Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association®
Learn and Live℠

Progression Is Accelerated From Prehypertension to Hypertension in Blacks

Anbesaw Selassie, C. Shaun Wagner, Marilyn L. Laken, M. LaFrance Ferguson, Keith C. Ferdinand and Brent M. Egan

Hypertension 2011, 58:579-587: originally published online September 12, 2011
doi: 10.1161/HYPERTENSIONAHA.111.177410
Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
Copyright © 2011 American Heart Association. All rights reserved. Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/58/4/579

Subscriptions: Information about subscribing to Hypertension is online at
http://hyper.ahajournals.org//subscriptions/

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail:
journalpermissions@lww.com

Reprints: Information about reprints can be found online at
http://www.lww.com/reprints

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

Progression Is Accelerated From Prehypertension to Hypertension in Blacks

Anbesaw Selassie, C. Shaun Wagner, Marilyn L. Laken, M. LaFrance Ferguson, Keith C. Ferdinand, Brent M. Egan

See Editorial Commentary, pp 546–547

Abstract—Prehypertension is a major risk factor for hypertension. Blacks have more prevalent and severe hypertension than whites, but it is unknown whether progression from prehypertension is accelerated in blacks. We examined this question in a prospective cohort study of 18 865 nonhypertensive persons (5733 black [30.4%] and 13 132 white [69.6%]) aged 18 to 85 years. Electronic health record data were obtained from 197 community-based outpatient clinics in the Southeast United States. Days elapsing from study entry to hypertension diagnosis, mainly blood pressure ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic on 2 consecutive visits established conversion time within a maximum observation period of 2550 days. Cox regression modeling was used to examine conversion to hypertension as a function of race, while controlling for age, sex, baseline systolic and diastolic blood pressures, body mass index, diabetes mellitus, and chronic kidney disease. The covariable adjusted median conversion time when 50% became hypertensive was 365 days earlier for blacks than whites (626 versus 991 days; $P<0.001$). Among covariables, baseline systolic blood pressure 130 to 139 mm Hg (hazard ratio: 1.77 [95% CI: 1.69 to 1.86]) and 120 to 129 mm Hg (hazard ratio: 1.52 [95% CI: 1.44 to 1.60]), as well as age ≥75 years (hazard ratio: 1.40 [95% CI: 1.29 to 1.51]) and 55 to 74 years (hazard ratio: 1.29 [95% CI: 1.23 to 1.35]) were the strongest predictors of hypertension. Additional predictors included age 35 to 54 years, diastolic blood pressure 80 to 89 mm Hg, overweight and obesity, and diabetes mellitus (all $P<0.001$). Conversion from prehypertension to hypertension is accelerated in blacks, which suggests that effective interventions in prehypertension could reduce racial disparities in prevalent hypertension. **(*Hypertension*. 2011;58:579-587.)**

Key Words: prehypertension ■ hypertension ■ race ■ black

In 1939, Robinson and Brucer[1] reported that individuals with blood pressures of 120 to 139/80 to 89 mm Hg were more likely to become hypertensive and die earlier than people with normal blood pressures <120/<80 mm Hg. They labeled this blood pressure range as prehypertension. The Joint National Committee on High Blood Pressure adopted the term prehypertension for the first time in its seventh report (JNC 7) in May 2003. As in 1939, the JNC 7 defined prehypertension by blood pressures 120 to 139/80 to 89 mm Hg.[2,3] Although prehypertension was controversial, several studies confirmed the 1939 report that prehypertension is a risk factor for hypertension and cardiovascular diseases (CVDs).[4] Among people with blood pressure (BP) 130 to 139 mm Hg systolic and/or 85 to 89 mm Hg diastolic (stage 2 prehypertension), the risk of developing hypertension is 3-fold that of normotensives with BP <120/<80 mm Hg.[5–7] The risk of CVD morbidity and mortality is ≈1.6- to 2.0-fold greater in stage 2 prehypertensives than normotensives, even without progression to hypertension.[7]

In the United States, blacks have a higher prevalence of hypertension and associated cardiovascular and renal complications than whites.[8,9] Moreover, even without progression to hypertension, prehypertensive blacks experience more CVD complications than whites.[10] These observations suggest that effective interventions, which lower BP in prehypertensives and retard the progression to hypertension, could potentially reduce black-white health disparities in prevalent hypertension.[3,11] In fact, the International Society on Hypertension in Blacks consensus statement recommends comprehensive lifestyle intervention in blacks with BP ≥115/≥75 mm Hg rather than ≥120/≥80 mm Hg, as in JNC 7.[12]

JNC 7 recommended therapeutic lifestyle change only for prehypertension in the absence of diabetes mellitus and clinical cardiovascular and renal disease.[1] Clinical efficacy

Received June 3, 2011; first decision June 14, 2011; revision accepted July 27, 2011.

From the Divisions of Biostatistics (A.S.) and General Medicine (C.S.W., B.M.E.), Department of Medicine, and College of Nursing (M.L.L.), Medical University of South Carolina, Charleston, SC; Beaufort-Jasper-Hampton Comprehensive Health Services (M.L.F.), Beaufort, SC; Division of Cardiology (K.C.F.), Department of Medicine, Emory University, Atlanta, GA.

Correspondence to Anbesaw Selassie, Department of Medicine, Medical University of South Carolina, 135 Ashley Ave, Charleston, SC 29425. E-mail selassie@musc.edu

© 2011 American Heart Association, Inc.

Hypertension **is available at http://hyper.ahajournals.org** **DOI: 10.1161/HYPERTENSIONAHA.111.177410**

Downloaded from http://hyper.ahajournals.org at FMRP SKANFO INC on October 17, 2011

studies document that lifestyle changes, for example, the Dietary Approaches to Stop Hypertension, lower BP in nonhypertensive persons, especially blacks.[13] However, adoption of healthy nutrition and physical activity patterns are limited in the US population whose dietary patterns have become less Dietary Approaches to Stop Hypertension–like as body mass index (BMI) and prevalent obesity have risen.[14,15]

These observations suggest that adoption of lifestyle interventions is limited in the population and that a large proportion of individuals with stage 2 prehypertension progress to hypertension within 4 years. Thus, safe and effective pharmacological options emerge as a logical complement to therapeutic lifestyle change for reducing prevalent hypertension.[3] If blacks with prehypertension progress to hypertension at a faster rate than whites, then the rationale for studying pharmacological interventions in this high-risk group would be strengthened. Although several studies examined progression from prehypertension to hypertension,[5,7,16] none addressed differences between black and white individuals. Our study addresses that important knowledge gap.

Methods

This study used the Outpatient Quality Improvement Network Hypertension Initiative database.[17] The Outpatient Quality Improvement Network captures data on patients from the Southeast United States who are receiving health care at practices with electronic health record systems. Data collection is facilitated through a business associate agreement with each clinic. The agreement addresses the Health Insurance Portability and Accountability Act regulations and includes a provision for use of deidentified data for research. The data file includes patient demographics (age, race, and sex), visits and visit dates, vital signs, diagnoses and procedure codes, medications, and laboratory data. The source of race information retrieved from the electronic health record was not specified. This study was approved by the Medical University of South Carolina Institutional Review Board.

This study examined differences in conversion rates between non-Hispanic blacks and non-Hispanic whites in a prospective observational cohort design. Patients were selected from among 1 720 242 patients seen at participating practices between January 1, 2003, and December 31, 2007. Subjects were eligible for this study if they were 18 to 85 years old and had ≥4 visits with a valid BP measurement over a period ≥2 years.

Patients were excluded if they had initial BP values ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic, a diagnosis of hypertension (*International Classification of Diseases, 9th Revision, Clinical Modification* [ICD-9-CM] 401 to 405), or prescription for antihypertensive medication. Persons with a history of active drug or alcohol abuse (ICD-9-CM 303 to 305), major psychiatric illness (ICD-9-CM 290 to 299), or malignancy (ICD-9-CM 140 to 208) were excluded. Persons with missing race, Hispanic ethnicity, or who did not meet inclusion criteria were excluded. Figure 1 depicts derivation of the study sample.

Recruitment was open ended and began January 1, 2003, and closed December 31, 2007. Data collection for patients enrolled during this 5-year period ended on December 31, 2009, which yielded a maximum observation period of 2550 days.

The primary end point was conversion from nonhypertensive, that is, normal BP (<120/<80 mm Hg) or prehypertension (120 to 139/80 to 89 mm Hg), to hypertensive status. From the electronic health record, new-onset hypertension was defined by the following: (1) systolic BP ≥140 mm Hg and/or diastolic BP ≥90 mm Hg on 2 consecutive visits; (2) new ICD-9-CM 401 to 405 diagnosis of hypertension; or (3) initiation of antihypertensive treatment identified from the medical chart. The prehypertensive BP range was divided into stage 1 prehypertension with BP 120 to 129 mm Hg systolic and/or 80 to 84 mm Hg diastolic and stage 2 prehypertension with SBP 130 to 139 mm Hg and/or DBP 85 to 89 mm Hg.[7] Based on the empirical joint distribution of systolic and diastolic BP values, 9 nonhypertensive BP categories were defined including normal BP and 8 categories of prehypertension to determine their influence on progression to hypertension.

The number of days elapsing from study entry to hypertension conversion established the survival time. The main independent variable, race, was obtained from demographic information in the electronic health record. For some patients living in South Carolina without race in the electronic health record, this information was obtained from the State Office of Research and Statistics Uniform Billing claims database. Race was categorized as black or white with exclusion of other race/ethnicity groups including Hispanic and unknown.

BMI (in kilograms per meter squared) was calculated. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate <60 mL/1.7 m^2 per minute or history of CKD (ICD-9-CM codes 403, 404, and 585). Diabetes mellitus was defined by ICD-9-CM code 250 and/or prescriptions for insulin or oral antidiabetic medications.

Data analyses were conducted with SAS software package (SAS version 9.03, Cary, NC).[18] Descriptive statistics for group comparisons included *t* tests for continuous variables and χ^2 for proportions. The relationship between the dependent variable (conversion to hypertension) and various risk factors or independent variables was examined as a function of time using survival analysis. Variables with bivariate association *P* values ≤0.20 were included in the multivariable model. Multicollinearity among covariates was evaluated by assessing deviations of regression coefficients and their SEs in the fitted univariate and multivariate models,[19] and none was detected. Covariates were entered simultaneously into the model. Age-adjusted Kaplan-Meier survival curves graphically presented the relationship of the cumulative proportion of conversions to hypertension among blacks and whites. A log-rank test was used to test the homogeneity of survival curves across racial strata.[20] *P* values <0.05 were considered significant.

Cox proportional hazards regression was used to estimate the prognostic influence of race on conversion to hypertension, while simultaneously controlling for the confounding effect of covariates. This model estimates the instantaneous relative risk of conversion to hypertension averaged over the entire time of follow-up. The proportional hazard assumption was tested with the goodness-of-fit χ^2 test, which compares the observed and expected survival probabilities, and by graphic means using the log-log Kaplan-Meier curves.[21] The heterogeneity of the stratum-specific hazard ratios (HRs) between systolic BP and conversion across the various stages of diastolic BP as proposed by Breslow and Day[22] for analysis of cohort data were used.[23] Adjusted HRs and 95% CIs are reported.

Results

In this study, 18 865 individuals (Figure 1) were followed through the end point of hypertension or the end point of 2550 days. Nonhypertensive subjects who met exclusion criteria except for race unknown or other than black or white (N=12 868) were younger, more likely to be men, overweight, and normotensive and to have CKD and diabetes mellitus and were less likely to have normal weight and BPs (data not shown, all *P* values <0.01). A total of 12 045 patients (63.8%) progressed to clinical hypertension. Significant differences were identified between converters and nonconverters in all of the covariables but sex (Table 1). The mean age of the cohort was 48.5 years (SD: ±15.7 years), 43% were obese, and 27.4% were diabetic. Converters were significantly older than nonconverters.

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

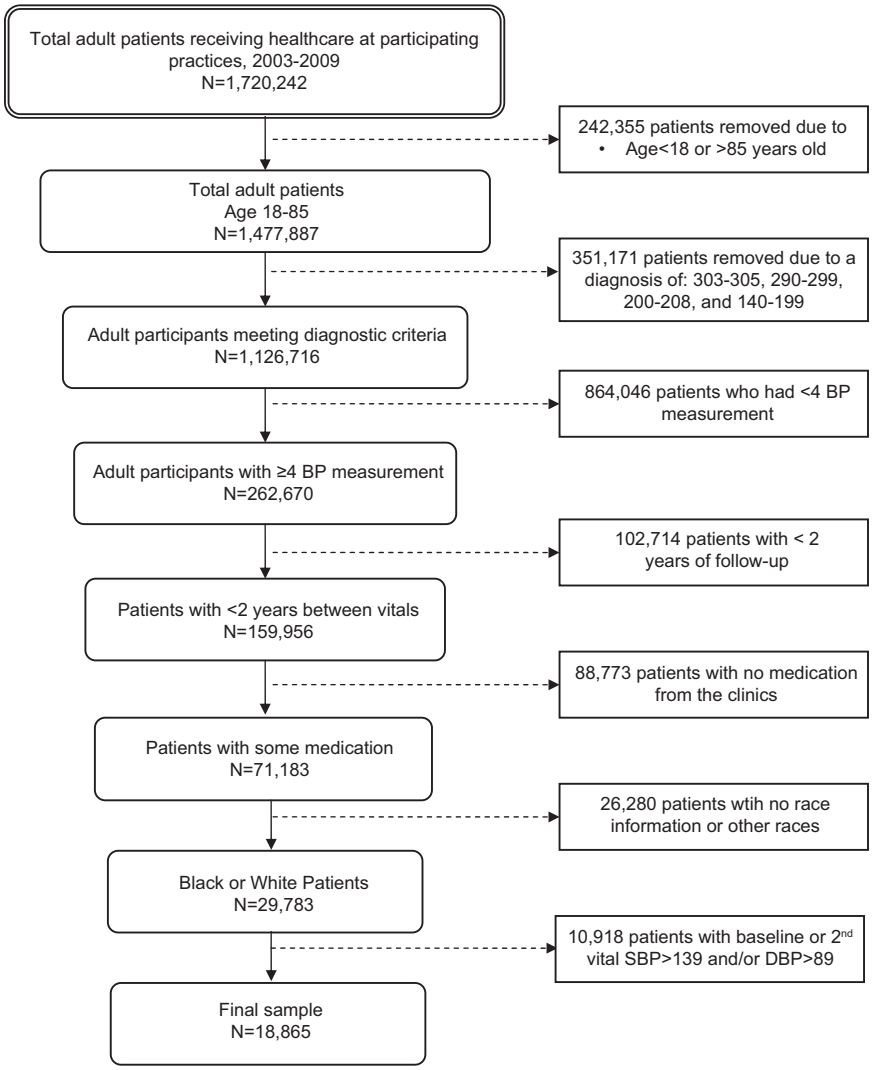

Figure 1. The stepwise process is shown by which the final sample of 18 865 nonhypertensive black and white subjects was selected from a total sample of 1 720 242 patients seen at participating network practices during 2003–2009.

Table 2 shows the baseline prevalence of prehypertension in this nonhypertensive cohort. Within this cohort, 28% were normotensive, 27.2% had stage 1 prehypertension (120 to 129/80 to 84 mm Hg), and 45.2% had stage 2 prehypertension (130 to 139/85 to 89 mm Hg).[7] Significant group differences were observed in several nonmodifiable covariables with patients who were black, male, older, diabetic, and with CKD having a higher prevalence of stage 2 prehypertension. BMI was the only readily modifiable covariable examined. There was a positive linear gradient of baseline stage 2 hypertension status with increasing BMI, with the highest rate (52.4%) among grade III obesity and the lowest (25.6%) among underweight individuals. All of the patients with CKD and 72% with diabetes mellitus had stage 2 prehypertension at baseline. Table 3 summarizes results of multivariable Cox proportional hazard regression analyses and risk of conversion to hypertension over 7-year follow-up. Crude risk ratios were larger than adjusted ratios, which indicates confounding effects of covariables in the model. The overestimation eliminated by adjusting for other covariables ranged from 62.0% for CKD to 3.2% for sex. Blacks had greater risk of conversion to hypertension than whites (HR: 1.35 [95% CI: 1.30 to 1.40]) after adjusting for covariables. The strongest predictor of conversion was stage 2 systolic prehypertension followed by stage 1 systolic prehypertension. The risk of progressing to hypertension increased with advancing age. Patients who ere ≥75 years old had 46% higher risk of conversion than those aged 18 to 34 years ($P<0.001$).

Persons with stage 2 and stage 1 diastolic prehypertension had significantly elevated risk of conversion independent of other covariables. Unlike stage 2 and stage 1 systolic prehypertension, risk for conversion to hypertension did not differ between stage 2 and stage 1 diastolic prehypertension.

Compared with individuals with normal BMI (18.5 to <25 kg/m^2), risk of new-onset hypertension rose with increasing BMI category (Table 3). Underweight was associated with a lower mean estimate of conversion to hypertension, although this was not statistically significant. CKD and diabetes mellitus increased risk of new-onset hypertension.

Table 4 shows the empirical distribution of 9 groups of nonhypertensive individuals and risk of each group for conversion to hypertension. The largest group is composed of isolated systolic prehypertension with 20% stage 1 and 16% stage 2. Generally, the higher the stage of prehypertension, the greater was the risk of new-onset hypertension. With

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

Table 1. Demographic and Clinical Characteristics of Prehypertension Cohorts by Conversion Status

Characteristics	Conversion Status: Converted (n=12 045), n (%)	Conversion Status: Unconverted (n=6820), n (%)	Total (N=18 865), n (%)
Race			
Black	4171 (34.6)	1562 (22.9)	5733 (30.4)
White	7874 (65.4)	5258 (77.1)	13132 (69.6)
Sex*			
Male	7471 (38.0)	4163 (39.0)	11634 (61.7)
Female	4574 (62.0)	2657 (61.0)	7231 (38.3)
Age group, y			
≥75	817 (6.8)	450 (6.6)	1267 (6.7)
55 to 74	3757 (31.2)	1911 (28.0)	5668 (30.1)
35 to 54	4159 (34.5)	2031 (29.8)	6190 (32.8)
18 to 34	3312 (27.5)	2428 (35.6)	5740 (30.4)
Age, mean (SD)	49.2 (±15.7)	47.2 (±16.1)	48.5 (±16.0)
Baseline systolic BP, mm Hg			
130 to 139 (stage 2 prehypertension)	5980 (49.7)	2083 (30.5)	8063 (42.7)
120 to 129 (stage 1 prehypertension)	2996 (24.9)	1612 (23.6)	4608 (24.4)
≤119 (normal systolic BP)	3069 (25.5)	3125 (45.8)	6194 (32.8)
Baseline systolic BP, mean (SD)	125.5 (±11.1)	119.6 (±13.0)	123.4 (±12.2)
Baseline diastolic BP, mm Hg			
85 to 89 (stage 2 prehypertension)	2404 (20.0)	702 (10.3)	3106 (16.5)
80 to 84 (stage 1 prehypertension)	2661 (22.1)	256 (18.4)	3917 (20.8)
≤79 (normal diastolic BP)	6980 (58.0)	4862 (71.3)	11842 (62.7)
Baseline diastolic BP, mean (SD)	75.9 (±9.1)	72.5 (±9.4)	74.7 (±9.3)
Average of quarterly BMI			
Obesity grade III (≥40.0)	1301 (10.8)	447 (6.6)	1748 (9.3)
Obesity grade II (35.0 to 39.0)	1764 (14.7)	811 (11.9)	2575 (13.7)
Obesity grade I (30.0 to 34.0)	3344 (27.8)	1734 (25.4)	5078 (26.9)
Overweight (25.0 to 29.0)	3509 (29.1)	2125 (31.2)	5634 (29.9)
Normal weight (18.5 to 24.0)	2073 (17.2)	1640 (24.1)	3713 (19.7)
Underweight (≤18.4)	54 (0.5)	63 (0.9)	117 (0.6)
BMI, mean (SD)	31.6 (±8.0)	29.8 (±7.1)	30.9 (±7.7)
Chronic kidney disease			
Yes	183 (1.5)	35 (0.5)	218 (1.2)
No	11862 (98.5)	6785 (99.5)	18647 (98.8)
Diabetes mellitus			
Yes	3684 (30.6)	1490 (21.9)	5174 (27.4)
No	8361 (69.4)	5330 (78.2)	13691 (72.6)

BMI indicates body mass index; BP, blood pressure.

*Data show significant differences between converters and nonconverters for all characteristics but sex ($P<0.01$).

normotensives (group 0, reference), a biological gradient was noted with progressive covariate-adjusted increasing risk from group 1 (normal systolic BP, stage 1 diastolic prehypertension), to group 8 (stage 2 systolic and diastolic prehypertension [linear trend of HR $P<0.001$]).

The 9 stages of nonhypertension indicated a transadditive effect of systolic and diastolic BPs on risk for hypertension. For example, patients with stage 2 systolic and diastolic prehypertension (group 8) had an HR for future hypertension of 2.42, which was greater than the sum of the separate components of isolated stage 2 systolic and isolated stage 2 diastolic prehypertension (HR: 1.75+1.21 [respectively]=1.96), as shown in Table 3. The small difference between the crude and adjusted HRs, expressed as crude/adjusted, indicate that the degree of confounding by covariables was <4% for all 9 grades of prehypertension. The differences in crude and adjusted HRs using the 9 groups were smaller than ratios using only 3 groups, that is, normal BP, stage 1 prehypertension, and stage 2 prehypertension (Table 3).

Figure 2 shows age-adjusted Kaplan-Meier probability curves of incident hypertension (percentage remaining nonhypertensive) by race over 2550 days. The probability of blacks and whites remaining hypertension free separated during the first few months. The median conversion time [$S(T)_{50}$] (where S indicates survival; T, time) of blacks was 365 days earlier than whites (626 versus 991; $P<0.001$). Similarly, at the midpoint or 1250 days, 65% of blacks had already converted to hypertension compared with 54% of the whites. By end or censoring point of day 2550, ≈70% of blacks and 56% of whites had converted.

Discussion

The principal study finding is that black race, as recorded in the electronic health record, is associated with an accelerated risk of new-onset hypertension. Our findings are based on community practice–based electronic health record system data and included adjustments for several confounding clinical and demographic covariables. In addition to race, several other clinical characteristics were independently associated with new-onset hypertension, including age, baseline systolic

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

Table 2. Demographic and Clinical Characteristics of the Cohort by Baseline BP Status

BP Category	Stage 2 pHTN	Stage 1 pHTN	Normal BP	P*
No.	8535 (45.24)	5134 (27.2)	5196 (27.5)	
Race				<0.001
Black	2824 (49.3)	1439 (25.1)	1470 (25.6)	
White	5711 (43.5)	3695 (28.1)	3726 (28.4)	
Sex				<0.001
Male	3507 (48.5)	1910 (26.4)	1814 (25.1)	
Female	5028 (43.2)	3224 (27.7)	3382 (29.1)	
Age group, y				<0.001
≥75	574 (45.3)	329 (26.0)	364 (28.7)	
55 to 74	2834 (50.0)	1401 (24.7)	1433 (25.3)	
35 to 54	2855 (46.1)	1678 (27.1)	1657 (26.8)	
18 to 34	2272 (39.6)	1726 (30.1)	1742 (30.4)	
Age, mean (SD)	49.2 (±15.7)	47.2 (±16.1)	48.5 (±16.0)	
Systolic BP, mm Hg	133.4±5.7	121.6±5.1	108.4±8.1	
Diastolic BP, mm Hg	79.0±8.6	75.5±6.8	66.6±7.0	
Average of quarterly BMI				<0.001
Obesity grade III (≥40.0)	915 (52.4)	398 (22.8)	435 (24.9)	
Obesity grade II (35.0 to 39.0)	1339 (52.0)	650 (25.2)	586 (22.8)	
Obesity grade I (30.0 to 34.0)	2451 (48.3)	1387 (27.3)	1240 (24.2)	
Overweight (25.0 to 29.0)	2448 (43.5)	1554 (27.6)	1632 (29.0)	
Normal weight (18.5 to 24.0)	1352 (36.4)	1119 (30.1)	1242 (33.5)	
Underweight (≤18.4)	30 (25.6)	26 (22.2)	61 (52.1)	
BMI, mean (SD)	31.8 (±7.8)‡	30.3 (±7.4)	30.1 (±7.8)	
Chronic kidney disease				<0.001†
Yes	218 (100.0)	0 (0.0)	0 (0.0)	
No	8317 (44.6)	5134 (27.5)	5196 (27.9)	
Diabetes mellitus				<0.001
Yes	3705 (71.6)	196 (3.8)	1273 (24.6)	
No	4830 (35.3)	4938 (36.1)	3923 (28.7)	

Data are No. (%), unless otherwise specified. pHTN indicates prehypertension; BMI, body mass index in kilograms per meter squared; BP, blood pressure.

*Data show the log likelihood ratio χ^2 test.

†Data show the Fisher exact test.

‡Only stage 2 is significantly different in BMI.

and diastolic BPs, BMI, CKD, and diabetes mellitus. These findings are consonant with previous reports on risk factors in prehypertension for CVD.[10,24–30] The dose-dependent risk of conversion noted with increasing BMI from underweight to grade III obesity is consistent with studies linking obesity and adiposity to the pathophysiology of elevated BP and hypertension.[31–33]

Another novel study finding was the transadditivity of systolic and diastolic BPs when both values were examined simultaneously as predictors of new-onset hypertension (Table 4). A biological gradient of risk was observed, which corresponded with the 8 categories of prehypertension when systolic and diastolic BPs are considered simultaneously rather than the 3 separate stages of systolic and diastolic pressures. Moreover, the difference between unadjusted and adjusted crude rates was reduced when 9 rather than 3 categories of nonhypertensive systolic and diastolic BP values were considered (Table 3). Thus, considering systolic and diastolic BPs simultaneously substantially reduces the confounding by covariables that occurs when systolic or diastolic pressures are examined separately. Although both systolic and diastolic prehypertension increase the risk of conversion to hypertension, the influence of systolic appears stronger. The stronger relationship of systolic than diastolic to cardiovascular events has also been reported, especially for people ≥50 years old.[2,34–36]

Isolated stage 1 and 2 systolic prehypertension with normal diastolic (grades 2 and 5) accounted for 36% of prehypertensive subjects in our cohort. Nearly two thirds of adults with isolated systolic prehypertension were ≥55 years of age, which is consistent with the notion that age-related arterial stiffening,[37,38] possibly reflecting or coincident with age-related increase in salt-sensitivity of BP,[16] contributes to prehypertension and progression to hypertension.[39]

In this study, blacks had a 35% greater risk of conversion to hypertension than whites after adjustment for multiple covariables (Table 3). Moreover, the median, age-adjusted conversion time when 50% of the group became hypertensive occurred after only ≈1.7 years of follow-up in blacks as compared with ≈2.7 years in whites (Figure 2). The median conversion time in our study, which did not have standardized BP measurements or visits frequencies, is comparable to the 2.2 years reported for the predominantly white stage 2 prehypertensives in the Trial of Preventing Hypertension (TROPHY), a rigorous clinical trial.[3] The longer median conversion time for whites in our study than the overall TROPHY is expected, because our report included stage 1 prehypertensive and normotensive individuals. On the other hand, patients with diabetes mellitus at baseline were at greater risk for incident hypertension, and TROPHY excluded these patients.

As noted, JNC 7 recommended therapeutic lifestyle change only for most individuals with prehypertension. Although lifestyle interventions, for example, Dietary Approaches to Stop Hypertension, are efficacious in lowering BP in nonhypertensive individuals,[13] adoption in the population is limited.[15] Even in a relatively intensive clinical efficacy study (Trials of Hypertension Prevention), the relative reduction in progression to hypertension over 4 years was ≈15%, with an absolute reduction of 6% to 7%.[40] The relative risk reduction for de novo hypertension over 4 years was virtually identical to TROPHY patients 2 years after angiotensin receptor blockade was discontinued.[5] At

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

Table 3. Univariable and Multivariable Adjusted Hazard Ratios of De Novo Hypertension

	Hazard Ratio (95% CI)		
Characteristics	Crude	Adjusted	*P* (Adjusted)
Race			
Black	1.41 (1.36 to 1.42)	1.35 (1.30 to 1.40)	<0.001
White	Reference	Reference	
Sex			
Male	0.97 (0.93 to 1.00)	0.94 (0.91 to 0.98)	0.001
Female	Reference	Reference	
Age group, y			
≥75	1.33 (1.23 to 1.44)	1.46 (1.30 to 1.58)	<0.001
55 to 74	1.32 (1.27 to 1.39)	1.32 (1.26 to 1.38)	<0.001
35 to 54	1.29 (1.23 to 1.44)	1.19 (1.14 to 1.25)	<0.001
18 to 34	Reference	Reference	
Base systolic BP, mm Hg			
130 to 139 (stage 2 prehypertension)	2.02 (1.94 to 2.11)	1.75 (1.67 to 1.84)	<0.001
120 to 129 (stage 1 prehypertension)	1.53 (1.46 to 1.61)	1.50 (1.42 to 1.58)	<0.001
≤119 (normal)	Reference	Reference	
Base diastolic BP, mm Hg			
85 to 89 (stage 2 prehypertension)	1.63 (1.56 to 1.71)	1.21 (1.15 to 1.28)	<0.001
80 to 84 (stage 1 prehypertension)	1.27 (1.22 to 1.33)	1.18 (1.13 to 1.24)	<0.001
≤79 (normal)	Reference	Reference	
Average of quarterly BMI, kg/m^2			
Obesity grade III (≥40.0)	1.63 (1.52 to 1.75)	1.42 (1.32 to 1.52)	<0.001
Obesity grade II (35.0 to 39.0)	1.39 (1.30 to 1.48)	1.23 (1.16 to 1.32)	<0.001
Obesity grade I (30.0 to 34.0)	1.27 (1.20 to 1.34)	1.16 (1.09 to 1.22)	<0.001
Overweight (25.0 to 29.0)	1.17 (1.11 to 1.23)	1.10 (1.04 to 1.16)	0.001
Underweight (≤18.4)	0.78 (0.59 to 1.02)	0.85 (0.65 to 1.12)	0.243
Normal weight (18.5 to 24.9)	Reference	Reference	
Chronic kidney disease			
Yes	1.91 (1.65 to 2.21)	1.18 (1.02 to 1.37)	0.034
No	Reference	Reference	
Diabetes mellitus			
Yes	1.32 (1.27 to 1.37)	1.11 (1.06 to 1.17)	<0.001
No	Reference	Reference	

BMI indicates body mass index; BP, blood pressure.

the 2-year time point when angiotensin receptor blockers were discontinued, the active treatment group developed hypertension at approximately one third of the rate of the placebo group (relative risk: 0.34 [95% CI: 0.25 to 0.44]; $P<0.001$). Only 79 of 772 evaluable patients in TROPHY were black, which limits assessment of black-white differences in response to treatment.

Study Limitations

This prospective cohort study relied on data in several different electronic health record systems obtained from a variety of outpatient clinical settings in the Southeast United States. Race ascertainment was not standardized. Unlike the National Health and Nutrition Examination Surveys, BP measurements were not standardized and likely included multiple suboptimal practices.[8,39] Unlike population studies, for example, the Framingham Heart Study, time between visits was not standardized. Of note, the Framingham report on incident hypertension was based on a single follow-up visit 4 years after baseline assessment.[5] Nonhypertensive patients excluded from the analysis for race unknown or other than black or white differed by age, sex, weight, BP category, and prevalence of diabetes and CKD. For these and other reasons, our sample and findings may not represent the broader population of nonhypertensive individuals. On the other hand, the data reflect findings in contemporary medical practice among a diverse group of clinical sites in the Southeast United

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

Table 4. Hazard Ratios of De Novo Hypertension by Various Combinations of Nonhypertensive Systolic and Diastolic BP Values

Grades of Prehypertension, (SBP)/(DBP), mm Hg	Total (n=18 865), n (%)	Conversion Status: Converted (n=12 045), n (%)	Conversion Status: Unconverted (n=6820), n (%)	Crude HR (95% CI)*	Adjusted HR (95% CI)*†
Grade 8, (130 to 139)/(85 to 89)	831 (4.4)	675 (81.2)	156 (18.8)	2.47 (2.27 to 2.69)	2.42 (2.23 to 2.64)
Grade 7, (130 to 139)/(80 to 84)	2440 (12.9)	1816 (74.4)	624 (25.6)	2.17 (2.04 to 2.30)	2.16 (2.03 to 2.29)
Grade 6, (120 to 129)/(85 to 89)	477 (2.5)	352 (73.8)	125 (26.2)	2.06 (1.84 to 2.30)	2.07 (1.85 to 2.32)
Grade 5, (130 to 139)/(≤79)	2996 (15.9)	2201 (73.5)	795 (26.5)	2.15 (2.03 to 2.28)	2.06 (1.94 to 2.18)
Grade 4, (≤119)/(85 to 89)	100 (0.5)	77 (77.0)	23 (23.0)	2.24 (1.79 to 2.81)	2.29 (1.82 to 2.87)
Grade 3, (120 to 129)/(80 to 84)	2098 (11.1)	1455 (69.4)	643 (30.7)	1.84 (1.72 to 1.96)	1.87 (1.75 to 2.00)
Grade 2, (120 to 129)/(≤79)	3751 (19.9)	2420 (64.5)	1331 (35.5)	1.61 (1.52 to 1.70)	1.59 (1.51 to 1.68)
Grade 1, (≤119)/(80 to 84)	905 (4.8)	545 (60.2)	360 (39.8)	1.43 (1.30 to 1.57)	1.47 (1.34 to 1.61)
Grade 0, (≤119)/(≤ 79)	5267 (28.0)	2504 (47.5)	2763 (52.5)	Referent	Referent

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, hazard ratio; BP, blood pressure.
*Data show *P* value for trend <0.001.
†Data were adjusted for age, race, sex, BMI, diabetes mellitus, and chronic kidney disease.

States. Despite limitations, black race was associated with an accelerated transition from nonhypertensive to hypertensive status, with 50% transitioning to hypertension in only 1.7 years versus 2.7 years in whites. The finding of racial differences in progression from hypertension to prehypertension does not necessarily implicate biological differences but can include sociocultural and economic factors.[41,42]

Our study findings are potentially relevant to national health goals for reducing prevalent hypertension and improving health equity. Healthy People 2000 and 2010 included a goal to reduce the prevalence of hypertension in the US population from 29% to 16%.[8,43,44] Despite JNC 7 efforts to facilitate a reduction of incident hypertension by resurrecting the 1939 term "prehypertension,"[1] the lifestyle-only focus in prehypertension has limited effectiveness in the population.[13,14] Perhaps in recognizing this reality, Healthy People 2020 set a more realistic goal of reducing prevalent hypertension to 26.9% for all race groups. Even this dilutional goal is unlikely to be obtained among blacks, who had an age-adjusted hypertension prevalence of 37.9% in 2007–2008,[8] without a safe, widely adopted, and effective pharmacological intervention for slowing the rapid progression from prehypertension to hypertension. Given the excess of prevalent hypertension and related complications in blacks,[9] their accelerated transition from prehypertension to hypertension, and greater risk of CVD complications even in the absence of progression,[10] this is an opportune time for clinical effectiveness trials addressing these critical issues.

Perspectives

Public health efforts over the past 20 years, focused mainly on therapeutic lifestyle change, have not succeeded in reduc-

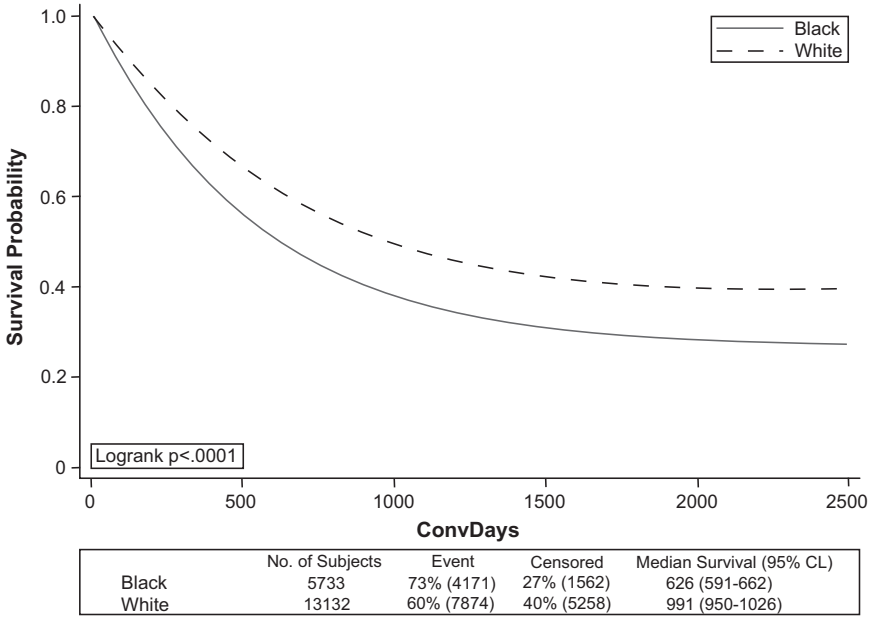

Figure 2. The age-adjusted probability of remaining nonhypertensive is depicted separately for black and white adults 18 to 85 years of age who were not hypertensive at time 0.

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

ing prevalent hypertension or racial differences in prevalent hypertension. Most hypertension progresses from the prehypertensive stage, but it was not known whether blacks with prehypertension progress to hypertension faster than whites. Our study indicates that progression to hypertension is significantly faster in blacks than whites with prehypertension. These findings raise the possibility that effective interventions in prehypertension could reduce incident hypertension and associated racial differences with longer-term potential to reduce the magnitude of prevalent hypertension and its impact on health disparities.

Sources of Funding

This work was supported by the state of South Carolina, US Army grant W81XWH-10-2-0057, National Institutes of Health Clinical Translational Science Award 1UL1RR029882, National Institutes of Health grant HL091841, National Institutes of Health grant DK067615, the American Society of Hypertension, and the South Carolina Department of Health and Environmental Control.

Disclosures

K.C.F. is on the Speakers' Bureau at AstraZeneca (less than $10 000), Novartis (less than $10 000), Forest (less than $10 000), and Daiichi-Sankyo (less than $10 000); has received honoraria from AstraZeneca (more than $10 000), Novartis (more than $10 000), and Forest (more than $10 000); and is a consultant/advisory board member for AstraZeneca (less than $10 000), Novartis (less than $10 000), and Forest (less than $10 000). B.M.E. has received grant support from Daiichi-Sankyo (more than $50 000), Novartis (more than $50 000), and Takeda (more than $50 000); is a lecturer with honoraria on continuing medical education–accredited programs for the American Society of Hypertension Carolinas-Georgia-Florida Chapter (more than $10 000), International Society of Hypertension in Blacks (more than $10 000); and is a consultant for NicOx (less than $10 000).

References

1. Robinson S, Brucer M. Range of normal blood pressure: a statistical and clinical study of 11,383 persons. *Arch Int Med*. 1939;64:409–444.
2. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.
3. Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, Black HR, Grimm RH Jr, Messerli FH, Oparil S, Schork MA. Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med*. 2006;354:1685–1697.
4. Egan BM, Julius S. Prehypertension: risk stratification and management considerations. *Curr Hypertens Rep*. 2008;10:359–366.
5. Leitschuh M, Cupples LA, Kannel W, Gagnon D, Chobanian A. High-normal blood pressure progression to hypertension in the Framingham Heart Study. *Hypertension*. 1991;17:22–27.
6. Winegarden CR. From "prehypertension" to hypertension? Additional evidence. *Ann Epidemiol*. 2005;15:720–725.
7. Egan B, Lackland D, Jones DW. Pre-hypertension: an opportunity for a new public health paradigm. In: Mensah GA, eds. *Cardiology Clinics: Hypertension and Hypertensive Heart Disease*. Philadelphia, PA: Saunders; 2010;561–569.
8. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988–2008. *JAMA*. 2010;303:2043–2050.
9. Mensah GA. Eliminating disparities in cardiovascular health: six strategic imperatives and a framework for action. *Circulation*. 2005;111:1332–1336.
10. Kshirsagar AV, Carpenter M, Bang H, Wyatt SB, Colindres RE. Blood pressure usually considered normal is associated with an elevated risk of cardiovascular disease. *Am J Med*. 2006;119:133–141.
11. Chobanian AV. Prehypertension revisited. *Hypertension*. 2006;48:812–814.
12. Flack JM, Sica DA, Bakris G, Brown AL, Ferdinand KC, Grimm RH Jr, Hall WD, Jones WE, Kountz DS, Lea JP, Nasser S, Nesbitt SD, Saunders E, Scisney-Matlock M, Jamerson KA. Management of high blood pressure in blacks: an update of the International Society on Hypertension in Blacks consensus statement. *Hypertension*. 2010;56:780–800.
13. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure: DASH Collaborative Research Group. *N Engl J Med*. 1997;336:1117–1124.
14. Ford ES, Zhao G, Li C, Pearson WS, Mokdad AH. Trends in obesity and abdominal obesity among hypertensive and nonhypertensive adults in the United States. *Am J Hypertens*. 2008;21:1124–1128.
15. Mellen PB, Gao SK, Vitolins MZ, Goff DC Jr. Deteriorating dietary habits among adults with hypertension: DASH dietary accordance, NHANES 1988–1994 and 1999–2004. *Arch Intern Med*. 2008;168:308–314.
16. Weinberger MH, Fineberg NS. Sodium and volume sensitivity of blood pressure: age and pressure change over time. *Hypertension*. 1991;18:67–71.
17. Egan B, Laken M, Wagner C, Mack S, Seymour-Edwards K, Dodson J, Zhao Y, Lackland DT. Impacting population cardiovascular health through a community-based practice network: update on an ASH-supported collaborative. *J Clin Hypertension (Greenwich)*. 2011;13:543–550.
18. SAS Institute Inc. *Statistical Analytical Software. Version 9.1.3*. Cary, NC: SAS Institute Inc; 2010.
19. Darlington GA. Collinearity. In: Armtage P, Colton T, eds. *Encyclopedia of Biostatistics*. Chichester, United Kingdom: John Wiley & Sons; 1998:788–789.
20. Allison PD. Estimating and comparing survival curves with proc lifetest. In: The SAS Institute I, ed. *Survival Analysis Using the SAS System: A Practical Guide*. 1st ed. Cary, NC: SAS Institute, Inc; 1995:29–59.
21. Kleinbaum DG. Evaluating the proportional hazards assumption. In: Kleinbaum DG. *Survival Analysis: A Self-Learning Text*. 1st ed. New York, NY: Springer-Verlag; 2010:130–166.
22. Breslow NE, Day NE. Modelling the relaionship between risk, dose, and time. In: International Agency for Research on Cancer, ed. *Statistical Method in Cancer Research: The Design and Analysis of Cohort Data*. Lyon, France: Oxford University Press; 1987:232–270.
23. Greenland S. Applications of stratified analysis methods. In: Rothman KJ GSLT, ed. *Modern Epidemiology*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2008:283–302.
24. Egan BM. Should metabolic syndrome patients with prehypertension receive antihypertensive therapy? In: Bakris GL, ed. *Therapeutic Strategies in Hypertension*. Oxford, United Kingdom: Clinical Publishing; 2006:9–25.
25. Hsia J, Margolis KL, Eaton CB, Wenger NK, Allison M, Wu L, LaCroix AZ, Black HR. Prehypertension and cardiovascular disease risk in the Women's Health Initiative. *Circulation*. 2007;115:855–860.
26. Liszka HA, Mainous AG III, King DE, Everett CJ, Egan BM. Prehypertension and cardiovascular morbidity. *Ann Fam Med*. 2005;3:294–299.
27. Ogden LG, He J, Lydick E, Whelton PK. Long-term absolute benefit of lowering blood pressure in hypertensive patients according to the JNC VI risk stratification. *Hypertension*. 2000;35:539–543.
28. Tsai SP, Wen CP, Chan HT, Chiang PH, Tsai MK, Cheng TY. The effects of pre-disease risk factors within metabolic syndrome on all-cause and cardiovascular disease mortality. *Diabetes Res Clin Pract*. 2008;82:148–156.
29. Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, Levy D. Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med*. 2001;345:1291–1297.
30. Zhang Y, Lee ET, Devereux RB, Yeh J, Best LG, Fabsitz RR, Howard BV. Prehypertension, diabetes, and cardiovascular disease risk in a population-based sample: the Strong Heart Study. *Hypertension*. 2006;47:410–414.
31. Bogaert YE, Linas S. The role of obesity in the pathogenesis of hypertension. *Nat Clin Pract Nephrol*. 2009;5:101–111.
32. Hall JE, Jones DW, Kuo JJ, da SA, Tallam LS, Liu J. Impact of the obesity epidemic on hypertension and renal disease. *Curr Hypertens Rep*. 2003;5:386–392.

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011

33. Jones DW, Kim JS, Andrew ME, Kim SJ, Hong YP. Body mass index and blood pressure in Korean men and women: the Korean National Blood Pressure Survey. *J Hypertens*. 1994;12:1433–1437.
34. Smulyan H. Clinical studies and therapeutic trials in systolic hypertension. *Pathol Biol (Paris)*. 1999;47:752–759.
35. Benetos A, Thomas F, Bean K, Gautier S, Smulyan H, Guize L. Prognostic value of systolic and diastolic blood pressure in treated hypertensive men. *Arch Intern Med*. 2002;162:577–581.
36. Qureshi AI, Suri MF, Kirmani JF, Divani AA, Mohammad Y. Is prehypertension a risk factor for cardiovascular diseases? *Stroke*. 2005;36:1859–1863.
37. Smulyan H, Safar ME. Systolic blood pressure revisited. *J Am Coll Cardiol*. 1997;29:1407–1413.
38. Smulyan H, Safar ME. The diastolic blood pressure in systolic hypertension. *Ann Intern Med*. 2000;132:233–237.
39. Whyte JL, Lapuerta P, L'Italien GJ, Franklin SS. The challenge of controlling systolic blood pressure: data from the National Health and Nutrition Examination Survey (NHANES III), 1988–1994. *J Clin Hypertens (Greenwich)*. 2001;3:211–216.
40. The Trials of Hypertension Prevention Collaborative Research Group. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure: the Trials of Hypertension Prevention, phase II. *Arch Intern Med*. 1997;157:657–667.
41. Link CL, McKinlay JB. Disparities in the prevalence of diabetes: is it race/ethnicity or socioeconomic status? Results from the Boston Area Community Health (BACH) Survey. *Ethn Dis*. 2009;19:288–292.
42. Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. *Ann N Y Acad Sci*. 2010;1186:69–101.
43. National Center for Health Statistics. *Healthy People 2000 Final Review*. http://www.cdc.gov/nchs/data/hp2000/hp2k01.pdf. 2001. Accessed March 23, 2010.
44. Healthy People 2010. *Heart Disease and Stroke*. http://www.cdc.gov/dhdsp/docs/hp2010.pdf. 2010. Accessed May 6, 2010.

Downloaded from http://hyper.ahajournals.org/ at FMRP SKANFO INC on October 17, 2011