Association Between Urinary Albumin Excretion and Coronary Heart Disease in Black vs White Adults

Orlando M. Gutiérrez, MD, MMSc; Yulia A. Khodneva, MD, PhD; Paul Muntner, PhD; Dana V. Rizk, MD; William M. McClellan, MD, MPH; Mary Cushman, MD, MSc; David G. Warnock, MD; Monika M. Safford, MD; for the REGARDS Investigators

**IMPORTANCE** Excess urinary albumin excretion is more common in black than white individuals and is more strongly associated with incident stroke risk in black vs white individuals. Whether similar associations extend to coronary heart disease (CHD) is unclear.

**OBJECTIVE** To determine whether the association of urinary albumin excretion with CHD events differs by race.

**DESIGN, SETTING, AND PARTICIPANTS** Prospective cohort study of black and white US adults aged 45 years and older who were enrolled within the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study between 2003 and 2007 with follow-up through December 31, 2009. We examined race-stratified associations of urinary albumin-to-creatinine ratio (ACR) in 2 groups: (1) incident CHD among 23 273 participants free of CHD at baseline; and (2) first recurrent CHD event among 4934 participants with CHD at baseline.

**MAIN OUTCOMES AND MEASURES** Expert-adjudicated incident and recurrent myocardial infarction and acute CHD death.

**RESULTS** A total of 616 incident CHD events (421 nonfatal MIs and 195 CHD deaths) and 468 recurrent CHD events (279 nonfatal MIs and 189 CHD deaths) were observed over a mean time of 4.4 years of follow-up. Among those free of CHD at baseline, age- and sex-adjusted incidence rates of CHD per 1000 person-years of follow-up increased with increasing categories of ACR in black and white participants, with rates being nearly 1.5-fold greater in the highest category of ACR (>300 mg/g) in black participants (20.59; 95% CI, 14.36-29.51) vs white participants (13.60; 95% CI, 7.60-24.25). In proportional hazards models adjusted for traditional cardiovascular risk factors and medications, higher baseline urinary ACR was associated with greater risk of incident CHD among black participants (hazard ratio [HR] comparing ACR >300 vs <10 mg/g, 3.21 [95% CI, 2.02-5.09]) but not white participants (HR comparing ACR >300 vs <10 mg/g, 1.49 [95% CI, 0.80-2.76]) (**P** value for interaction = .03). Among those with CHD at baseline, fully adjusted associations of baseline urinary ACR with first recurrent CHD event were similar between black participants (HR comparing ACR >300 vs <10 mg/g, 2.21 [95% CI, 1.22-4.00]) vs white participants (HR comparing ACR >300 vs <10 mg/g, 2.48 [95% CI, 1.61-3.78]) (**P** value for interaction = .53).

**CONCLUSIONS AND RELEVANCE** Higher urinary ACR was associated with greater risk of incident but not recurrent CHD in black individuals when compared with white individuals. These data confirm that black individuals appear more susceptible to vascular injury.
Increased urinary albumin excretion (generally defined as an albumin-to-creatinine ratio [ACR] ≥30 mg/g) is an important marker of kidney injury and a strong risk factor for cardiovascular disease. Black individuals have higher levels of urinary albumin excretion than white individuals, which may contribute to racial disparities in cardiovascular outcomes. In support of this, in participants of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study free of stroke at baseline, we previously showed that the association of urinary ACR with incident stroke differed by race, such that higher urinary ACR was independently associated with a greater risk of incident stroke in black individuals but not in white individuals. Although these data suggest that higher urinary albumin excretion may be a stronger risk factor for cardiovascular disease events in black individuals than in white individuals, little is known about racial differences in the association of urinary ACR with cardiovascular outcomes apart from stroke events. In particular, no study to our knowledge has specifically examined associations of urinary ACR with both incident and recurrent CHD disease (CHD) differs by race. Accordingly, we examined the associations of ACR with both incident and recurrent CHD events in black and white participants of the REGARDS study.

Methods

Study Participants

The REGARDS study is a population-based investigation of stroke incidence in black and white US adults aged 45 years and older. Details of the study design have been reviewed previously. Briefly, the study was designed to provide approximately equal representation of men and women and oversampled individuals who were black (race/ethnicity was self-reported), as well as individuals living in the US stroke belt (Alabama, Arkansas, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Tennessee). Trained personnel conducted computer-assisted telephone interviews to obtain information including participants’ sociodemographics, cardiovascular risk factors, cigarette smoking, physical activity, and use of medications. Following the interview, certified health professionals conducted an in-home study visit that included an electrocardiograph (ECG) recording and inventory of medications. In addition, fasting blood and urine samples were collected during the in-home visit and shipped to the University of Vermont central laboratory using standardized procedures. The REGARDS study protocol was approved by the institutional review boards governing research in human subjects at the participating centers and all participants provided written informed consent.

Primary Exposure of Interest

The exposure of interest was baseline urinary ACR. Urine albumin was measured by nephelometry using the BNII ProSpec nephelometer (Siemens AG), and urine creatinine was measured by the rate Jaffé method using the Modular-P chemistry analyzer (Roche/Hitachi).

Ascertainment of Outcomes

The outcomes of interest were incident and recurrent CHD events, defined as acute myocardial infarction (MI) or acute CHD death. Suspected CHD events were detected via telephone follow-up with participants every 6 months with corresponding medical records reviewed by 2 expert adjudicators, blinded to ACR results, to validate potential events using published guidelines. For suspected MI, medical records were examined for signs or symptoms of ischemia; an increasing and/or decreasing pattern in cardiac troponin or creatine phosphokinase-MB concentration over 6 or more hours with a peak concentration greater than twice the upper limit of normal; and ECG changes consistent with ischemia, guided by the Minnesota code and classified as evolving diagnostic, positive, nonspecific, or not consistent with ischemia. Define MI was defined as that with diagnostic enzymes or ECG, and probable MI was defined as that with equivocal diagnostic enzymes with a positive but not diagnostic ECG or, if enzymes were missing, with a positive ECG in the presence of ischemic signs or symptoms. Only definite or probable MIs were included as CHD events. Coronary revascularizations were not included, since racial contrasts were a major interest of this study and because of the known relatively low use of these procedures among black individuals. For fatal events, the medical history, hospital records, interviews with next of kin or proxies, and death certificates or National Death Index data were reviewed to adjudicate the cause of death, with definite or probable CHD death used in this analysis (eBox in Supplement for expanded definition). In prespecified analyses, we tested for but did not detect a statistically significant difference in the association of ACR with CHD type (fatal vs nonfatal) by race; therefore, we examined the composite of fatal or nonfatal CHD events as the main outcome.

Covariates of Interest

Age, sex, smoking history, annual family income, and educational attainment were determined by self-report. Systolic blood pressure was defined as the average of 2 seated measures taken after a 3-minute rest. History of CHD was defined as having any of the following: evidence of MI on the baseline ECG, self-report of a prior history of a cardiac procedure (coronary artery bypass surgery or percutaneous angioplasty), or self-reported history of MI. Diabetes was defined as self-reported use of insulin or oral hypoglycemic agents, fasting serum glucose concentration of at least 126 mg/dL, or a nonfasting serum glucose concentration of at least 200 mg/dL. Using height and weight measured during the in-home study visit, body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) was calculated. Waist circumference was measured during the in-home visit using a tape measure midway between the lowest rib and the iliac crest with...
the participant standing. Use of lipid-lowering and antihypertensive medications was based on self-report and pill bottle review during the home visit. Serum concentrations of total cholesterol, high-density lipoprotein (HDL), triglycerides, and high-sensitivity C-reactive protein (hsCRP) were measured using established assays, and estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration formula.13

Statistical Analyses
The end of follow-up for this analysis was December 31, 2009. Follow-up time for each participant was calculated from the date of the in-home visit to the date of first incident or first recurrent CHD event after study enrollment, death, or last telephone follow-up. Age- and sex-adjusted incidence rates for CHD were calculated by strata of ACR in participants with and without CHD at baseline, stratified by race. After confirming the proportionality of hazards, Cox proportional hazards models were used to estimate the hazard ratio of incident or recurrent CHD separately, as a function of ACR in sequential models, stratified by race. Model 1 was adjusted for age, sex, and geographic region of residence (stroke belt, stroke buckle [Georgia, North Carolina, and South Carolina], or other). Model 2 was adjusted for variables in model 1 plus annual family income (< vs ≥$20 000/y), educational achievement (< or ≥ a high school diploma), health insurance (yes/no), waist circumference (continuous), systolic blood pressure (continuous), total and HDL cholesterol (continuous), triglycerides (continuous), eGFR (continuous), natural log-transformed hsCRP (continuous), diabetes (yes/no), smoking status (current vs non-current tobacco use), physical activity (none vs any), use of statins (yes/no), use of aspirin (yes/no), use of any antihypertensive medications (yes/no), and use of angiotensin II receptor blockers or angiotensin-converting enzyme inhibitors (yes/no). In all models, urinary ACR was analyzed as a categorical variable (<10, 10-29.99, 30-300, and >300 mg/g),14 with the lowest category (<10 mg/g) serving as the referent group or as a continuous, natural log-transformed variable.

All multivariable-adjusted Cox proportional hazards models were fitted with imputed data to account for missing covariate data, using multiple imputation by chained equations with 5 data sets. The decision to stratify all analyses by race was made a priori. We also formally examined for effect modification by race by testing the statistical significance of ACR category × race interaction terms in multivariable-adjusted Cox models using a postestimation Wald test to obtain an omnibus P value for interaction between ACR categories and race. In addition, we tested the statistical significance of ACR × race interaction terms modeling ACR as a continuous, natural log-transformed variable. In sensitivity analyses, death from non-CHD-related deaths was analyzed as a competing risk. Finally, point estimates and CIs for the Harrell c-index and change in c-indices for the fully adjusted models with and without ACR were calculated from 1000 bootstrap replicates; each replicate included the same number of observations in the original data sets. To account for the additional variability due to multiple imputation, bootstrap replicates were drawn randomly with replacement from the pool of all 5 imputed data sets. A 2-sided P value of .05 was considered statistically significant for all analyses, which were conducted using SAS software version 9.2 (SAS Institute), STATA version 12 (STATA Inc), and Rv3.0.1 (R Foundation for Statistical Computing).

Results
Study Participants
Overall, 30 239 black and white adults were enrolled between January 2003 and October 2007. We excluded 1400 individuals missing urinary ACR at baseline, 569 individuals missing follow-up data, and 63 participants receiving hemodialysis at baseline, leaving a total of 28 207 participants in the final analysis. Of these, 5076 were missing data for demographic, clinical, or lifestyle covariates, 5306 for biochemical covariates, and 587 for medication use. We reported the baseline characteristics of the 23 273 study participants without CHD (Table 1) and the 4934 participants with CHD (Table 2), stratified by categories of urinary ACR and race. In general, irrespective of race and CHD status at baseline, participants who had higher urinary ACR values were more likely to be older, men, less educated, lower income (annual family), current smokers, currently taking statins and antihypertensive medications; and to have higher systolic blood pressure, higher waist circumference, lower mean eGFR, higher median hsCRP concentrations, and a history of diabetes, hypertension, and dyslipidemia.

Associations of ACR With Incident CHD
Over a median 4.5 years of follow-up (interquartile range, 3.1-5.5), a total of 616 incident CHD events (259 among black participants and 357 among white participants) were observed. Of these, 421 were nonfatal MIs (153 among black participants and 268 among white participants) and 195 were CHD-related deaths (106 among black participants and 89 among white participants) (eTable 1 in Supplement). Age- and sex-adjusted incidence rates (IRs) of CHD per 1000 person-years of follow-up increased in the higher categories of urinary ACR in both black and white participants (Table 3). The adjusted IRs in the 2 highest categories of ACR were approximately 1.5-fold greater in black participants when compared with white participants (30-300 mg/g; IR, 11.23; 95% CI, 8.64-14.58 in black participants vs IR, 8.04; 95% CI, 6.03-10.73 in white participants; and >300 mg/g; IR, 20.59; 95% CI, 14.36-29.51 in black participants vs IR, 13.60; 95% CI, 7.64-24.26 in white participants).

The adjusted hazard ratios [HRs] of incident CHD according to categories of urinary ACR and stratified by race are reported in Table 4. Among both black and white participants, higher urinary ACR was associated with greater risk of incident CHD in analyses adjusted for age, sex, and geographic region of residence. After further adjustment for traditional cardiovascular risk factors and medication use, higher categories of ACR remained associated with greater risk of incident CHD among black individuals, such that in the fully adjusted model, black participants with an ACR greater than 300 mg/g had a 3-fold greater risk of incident CHD as compared with black participants with an ACR of less than 10 mg/g (HR, 3.21; 95%CI,
2.02-5.09). In contrast, in the fully adjusted model among white individuals, the association of higher ACR with incident CHD was attenuated and no longer statistically significant (HR comparing ACR >300 vs ACR <10 mg/g, 1.49; 95% CI, 0.80-2.76). Similarly, when modeling ACR as a continuous variable in fully adjusted models, higher ACR was significantly associated with greater risk of incident CHD in black individuals (HR per doubling of ACR, 1.18; 95% CI, 1.12-1.24) but not white individuals (HR per doubling of ACR, 1.06; 95% CI, 1.00-1.13 (P for interaction = .03). In fully adjusted models, addition of ACR decreased the c-index of the model from 0.723 (95% CI, 0.698-0.749) to 0.746 (95% CI, 0.723-0.770) among black participants (mean difference, 0.023; 95% CI, 0.011-0.036), whereas there was no change among white participants with the addition of ACR to the c-index of the model (0.745; 95% CI, 0.726-0.765 without vs 0.745; 95% CI, 0.725-0.765 with ACR; mean difference, −0.000 [95% CI, −0.002 to 0.002]). In sensitivity analyses using death as a competing risk, the results did not meaningfully change (eTable 2 in Supplement).

The Figure reports the HRs of incident CHD according to race and baseline ACR, with white participants in the lowest ACR risk category serving as the reference group. In fully adjusted models, compared with white participants with an ACR of less than 10 mg/g, the HR of incident CHD was significantly increased in black participants with an ACR 30 mg/g or greater, whereas there was no statistically significant association of increasing ACR with incident CHD among white participants.

---

**Table 1. Baseline Characteristics of REGARDS Participants, by ACR Categories and Race, Without CHD at Baseline**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>White (n = 13 526)</th>
<th>Black (n = 9747)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Participants (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR Category, mg/g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10 (n = 9105)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-29.99 (n = 3015)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-300 (n = 1254)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;300 (n = 5869)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Abbreviations:
- ACE: angiotensin-converting enzyme
- ACR: urinary albumin-to-creatinine ratio
- ARB: angiotensin II receptor blockers
- BMI: body mass index
- CHD: coronary heart disease
- CRP: C-reactive protein
- DBP: diastolic blood pressure
- eGFR: estimated glomerular filtration rate
- IQR: interquartile range
- REGARDS: Reasons for Geographic and Racial Differences in Stroke
- SBP: systolic blood pressure
- SBP: systolic blood pressure

---

**Notes:**
- Indicates annual family income.
- BMI was calculated as weight in kilograms divided by height in meters squared.
- Baseline CHD is defined as history of self-reported myocardial infarction.
Urinary Albumin Excretion and Heart Disease

Table 2. Baseline Characteristics of REGARDS Participants, by ACR Categories and Race, With CHD at Baselinea

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>White (n = 3236)</th>
<th>Black (n = 1698)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR Category, mg/g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%) of Participants</td>
<td>&lt;10 (n = 1697)</td>
<td>10-29.99 (n = 892)</td>
<td>30-300 (n = 516)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>68.0 (8.6)</td>
<td>71.1 (8.9)</td>
<td>71.3 (8.8)</td>
</tr>
<tr>
<td>Women</td>
<td>520 (30.6)</td>
<td>340 (38.1)</td>
<td>142 (27.5)</td>
</tr>
<tr>
<td>Education &lt;high school</td>
<td>162 (9.6)</td>
<td>108 (12.1)</td>
<td>80 (15.5)</td>
</tr>
<tr>
<td>Income &lt;$20 000b</td>
<td>222 (13.1)</td>
<td>169 (19.0)</td>
<td>105 (20.4)</td>
</tr>
<tr>
<td>Health insurance</td>
<td>1653 (97.5)</td>
<td>867 (97.2)</td>
<td>505 (97.9)</td>
</tr>
<tr>
<td>BMI, mean (SD)c</td>
<td>28.5 (5.2)</td>
<td>28.4 (5.3)</td>
<td>29.2 (6.0)</td>
</tr>
<tr>
<td>Waist circumference, mean (SD), cm</td>
<td>97.9 (14.2)</td>
<td>98.4 (16.7)</td>
<td>101.8 (16.1)</td>
</tr>
<tr>
<td>SBP, mean (SD), mm Hg</td>
<td>124.9 (15.0)</td>
<td>130.2 (17.2)</td>
<td>132.5 (18.4)</td>
</tr>
<tr>
<td>DBP, mean (SD), mm Hg</td>
<td>73.6 (9.1)</td>
<td>74.4 (9.3)</td>
<td>75.1 (10.0)</td>
</tr>
<tr>
<td>Lifestyle habits</td>
<td>189 (11.2)</td>
<td>129 (14.5)</td>
<td>87 (16.9)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>528 (31.5)</td>
<td>333 (37.8)</td>
<td>213 (42.3)</td>
</tr>
<tr>
<td>Exercise (none)</td>
<td>306 (18.5)</td>
<td>267 (31.1)</td>
<td>223 (44.0)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>1004 (59.5)</td>
<td>661 (74.2)</td>
<td>393 (76.3)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1346 (80.6)</td>
<td>687 (78.9)</td>
<td>411 (81.4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1029 (61.1)</td>
<td>545 (61.7)</td>
<td>306 (59.9)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>82.2 (69.0-91.9)</td>
<td>78.1 (62.4-89.8)</td>
<td>69.8 (53.4-86.1)</td>
</tr>
<tr>
<td>eGFR, median (IQR), ml/min/1.73 m²</td>
<td>1264 (74.5)</td>
<td>651 (73.0)</td>
<td>366 (70.9)</td>
</tr>
<tr>
<td>CRP, median (IQR), mg/L</td>
<td>1.8 (0.8-3.8)</td>
<td>1.9 (0.9-4.6)</td>
<td>2.9 (1.3-6.8)</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; ACR, urinary albumin-to-creatinine ratio; ARB, angiotensin II receptor blockers; CHD, coronary heart disease; CRP, C-reactive protein; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; IQR, interquartile range; REGARDS, Reasons for Geographic and Racial Differences in Stroke; SBP, systolic blood pressure.

*a* Baseline CHD is defined as history of self-reported myocardial infarction.

**Associations of ACR With First Recurrent CHD**

Over 4.4 years of follow-up (interquartile range, 2.8-5.4 years), 468 recurrent CHD events (137 among black participants and 331 among white participants) were observed. Of these events, 279 were nonfatal MIs (86 among black participants and 193 among white participants) and 189 were CHD-related deaths (51 among black participants and 138 among white participants). Age- and sex-adjusted incidence rates of CHD rose with increasing categories of urinary ACR in both black and white participants (Table 3). In Cox models adjusted for age, sex, and geographic region of residence, higher urinary ACR was associated with greater risk of recurrent CHD among black and white participants (Table 4). After further adjustment for traditional cardiovascular risk factors and medication use, higher ACR continued to be associated with greater risk of recurrent CHD among both black and white participants, with no statistically significant difference in these relationships by race whether modeling ACR as a categorical variable (P for interaction = .53) or a continuous one (P for interaction = .44). Addition of ACR to the fully adjusted model resulted in an increase in the c-index of the model in white participants (0.691 [95% CI, 0.667-0.715] without ACR vs 0.703 [95% CI, 0.679-0.727] with ACR; mean difference, 0.012 [95% CI, 0.004-0.022]), but not in black participants (0.710 [95% CI, 0.679-0.742] without ACR vs 0.721 [95% CI, 0.689-0.751] with ACR; mean difference, 0.011 [95% CI, −0.000 to 0.026]).

**Discussion**

In this national cohort of community-dwelling adults, higher urinary albumin excretion was associated with a higher risk of incident CHD, with the strength and magnitude of this association being greater in black individuals than in white individuals. In contrast, no racial differences in the association of urinary ACR with recurrent CHD were noted. These findings confirm the results of prior studies showing that urinary ACR is an important biomarker for CHD risk in the general population.
population, even among individuals with ACR values that are less than the current threshold for defining microalbuminuria (30 mg/g). Additionally, to our knowledge, this is the first study to demonstrate that the higher risk of incident CHD associated with excess ACR differs by race.

A growing body of evidence suggests that black individuals are more susceptible to vascular injury and its consequences such as stroke and CHD than white individuals. In a recent analysis from the REGARDS study, racial differences in the effect of systolic blood pressure on stroke risk were observed, such that the risk of incident stroke associated with a 10-mm Hg difference in systolic blood pressure was 3-times higher in black participants when compared with white participants. Similarly, we previously showed that the risk of incident stroke associated with any given strata of urinary ACR above the normal range was significantly higher in black individuals than in white individuals, even after accounting for traditional cardiovascular risk factors and eGFR. The results of the current study extend these findings by showing that higher urinary ACR confers a 2-times greater relative risk of incident CHD in black individuals when compared with white individuals with an ACR of at least 30 mg/g. Although the absolute risk differences in the 2 highest categories of ACR were relatively small (approximately equal to 4 and 7 extra events per 1000 person-years of follow-up in black vs white participants, respectively), given the link between elevated urinary ACR and systemic microvascular injury, these data suggest that black individuals have greater susceptibility to vascular disease than white individuals, which, in turn, may account for much of their excess risk of cardiovascular disease events such as stroke and CHD.

Given that elevated urinary ACR is also an important marker of kidney injury, a further potential explanation for these findings is that kidney disease may confer a higher risk of CHD in black individuals than in white individuals. Arguing against this possibility is the finding that black vs white differences in the association of urinary ACR with incident CHD were observed even after adjusting for baseline eGFR. Nonetheless, creatinine-based eGFR measurements are known to have relatively poor sensitivity for detecting chronic kidney disease in its earliest stages, whereas albuminuria is thought to be among the earliest biomarkers of kidney injury. Given that black individuals tend to have faster rates of kidney function decline than white individuals, faster chronic kidney disease progression among black individuals could potentially explain the difference in the relationship between excess urinary ACR and CHD risk by race in this study.

The reason for the absence of racial differences in the association of urinary ACR and first recurrent CHD events was unclear. It is conceivable that racial differences in the management of CHD risk factors before as opposed to after a CHD event could account for these findings. Studies have
shown that black individuals are less likely to receive primary preventive care for CHD, including maintaining normal cholesterol levels, controlling blood pressure, and stopping tobacco use.26 This likely plays a key role in the higher incidence of CHD events in black individuals vs white individuals in the United States since the higher burden of traditional CHD risk factors among black individuals almost completely accounted for their increased risk of fatal CHD in the REGARDS cohort.10 Following a CHD event, however, black individuals (like white individuals) are more likely to receive secondary preventive therapies such as lipid-lowering medications and aspirin and tobacco cessation counseling, which perhaps mitigates racial differences in the risk for recurrent CHD events associated with higher urinary ACR (and by extension systemic vascular injury).

In conclusion, as compared with white participants in this large national cohort, higher urinary ACR was a stronger risk factor for incident CHD events but not recurrent CHD events among black participants. Future studies should examine whether addition of ACR can improve the diagnosis and management of CHD in black individuals.

Table 4. HRs for CHD Events by ACR Level and Race in Participants Without and With Coronary Heart Disease at Baseline

<table>
<thead>
<tr>
<th></th>
<th>ACR, mg/g</th>
<th>&lt;10</th>
<th>10-29.99</th>
<th>30-300</th>
<th>&gt;300</th>
<th>P Value for Interactionb</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD events among participants without CHD at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, sex, regionc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>13 526</td>
<td>1 [Reference]</td>
<td>1.45 (1.13-1.86)</td>
<td>1.76 (1.30-2.39)</td>
<td>2.98 (1.66-5.35)</td>
<td>.03</td>
</tr>
<tr>
<td>Black</td>
<td>9747</td>
<td>1 [Reference]</td>
<td>2.17 (1.58-2.97)</td>
<td>3.27 (2.37-4.50)</td>
<td>6.14 (4.11-9.18)</td>
<td></td>
</tr>
<tr>
<td>Multivariabled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>13 526</td>
<td>1 [Reference]</td>
<td>1.23 (0.96-1.59)</td>
<td>1.19 (0.86-1.64)</td>
<td>1.49 (0.80-2.76)</td>
<td>.03</td>
</tr>
<tr>
<td>Black</td>
<td>9747</td>
<td>1 [Reference]</td>
<td>1.84 (1.34-2.53)</td>
<td>2.40 (1.72-3.36)</td>
<td>3.21 (2.02-5.09)</td>
<td></td>
</tr>
<tr>
<td>CHD events among participants with CHD at baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, sex, regionc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3236</td>
<td>1 [Reference]</td>
<td>1.53 (1.17-2.01)</td>
<td>2.32 (1.74-3.08)</td>
<td>4.50 (3.08-6.57)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1698</td>
<td>1 [Reference]</td>
<td>1.07 (0.67-1.70)</td>
<td>1.84 (1.21-2.82)</td>
<td>2.74 (1.64-4.58)</td>
<td>.39</td>
</tr>
<tr>
<td>Multivariabled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>3236</td>
<td>1 [Reference]</td>
<td>1.27 (0.96-1.67)</td>
<td>1.54 (1.13-1.67)</td>
<td>2.45 (1.59-3.77)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1698</td>
<td>1 [Reference]</td>
<td>1.05 (0.66-1.69)</td>
<td>1.73 (1.11-2.69)</td>
<td>2.16 (1.18-3.95)</td>
<td>.53</td>
</tr>
</tbody>
</table>

Abbreviations: ACR, urinary albumin-to-creatinine ratio; CHD, coronary heart disease; HR, hazard ratio.

a Indicates HRs were adjusted for age, sex, and region.

b Multivariable adjustment of HRs includes age, sex, geographic region of residence, income, education, health insurance coverage, waist circumference, systolic blood pressure, total and high-density lipoprotein cholesterol, triglycerides, estimated glomerular filtration rate, C-reactive protein, diabetes, smoking status, physical activity, use of statins, use of any antihypertensive medications, use of angiotensin II receptor blockers or angiotensin-converting enzyme inhibitors, and regular aspirin use.

d Multivariable model was adjusted for age, sex, geographic region of residence, income, education, health insurance coverage, waist circumference, systolic blood pressure, total and high-density lipoprotein cholesterol, triglycerides, estimated glomerular filtration rate, C-reactive protein, diabetes, smoking status, physical activity, use of statins, and use of any antihypertensive medications, angiotensin II receptor blockers, or angiotensin-converting enzyme inhibitors.
Urinary Albumin Excretion and Heart Disease

Original Investigation Research

Cushman, Safford.

Administrative, technical, or material support:
Study concept and design:
data and the accuracy of the data analysis.
Statistical analysis:
Study supervision:

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Drs Gutiérrez and Warnock report receipt of research support from Amgen. Dr Muntner reports receipt of a grant to the institution and consultancy fees from Amgen. Dr Richman reports receipt of consultancy fees from Amgen and receipt of a grant to the institution from Amgen for the EVOLVE trial and from REATA Pharmaceuticals for the BEACON trial and the Bardoxilone pharmacokinetic studies. Dr McClellan reports board membership with Arbor Research. Dr Cushman reports receipt of a grant to the institution through a project subcontract from the University of Alabama at Birmingham to the University of Vermont (Burlington) from Amgen. Dr Warnock reports being a member of the Amgen National Nephrology Advisory Board, receipt of honoraria from Amgen and Sanofi-Genzyme for consultancy services, and stock or stock options with REATA. Dr Safford reports receipt of consultancy fees from diaDexus. Dr Khodneva reports no financial disclosures.

Funding/Support: This study was supported by a cooperative agreement from the National Institute of Neurological Disorders and Stroke (NINDS, U01 NS041588) and from the National Heart, Lung, and Blood Institute (NHLBI, ROI HL080477). Dr Gutiérrez was supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, K23DK081673 and R03DK095005) and from NINDS (ROI NS080850). Additional funding was provided by an investigator-initiated grant-in-aid from Amgen.

Role of the Sponsor: The manuscript was sent to Amgen for review prior to submission for publication. Amgen representatives were involved in the review of the manuscript. Amgen did not have any role in the design and conduct of the study, the collection, management, data analysis, or interpretation of the data, the preparation of the manuscript, or the decision to submit the manuscript.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of NIDDK, NINDS, NHLBI, or the National Institutes of Health.

Additional Contributions: We thank the other investigators, the staff, and the participants of the REGARDS study for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at http://www.regardsstudy.org. We also thank Joshua S. Richman, MD, PhD, University of Alabama at Birmingham, for his assistance with the analyses. Dr Richman did not receive compensation in association with his contribution to this article.

REFERENCES