

Blood Pressure and the Risk of Developing Diabetes in African Americans and Whites

ARIC, CARDIA, and the Framingham Heart Study

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OBJECTIVE—We examined the association between high blood pressure and incident type 2 diabetes in African Americans and whites aged 35–54 years at baseline.

RESEARCH DESIGN AND METHODS—We combined data from the Atherosclerosis Risk in Communities (ARIC) study, the Coronary Artery Risk Development in Young Adults (CARDIA) study, and the Framingham Heart Study offspring cohort. Overall, 10,893 participants (57% women; 23% African American) were categorized by baseline blood pressure (normal, prehypertension, hypertension) and examined for incident diabetes (median follow-up 8.9 years).

RESULTS—Overall, 14.6% of African Americans and 7.9% of whites developed diabetes. Age-adjusted incidence was increasingly higher across increasing blood pressure groups (*P* values for trend: <0.05 for African American men; <0.001 for other race-sex groups). After adjustment for age, sex, BMI, fasting glucose, HDL cholesterol, and triglycerides, prehypertension or hypertension (compared with normal blood pressure) was associated with greater risks of diabetes in whites (hazard ratio [HR] for prehypertension: 1.32 [95% CI 1.09–1.61]; for hypertension: 1.25 [1.03–1.53]), but not African Americans (HR for prehypertension: 0.86 [0.63–1.17]; for hypertension: 0.92 [0.70–1.21]). HRs for developing diabetes among normotensive, prehypertensive, and hypertensive African Americans versus normotensive whites were: 2.75, 2.28, and 2.36, respectively (*P* values <0.001).

CONCLUSIONS—In African Americans, higher diabetes incidence among hypertensive individuals may be explained by BMI, fasting glucose, triglyceride, and HDL cholesterol. In whites, prehypertension and hypertension are associated with greater risk of diabetes, beyond that explained by other risk factors. African Americans, regardless of blood pressure, have greater risks of developing diabetes than whites.

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Age, race, and adiposity are well-established risk factors for type 2 diabetes (1,2). Other cardiometabolic traits such as hypertension, fasting

blood glucose, and lipid levels have also been identified as independent variables in clinical predication models (3). Recently, hypertension has further emerged

as a potential risk factor based on several longitudinal studies' findings that higher blood pressure is associated with increased risk of diabetes (4–9). These studies, however, all had limitations. Some relied on self-reported diabetes or blood pressure (4,5,7). Some were single-sex studies (4,5,7). All but one had few or no African American participants (4,5,7–9). Most also lacked information on important baseline characteristics, such as fasting glucose, lipid profile, or waist circumference, that could confound the relationship (4–9). It thus still remains unclear whether hypertension is associated with diabetes above and beyond known risk factors. Large longitudinal studies are needed to further examine this issue, especially in order to more precisely estimate the association in African Americans, a population with disproportionate levels of hypertension and diabetes.

We therefore conducted pooled analyses using individual participant-level data from three large well-characterized community-based cohort studies in the U.S. Together, the Atherosclerosis Risk in Communities (ARIC) study, the Coronary Artery Risk Development in Young Adults (CARDIA) study, and the Framingham Heart Study provide a rich resource to examine whether higher blood pressure is a risk factor for new-onset diabetes in middle-aged African American and white persons in the community.

RESEARCH DESIGN AND METHODS

ARIC is a longitudinal study of 15,792 adults aged 45–64 years at enrollment in 1987–1989 in four communities: Forsyth County, NC; Jackson, MS (African Americans only); the northwestern suburbs of Minneapolis, MN; and Washington County, MD. Participants attended three subsequent examinations approximately every 3 years (1990–1992; 1993–1995; and 1996–1999).

CARDIA is a longitudinal study investigating 5,115 African American and white men and women aged 18–30 years

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at enrollment in 1985–1986 in four communities: Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA. Participant recruitment was approximately balanced on age, sex, race, and education status at each community. Six subsequent examinations were conducted (1987–1988, 1990–1991, 1992–1993, 1995–1996, 2000–2001, and 2005–2006).

The offspring cohort of the Framingham Heart Study began in 1971–1975, enrolling 5,124 offspring and spouses of the offspring of the Framingham Heart Study's original cohort. The offspring cohort participants were aged 5–70 years at their first examination. They were next examined 8 years later and then about every 4 years through the seventh examination, followed by the eighth examination approximately 6.5 years later (2005–2008).

Details of these three studies have been reported elsewhere (10–12). The studies were approved by their institutional review boards of the participating institutions. All participants provided written informed consent at each examination.

Participants

Initial eligibility criteria for these analyses included participants aged 35–54 years old and nondiabetic (defined as fasting blood glucose <126 mg/dL, and no prior history of and not on medication for diabetes) at their index or “baseline” examination (as detailed below). This yielded 12,119 participants: 8,170 from ARIC, 2,111 from CARDIA, and 1,838 from the Framingham Heart Study. Participants were further excluded if they were not African American or white ($n = 30$); failed to return for follow-up or did not have at least one follow-up visit to determine diabetes status ($n = 709$); or at the index examination were either pregnant ($n = 12$), did not fast >8 h ($n = 330$), or had missing data on systolic (SBP) or diastolic blood pressure (DBP) or any of the following cardiometabolic traits: fasting blood glucose, insulin, HDL cholesterol (HDL-C), or triglycerides, waist circumference, or BMI ($n = 232$). After these exclusions, 10,893 participants remained eligible. Those excluded were more likely to be African American (40.5 vs. 23.4%), not finished high school (21.1 vs. 12.4%), have higher SBP (mean 119 vs. 116 mmHg), and prevalence of hypertension (28.1 vs. 21.5%), consume more alcohol (mean 4.8 vs. 3.8 drinks/week), and be a smoker (40.8 vs. 25.2%).

For CARDIA and the Framingham Heart Study offspring cohort, their fifth

examination cycle (conducted in 1995–1996 and 1991–1995, respectively) was considered the index examination, for an approximate follow-up period of 10 and 14 years, respectively. These were chosen over prior examinations to ensure a more contemporary sample while allowing for sufficient follow-up of approximately 1 decade. Because the most recent ARIC exam occurred in 1996–1999, its first examination (conducted in 1987–1989) was considered the index examination, for 9 years of follow-up.

Assessment of blood pressure, covariates, and incident diabetes

Blood pressure was measured with participants seated after a 5-minute rest using a random-zero mercury sphygmomanometer in ARIC and CARDIA, and a standard mercury-column sphygmomanometer in the Framingham Heart Study. The average of two readings was used. Three mutually exclusive blood pressure categories were established: hypertension was defined if SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, or reported use of antihypertensive medication; prehypertension was defined as not having hypertension, and SBP 120–139 mmHg or DBP 80–89 mmHg; normal included SBP <120 mmHg and DBP <80 mmHg and not using antihypertensive medication.

Height, weight, and waist circumference were measured with participants in light clothing. BMI was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured at the level of the umbilicus in ARIC and the Framingham Heart Study, and at the level of the smallest waist circumference in CARDIA. Self-reported information included race, education level, parental history of diabetes (one or both parents with diabetes), smoking status, alcohol use, and physical activity. Participants were instructed to fast overnight before providing blood specimens for measuring glucose, lipid, and insulin levels.

Participants were considered to have incident diabetes if any of the following was present at a follow-up examination: fasting blood glucose ≥ 126 mg/dL, casual blood glucose ≥ 200 mg/dL, or using insulin or oral hypoglycemic medication. Time-to-diabetes was estimated using a previously described method by Duncan et al. (13). For cases ascertained based on blood glucose value, the incident date was estimated by linear interpolation using the glucose values at the ascertaining

and previous examinations. For cases ascertained based on the use of diabetic medications, the time-to-diabetes was estimated by using their fasting glucose at the earlier visit and a slope estimated using information from all diabetic subjects who had been unaware of their status (because the fasting glucose at ascertainment for those who were on diabetic medication may have been affected by their knowledge of their diabetes status).

Statistical analysis

Baseline characteristics by study were examined using simple means and proportions. General linear models were used to compare characteristics by blood pressure categories after adjustment for age and sex (regression models for continuous traits and Poisson regression for categorical traits). In multivariable analyses, triglycerides were natural-log transformed because of their skewed distribution.

Diabetes incidence was calculated using person-years of observation. Age-specific rates were first calculated and then weighted to the standard year 2000 U.S. population to derive age-adjusted incidence rates by race, sex, and blood pressure category. Confidence intervals and trend tests across blood pressure category within race and sex groups were estimated using 2,000 bootstrap resamples. A standard normal distribution in the rates was assumed because the bias between the sample population estimates and the mean of the bootstrap estimates was less than 1%.

Proportional hazards models were fitted to assess the association of blood pressure category with incident diabetes. Tests for effect modification by sex were evaluated in race-specific models that adjusted for age and sex, whereas effect modification by race was tested in age-, race-, and sex-adjusted models. Effect modification by study was also tested. Nonproportionality of hazards over time was tested in race-specific models using time-dependent covariates for the blood pressure categories.

For multivariable analyses, Cox proportional hazards models were constructed to calculate the hazard ratio (HR) and 95% CIs to compare incident diabetes across blood pressure categories, using normal blood pressure as the reference group. The base model adjusted for age and sex. The second model then added BMI. The third, considered our primary model, further adjusted for fasting glucose, HDL-C, and triglyceride. Fasting

glucose was included to account for its potential confounding effect on blood pressure and incident diabetes because its levels were positively associated with increasing blood pressure categories in both race groups. The fourth model included a longer list of cardiometabolic risk factors by also introducing fasting insulin and waist circumference. To directly compare the racial differences in the association of blood pressure and incident diabetes, we also combined both races in multivariable analyses with race-specific blood pressure categories using normotensive whites as the referent group.

Sensitivity analyses included constructing models with additional groups of covariates or varying the exclusion criteria. The additional covariates included: current smoking, alcohol use, class of antihypertensive drugs, and physical activity level, as well as education level and parental history of diabetes. Finally, because those with higher blood pressure also tend to have higher fasting glucose level, which is a strong predictor of diabetes, we performed separate multivariable analyses after lowering our exclusion threshold for baseline fasting glucose to 110 mg/dL from 126 mg/dL (i.e., excluding individuals with borderline elevated levels at the index examination).

Antihypertensive medications were classified into one of four categories: β -blockers, thiazides, ACE inhibitors or angiotensin-receptor blockers, or other single-agent medications. Combination or multiple medications were sorted into nonmutually exclusive categories (for example, someone taking a β -blocker and thiazide was included in each of those two drug classes). Questionnaires assessing physical activity were not standardized across studies. Therefore, each study's physical activity summary score (sum of leisure, sport, and work activity scores in ARIC and CARDIA, and total physical activity in kilocalories over the past year in Framingham) was standardized (mean = 0, SD = 1) for analytic purposes. To achieve a normal distribution in the Framingham physical activity score, natural-log transformation of the original score was performed. All analyses were performed using SAS 9.1 (Cary, NC).

RESULTS

Baseline characteristics

More than half (57%) were women. Nearly one-quarter (23.4%) were African Americans, all from ARIC and CARDIA.

Mean age (SD) in years in CARDIA, ARIC, and Framingham Heart Study were 37.7 (1.72), 49.9 (3.15), and 47.5 (5.00), respectively (Supplementary Table A). Table 1 shows that at baseline, within each race increasingly higher blood pressure categories were significantly associated with lower educational level, HDL-C, and physical activity scores, as well as older age, higher fasting glucose, triglycerides and insulin levels, and greater waist circumference, BMI, and alcohol consumption. Higher blood pressure was also associated with higher proportion of men, current smoker, and parental history of diabetes in whites. Overall, whites had more favorable profiles in blood pressure, adiposity, fasting glucose and insulin levels, prevalence of smoking, and education, whereas African Americans had more favorable lipid levels.

Incident diabetes

During median follow-up of 8.9 years, 14.6% ($n = 372$; 239 women) of African Americans and 7.9% ($n = 657$; 271 women) of whites developed diabetes. Within each race-sex group, age-adjusted rates were increasingly higher across baseline blood pressure categories, with the incidence lowest in the normal blood pressure group and highest in the hypertension group (Fig. 1) (P values for trend: <0.05 for African American men; <0.001 for other race-sex groups). The rates ranged from 2.8 per 1,000 person-years in normotensive white women to 28.9 per 1,000 person-years in hypertensive African American women.

Multivariable analyses

The assumption of proportionality of hazards was confirmed. Race-stratified multivariable analyses were performed because tests for race-by-blood-pressure-category interactions were significant (P values-for-interaction for prehypertension and hypertension: 0.004 and 0.003, respectively). Within race-specific models, effect modification by sex was not present (P values-for-interaction for prehypertension and hypertension: 0.68 and 0.92 in African Americans, and 0.37 and 0.052 in whites, respectively); therefore, sex-pooled models were used for all analyses. In models with interaction terms for study-by-blood-pressure-category, none of the terms approached statistical significance ($P \geq 0.194$).

The age- and sex-adjusted HR for diabetes among African Americans (Table 2) with hypertension was 1.95 (95% CI

1.50–2.54), using normal blood pressure group as the referent; the risk was not significant for prehypertension ($P = 0.23$). After further adjusting for BMI, the diabetes risk associated with hypertension was attenuated but remained statistically significant (HR 1.48 [95% CI 1.13–1.94]); but when fasting glucose, HDL-C, and triglyceride levels were added, the effect was further attenuated and there was no longer a significant association (0.92 [0.70–1.21]).

Among whites (Table 2), after adjusting for age and sex, compared with normal blood pressure group, hypertension had a more than threefold increased risk of developing diabetes (HR 3.26 [95% CI 2.70–3.94]), and prehypertension had a twofold increased risk (1.99 [1.64–2.41]). These associations remained statistically significant, though attenuated, after also adjusting for BMI, fasting glucose, HDL-C, and triglyceride levels (HR for prehypertension: 1.32 [95% CI 1.09–1.61]; for hypertension: 1.25 [1.03–1.53]).

The race-specific results remained similar even when the modeling included additional baseline covariates (first, waist circumference and fasting insulin; then also antihypertensive drug class, smoking, alcohol, and physical activity; and finally also education level and parental history of diabetes). Statistically significant associations between prehypertension or hypertension and incident diabetes were again observed in whites only (Supplementary Table B). Of note, in the multivariable analyses no antihypertensive drug class was significantly associated with incident diabetes (results not shown).

In race-combined primary multivariable model (i.e., adjusting for age, sex, BMI, fasting glucose, HDL-C, and triglyceride) using normotensive whites as referent, the HR (95% CI) for developing diabetes in normotensive, prehypertensive, and hypertensive African Americans were 2.75 (2.14–3.53), 2.28 (1.76–2.95), and 2.36 (1.93–2.90), respectively, and in prehypertensive and hypertensive whites were 1.36 (1.12–1.65) and 1.33 (1.10–1.62), respectively. A similar pattern was observed after additionally adjusting for other differences in baseline characteristics: education, fasting insulin, waist circumference, smoking, alcohol, and parental history of diabetes (results not shown).

When repeating our primary multivariable model after lowering the baseline exclusion glucose cut point to 110 mg/dL

Table 1—Age- and sex-adjusted means or proportions of baseline characteristics by race and blood pressure category* at baseline

	African American			White			P for trends	P for trends	White	P	
	Normal BP	Prehypertension	Hypertension	Normal BP	Prehypertension	Hypertension					
	n	n	n	n	n	n					
n	954	663	935	4,970	1,968	1,403			2,552	8,341	
Age (years)	43.8 (6.1)	46.2 (5.9)	48.7 (4.8)	47.0 (5.6)	48.4 (5.1)	50.1 (4.0)	<0.001	<0.001	46.2 (6.0)	47.9 (5.4)	<0.001
Women (%)	66.4	56.4	63.8	60.7	45.0	50.3	0.511	<0.001	62.9	55.2	<0.001
Education < HS (%)	18.1	21.7	25.2 (0.5)	7.0	6.7	9.1	<0.001	0.006	24.1	8.4	<0.001
SBP (mmHg)	107.0 (7.5)	123.7 (7.3)	134.8 (21.0)	105.6 (8.3)	124.6 (6.7)	131.3 (17.5)	<0.001	<0.001	122.7 (18.8)	114 (15.2)	<0.001
DBP (mmHg)	69.1 (6.2)	80.2 (5.9)	87.5 (12.5)	66.9 (6.9)	77.9 (6.4)	81.7 (10.7)	<0.001	<0.001	79.2 (11.8)	71.8 (9.9)	<0.001
HDL-C (mg/dL)	55.5 (16.2)	56.3 (18.8)	53.2 (17.1)	52.1 (16.0)	51.0 (15.4)	48.3 (15.8)	0.005	<0.001	54.3 (17.2)	51.4 (16.0)	<0.001
Triglycerides (mg/dL)†	77.7 (48.5)	84.4 (89.6)	97.5 (72.7)	97.1 (67.5)	113.3 (92.9)	130.5 (112.0)	<0.001	<0.001	89.6 (71.1)	104.6 (85.0)	<0.001
Fasting glucose (mg/dL)	94.2 (9.5)	95.8 (9.8)	98.6 (10.4)	94.8 (8.6)	96.5 (9.1)	98.8 (9.5)	<0.001	<0.001	97.1 (10.3)	95.6 (9.1)	<0.001
Fasting insulin (μU/mL)	11.9 (7.6)	13.2 (8.8)	16.4 (11.1)	8.3 (5.2)	10.4 (7.5)	13.4 (9.7)	<0.001	<0.001	13.9 (9.5)	9.7 (7.0)	<0.001
WC (cm)	90.1 (13.3)	94.9 (14.3)	99.4 (15.9)	89.6 (12.7)	94.1 (13.5)	98.3 (14.6)	<0.001	<0.001	96 (15.4)	91.8 (13.9)	<0.001
BMI (kg/m ²)	27.4 (5.6)	29.5 (6.2)	31.2 (6.8)	25.5 (4.1)	27.4 (4.9)	29.0 (5.7)	<0.001	<0.001	29.4 (6.4)	26.5 (4.8)	<0.001
Alcohol (drinks/week)	2.7 (8.3)	3.4 (8.9)	3.8 (8.2)	3.7 (6.5)	4.6 (8.1)	4.4 (8.1)	0.006	0.001	3.4 (8.4)	4 (7.2)	0.001
Current smoker (%)	30.7	31.5	28.7	25.8	19.7	20.6	0.459	<0.001	31.0	23.6	<0.001
Parent history of DM (%)	28.7	26.2	28.4	21.3	24.1	24.7	0.901	0.025	28.0	22.6	<0.001
Physical activity‡	0.12 (0.97)	0.09 (0.98)	-0.06 (0.97)	0.07 (0.98)	-0.04 (1.00)	-0.06 (0.99)	<0.001	<0.001	0.04 (0.98)	0.03 (0.99)	0.508

Data are mean (SD) or percent, unless otherwise indicated. SD is from the unadjusted distribution. BP, blood pressure; DM, diabetes; HS, high school; WC, waist circumference. * Blood pressure categories: normal, SBP <120 and DBP <80 mmHg and not using antihypertensive medication; prehypertension, not hypertension and SBP 120–139 or DBP 80–89 mmHg; hypertension, SBP ≥140, DBP ≥90 mmHg, or using antihypertensive medication. †Exponent of log transformed triglycerides, therefore is approximately the median of the distribution of log (triglycerides). ‡SP value from a simple linear contrast. ‡‡Data are z scores. Each study's physical activity measures were normalized to that study's population. A higher z score means a greater physical activity level of that participant relative to others in the same study. For example, a z score of 1.96 means that that participant was more physically active than ~95% of the participants in that study.

from 126 mg/dL, the significant associations persisted among whites (HR for prehypertension: 1.42 [95% CI 1.11–1.82]; HR for hypertension: 1.52 [1.17–1.98]). In African Americans, there was now a trend toward higher risk of diabetes in prehypertension group (1.18 [0.80–1.73]) and a marginally statistically significant association in hypertension group (1.44 [1.01–2.05]), which was no longer significant after additionally adjusting for fasting insulin and waist circumference (P value 0.062). In a race-pooled multivariable model with baseline glucose <110 mg/dL and using normotensive whites as referent, the race-by-blood-pressure-category interaction terms were not significant (P values >0.395).

CONCLUSIONS—Middle-aged African Americans and whites with higher blood pressure are more likely to develop diabetes than those with normal blood pressure. In African Americans, the higher incidence of diabetes among hypertensive individuals may be explained by concomitantly greater adiposity and other cardiometabolic risk factors. In whites, the association of both prehypertension and hypertension with incident diabetes is partially explained by these and other risk factors. Regardless of baseline blood pressure status, African Americans have a greater risk of developing diabetes than whites.

Only one prior ARIC publication from a decade ago included substantial numbers of African Americans when studying the relationship between blood pressure and new-onset diabetes; however, race-specific results were not presented (6). We found significant race-by-blood-pressure-category interaction for incident diabetes in our primary analysis, thus needing separate analyses by race. Although after accounting for age- and sex-differences hypertensive African Americans were more than twice as likely to develop diabetes as normotensive African Americans, after further adjusting for baseline BMI, fasting glucose, HDL-C, and triglyceride levels, the effect size was greatly attenuated and no longer significant. For whites, our finding validates prior reports that high blood pressure is a risk factor for diabetes (4,5,9). This finding is in contrast to a recent paper from the San Antonio Heart Study, where no association between prehypertension and diabetes was observed in 2,767 Mexican Americans and non-Hispanic white participants after multivariable analysis

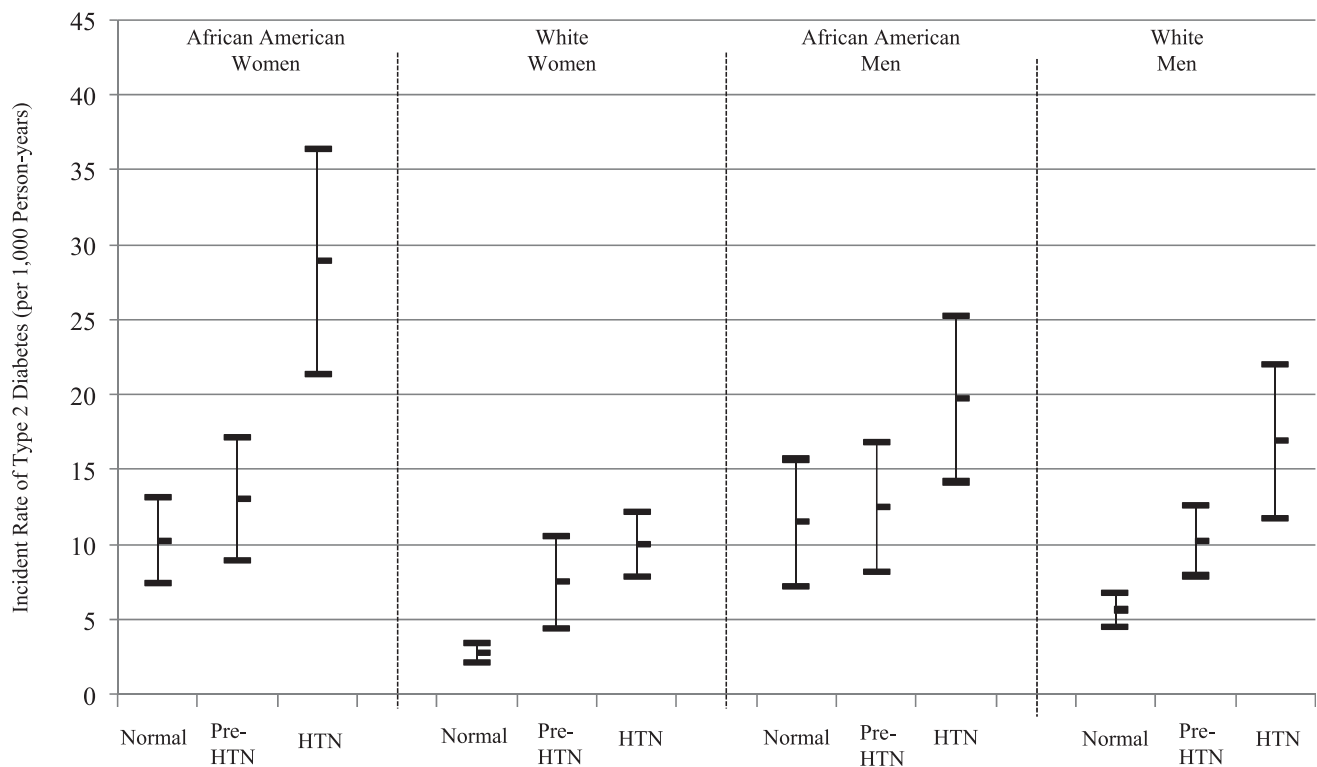


Figure 1—Age-adjusted rate of incident diabetes and 95% CI by baseline blood pressure category, sex, and race. Rate per 1,000 person-years, age-adjusted to the year 2000 standard population; 95% CI from normal approximation after 2,000 bootstrap samples. P values for trend all race and sex groups <0.0001 , except for African American men, for which P value for trend was 0.0219. Normal blood pressure: SBP <120 and DBP <80 mmHg and not using antihypertensive medication; prehypertension: not hypertension and SBP 120–139 or DBP 80–89 mmHg; and hypertension: SBP ≥ 140 , DBP ≥ 90 mmHg, or using antihypertensive medication. HTN, hypertension.

(14). Although their age-, sex-, and race-adjusted model of prehypertension was associated with incident diabetes, it was no longer significant after further adjusting for BMI, impaired glucose tolerance, insulin resistance and secretion, and family history. However, the multivariable-adjusted odds ratio of incident diabetes for prehypertension versus normal blood pressure at 1.42 (95% CI 0.99–2.02) was comparable to that of our prehypertensive whites.

African Americans generally have higher levels of cardiovascular risk factors than whites except for lipid profile (15,16). Even after we accounted for these differences, the racial variation in the association between blood pressure and incident diabetes persisted. However, when lowering the exclusion-criteria threshold for baseline fasting glucose to 110 mg/dL, the positive results in whites remained robust, whereas trends toward positive associations were newly observed in African Americans. In a race-pooled model with this lower exclusion cutpoint and using normotensive whites as referent, the race-by-blood pressure-category interaction

terms also became no longer significant. Taken together, this suggests that the null association from our primary analyses of African Americans may have been largely driven by their higher overall baseline glucose levels.

Although African Americans are known to have greater risks of developing diabetes than whites, potentially modifiable factors including obesity, education, physical inactivity, smoking, alcohol, and dietary intake have accounted for only about half of the disparity (2). We further found that this disparity cannot be explained by African Americans' higher prevalence of prehypertension and hypertension. Even after accounting for racial differences in several risk factors, their risk of diabetes remained higher than whites across all blood pressure categories. Notably, education is a limited proxy for socioeconomic status, and other measures such as income and healthcare access are needed. Higher fasting insulin levels may be one potential biological mechanism to explain the excess incidence of diabetes, though only in nonobese African American women (17). Future studies

should investigate additional factors such as insulin sensitivity, inflammation, and endothelial dysfunction, the pathways of which, like insulin resistance, are shared by hypertension and diabetes (13,18–20).

Strengths of the present article include the large sample size, multiethnic sample, measured instead of self-reported blood pressure and blood glucose; and extensive data on potential confounders. Limitations should be recognized. First, as with all observational studies, residual confounding cannot be ruled out. Second, the African American participants were only from ARIC and CARDIA. In ARIC, $>90\%$ of the African Americans were recruited from one site (Jackson, MS). Given the nonoverlapping age-range between ARIC and CARDIA participants, we did not test whether African Americans differ between these studies. Though possible that the observed race-and-blood pressure interaction might have been confounded by racial differences in geographical distribution, CARDIA included balanced biracial cohorts from four other cities, making this concern less likely. Third, whether causal relationship exists

Table 2—HRs for the association of baseline prehypertension and hypertension with incident diabetes

	African American			White		
	HR	95% CI	P value	HR	95% CI	P value
N (events)	2,552 (372)			8,341 (657)		
Model 1*						
Age (5 years)	1.35	(1.22–1.49)	<0.001	1.23	(1.13–1.33)	<0.001
Women	1.04	(0.84–1.29)	0.693	0.61	(0.53–0.72)	<0.001
Prehypertension	1.20	(0.89–1.63)	0.229	1.99	(1.64–2.41)	<0.001
Hypertension	1.95	(1.50–2.54)	<0.001	3.26	(2.70–3.94)	<0.001
Model 2†						
Age (5 years)	1.40	(1.27–1.55)	<0.001	1.27	(1.17–1.38)	<0.001
Women	0.84	(0.68–1.05)	0.128	0.62	(0.53–0.72)	<0.001
Prehypertension	1.03	(0.76–1.40)	0.841	1.56	(1.28–1.89)	<0.001
Hypertension	1.48	(1.13–1.94)	0.004	2.02	(1.66–2.47)	<0.001
BMI (5 units)	1.39	(1.30–1.48)	<0.001	1.71	(1.61–1.82)	<0.001
Model 3‡						
Age (5 years)	1.10	(0.98–1.22)	0.095	1.08	(0.99–1.18)	0.081
Women	1.36	(1.07–1.72)	0.011	1.19	(1.00–1.41)	<0.050
Prehypertension	0.86	(0.63–1.17)	0.342	1.32	(1.09–1.61)	<0.005
Hypertension	0.92	(0.70–1.21)	0.540	1.25	(1.03–1.53)	0.026
BMI (5 units)	1.26	(1.17–1.34)	<0.001	1.37	(1.28–1.47)	<0.001
HDL-C (15 mg/dL)	0.89	(0.79–1.00)	0.044	0.72	(0.63–0.81)	<0.001
Glucose (10 mg/dL)	2.89	(2.58–3.24)	<0.001	3.07	(2.81–3.35)	<0.001
Ln(triglycerides)	1.39	(1.10–1.75)	0.006	1.59	(1.34–1.88)	<0.001

*Using normal blood pressure (SBP <120 and DBP <80 mmHg and not using antihypertensive medication) as referent for comparing prehypertension (not hypertension and SBP 120–139 or DBP 80–89 mmHg) and hypertension (SBP ≥ 140, DBP ≥ 90 mmHg, or using antihypertensive medication). Diabetes during follow-up defined as fasting glucose ≥126 mg/dL, casual glucose ≥200 mg/dL, or use of diabetic drugs. †Model 1 + BMI. ‡Model 2 + fasting glucose, HDL, and triglycerides.

and whether treating high blood pressure prevents diabetes are outside the scope of observational studies. Clinical trials unfortunately have also been unable to address this sufficiently. Trials on prehypertension are few and none reported incident diabetes as an outcome (21,22). For hypertension, several meta-analyses of antihypertensive drug trials that reported incident diabetes identified inhibitors of the renin-angiotensin system to lower the risk (23,24). In contrast, other antihypertensive drugs such as β-blockers and diuretics were implicated as putative risk-promoting factors (6,25). Moreover, drug trials have been inherently limited in their inability to distinguish any protective effects of blood pressure-lowering per se from any direct pharmacological effects on diabetes development.

In summary, high blood pressure in middle age is associated with greater likelihood of developing diabetes. In African Americans with hypertension, this association may be explained by greater adiposity and other cardiometabolic risk factors. In whites, both prehypertension and hypertension are associated with increased risk of developing diabetes

beyond that explained by adiposity and other risk factors. Whether lowering blood pressure slows or prevents the onset of diabetes deserves further clinical investigation. Regardless of blood pressure status, African Americans have greater risks of developing diabetes than whites. Future studies are also needed to determine the etiology for the excess risks in African Americans.

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