

# Racial Differences in the Prevalence of Chronic Kidney Disease among Participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Cohort Study

William McClellan,<sup>\*†</sup> David G. Warnock,<sup>†</sup> Leslie McClure,<sup>‡</sup> Ruth C. Campbell,<sup>§</sup> Britt B. Newsome,<sup>§||</sup> Virginia Howard,<sup>¶</sup> Mary Cushman,<sup>\*\*</sup> and George Howard<sup>‡</sup>

<sup>\*</sup>Emory University School of Medicine, Renal Division, Atlanta, Georgia; <sup>†</sup>Department of Medicine, <sup>‡</sup>Department of Biostatistics, School of Public Health, Divisions of <sup>§</sup>Nephrology and <sup>¶</sup>Preventive Medicine, Department of Medicine, and <sup>||</sup>Department of Epidemiology, University of Alabama at Birmingham, Birmingham, Alabama; and <sup>\*\*</sup>Departments of Medicine and Pathology, University of Vermont College of Medicine, Burlington, Vermont

The racial disparity in the incidence of ESRD exemplified by the three- to four-fold excess risk among black compared with white individuals in the United States is not reflected in the prevalence of less severe degrees of impaired kidney function among black compared with white individuals. The four-variable Modification of Diet in Renal Disease study equation was used to evaluate the black-to-white prevalence of impaired kidney function with increasing severity of impairment among participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a nationally representative, population-based cohort of individuals who are 45 yr and older. An estimated GFR (eGFR) <60 ml/min per 1.73 m<sup>2</sup> was present in 43.3% of the 20,667 REGARDS participants and was slightly less prevalent among black than white patients (33.7 versus 49.9%; prevalence odds ratio 0.51; 95% confidence interval [CI] 0.48 to 0.54). The lower prevalence among black patients was not uniform as eGFR declined. After controlling for other patient characteristics, the black-to-white odds ratio was 0.42 (95% CI 0.40 to 0.46) at an eGFR of 50 to 59 ml/min per 1.73 m<sup>2</sup> and increased to 1.73 (95% CI 1.02 to 2.94) at an eGFR of 10 to 19 ml/min per 1.73 m<sup>2</sup>. The disparity in prevalence of impaired kidney function among white compared with black patients reversed as the severity of impaired kidney function increased. Factors that are responsible for the increasing prevalence of severely impaired kidney function among black patients remain to be determined.

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Black compared with white individuals in the United States have a disproportionate risk for ESRD (1). Black Americans comprise approximately 13% of the population and account for 28.6% of incident ESRD patients who started therapy during 2000. This contrasts to white patients, who accounted for 64% of the incident ESRD population and 77% of the US population in 2000. Age-adjusted ESRD rates are 982 people per million among black and 256 people per million for white individuals, a 3.8-fold racial disparity (1). This disparity persists after controlling for the prevalence of hypertension and diabetes, demographic characteristics, socioeconomic status, and access to health care (2–7). The excess incidence of ESRD among black individuals suggests that black individuals have a higher prevalence of antecedent chronic kidney disease (CKD). This assumption has been challenged by recent reports that the prevalence of CKD is comparable among US black and

white individuals (8). This report extends these observations and describes the prevalence of CKD among a representative sample of older black and white Americans who participated in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study (9).

## Materials and Methods

### Study Design

REGARDS is a population-based cohort study of a representative sample of individuals who are 45 yr and older with follow-up that will extend up to 4 yr (9,10). The purpose of REGARDS is to identify factors that contribute to the excess stroke mortality among black individuals and in the Southeastern United States. REGARDS has a targeted sample size of 30,000 participants, and our report examines the prevalence of CKD at baseline among the first 20,667 participants enrolled.

### Participants

The cohort is recruited from a national stratified random probability sample with 20% of participants recruited from the coastal plain of North Carolina, South Carolina, and Georgia (the “buckle” of the southeastern stroke belt), 30% from the remainder of the stroke belt (North Carolina, South Carolina, and Georgia and the southeastern states of Tennessee, Mississippi, Alabama, Louisiana, and Arkansas), and 50% from the remaining 42 contiguous states.

Cohort recruitment selects individuals who are 45 yr and older with one half black and one half male. Exclusions include active treatment

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**Address correspondence to:** Dr. William McClellan, Emory University School of Medicine, Renal Division, Rollins School of Public Health, 4th Floor, 1518 Clifton Road NE, Atlanta, Georgia 30322. Phone: 404-727-6976; 404-650-7023; E-mail: [wmcclle@sph.emory.edu](mailto:wmcclle@sph.emory.edu)

for cancer, any serious medical condition that would prevent long-term participation, cognitive impairment as judged by an interviewer, living in a nursing home or on the waiting list for a nursing home, and a language barrier (speaks other than English). Furthermore, we excluded patients who reported being treated for ESRD.

### Data Collection

Data are obtained from each participant in a multistep manner. First, telephone contact is made and verbal informed consent is obtained. A trained interviewer conducts a computer-assisted telephone interview to obtain demographic information and self-report of physician diagnosis of major comorbid conditions (diabetes, hypertension, myocardial infarction, and stroke) and cigarette smoking status. Arrangements are made for an in-home examination by a nurse or other health professional who is trained in REGARDS data collection. During the in-home examination, written informed consent is obtained with institutional review board approved methods. Measurements of BP, height, weight, electrocardiogram, and anthropometric measurements are done; urine and blood specimens are obtained; and a medication history is collected. Blood is analyzed at a central laboratory, and the electrocardiogram is coded at a central reading center.

### Data

BP was estimated by the average of three measurements. Hypertension was defined as systolic BP >140 mmHg, diastolic BP >90 mmHg, or self-reported current treatment for hypertension. Diabetes was defined as fasting glucose  $\geq$ 126 mg/dl, nonfasting glucose  $\geq$ 200 mg/dl, or self-reported current treatment for diabetes.

We estimated the GFR (eGFR) using the four-variable Modification of Diet in Renal Disease study (MDRD) equation in the following manner (11):  $eGFR \text{ (ml/min per } 1.73 \text{ m}^2) = 186 \times (SCr)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$ , where SCr is serum creatinine. Even though only a single creatinine measurement was obtained at the time of the home visit, we assume that the calculated GFR represents the kidney function on a chronic basis. We calibrated the REGARDS SCr to values reported by the Cleveland Clinic Foundation (CCF) by submitting 250 serum samples for duplicate testing in the two laboratories. On average, the REGARDS value is lower than the CCF value; however, the spread of the distribution is approximately the same. The resulting least squares linear regression was done to determine an equation for translating REGARDS to CCF creatinine values: Calibrated creatinine =  $0.1363 + 1.0306 \times \text{REGARDS value}$ . All estimates of GFR use the CCF-calibrated SCr.

We defined CKD as an estimated MDRD GFR of <60 ml/min per

1.73 m<sup>2</sup>. We conducted similar analyses using the Cockcroft-Gault equation to estimate creatinine clearance (Ccr):

$$Ccr = (140 - \text{age}) \times (\text{weight}) \times 0.85 \text{ (if female)} / (SCr \times 72)$$

### Statistical Analyses

Means and proportions were used to describe the baseline characteristics and *t* test and  $\chi^2$  tests to test differences between groups. Patient characteristics that independently were associated with levels of CKD were assessed using multivariate polytomous logistic regression models (12). For these analyses, we used 10-ml/min per 1.73 m<sup>2</sup> decrements in eGFR <60 ml/min per 1.73 m<sup>2</sup> as outcome categories and eGFR  $\geq$ 60 ml/min per 1.73 m<sup>2</sup> as the referent category. In addition, we examined the robustness of our results to the method that was used to compute the eGFR, by repeating our analysis using the Cockcroft-Gault equation to compute Ccr. Analyses were done using SAS and Epi-Info (13,14).

### Results

As of December 1, 2005, there were 20,667 REGARDS participants included in the analysis; 41.7% were black, and 48.8% were male. Black participants were younger; more likely to be male and to report a history of hypertension, diabetes, and stroke; and less likely to report a previous myocardial infarction (Table 1). Black participants were more likely to be current smokers compared with white participants. CKD was highly prevalent among REGARDS participants (Table 2). These estimates of the prevalence of CKD are higher than a preliminary description of this cohort (10), as a result of the use of calibrated SCr measurements in this report.

An eGFR of <60 ml/min per 1.73 m<sup>2</sup> was present in 43.3% of REGARDS participants. The prevalence of impaired kidney function was higher with increasing age: Among individuals aged 45 to 54 yr, 19.3% had CKD compared with 31.6% among those who were aged 55 to 64 yr (odds ratio [OR] 1.93; 95% confidence interval [CI] 1.69 to 2.12), 51.5% among those who were aged 65 to 74 yr (OR 4.45; 95% CI 3.89 to 5.10), 62.7% among those who were aged 75 to 84 yr (OR 7.06; 95% CI 6.10 to 8.16), and 71.0% among those who were 85 yr and older (OR 10.25; 95% CI 7.97 to 13.19). Impaired kidney function was more prevalent among women than men (47.5 versus 38.9%; OR 1.42; 95% CI 1.34 to 1.51), individuals with hypertension (47.8 versus

Table 1. Characteristics of study group

Characteristic	All (n = 20,669)	Black (n = 8617)	White (n = 12,053)	P
Age (mean [SD])	66.2 (9.0)	65.6 (8.8)	66.7 (9.1)	<0.0001
Male (%)	48.8	41.0	54.4	<0.0001
Hypertension (%)	58.7	70.5	50.2	<0.0001
Diabetes (%)	22.8	30.9	17.0	<0.0001
Stroke (%)	7.0	8.6	5.7	<0.0001
Myocardial infarction (%)	9.2	8.2	9.9	<0.0001
Smoking (%)				<0.0001
current	14.5	17.6	12.3	
past	42.3	44.9	44.9	
never	43.2	43.6	42.8	

Table 2. Racial differences in renal function by level of MDRD eGFR and odds of a low GFR in black compared with white individuals<sup>a</sup>

GFR (ml/min per 1.73 m <sup>2</sup> )	N (%)		OR	aOR <sup>b</sup>
	Black (n = 8139)	White (n = 11620)		
>60	5394 (66.3)	5817 (50.1)	Reference	Reference
50 to 59	1541 (18.9)	3611 (31.1)	0.46 (0.43 to 0.49)	0.42 (0.40 to 0.46)
40 to 49	693 (8.5)	1506 (13.0)	0.50 (0.45 to 0.55)	0.37 (0.33 to 0.41)
30 to 39	287 (3.5)	521 (4.5)	0.59 (0.51 to 0.67)	0.38 (0.32 to 0.45)
20 to 29	116 (1.4)	131 (1.1)	0.95 (0.74 to 1.22)	0.48 (0.36 to 0.64)
10 to 19	60 (0.7)	25 (0.2)	2.56 (1.62 to 4.13)	1.73 (1.02 to 2.94)
<10	48 (0.6)	9 (0.08)	5.75 (2.82 to 11.7)	4.19 (1.90 to 9.24)

<sup>a</sup>A total of 2029 participants were excluded from analyses because of missing values for MDRD components. OR, odds ratio; aOR, adjusted odds ratio; eGFR, estimated GFR; MDRD, Modification of Diet in Renal Disease.

<sup>b</sup>aOR controlling for age, gender, hypertension, diabetes, previous stroke or myocardial infarction, region, and smoking status.

36.8%; OR 1.57; 95% CI 1.48 to 1.67), and those with diabetes (45.4 versus 42.7%; OR 1.12; 95% CI 1.05 to 1.20). Furthermore, the prevalence of impaired kidney function was increased among individuals who reported a history of myocardial infarction (54.3 versus 42.1%; OR 1.64; 95% CI 1.48 to 1.80) and in those with a history of stroke (54.0 versus 42.5%; OR 1.59; 95% CI 1.42 to 1.78).

There was substantial difference in the distribution of kidney function between black and white participants. The mean MDRD eGFR for black participants was 65.9 (17.0) ml/min per 1.73 m<sup>2</sup> and for white participants was 60.1 (12.9) ml/min per 1.73 m<sup>2</sup> (*P* < 0.0001). The distribution of the eGFR by race is shown in Figure 1. CKD was more prevalent among white than black participants (49.9 versus 33.7%; OR 0.51; 95% CI 0.48, 0.54). Compared with white participants, fewer black participants had an eGFR between 50 and 59 ml/min per 1.73 m<sup>2</sup> (OR 0.46; 95% CI 0.43 to 0.49; Table 2). The odds of lower eGFR in black compared with white participants converged at lower levels of kidney function so that the proportion of black participants (0.7%) with an eGFR of 10 to 19 ml/min per 1.73 m<sup>2</sup> was nearly three times that of white participants (0.2%; OR 2.56;

95% CI, 1.62, 4.13; Table 2 and Figure 2), and this disparity persisted after controlling for other patient factors.

After adjustment for other patient characteristics, the increasing black-to-white OR (95% CI) with lower eGFR was attenuated (Table 2). Compared with an eGFR of 60 ml/min per 1.73 m<sup>2</sup>, the adjusted black-to-white OR for an eGFR of 50 to 59 ml/min per 1.73 m<sup>2</sup> was 0.43 (0.40 to 0.46), for eGFR 40 to 49 ml/min per 1.73 m<sup>2</sup> was 0.37 (0.33 to 0.41), for eGFR 30 to 39 ml/min per 1.73 m<sup>2</sup> was 0.38 (0.32 to 0.45), for eGFR 20 to 29 ml/min per 1.73 m<sup>2</sup> was 0.48 (0.36 to 0.64), for eGFR 10 to 19 ml/min per 1.73 m<sup>2</sup> was 1.73 (1.01 to 2.94), and for eGFR <10 ml/min per 1.73 m<sup>2</sup> was 4.19 (1.90 to 9.24; Table 2).

A similar association with the black-to-white OR increasing as the kidney function declined was observed when we used the uncalibrated SCr with the Cockcroft-Gault equation to estimate Ccr (Table 3). In contrast to MDRD estimates for GFR, black participants were more prevalent at each level of impaired kidney function, and the adjusted black-to-white OR increased from 1.22 (95% CI 1.10 to 1.36) for Ccr level of 50 to 59 ml/min to 4.16 (95% CI 2.28 to 7.59) for a Ccr of 10 to 19 ml/min (Table 3).

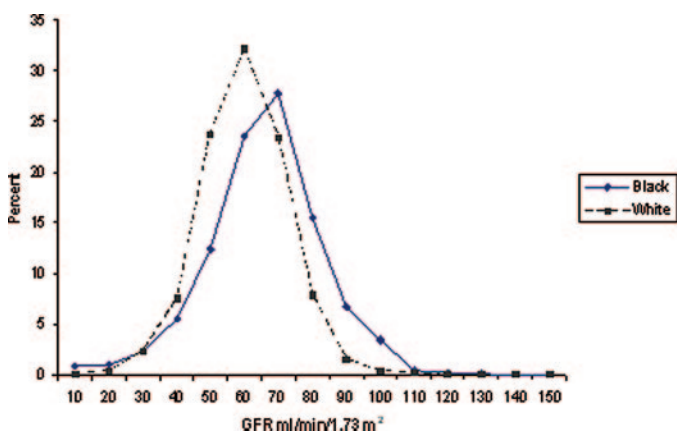


Figure 1. Distribution of four-variable Modification of Diet in Renal Disease estimated GFR by race.

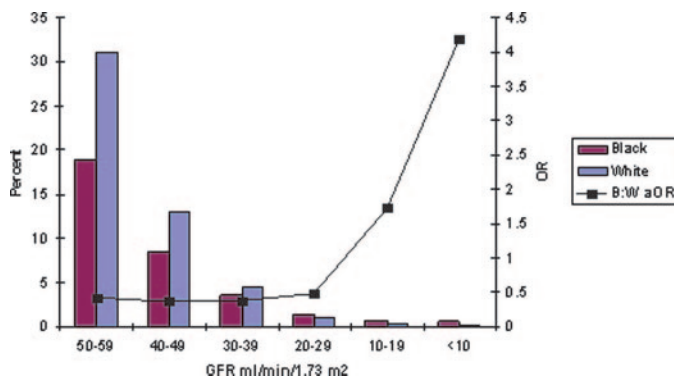


Figure 2. Prevalence of race by level of GFR and prevalence odds ratio (POR) for black compared with white individuals.

Table 3. Racial differences in renal function by level of Cockcroft-Gault estimated creatinine clearance (Ccr) and odds of a low GFR in black compared with white individuals<sup>a</sup>

Ccr (ml/min)	N (%)		OR	aOR <sup>b</sup>
	Black (n = 5793)	White (n = 8232)		
>60	6131 (76.1)	9072 (78.6)	Reference	Reference
50 to 59	874 (10.8)	1269 (11.0)	1.02 (0.93 to 1.12)	1.22 (1.10 to 1.36)
40 to 49	548 (6.8)	731 (7.3)	1.11 (0.99 to 1.24)	1.24 (1.07 to 1.42)
30 to 39	295 (3.7)	334 (2.9)	1.31 (1.11 to 1.53)	1.41 (1.16 to 1.70)
20 to 29	131 (1.6)	116 (1.0)	1.67 (1.23 to 2.15)	1.77 (1.32 to 2.37)
10 to 19	52 (0.7)	17 (0.2)	4.53 (2.62 to 7.83)	4.16 (2.28 to 7.59)
<10	28 (0.4)	3 (0.03)	13.76 (4.19 to 45.19)	13.06 (3.81 to 44.8)

<sup>a</sup>A total of 674 participants were excluded from analyses, due to missing values for Cockcroft-Gault components. Ccr, creatinine clearance.

<sup>b</sup>aOR controlling for age, gender, hypertension, diabetes, previous stroke or myocardial infarction, region, and smoking status.

## Discussion

This is the first report that the prevalence of impaired kidney function in black compared with white individuals increases as kidney function declines and that this association persists after accounting for other factors that are associated with increased risk for kidney disease. This pattern persisted after controlling for other risk factors that are associated with increased risk for CKD: Older age, gender, diabetes, hypertension, cardiovascular disease, and smoking status. This relationship was observed when we used either the more accurate MDRD equation with calibrated SCr measurements, which includes a term for race, or the race-neutral Cockcroft-Gault equation. Our observations are consistent with the hypothesis that the marked disparity in the incidence of ESRD that is observed in the US black and white individuals may be due to differences in the rate of progression of CKD and in overall survival between black and white individuals with advanced stages of CKD.

The genesis of our study is the marked disparity in age- and gender-adjusted risk for ESRD among black compared with white individuals that has persisted for the past two decades. The ESRD incidence in 1980 was 283 people per million population for black individuals and 59 people per million for white individuals, a 4.8-fold black-to-white difference in risk for ESRD. In 2002, the respective rates were 982 and 256 people per million, a 3.8-fold difference in risk (1). Disparities in ESRD rates between black and white individuals are unlikely to misrepresent patterns of dialysis and transplantation in the US population. The United States Renal Data System (USRDS) is a national population-based registry that has collected information on >90% of all incident ESRD patients in the United States for more than three decades (1). Case ascertainment is based on establishing insurance eligibility for Medicare reimbursement, which is the source of health care for incident ESRD patients in the United States regardless of age. A standard enrollment form is completed for incident dialysis patients, which is transmitted to the USRDS for case identification. Enrollment is tracked and reconciled for the USRDS by regional ESRD networks that independently identify incident dialysis patients.

The racial disparities in risk for ESRD in the US population led to the expectation that similar differences would be observed for less severe degrees of impaired kidney function. Contrary to this expectation, the findings in our study are consistent with previous studies that used a national population-based survey (Third National Health and Nutrition Examination Survey [NHANES III]), which failed to find comparable racial disparities in the prevalence of kidney disease in the US population. Clase *et al.* (8) observed that the prevalence of CKD among adults who were 20 yr and older and did not have diabetes, defined by an eGFR of <60 ml/min per 1.73 m<sup>2</sup>, was 9.2% among white men and 17.8% for white women. Comparable prevalence rates for black men and women were 9.2 and 6.3%, respectively. Clase *et al.* also used the Cockcroft-Gault equation and found that the white and black, gender-specific prevalence rates of CKD were 8.2 and 20.7% for white men and women and 9.3 and 12.3% for black men and women.

Coresh *et al.* (15) also estimated the prevalence of CKD, defined as eGFR of <60 ml/min per 1.73 m<sup>2</sup>, in all NHANES III participants who were 20 yr and older. They adjusted the value for SCr to account for calibration differences between the MDRD and NHANES III laboratories that might bias GFR estimates (16). They found a prevalence of eGFR of <60 ml/min per 1.73 m<sup>2</sup> of 5.0% for white individuals and 3.4% for black individuals, consistent with our observations. The increased prevalence of CKD persisted among white individuals after controlling for age, hypertension, and diabetes. When Coresh *et al.* estimated kidney function using the Cockcroft-Gault equation, the prevalence of CKD was 7.5% of white individuals and 7.8% of black individuals.

It is clear from these analyses that the prevalence of CKD in the US population is not consistent with the disproportionate risk for ESRD that is experienced by black Americans, although the extent of racial disparity in CKD depends on the approach used to estimate GFR. The dependence of black-to-white differences in the prevalence of CKD on the level of kidney function has been observed in clinical populations. Go *et al.* (17) used the MDRD equation to estimate GFR among >1.1 million



participants in a managed health care program. Calculations based on Table 1 of their report shows that the prevalence of an eGFR  $\geq 60$  ml/min per  $1.73 \text{ m}^2$  was found in 80.3% for black individuals and 76.5% for white individuals. Comparable black and white prevalence rates for eGFR between 45 and 59 ml/min per  $1.73 \text{ m}^2$  were 8.7 and 18.4%; for GFR between 30 and 44 ml/min per  $1.73 \text{ m}^2$  were 2.8 and 4.3%; for GFR between 15 and 29 ml/min per  $1.73 \text{ m}^2$  were 0.9 and 0.82%; and for eGFR  $< 15$  ml/min per  $1.73 \text{ m}^2$  were 0.3 and 0.1%, respectively. Although the pattern of these estimates of the prevalence of CKD in black and white individuals that we derived from Table 1 of the study of Go *et al.* (17) are similar to the our findings, the estimates may lack precision because the degree of missing data on race varies with severity of CKD in that study.

One possible explanation for lower rates of impaired kidney function and higher rates of ESRD in black compared with white individuals is that kidney disease may progress more rapidly in black individuals. Hsu *et al.* (18,19) examined this possibility in a series of analyses using NHANES and USRDS data. They estimated that among black participants who had an eGFR between 15 and 59 ml/min per  $1.73 \text{ m}^2$  in the NHANES III, 5% will develop ESRD during a 5-yr period compared with 1% of white participants (18). It is interesting that when ESRD incidence rates for individuals with prevalent CKD in the US population in NHANES II (1976 to 1980) and NHANES III (1988 to 1994) were estimated using USRDS data, a 70% increase in ESRD incidence was noted for each 1000 prevalent white individuals compared with a 40% increase for black individuals with CKD (19). These observations suggest that the racial disparity in risk for progressive ESRD may have attenuated during the 20-yr interval represented by the two NHANES surveys for as yet unexplained reasons.

Other observations support the possibility that the rate of progression of CKD is greater in black than in white individuals. Most important are those from the MDRD study, in which race, greater urine protein excretion, diagnosis of polycystic kidney disease, lower serum transferrin, higher mean arterial pressure, and lower serum HDL cholesterol were independent predictors of a greater rate of loss of kidney function among individuals with moderate and advanced CKD (20). The reasons for these differences in the rate of progression remain a subject of intense investigation (21) and may reflect variations in access and adequacy of health care (22); poor control of hypertension or other modifiable risk factors for progression (23); or differences in prevalence of genetic, environmental, and behavioral risk factors that are associated with increased risk for kidney disease and ESRD (24–26). An interesting corollary of the differential progression hypothesis is that there are differences in the prevalence of subpopulations of individuals who more rapidly progress to ESRD. Longitudinal studies with repeated estimates of kidney function will be required to address this issue.

Hsu *et al.* (18) also noted that their results were consistent with the possibility that more white than black individuals with CKD die before reaching ESRD. Support for this possibility of a “survivor effect” is found in recent reports of better survival among older black individuals with CKD and either heart

failure or myocardial infarction compared with white individuals (27,28). Furthermore, after the start of renal replacement therapy for ESRD, white individuals have a substantially greater risk for death than do black individuals (29).

A major strength of our study is that, although the REGARDS study oversamples the southeastern United States, it is a large representative sample of the entire US population that is most at risk for CKD and ESRD. REGARDS provides sufficient numbers of cases for statistically valid estimates of patterns and risk factors for moderate to severe impairment of kidney function. Because REGARDS is a random sample of the US population, it is unlikely that the racial differences in the prevalence of CKD that we report are due to differences in participation rates or case ascertainment. A major weakness of our observations is that we must estimate rather than measure directly GFR, and at this time, only a single measurement of SCr is available for each participant. This is because of the expense and inherent difficulties in measuring GFR or collecting accurate Ccr in a cohort the size of the REGARDS study from across the entire continental United States.

While the current MDRD equation is systematically biased for higher GFR and explicitly includes an adjustment to higher GFR for race, we do not think that these factors can explain our observations for several reasons. First, the reversal in black-to-white prevalence in CKD is observed in the range of GFR, where the estimates of GFR are most accurate for both races. Second, the black-to-white pattern of CKD that we observed is an attenuation of the shift to higher GFR that results from the race term in the MDRD equation. Third, analyses that are consistent with our observation have been reported from studies that used the less accurate but race-neutral Cockcroft-Gault equation or SCr alone, and we found similar relationships when we used the Cockcroft-Gault equation to estimate Ccr. Finally, our eGFR accounted for calibration differences (16), which have the effect of adding the same constant to the SCr measures for both black and white REGARDS participants and therefore cannot account for the difference in CKD prevalence between the two groups of participants.

## Conclusion

The increased risk for ESRD that is experienced by black Americans is not reflected by increases in the prevalence of earlier stages of impaired kidney function compared with white individuals in the US population. White, not black, individuals predominate among older individuals with a GFR  $< 60$  ml/min per  $1.73 \text{ m}^2$  until GFR falls below 20 ml/min per  $1.73 \text{ m}^2$ . This disproportionate and variable black-to-white prevalence of advanced stages of CKD is not explained by risk factors that are associated with increased risk for CKD. Our findings extend previous reports of this unexpected black-to-white difference that will require longitudinal studies with repeated estimates of GFR in the same participants to identify and understand fully the risk factors that account for the increased incidence of ESRD in the black population in the United States.

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