increased incidence of CVD for each of the BP categories when compared with the referent group that was free of hypertension (Figure 1).

Individuals in category 2 (“needs BP medications by JNC 7, no medications by JNC 8”) had higher absolute IR of CVD in both cohorts compared to those without hypertension (Table 2). Upon multivariable adjustment, these individuals had approximately 90% increased risk of CVD compared to the referent group among FHS participants and in the meta-analyzed results, while the risk in JHS was of borderline statistical significance (Figure 2).

Category 3 participants (“successfully treated by JNC 7, unnecessarily treated by JNC 8”) displayed elevated risk of CVD, with a 2-3 fold higher risk than those with no hypertension in both the FHS and JHS in multivariable-adjusted models (Figure 2). The observed relations with CVD were also elevated for category 5 individuals (“hypertension by JNC 7 and JNC 8”), but were, overall, similar to other BP categories with a 2-3.3-fold higher risk of CVD in multivariable-adjusted analyses (Figure 2).

Individuals in category 4 (“inadequately treated by JNC 7, successfully treated by JNC 8”) had particularly high absolute IR of CVD in the FHS, and the incidence was also elevated in the JHS (Table 2). These relations persisted in multivariable-adjusted Cox models, with a 2.7 to 3.5-fold higher risk of CVD in this group compared with the referent group in both cohorts (Figure 2).

In secondary analyses, we evaluated the associations of BP category with incident CVD after including age as a continuous variable in the multivariable-adjusted model (Supplemental Figure 1) and the results were similar, although the hazard ratios were somewhat lower on average.

Evidence for modification of the effect of BP treatment group on incident CVD was observed for age group (p for interaction 0.0002) and diabetes status (p for interaction 0.009), but not for sex (p for interaction 0.23) in the FHS. In the JHS analyses, no effect modification by age group, diabetes status or sex was observed (p for interaction >0.05 for all).

Effect of Age Group

We performed subgroup analyses stratified by age group. Due to low numbers of individuals in certain BP categories, the statistical power in each cohort was limited (Supplemental Table 2). Among those aged <60 years, we observed similar results in the meta-analysis as we did in the overall analyses, with each BP category demonstrating a statistically significant increase in the hazards of CVD when compared with the referent group, and the highest individual risk was observed for category 4 (“inadequately treated by JNC 7, successfully treated by JNC 8”), Table 3. For those ≥60 years of age, the relative hazards for each BP category were lower due to an increased risk of CVD in the non-hypertensive group

(category 1), Table 2. In the ≥ 60 years of age subgroup, no statistically significant increase in CVD risk was observed for individuals in category 2 (“needs BP meds by JNC 7, no meds by JNC 8”). Individuals in category 3 (“successfully treated by JNC 7, unnecessarily treated by JNC 8”) displayed a 59% increased risk of CVD. Again, the highest hazard ratio was observed for category 4 participants (“inadequately treated by JNC 7, successfully treated by JNC 8”) who demonstrated a 2.6-fold increased risk of CVD (Table 3).

Effect of Diabetes Status

We then stratified by diabetes status, given the statistical evidence of effect modification in the FHS as noted above. The absolute incidence rates were substantially higher for those with diabetes versus those without (Supplemental Table 3). Associations observed in individuals without diabetes were consistent with our overall results. However, the number of participants in each BP category with diabetes was low, and therefore our statistical power to detect statistically significant associations in those with diabetes was limited.

Sensitivity Analyses

In our sensitivity analyses comparing the results from the fixed effect approach to the random effects approach within the meta-analysis, we found that although some of the I^2 statistics for the BP categories indicated a moderate to high degree of heterogeneity between FHS and JHS, the hazard ratios and corresponding confidence intervals from both approaches were identical to the second decimal digit.

We performed further sensitivity analyses in the Framingham sample by adjusting our multivariable models for additional clinical variables including pack years smoking (Supplemental Table 4), lipid treatment, microalbuminuria, and left ventricular hypertrophy (Supplemental Table 5) with only slight changes observed in the effect estimates for the relations between BP category and incident CVD (these additional variables were not available in a substantial proportion of the JHS sample, precluding extension of these sensitivity analyses to that cohort).

DISCUSSION

Using prospective data from two large community-based cohorts, we evaluated the incidence of CVD in individuals whose BP management strategy would change with the adoption of JNC 8 versus JNC 7 Guidelines in whites and blacks. Absolute incidence rates were over 2-fold higher for each BP category when compared with the non-hypertensive referent category, and particularly high absolute incidence rates were observed for the individuals with treated SBP 140-149 mm Hg and DBP <90 mm Hg, a group that is discordant between JNC 7 vs. JNC 8 management strategies. These relations persisted in multivariable models adjusted for standard cardiovascular risk factors. In age-stratified analyses, individuals with treated SBP 140-149 mm Hg and DBP <90 mmHg appeared to be at high risk in both the FHS analyses and the meta-analysis sample regardless of their age group (< 60 vs. ≥ 60 years).

Differences Between Cohorts

The present investigation was conducted in two community-based cohorts: the JHS consisting of black adults living in and around Jackson Mississippi, and the FHS consisting of mostly white individuals of European descent predominantly residing in Massachusetts. However, a direct comparison between racial groups in this study is challenging because of several factors including secular changes in the distribution of risk factors and hypertension treatment between the two cohorts. We included participants from the FHS with baseline examinations in the 1970s, 1980s and 1990s (to enhance our statistical power), while the JHS participants were enrolled beginning in 2000. Increasing awareness and treatment of hypertension over the course of the study period likely contributed to the higher prevalence of hypertension treatment in the JHS, and particularly to the number of participants who achieved on treatment SBP of <140 mm Hg. Relatively high rates of hypertension treatment and of BP control in JHS compared with other predominantly black samples have been reported previously [14]. A healthy survivor bias might also exist when comparing JHS and FHS due to the higher mean age of the JHS sample included in the present investigation. Furthermore, current smoking was more prevalent in FHS participants, whereas the JHS sample had a higher proportion of women. These factors likely explain the lower absolute CVD incidence rates that we observed in the JHS sample in a contemporary time period when compared with the FHS sample where observations used in the present study were accrued over a wider time-window from an earlier era. These data contrast with the most recent population-level data suggesting that blacks have similar rates of coronary heart disease but higher rates of stroke than non-Hispanic whites [15]. Nonetheless, the consistency of our results evaluating the association of the BP groups with CVD in both samples is striking, bearing in mind the effects of secular trends in BP treatment and in racial differences across the two racial groups.

Applicability of Findings to Recent US Guideline Changes

Our findings identify specific BP treatment categories that would be at increased risk assuming full implementation of the JNC 8 Guidelines. Participants with treated SBP of 140-149 mm Hg and DBP <90 mm Hg (category 4) were at particularly high risk in the unadjusted and multivariable-adjusted analyses, and these findings were consistent when restricted to those individuals 60 years of age or older. The JNC 8 Guidelines recommend against further BP lowering in individuals in this category who are ≥60 years. Our findings suggest that this group is at considerable risk of developing CVD over the next 12 years if left untreated or uncontrolled to a level below 140 mm Hg systolic BP. Future studies and guidelines should seek to define optimal treatment strategies to minimize CVD risk in this group.

The JNC 8 Guidelines also recommend against initiating treatment for individuals with untreated SBP of 140-149 mm Hg and DBP <90 mm Hg (category 2) who are ≥60 years. We observed increased unadjusted incidence rates of CVD in these individuals in both cohorts, and in multivariable-adjusted models in the FHS and the meta-analysis samples. After stratifying by age ≥60 years, no statistically significant associations were observed. However, the number of individuals in this subgroup was small and our statistical power to

detect important associations may have been limited. Therefore, our results neither support nor question the JNC 8 recommendations for this group.

While our findings indicate specific subgroups of hypertensive individuals who may be at particularly high risk of CVD if treated according to the less aggressive JNC 8 recommendations, our study was purely observational. Hence, inferring that these individuals would experience improved outcomes if a different treatment strategy were pursued is speculative and must be further investigated through clinical trials designed to test this premise. Numerous factors might contribute to differences in outcomes according to treated BP levels in our observational study. For example, individuals might be treated less or more aggressively as a consequence of other comorbidities, or by their physician's impression that they would be at increased risk from adverse effects with additional BP lowering. Moreover, pretreatment blood pressure, antihypertensive medication class, and number of BP lowering agents used were not included in our analysis. Furthermore, secular trends in the awareness and treatment of hypertension (driven partly by changing blood pressure treatment guidelines over time) also may partially affect our results. Additionally, in observational studies, hypertension treatment may be a marker of both the chronicity and the severity of BP elevation. Our findings should, therefore, not be interpreted as supporting a more aggressive BP treatment strategy, but rather as demonstrating that groups of individuals remain at considerable residual risk of CVD if they are observed under conditions of a less aggressive (JNC 8) BP-lowering strategy.

Findings in the Context of International Guidelines

While the present investigation focused on recent changes to US hypertension treatment guidelines, it is important to consider our findings within the context of other leading international guidelines. The most recent European Society of Hypertension/European Society of Cardiology Guidelines for the Management of Arterial Hypertension (last revised in 2013) [16] and National Institute for Health and Care Excellence (NICE, published in 2011) [17] both differ substantially from the JNC 8 guideline. Both consider BP treatment targets in the context of other cardiovascular risk factors and global CVD risk assessment. Furthermore, both of these guideline documents describe elderly individuals as being 80 years and while treatment recommendations are less definite for this age group, targets of <140/<90 are recommended for select patients. The recommendation for less aggressive treatment targets for individuals 60 years or older is unique to the JNC 8 guidelines. Our findings indicate that that these individuals are at particularly high risk for CVD if JNC 8 guidelines are followed.

Comparison with Prior Observational Studies

Using registry-level data, Xu *et al* found SBP intensification thresholds >150 mm Hg, but not >140 mm Hg, to be associated with increased risk of CVD over a 10 year period [16]. However, there are a number of differences between this study and the present investigation. In the study by Xu *et al*, all participants had been diagnosed with hypertension and were already treated with at least one antihypertensive medication, which was recently started or intensified. Furthermore, Xu *et al* used the "systolic intensification threshold" as the

exposure variable, which was estimated from the lowest achieved SBP during the assessment period, whereas we categorized participants based on their baseline BP readings.

In a report from the Northern Manhattan Study, Dong *et al* demonstrated elevated risks of stroke in individuals with SBP 140-149 mm Hg compared with those with an SBP <140 mm Hg, consistent with our findings [17]. In their sample, the increased risk was especially profound among Hispanics and non-Hispanic blacks. In the present investigation, we did not observe a higher risk among blacks, but several features of our study samples may explain this finding, as discussed above.

Methodological Considerations

The present investigation was observational in design. Therefore, although we observed a particularly high risk of CVD in individuals with treated SBP of 140-149 mm Hg, we cannot infer that this risk would be modified by more aggressive treatment. Unmeasured confounding and other factors that may affect decisions regarding BP targets in individual patients (detailed above) are likely to partially affect our findings. Despite the relatively large sample sizes, our statistical power was limited to detect differences in outcomes for certain subgroups, especially for those with diabetes. Furthermore, there were too few participants in our sample with CKD and we therefore excluded them from the analyses. Therefore, we cannot assess the outcomes in individuals with diabetes or CKD whose treatment recommendations were changed by JNC 8 Guidelines. Lastly, we categorized individuals using resting blood pressures at the FHS clinic; other techniques such as ambulatory BP monitoring might more accurately reflect true hypertension burden [18]. Notwithstanding these limitations, our study has a number of important strengths, including long-term follow-up, comprehensive ascertainment of outcomes, and the ability to compare results from two large community-based cohorts with different racial and geographic characteristics.

CONCLUSIONS

In two well-characterized community-based samples with long-term follow-up, we observed higher absolute incidence and risk factor-adjusted hazards of CVD in white and black individuals whose treatment recommendations would change based on adoption of the JNC 8 versus JNC 7 recommendations for the treatment of high BP. The risk was particularly high for individuals with treated SBP of 140-149 mm Hg and DBP <90 mm Hg, and was consistent in those 60 years of age or older, and in blacks and whites. Our findings demonstrate the absolute incidence and the relative hazards of CVD for individuals who may be potentially affected by recent changes to BP treatment guidelines, and we identify specific subgroups of hypertensive individuals that would be at substantial residual CVD risk when treated per the JNC 8 guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

a. Cumulative incidence of CVD by blood pressure category in the Framingham Heart Study

b. Cumulative incidence of CVD by blood pressure category in the Jackson Heart Study

Multivariable models adjusted for age (<60 years, ≥60 years), sex, total/HDL cholesterol, diabetes status, and current smoking.

Figure 2.

a. Unadjusted association of blood pressure category with incident CVD

b. Multivariable-adjusted association of blood pressure category with incident CVD

Table 1

Baseline characteristics of the study samples

Characteristics	Framingham Heart Study (n=11,237)	Jackson Heart Study (n=2,948)
Age (years)	46±13	55±11
Women, n (%)	5914 (53)	2027 (69)
Body mass index (kg/m ²)	26.1±4.8	32.2±7.1
Diabetes mellitus, n (%)	438 (4)	593 (20)
Total cholesterol (mg/dL)	205±40	201±40
HDL cholesterol (mg/dL)	52±16	52±14
Current smoking, n (%)	3540 (32)	316 (11)
Systolic blood pressure (mm Hg)	124±17	127±17
Diastolic blood pressure (mm Hg)	78±10	80±10
Hypertension treatment, n (%)	1381 (12)	(59)
Blood pressure categories		
1. No hypertension by JNC 7 or JNC 8, n (%)	8189 (73)	2)
2. Needs BP meds by JNC 7, no meds by JNC 8, n (%)	390 (3)	50 (2)
3. Successfully treated by JNC 7, unnecessarily treated by JNC 8, n (%)	692 (6)	1181 (40)
4. Inadequately treated by JNC 7, successfully treated by JNC 8, n (%)	186 (2)	(5)
5. Hypertension by JNC 7 and JNC 8, n (%)	1780 (16)	621 (21)

Values are mean ± SD for continuous variables and n (%) for categorical variables

HDL indicates high-density lipoprotein; JNC 7, The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [2]; JNC 8, Evidence-Based Guidelines for the Management of Blood Pressure in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee [1]; BP, blood pressure; meds, medications

Table 2

Absolute incidence rates of CVD by blood pressure category

Blood pressure category	Framingham Heart Study		
	Overall (# events/# at risk) n=11,237	Age <60 years (# events/# at risk) n=9417	Age ≥ 60 years (# events/# at risk) n=1820
1. No hypertension by JNC 7 or JNC 8	5.3 (489/8189)	4.3 (358/7354)	15.3 (131/835)
2. Needs BP meds by JNC 7, no meds by JNC 8	14.4 (58/390)	10.8 (28/242)	20.8 (30/148)
3. Successfully treated by JNC 7, unnecessarily treated by JNC 8	18.0 (127/692)	14.4 (65/431)	24.3 (62/261)
4. Inadequately treated by JNC 7, successfully treated by JNC 8	36.7 (61/186)	19.1 (12/63)	47.5 (49/123)
5. Hypertension by JNC 7 and JNC 8	16.8 (312/1780)	13.8 (196/1327)	26.9 (116/453)
Blood pressure category	Jackson Heart Study		
	Overall (# events/# at risk) n=2,948	Age <60 years (# events/# at risk) n=1,861	Age ≥ 60 years (# events/# at risk) n=1,087
1. No hypertension by JNC 7 or JNC 8	2.7 (23/956)	1.5 (10/753)	6.9 (13/203)
2. Needs BP meds by JNC 7, no meds by JNC 8	13.4 (6/50)	9.4 (2/24)	17.0 (4/26)
3. Successfully treated by JNC 7, unnecessarily treated by JNC 8	11.5 (121/1181)	7.0 (40/639)	16.7 (81/542)
4. Inadequately treated by JNC 7, successfully treated by JNC 8	12.7 (16/140)	9.0 (4/48)	14.6 (12/92)
5. Hypertension by JNC 7 and JNC 8	11.8 (64/621)	9.3 (32/397)	16.3 (32/224)

Incidence rates are calculated per 1000 person-years.

Table 3
Meta-analysis of association of blood pressure category with incident CVD stratified by age group

Blood pressure category	Age <60 years HR (95% CI)	p value	I ²	Age ≥60 years HR (95% CI)	p value	I ²
1. No hypertension by JNC 7 or JNC 8	Referent	–	–	Referent	–	–
2. Needs BP meds by JNC 7, no meds by JNC 8	2.33 (1.43, 3.78)	<0.0001	0.00	1.36 (0.86, 2.16)	0.39	0.00
3. Successfully treated by JNC 7, unnecessarily treated by JNC 8	2.89 (2.04, 4.09)	<0.0001	0.00	1.59 (1.13, 2.23)	0.0031	0.36
4. Inadequately treated by JNC 7, successfully treated by JNC 8	3.39 (1.67, 6.89)	<0.0001	0.00	2.61 (1.75, 3.90)	<0.0001	0.00
5. Hypertension by JNC 7 and JNC 8	2.88 (2.30, 3.60)	<0.0001	0.53	1.64 (1.21, 2.20)	0.0001	0.00

HR represents hazards ratio for each group compared with the referent.

Multivariable model is adjusted for sex, total/HDL cholesterol, diabetes status, and current smoking.

A Bonferroni adjustment was used when calculating confidence intervals and p-values to account for multiple comparisons.