NHANES III: Influence of Race on GFR Thresholds and Detection of Metabolic Abnormalities

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ABSTRACT

Whether the creatinine-based glomerular filtration rate (GFR) thresholds used to define chronic kidney disease (CKD) identify metabolic abnormalities similarly in minority and nonminority populations is unknown. We addressed this question among adult participants in the Third National Health and Nutrition Examination Survey (NHANES III) (n = 15,837). GFR was estimated from serum creatinine values and metabolic abnormalities were defined by 5th or 95th percentile values. After adjustment for age, demographic characteristics, and GFR, black participants were significantly more likely than white participants to have abnormal levels of systolic and diastolic blood pressure, hemoglobin, phosphorus, and uric acid. Hispanic subjects were significantly more likely to have abnormal levels of systolic blood pressure, hemoglobin, bicarbonate, and phosphorus. Among participants with GFR $<$ 60 mL/min per 1.73 m^2, black participants were significantly more likely to have abnormal levels of systolic and diastolic blood pressure, hemoglobin, and uric acid; Hispanic subjects were significantly more likely to have abnormal systolic blood pressure levels. Metabolic abnormalities were more common in minority populations, and low GFR appeared to have a multiplicative effect. Defining CKD using a single GFR threshold may be disadvantageous for minority populations because metabolic abnormalities are present at higher levels of GFR.

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Estimates indicate that approximately 19 million adults in the United States have chronic kidney disease (CKD),[1] and recent public health initiatives have focused on harmonizing case definitions and early identification in the general population.[2–4] Several community-based studies have shown a graded association between GFR and the risk for cardiovascular disease and death, providing further support for the hypothesis that earlier detection of CKD leads to public health improvement.[1,5–9] Risk factors for CKD include older age, hypertension, diabetes, cardiovascular disease, and family history of CKD.

Several national guidelines have recommended the use of serum creatinine levels to measure GFR, with 60 ml/min per 1.73 m^2 considered a watershed value, in part because treatable renal abnormalities become increasingly prevalent as GFR falls below this level.[2,10–12] At the level of public health policy, demonstrating a GFR value below this threshold before embarking on an exhaustive search for renal complications would seem to be a rational use of these guidelines. Surprisingly, it is unknown whether such a two-stage strategy performs similarly in minority and nonminority populations. In particular, if GFR thresholds are to become the gatekeeper to more intensive investigation and intervention, then it would seem important to know whether renal abnormalities develop at similar GFR values among individuals of different races and ethnicities. Hence, the objectives of this national study

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were to test the following hypotheses among the adult population of the United States:

1. Overall prevalence of metabolic abnormalities varies by race/ethnicity.
2. Prevalence of metabolic abnormalities varies by race/ethnicity, independent of GFR level.
3. Prevalence of renal abnormalities varies by race/ethnicity among individuals with GFR <60 ml per min per 1.73 m^2.

RESULTS

Of the 15,837 study participants, 76.9% were white, 10.4% were black, 5.1% were Hispanic, and 7.6% were of other race or ethnicity (Table 1). The corresponding mean GFR values were 90.8 ml/min per 1.73 m^2 for white individuals, 104.7 for black individuals, 108.5 for Hispanic individuals, and 99.8 for others ($P < 0.0001$).

Table 2 shows comparisons of mean values of metabolic and BP variables, by race and ethnicity, in the overall population and in the subgroups defined by GFR category. In the overall population, participants with GFR <60 ml/min per 1.73 m^2 had higher systolic BP (SBP), potassium, phosphorus, and uric acid levels and lower hemoglobin levels than participants with GFR ≥60 ml/min per 1.73 m^2. Compared with white individuals, black individuals had higher SBP, diastolic BP (DBP), phosphorus, and uric acid levels and lower potassium and hemoglobin levels; Hispanic individuals had higher phosphorus and lower SBP, DBP, and potassium levels. Formal testing showed statistically significant interactions between race and ethnicity and GFR for SBP, DBP, and uric acid. Among individuals with GFR <60 ml/min per 1.73 m^2, black individuals had higher SBP, DBP, and uric acid levels and lower hemoglobin levels; Hispanic individuals had higher SBP and phosphorus levels and lower bicarbonate and calcium levels.

Table 3 is similar to Table 2, with adjustment for the characteristics shown in Table 1. In the overall population, individuals with GFR <60 ml/min per 1.73 m^2 had higher SBP, DBP, potassium, calcium, phosphorus, and uric acid levels and lower hemoglobin and bicarbonate levels than individuals with GFR ≥60 ml/min per 1.73 m^2. Compared with white individuals, black individuals had higher SBP, DBP, and phosphorus levels and lower potassium and hemoglobin levels; Hispanic individuals had higher SBP and phosphorus levels and lower potassium and hemoglobin levels. Formal testing showed a statistically significant interaction between race and ethnicity and GFR for DBP, bicarbonate, and uric acid. Among individuals with GFR <60 ml/min per 1.73 m^2, black individuals had higher SBP, DBP, and uric acid levels and lower hemoglobin levels; Hispanic individuals had higher SBP levels and lower hemoglobin levels.

Table 4 shows unadjusted odds risk for laboratory and BP variables ≤5th or ≥95th percentiles. In the overall population, individuals with GFR <60 ml/min per 1.73 m^2 were more likely to have abnormal levels of each variable studied except calcium. Black individuals were more likely to have abnormal levels of each variable except high potassium and low calcium, and Hispanic individuals were more likely to have abnormal levels of bicarbonate, phosphorus, and uric acid. Formal testing showed a statistically significant interaction between race and ethnicity and GFR for abnormal levels of SBP, DBP, potassium, and uric acid. Among individuals with GFR <60 ml/min

Table 1. Population characteristics compared by race and ethnicity ($N = 15{,}837$)[a]

Variable	Racial/Ethnic Group					*P* Race/Ethnicity
	All	White	Black	Hispanic	Other	
All (% [SE], *n*)		76.9 (1.2), 6700	10.4 (0.6), 4219	5.1 (0.4), 4292	7.6 (0.8), 626	
GFR (mean [SE])	93.8 (0.5)	90.8 (0.6)	104.7 (0.8)	108.5 (0.8)	99.8 (1.5)	<0.0001
<60 (% [SE], *n*)	5.8 (0.3), 1325	6.5 (0.4), 922	4.1 (0.3), 228	1.7 (0.2), 136	9.4 (3.5), 39	<0.0001
Serum creatinine (μmol/L; mean [SE])	74.3 (0.3)	74.4 (0.3)	80.7 (0.8)	66.8 (0.4)	69.7 (0.8)	<0.0001
Urinary albumin/creatinine ratio (mg/g; mean [SE])[b]	2.0 (<0.1)	2.0 (<0.1)	1.9 (<0.1)	1.8 (0.1)	1.8 (0.1)	0.0073
≥30 (% [SE], *n*)	10.1 (0.4), 2176	9.7 (0.5), 910	13.4 (0.5), 625	9.9 (0.6), 565	10.1 (1.8), 76	<0.0001
Age (yr; mean [SE])	44.7 (0.5)	46.0 (0.6)	41.6 (0.4)	37.6 (0.4)	41.0 (1.0)	<0.0001
Female gender (% [SE], *n*)	52.1 (0.4), 8426	51.9 (0.5), 3592	55.8 (1.0), 2333	47.6 (0.7), 2143	52.3 (2.0), 358	<0.0001
BMI (kg/m^2; mean [SE])	26.6 (0.1)	26.4 (0.1)	27.80 (0.1)	27.4 (0.1)	25.9 (0.3)	<0.0001
Born outside United States (% [SE], *n*)	13.6 (1.1), 3307	5.1 (0.6), 348	7.0 (1.2), 269	54.9 (3.1), 2183	81.3 (2.3), 507	<0.0001
Self-reported diabetes (% [SE], *n*)	5.4 (0.3), 1332	5.2 (0.3), 489	7.6 (0.5), 363	6.8 (0.4), 441	4.2 (0.8), 39	0.0001
Self-reported hypertension (% [SE], *n*)	23.7 (0.7), 4387	24.1 (0.9), 2044	29.1 (0.9), 1336	16.5 (1.0), 869	16.7 (1.7), 138	<0.0001
ACEI therapy (% [SE], *n*)	3.8 (0.2), 747	4.0 (0.3), 394	4.3 (0.4), 204	2.2 (0.3), 131	2.5 (0.7), 18	<0.0001
Diuretic therapy (% [SE], *n*)	6.6 (0.4), 1416	7.0 (0.4), 815	8.7 (0.4), 421	2.3 (0.3), 154	2.6 (0.6), 26	<0.0001
Serum ferritin (μg/ml; mean [SE])	128.9 (2.1)	127.1 (2.5)	149.1 (4.0)	114.9 (1.9)	128.7 (7.8)	<0.0001
Red blood cell folate (nmol/L; mean [SE])	452.6 (6.1)	475.7 (7.3)	338.1 (3.6)	396.3 (8.8)	413.9 (8.5)	<0.0001

[a]ANOVA and χ^2 analysis, respectively, were used for between-group comparisons of continuous and categorical variables. ACEI, angiotensin-converting enzyme inhibitor; BMI, body mass index. GFR values are given as ml/min per 1.73 m^2.
[b]Urinary albumin/creatinine ratios showed non-Gaussian distribution characteristics and were logarithmically transformed. The exponents of 2.0, 1.9, and 1.8 are 7.4, 6.7, and 6.1, respectively.

Table 2. BP and laboratory variables compared by categories of GFR and race and ethnicity[a]

Variable	Racial/Ethnic Group					*P*	
	All	White	Black	Hispanic	Other	Race/Ethnicity	Race/Ethnicity × GFR
SBP (mmHg)							
all	122.20 (0.40)	122.40 (0.50)	124.28 (0.40)	119.77 (0.39)	119.00 (0.99)	<0.0001	0.0014
GFR <60	140.52 (1.02)	139.65 (1.16)	147.51 (1.75)	146.03 (2.72)	143.20 (2.81)	0.0026	
GFR ≥60	121.14 (0.37)[b]	121.28 (0.46)	123.33 (0.40)	119.34 (0.38)	118.13 (0.92)	<0.0001	
DBP (mmHg)							
all	74.19 (0.18)	74.08 (0.21)	75.58 (0.29)	73.14 (0.40)	74.05 (0.55)	<0.0001	0.0016
GFR <60	75.15 (0.53)	74.44 (0.57)	79.82 (1.20)	76.21 (1.49)	80.17 (2.54)	0.0017	
GFR ≥60	74.13 (0.18)	74.06 (0.21)	75.41 (0.30)	73.09 (0.40)	73.83 (0.53)	<0.0001	
Potassium (mmol/L)							
all	4.06 (0.01)	4.07 (0.01)	4.00 (0.01)	4.01 (0.02)	4.02 (0.03)	<0.0001	0.0937
GFR <60	4.20 (0.02)	4.21 (0.02)	4.12 (0.06)	4.20 (0.04)	4.30 (0.06)	0.1503	
GFR ≥60	4.05 (0.01)[b]	4.07 (0.01)	4.00 (0.01)	4.01 (0.02)	4.01 (0.02)	<0.0001	
Hemoglobin (g/L)							
all	141.52 (0.32)	142.56 (0.36)	133.84 (0.33)	142.82 (0.38)	140.66 (0.77)	<0.0001	0.8854
GFR <60	136.18 (0.52)	137.14 (0.56)	124.36 (1.25)	133.93 (2.37)	138.21 (3.56)	<0.0001	
GFR ≥60	141.84 (0.32)[b]	142.93 (0.36)	134.25 (0.35)	142.97 (0.38)	140.75 (0.76)	<0.0001	
Bicarbonate (mmol/L)							
all	28.12 (0.23)	28.21 (0.25)	27.76 (0.24)	27.61 (0.30)	28.03 (0.37)	0.1368	0.0539
GFR <60	28.05 (0.31)	28.16 (0.33)	27.65 (0.41)	26.75 (0.53)	27.09 (0.45)	0.0213	
GFR ≥60	28.12 (0.23)	28.21 (0.25)	27.76 (0.25)	27.63 (0.30)	28.06 (0.37)	0.1387	
Calcium (mmol/L)							
all	2.32 (0.01)	2.32 (0.01)	2.31 (<0.01)	2.31 (0.01)	2.31 (0.01)	0.0998	0.5715
GFR <60	2.34 (0.01)	2.34 (0.01)	2.34 (0.01)	2.28 (0.02)	2.32 (0.02)	0.0110	
GFR ≥60	2.31 (0.01)[b]	2.32 (0.01)	2.32 (0.00)	2.31 (0.01)	2.30 (0.01)	0.1373	
Phosphorus (mmol/L)							
all	1.11 (<0.01)	1.11 (<0.01)	1.13 (<0.01)	1.13 (<0.01)	1.12 (<0.01)	0.0002	0.8931
GFR <60	1.13 (0.01)	1.13 (0.01)	1.16 (0.02)	1.19 (0.02)	1.14 (0.05)	0.0765	
GFR ≥60	1.11 (<0.01)[c]	1.11 (<0.01)	1.12 (<0.01)	1.13 (<0.01)	1.12 (<0.01)	0.0001	
Uric acid (mmol/L)							
all	317.03 (1.27)	316.56 (1.53)	321.85 (2.38)	312.78 (2.38)	317.99 (3.74)	0.0394	0.0012
GFR <60	389.60 (4.41)	384.58 (4.77)	432.39 (7.70)	399.72 (11.87)	411.43 (8.17)	<0.0001	
GFR ≥60	312.57 (1.22)[b]	311.83 (1.48)	317.08 (2.15)	311.32 (2.16)	314.57 (3.91)	0.1812	

[a]Data are means (SE). ANOVA was used for between-group comparisons. GFR values are given as ml/min per 1.73 m^2.
[b]$P < 0.0001$ for comparison of GFR categories.
[c]$P < 0.001$ for comparison of GFR categories.

per 1.73 m^2, black individuals were more likely to have abnormal SBP, DBP, hemoglobin, and uric acid levels; Hispanic individuals were more likely to have abnormal SBP, DBP, bicarbonate, calcium, and phosphorus levels.

With covariate adjustment (Table 5), individuals with GFR <60 ml/min per 1.73 m^2 were more likely to have abnormal levels of each variable studied except SBP, DBP, and calcium. Black individuals were more likely to have abnormal SBP, DBP, hemoglobin, and phosphorus levels, and Hispanic individuals were more likely to have abnormal SBP, hemoglobin, bicarbonate, and phosphorus levels. Formal testing showed statistically significant interactions between race and ethnicity and GFR for abnormal levels of SBP, DBP, potassium, and uric acid. Among individuals with GFR <60 ml/min per 1.73 m^2, black individuals were more likely to have abnormal SBP, DBP, hemoglobin, and uric acid levels; Hispanic individuals were more likely to have abnormal SBP levels.

Among individuals with GFR <60 ml/min per 1.73 m^2, adjusted odds ratios (OR) for abnormal levels of several variables were higher among participants from minority populations. Figure 1 shows adjusted OR of detecting these abnormalities when different GFR thresholds (in 5-ml/min per 1.73 m^2 increments) were used for case definition among black, Hispanic, and other-race participants, using a fixed threshold value of 60 ml/min per 1.73 m^2 for white participants. With this approach, none of the GFR thresholds led to statistical neutrality for abnormal SBP, DBP, or hemoglobin levels. Statistical neutrality was achieved with GFR thresholds of 65, 80, and 65 ml/min per 1.73 m^2, respectively, for phosphorus, uric acid, and the presence of one or more abnormalities among black, Hispanic, and other-race participants.

DISCUSSION

We found that metabolic abnormalities were more common in

Table 3. Multivariate analysis of BP and laboratory variables with linear regression[a]

Variable	GFR		Race/Ethnicity (*versus* White)			*P*	
	<60 *versus* ≥60 ml/min per 1.73 m^2	*P*	Black	Hispanic	Other	Race/ Ethnicity	Race/ Ethnicity × GFR
SBP (mmHg)							
all	3.28 (0.81)	0.0002	3.29 (0.33)	1.93 (0.33)	0.55 (0.82)	<0.0001	0.0726
GFR <60			6.78 (2.19)	8.90 (3.31)	3.35 (3.78)	0.0044	
GFR ≥60			3.10 (0.35)	1.76 (0.32)	0.41 (0.78)	<0.0001	
DBP (mmHg)							
all	−1.51 (0.50)	0.0039	1.08 (0.29)	−0.52 (0.35)	1.04 (0.71)	0.0004	0.0048
GFR <60			4.48 (1.30)	0.26 (1.64)	5.68 (2.60)	0.0008	
GFR ≥60			0.95 (0.31)	−0.52 (0.34)	0.89 (0.68)	0.0024	
Potassium (mmol/L)							
all	0.16 (0.02)	<0.0001	−0.05 (0.01)	−0.06 (0.02)	−0.05 (0.03)	0.0014	0.0687
GFR <60			−0.05 (0.06)	−0.05 (0.05)	0.04 (0.07)	0.3600	
GFR ≥60			−0.05 (0.01)	−0.06 (0.02)	−0.05 (0.03)	0.0016	
Hemoglobin (g/L)							
all	−2.97 (0.60)	<0.0001	−9.30 (0.29)	−1.30 (0.47)	−2.28 (0.58)	<0.0001	0.4991
GFR <60			−15.07 (1.31)	−5.21 (2.10)	2.17 (3.70)	<0.0001	
GFR ≥60			−9.01 (0.30)	−1.24 (0.48)	−2.43 (0.62)	<0.0001	
Bicarbonate (mmol/L)							
all	−0.93 (0.17)	<0.0001	−0.20 (0.24)	−0.35 (0.38)	−0.05 (0.31)	0.7087	0.0346
GFR <60			−0.42 (0.60)	−1.10 (0.64)	−0.57 (0.72)	0.3835	
GFR ≥60			−0.17 (0.23)	−0.33 (0.38)	−0.02 (0.31)	0.7473	
Calcium (mmol/L)							
all	0.03 (0.01)	<0.0001	<0.01 (0.01)	<0.01 (0.01)	<0.01 (0.01)	0.6716	0.3904
GFR <60			<0.01 (0.01)	−0.04 (0.02)	0.02 (0.03)	0.2047	
GFR ≥60			<0.01 (0.01)	<0.01 (0.01)	<0.01 (0.01)	0.6576	
Phosphorus (mmol/L)							
all	0.04 (0.01)	<0.0001	0.02 (<0.01)	0.03 (0.01)	0.02 (0.01)	0.0009	0.6057
GFR <60			0.04 (0.02)	0.05 (0.02)	−0.02 (0.04)	0.0803	
GFR ≥60			0.01 (0.01)	0.03 (0.01)	0.02 (0.01)	0.0007	
Uric acid (mmol/L)							
all	62.28 (3.51)	<0.0001	1.52 (2.24)	−4.78 (2.58)	6.68 (4.94)	0.0158	0.0040
GFR <60			31.21 (8.58)	10.60 (12.12)	24.43 (12.70)	0.0042	
GFR ≥60			−0.03 (2.22)	−5.58 (2.64)	5.55 (5.04)	0.0164	

[a]Data are β coefficients (SE). Linear regression modeling was used, with BP and laboratory variables as outcome variables. Race/ethnicity, age, gender, BMI, born outside United States, self-reported diabetes, self-reported hypertension, ACEI therapy, diuretic therapy, serum ferritin, and red blood cell folate were included as adjustment variables in all models. GFR category was also included in analyses of the overall population. GFR values are given as ml/min per 1.73 m^2.

black and Hispanic adults than in white adults, an association that was evident regardless of whether CKD was present. As expected, the presence of CKD seemed to multiply prevalence estimates, irrespective of race. In aggregate, these observations seem to suggest that CKD management strategies based on single GFR thresholds may be disadvantageous to populations in which these complications are more prevalent, namely ethnic and racial minorities. In particular, the findings suggest that GFR thresholds >60 ml/min per 1.73 m^2 may be appropriate for detecting several metabolic abnormalities in minority populations.

It was been known for several years that the burden of ESRD (requiring renal replacement therapy) differs substantially in different racial and ethnic groups in the United States, with much higher event rates among black individuals.[13–17] Progress has been made in the arena of CKD, especially with regard to interventions that slow the progression of important causes, such as diabetic nephropathy and hypertensive nephrosclerosis.[18,19]

We found that black individuals have a lower prevalence of GFR <60 ml/min per 1.73 m^2, mirroring recent findings of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study.[20] People of Hispanic or Latino ethnicity now form the largest single minority population in the United States,[21] and there is little reason to suspect that they should have intrinsically lower risk for kidney disease; unfortunately, very few studies have attempted to quantify the burden of CKD in this population.

We found that, unlike several other variables, mean potassium levels were lower in black individuals, when adjustment was made for GFR. A substantial body of evidence suggests that black individuals may be relatively potassium deficient compared with white individuals. For example, urinary potassium excretion seems to be lower on random diets[22–25] and on diets

Table 4. Unadjusted OR of BP and laboratory variables ≤5th or ≥95th percentiles, compared by categories of GFR and race/ethnicity[a]

Variable	GFR		Race/Ethnicity (*versus* White)			*P*	
	<60 *versus* ≥60 ml/min per 1.73 m^2	*P*	Black	Hispanic	Other	Race/Ethnicity	Race/Ethnicity × GFR
SBP ≥156.0 mmHg							
all	5.60 (4.47 to 7.02)	<0.0001	1.53 (1.25 to 1.88)	0.71 (0.58 to 0.87)	0.86 (0.56 to 1.31)	<0.0001	<0.0001
GFR <60			1.84 (1.27 to 2.66)	1.97 (1.13 to 3.44)	2.20 (1.35 to 3.58)	0.0005	
GFR ≥60			1.61 (1.31 to 2.05)	0.76 (0.63 to 0.92)	0.79 (0.55 to 1.14)	<0.0001	
DBP ≥90.7 mmHg							
all	1.54 (1.09 to 2.16)	0.0147	1.93 (1.52 to 2.46)	0.95 (1.52 to 2.46)	1.01 (0.67 to 1.53)	<0.0001	0.0010
GFR <60			3.01 (1.79 to 5.05)	1.77 (1.79 to 5.05)	5.27 (1.91 to 14.55)	0.0004	
GFR ≥60			1.89 (1.47 to 2.43)	0.95 (0.73 to 1.22)	0.87 (0.58 to 1.31)	<0.0001	
Potassium ≥4.6 mmol/L							
all	4.03 (3.15 to 5.16)	<0.0001	0.75 (0.57 to 0.90)	0.63 (0.45 to 0.90)	0.65 (0.40 to 1.08)	0.0060	0.0006
GFR <60			0.72 (0.36 to 1.43)	1.29 (0.73 to 2.28)	1.92 (1.22 to 3.01)	0.0139	
GFR ≥60			0.79 (0.60 to 1.04)	0.68 (0.48 to 0.96)	0.58 (0.34 to 0.98)	0.0229	
Hemoglobin ≤118.0 g/L							
all	2.21 (1.69 to 2.90)	<0.0001	3.44 (2.46 to 4.82)	1.37 (0.96 to 3.39)	1.29 (0.77 to 2.17)	<0.0001	0.7936
GFR <60			3.96 (2.66 to 5.88)	1.77 (0.88 to 3.59)	1.77 (0.88 to 3.59)	<0.0001	
GFR ≥60			3.54 (2.41 to 5.19)	1.45 (0.97 to 2.17)	1.38 (0.78 to 2.42)	<0.0001	
Bicarbonate ≤22.5 mmol/L							
all	1.77 (1.27 to 2.48)	0.0013	1.52 (1.10 to 2.09)	2.03 (1.22 to 3.39)	0.73 (0.39 to 1.38)	0.0010	0.8822
GFR <60			1.44 (0.73 to 2.87)	2.34 (1.09 (5.05)	0.92 (0.09 to 9.52)	0.1344	
GFR ≥60			1.55 (1.12. to 2.15)	2.11 (1.25 to 2.15)	0.74 (0.36 to 1.54)	0.0012	
Calcium ≤2.1 mmol/L							
all	0.83 (0.56 to 1.23)	0.3537	0.99 (0.74 to 1.33)	1.18 (0.83 to 1.68)	1.66 (1.03 to 2.68)	0.0818	0.4703
GFR <60			1.99 (0.72 to 5.53)	3.29 (1.13 to 9.58)	1.91 (0.33 to 11.16)	0.1391	
GFR ≥60			0.96 (0.72 to 1.28)	1.14 (0.81 to 1.62)	1.64 (1.03 to 2.63)	0.0733	
Phosphorus ≥1.4 mmol/L							
all	1.73 (1.30 to 2.30)	0.0003	1.46 (1.22 to 1.74)	1.52 (1.27 to 1.83)	1.19 (0.78 to 1.81)	0.0001	0.4858
GFR <60			1.42 (0.79 to 2.54)	2.15 (1.07 to 4.32)	0.64 (0.12 to 3.41)	0.1334	
GFR ≥60			1.49 (1.24 to 1.79)	1.57 (1.30 to 1.89)	1.25 (0.82 to 1.92)	0.0001	
Uric acid ≥469.9 μmol/L							
all	6.02 (4.91 to 7.39)	<0.001	1.42 (1.17 to 1.73)	0.79 (0.61 to 1.02)	1.18 (0.82 to 1.71)	0.0008	0.0204
GFR <60			3.03 (2.04 to 4.49)	1.18 (0.61 to 2.28)	2.55 (1.47 to 4.43)	<0.0001	
GFR ≥60			1.38 (1.08 to 1.75)	0.91 (0.69 to 1.18)	1.18 (0.72 to 1.93)	0.0338	
≥1 abnormality							
all	3.56 (3.00 to 4.23)	<0.0001	1.74 (1.55 to 1.96)	1.15 (1.02 to 1.31)	0.97 (0.82 to 1.15)	<0.0001	0.4277
GFR <60			2.35 (1.49 to 3.70)	1.83 (1.28 to 2.61)	1.12 (0.57 to 2.22)	0.0008	
GFR ≥60			1.80 (1.61 to 2.03)	1.23 (1.08 to 1.40)	1.01 (0.85 to 1.20)	<0.0001	

[a]Data are OR (95% CI). GFR values are given as ml/min per 1.73 m^2. White race and GFR ≥60 were reference categories.

with fixed potassium contents.[26,27] Given the reciprocal relationship between potassium deficiency and sodium retention, intrinsic differences in potassium handling may contribute to higher-than-expected prevalence of hypertension among black individuals.[28]

Formal, gold-standard measurement of GFR was not a design feature of the Third National Health and Nutrition Examination Survey (NHANES III). Therefore, it was not possible to determine whether associations between serum creatinine and true GFR values differ in community-dwelling adults of different races and ethnicities and similar age and gender distribution. Similarly, it was not possible to determine whether complications associated with declining GFR develop at different GFR levels or whether the higher prevalence of GFR-associated complications in minority groups with GFR <60 ml/min per 1.73 m^2 reflects a greater prevalence of these complications in general, irrespective of GFR level. The data presented here tend to support the latter hypothesis. For example, in this study, compared with white participants, black participants had higher adjusted OR for high BP and low hemoglobin levels, regardless of whether GFR levels were <60 ml/min per 1.73 m^2. For Hispanic participants, similar between-GFR category parallels were seen for high BP, low hemoglobin, and high phosphorus.

The limitations of our study should be pointed out. It was cross-sectional, and longitudinal measures were not available. Mirroring clinical reality, gold-standard measures of GFR, such as those based on inulin or isotope clearance methods, were not used. Limitations notwithstanding, we believe that this study has useful features. The study design facilitates quantification of the burden and the complications of CKD in a nationally representative sample. Overall, this study suggests

Table 5. Adjusted OR of BP and laboratory variables ≤5th or ≥95th percentiles, compared by categories of GFR and race/ethnicity[a]

Variable	GFR		Race/Ethnicity (*versus* White)			*P*	
	<60 *versus* ≥60 ml/min per 1.73 m²	*P*	Black	Hispanic	Other	Race/ Ethnicity	Race/ Ethnicity × GFR
SBP ≥156.0 mmHg							
all	0.99 (0.76 to 1.30)	0.9570	2.36 (1.87 to 2.99)	1.69 (1.31 to 2.17)	1.63 (0.97 to 2.74)	<0.0001	0.0383
GFR <60			1.79 (1.11 to 2.88)	2.53 (1.19 to 5.37)	2.21 (1.11 to 4.39)	0.0087	
GFR ≥60			2.44 (1.92 to 3.09)	1.64 (1.28 to 2.10)	1.51 (0.84 to 2.69)	<0.0001	
DBP ≥90.7 mmHg							
all	1.18 (0.80 to 1.72)	0.3998	1.92 (1.48 to 2.48)	1.18 (0.88 to 1.58)	1.38 (0.88 to 1.72)	0.0001	0.0088
GFR <60			2.23 (1.25 to 3.97)	1.29 (0.40 to 4.20)	8.23 (3.23 to 21.00)	0.0001	
GFR ≥60			1.89 (1.44 to 2.47)	1.18 (0.87 to 1.60)	1.21 (0.76 to 1.91)	0.0003	
Potassium ≥4.6 mmol/L							
all	2.60 (1.87 to 3.61)	<0.0001	0.93 (0.69 to 1.25)	0.76 (0.48 to 1.22)	0.70 (0.40 to 1.23)	0.5421	0.0031
GFR <60			0.74 (0.30 to 1.82)	1.17 (0.52 to 2.65)	1.81 (0.87 to 3.75)	0.3259	
GFR ≥60			0.96 (0.71 to 1.29)	0.74 (0.46 to 1.20)	0.60 (0.31 to 1.15)	0.4307	
Hemoglobin ≤118.0 g/L							
all	1.97 (1.31 to 2.98)	0.0018	4.13 (2.78 to 6.14)	1.71 (1.16 to 2.52)	1.48 (0.85 to 2.58)	<0.0001	0.7977
GFR <60			5.06 (2.92 to 8.77)	2.10 (0.93 to 4.74)	0.77 (0.16 to 3.62)	<0.0001	
GFR ≥60			4.07 (2.68 to 6.16)	1.69 (1.12 to 2.57)	1.54 (0.84 to 2.81)	<0.0001	
Bicarbonate ≤22.5 mmol/L							
all	2.87 (1.93 to 4.18)	<0.0001	1.29 (0.88 to 1.89)	2.13 (1.13 to 3.99)	0.88 (0.44 to 1.76)	0.0289	0.7529
GFR <60			1.25 (0.52 to 2.98)	1.55 (0.66 to 3.64)	0.74 (0.08 to 6.55)	0.7338	
GFR ≥60			1.28 (0.87 to 1.89)	2.21 (1.17 to 4.17)	0.91 (0.40 to 2.07)	0.0364	
Calcium ≤2.1 mmol/L							
all	0.63 (0.38 to 1.05)	0.8189	0.99 (0.73 to 1.32)	0.99 (0.64 to 1.54)	1.27 (0.66 to 2.46)	0.8189	0.3138
GFR <60			2.22 (0.82 to 6.01)	1.83 (0.39 to 8.65)	0.54 (0.09 to 3.10)	0.2166	
GFR ≥60			0.93 (0.69 to 1.26)	0.98 (0.63 to 1.51)	1.28 (0.65 to 2.52)	0.6673	
Phosphorus ≥1.4 mmol/L							
all	1.95 (1.40 to 2.72)	0.0001	1.49 (1.23 to 1.80)	1.81 (1.45 to 2.26)	1.44 (0.93 to 2.23)	<0.0001	0.5387
GFR <60			1.45 (0.72 to 2.92)	1.30 (0.51 to 3.33)	0.25 (0.04 to 1.64)	0.2222	
GFR ≥60			1.50 (1.22 to 1.83)	1.90 (1.54 to 2.36)	1.62 (1.03 to 2.54)	<0.0001	
Uric acid ≥469.9 μmol/L							
all	5.42 (3.97 to 7.40)	<0.0001	1.41 (1.12 to 1.78)	1.02 (0.73 to 1.42)	1.72 (1.00 to 2.94)	0.0087	0.0482
GFR <60			2.94 (1.64 to 5.28)	1.28 (0.57 to 2.89)	3.84 (1.50 to 9.82)	0.0002	
GFR ≥60			1.25 (0.96 to 1.64)	0.96 (0.67 to 1.37)	1.51 (0.79 to 2.90)	0.2556	
≥1 abnormality							
all	2.17 (1.79 to 2.62)	<0.0001	1.85 (1.64 to 2.08)	1.44 (1.23 to 1.69)	1.17 (0.94 to 1.47)	<0.0001	0.5331
GFR <60			2.01 (1.21 to 3.32)	1.66 (0.98 to 2.79)	0.65 (0.33 to 1.27)	0.0296	
GFR ≥60			1.82 (1.62 to 2.04)	1.44 (1.23 to 1.70)	1.19 (0.94 to 1.51)	<0.0001	

[a]Data are OR (95% confidence intervals). GFR values are given as ml/min per 1.73 m². Race/ethnicity, age, gender, BMI, born outside United States, self-reported diabetes, self-reported hypertension, ACEI therapy, diuretic therapy, serum ferritin, and red blood cell folate were included as adjustment variables in all models. GFR category was also included in analyses of the overall population.

that strategies in which detection of treatable renal abnormalities are predicated on a single threshold of estimated GFR might be disadvantageous to racial minorities. Research focusing on efficient, equitable identification of covert kidney disease is urgently needed.

CONCISE METHODS

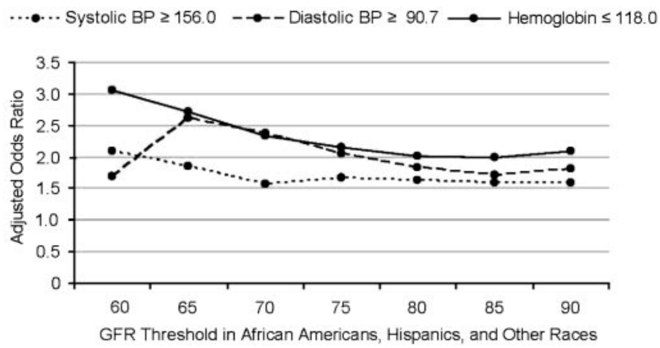
Design

NHANES III, conducted between 1988 and 1994, used stratified, multistage, probability sampling methods to assemble a nationwide probability sample of the noninstitutionalized population of the United States.[29] Calibration factors can have an impact on creatinine-based estimates of glomerular filtration, and NHANES III data have been directly calibrated with reference standards. All NHANES III participants aged 20 yr or older were eligible for determination of hematologic and biochemical profiles at the mobile examination center.

Measurements and Definitions

GFR.

Serum creatinine, measured at White Sands Research Center (Alamogordo, NM) with the modified kinetic Jaffe reaction and a Hitachi 737 analyzer (Boehringer Mannheim, Indianapolis, IN), was recalibrated to results obtained at the Cleveland Clinic (Cleveland, OH), using the method of Coresh *et al.*[30] Estimated GFR levels were derived from the re-expressed Modification of Diet in Renal Disease (MDRD) Study formula, namely, 175 × (serum creatinine value)$^{-1.154}$ × age$^{-0.203}$ × (0.742 for women) × (1.21 if black).[12]



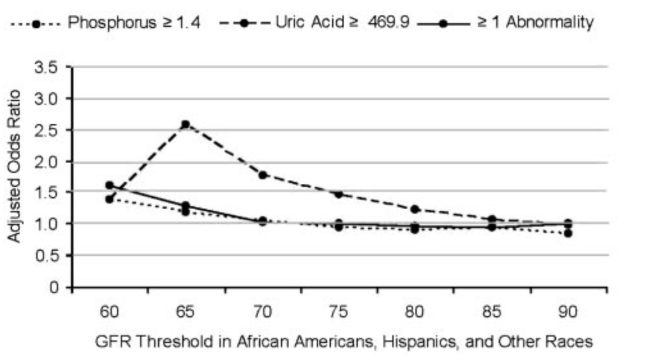


Figure 1. OR, from logistic regression models, of BP and laboratory variables ≤5th or ≥95th percentiles. In each model, white individuals with GFR <60 ml/min per 1.73 m^2 are compared successively with black, Hispanic, and other-race individuals with GFR thresholds varying in 5-ml/min per 1.73 m^2 increments from 60 to 90. Adjustment was made for age, gender, body mass index, born outside United States, self-reported diabetes, self-reported hypertension, angiotensin-converting enzyme inhibitor therapy, diuretic therapy, serum ferritin, and red blood cell folate. (Top) $P < 0.05$ for all odds ratios. (Bottom) $P < 0.05$ for phosphorus at GFR 60 ml/min per 1.73 m^2; uric acid at GFR 60, 65, 70, and 75 ml/min per 1.73 m^2; and one or more abnormalities at GFR 60 ml/min per 1.73 m^2.

Metabolic Abnormalities.

These were defined by the fifth or 95th percentiles of their respective distributions in the overall population. The specific threshold values were as follows: SBP ≥156.0 or DBP ≥90.7 mmHg, potassium ≥4.6 mmol/L, hemoglobin ≤118 g/L, bicarbonate ≤22.2 mmol/L, calcium ≤2.13 mmol/L, phosphorus ≥1.36 mmol/L, and uric acid ≥0.47 mmol/L.

Other Variables.

Self-reported diabetes was defined as an affirmative answer to the question, "Have you ever been told by a doctor that you have diabetes or sugar diabetes?" Self-reported hypertension was defined as an affirmative answer to the question, "Have you ever been told by a doctor or other health professional that you have hypertension, also called high BP?"

Statistical Analyses

χ^2 analysis and ANOVA were used for unadjusted comparisons of baseline variables between racial/ethnic groups. Considered as continuous parameters, unadjusted and adjusted associations of metabolic and BP variables were explored with ANOVA and multiple linear regression, respectively. Unadjusted and adjusted logistic regression analyses were used to explore the corresponding associations when abnormal values of metabolic and BP variables were considered as binary (yes/no) variables. National estimates of each parameter were adjusted for the sampling weights implicit in complex survey designs, using SUDAAN software (Research Triangle Institute, Research Triangle Park, NC) for complex sample surveys. SAS Version 8.2 (SAS Institute, Cary, NC) was used for data assembly.

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DISCLOSURES

None.

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