National Estimates of CKD Prevalence and Potential Impact of Estimating Glomerular Filtration Rate Without Race

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ABSTRACT

Background The implications of removing the adjustment for Black race in equations to eGFR on the prevalence of CKD and management strategies are incompletely understood.

Methods We estimated changes in CKD prevalence and the potential effect on therapeutic drug prescriptions and prediction of kidney failure if race adjustment were removed from the CKD-EPI GFR estimating equation. We used cross-sectional and longitudinal data from adults aged ≥18 years in the National Health and Nutrition Examination Survey (NHANES) from 2015 to 2016, and the Veterans Affairs (VA) Health Care System in 2015. In the VA cohort, we assessed use of common medications that require dose adjustment on the basis of kidney function, and compared the prognostic accuracy of the Kidney Failure Risk Equation with versus without race adjustment of eGFR.

Results The prevalence of CKD among Black adults increased from 5.2% to 10.6% in NHANES, and from 12.4% to 21.6% in the VA cohort after eliminating race adjustment. Among Black veterans, 41.0% of gabapentin users, 33.5% of ciprofloxacin users, 24.0% of metformin users, 6.9% of atenolol users, 6.6% of rosuvastatin users, and 5.8% of tramadol users were reclassified to a lower eGFR for which dose adjustment or discontinuation is recommended. Without race adjustment of eGFR, discrimination of the Kidney Failure Risk Equation among Black adults remained high and calibration was marginally improved overall, with better calibration at higher levels of predicted risk.

Conclusions Removal of race adjustment from CKD-EPI eGFR would double the estimated prevalence of CKD among Black adults in the United States. Such a change is likely to affect a sizeable number of drug-dosing decisions. It may also improve the accuracy of kidney failure risk prediction among higher-risk Black adults.

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Estimation of GFR plays a central role in public health surveillance and clinical care of patients with CKD. Because direct measurement of GFR is cumbersome, GFR estimation from serum creatinine is the primary method for assessing kidney function in public health, research, and clinical decision making. The most commonly used equation to estimate GFR, the CKD Epidemiology Collaboration (CKD-EPI) equation, includes an adjustment for race, categorizing individuals as Black or non-Black.1 In the derivation of this estimating equation, Black persons were found to have higher serum creatinine concentrations relative to persons

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of other races at a given level of measured GFR, thought to reflect non-GFR determinants of serum creatinine. The inclusion of race in the equation has been questioned on the basis that race is a social rather than biologic construct, and that binary race classification ignores ancestral diversity within racial and ethnic groups.

In response to these concerns, several healthcare institutions no longer report estimated GFR with adjustment for race, and the National Kidney Foundation and American Society of Nephrology have established a task force to assess the removal of race from creatinine-based GFR-estimating equations. Removal of the race adjustment results in lower eGFR for persons identified as Black race. A systematic change in the method for estimating GFR could have wide-ranging effects on clinical decisions such as medication dosing, radiograph contrast administration, referrals for specialty care, and eligibility for kidney transplantation and kidney donation. A preliminary report estimated the prevalence of CKD would increase by 3.5% among Black adults. How these changes might affect clinical care is unclear, because the effects depend on baseline use of a given intervention and the number of individuals who are reclassified to a lower level of kidney function. Furthermore, because equations to predict risk of kidney failure rely on eGFR, the accuracy of these tools may be affected when the race adjustment is eliminated.

To understand the effect of removing race from the CKD-EPI equation, we set out to estimate the prevalence of CKD and quantify the proportion of persons who would be reclassified into a more advanced stage of CKD in two large contemporary national cohorts from the National Health and Nutrition Examination Survey (NHANES) and the Department of Veterans Affairs (VA) health care system. We also assessed the potential clinical effect on persons receiving commonly prescribed medications that require dose adjustment for impaired kidney function and the accuracy of kidney failure risk prediction.

**METHODS**

**Study Population**
We estimated the prevalence of CKD in a population sample from the NHANES and a clinical sample from the VA health care system. NHANES uses a cross-sectional, multistage, stratified, clustered probability-sampling design to select participants representative of the noninstitutionalized civilian population of the United States. The survey oversamples groups of interest, including non-Hispanic Black individuals, to ensure greater reliability and precision of estimates. We utilized data collected in the 2015–2016 wave of NHANES and limited the cohort to participants aged ≥18 years with nonmissing data for age, sex, race, and serum creatinine measurements, excluding those who noted dialysis treatment in the preceding year (n=5369, Supplemental Figure 1).

**Assessment of Race and Demographic Characteristics**
We categorized individuals into Black and non-Black race to coincide with race categories utilized in the CKD-EPI equation. In NHANES, the assignment of race categories was on the basis of self-report during the survey interview. We categorized participants reported as “Non-Hispanic Black” as Black race, and those reported in other categories, including “Other Race—Including Multi-Racial,” as non-Black race. Within the VA cohort, we categorized those identified as “Black or African-American” as Black race, and those with other racial self-identification, including multiple races, as non-Black race.

In addition to race, we recorded age, sex, height, and weight for each participant. Where available, we recorded the urine albumin-creatinine ratio (UACR) in milligrams of albumin per gram of creatinine. For the VA cohort, we allowed a look-back window of 6 months to obtain UACR values. We also recorded diabetes status on the basis of participant self-report in NHANES, and International Classification of Disease, Ninth and Tenth revision codes in VA.

**Assessment of Potential Clinical Effects**
We assessed potential clinical effects of the change in GFR estimation on medication dosing, and prediction of kidney failure.

To complement data from NHANES, we used clinical data collected from the VA, the largest integrated health care system in the United States, to assemble a period-prevalent cohort of Veterans. Using data from the VA Corporate Data Warehouse, we identified persons aged ≥18 with an outpatient serum creatinine measurement in 2015, and nonmissing data for age, sex, and race. When multiple serum creatinine measurements were available, the first value during the calendar year was utilized. We excluded 28,491 persons who were receiving dialysis or had received a kidney transplant on or before the index date, using International Classification of Disease, Ninth and Tenth revisions, Current Procedural Terminology codes, and a linkage to the United States Renal Data System, a national registry of treated kidney failure, resulting in an analytic cohort of n=4,447,675 veterans (Supplemental Figure 1).

The study was approved by the Institutional Review Board at Stanford University and the VA Palo Alto R&D Committee.
failure using VA data. From the 2015 Medical Expenditure Panel Survey, we identified the five most commonly prescribed medications with dosing recommendations dependent on kidney function—metformin, gabapentin, tramadol, atenolol, and rosuvastatin. In addition to these chronic medications, we included an antibiotic, ciprofloxacin, with dosing recommendations that are dependent on kidney function. We identified active users on the basis of a pharmacy prescription within 90 days after the eGFR measurement and estimated the number of individuals potentially affected if the eGFR without race adjustment dropped below a level at which dose adjustment or discontinuation is recommended (described in Supplemental Table 1).

We identified individuals who progressed to kidney failure from the index creatinine measurement in 2015 over 2 years of follow-up through a linkage with the United States Renal Data System. To assess the effect of removing race adjustment on prognostic accuracy, we used the four-variable Kidney Failure Risk Equation (KFRE), a validated equation that predicts the 2-year risk for kidney failure with age, sex, eGFR, and UACR.

We assessed the accuracy of the KFRE with versus without race adjustment of eGFR among the subset of individuals, with a non-race-adjusted index eGFR < 60 ml/min per 1.73 m² sustained for more than 90 days before the index date (n = 495,959).

Statistical Analyses

Descriptive statistics are reported as means (SD) for continuous variables. We estimated the prevalence of CKD using the Kidney Disease International Improving Global Outcomes CKD Classification from GFR estimates with and without race adjustment. We estimated the number of individuals reclassified into a lower CKD stage and the absolute change in prevalence of each CKD stage using GFR estimates without versus with race adjustment. We performed subgroup analyses stratified by race (Black versus non-Black), and by age group and diabetes status. Sample weights from the NHANES Mobile Examination Center were applied using the “survey” package in R.

We followed the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis guidelines for updating a prediction model. The 2-year risk of kidney failure was calculated for each individual employing GFR estimates with and without race adjustment. Approximately 83% of the cohort was missing UACR measurements. We handled this with multiple imputation performed separately for Black and non-Black participants, and used Rubin’s rules to combine the results.

We assessed discrimination of the KFRE with and without race adjustment of eGFR with the c-statistic and calculated 95% confidence intervals using the bootstrap. We assessed calibration graphically by plotting the predicted and observed 2-year probability of kidney failure by risk categories (<1%, 1% to <2%, 2% to <5%, 5% to <10%, 10% to <20%, and ≥20%). We compared the Brier score, the squared difference between the observed versus predicted outcome, with and without race adjustment of eGFR. To assess whether the results were affected by imputation of missing UACR measurements, we also conducted a complete case analysis (n = 124,289).

Data were prepared using SAS Enterprise Guide, version 7.1 (SAS Institute, Inc., Cary, NC) or R, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). Statistical analyses were performed in R and SAS between June 2020 and January 2021.

RESULTS

Cohort Characteristics

The characteristics for the NHANES and VA cohorts are displayed in Table 1. In the NHANES population, a weighted 10.9% of the non-institutionalized US population self-reported as Black race, whereas 784,337 veterans (17.5%) were identified as Black race within the VA.

CKD Prevalence and Reclassification in NHANES

In the NHANES cohort, the mean (SD) eGFR was 96.3 (22.5) ml/min per 1.73 m² with the original CKD-EPI equation, and 94.7 (22.0) ml/min per 1.73 m² without race adjustment (Supplemental Figure 2, Table 2). In the subset of persons who self-reported as Black race, the eGFR was 104.5 (27.2) ml/min per 1.73 m² with the original CKD-EPI equation, and 90.2 (23.5) ml/min per 1.73 m² without race adjustment. The overall estimated prevalence of CKD, defined as GFR < 60 ml/min per 1.73 m², increased from 5.9% to 6.5% of the population after race adjustment was removed. Among persons identified as Black race, the estimated prevalence of CKD increased from 5.2% to 10.6%. Change in estimated prevalence of eGFR category by age group, sex, and diabetes status is displayed in Figure 1.

Based on the NHANES sample, an estimated 214,096,576 US adults (94.1%) had an eGFR ≥ 60 ml/min per 1.73 m² using the original CKD-EPI equation, 11.0% of whom were self-reported as Black race. Among Black individuals, 5.6% (95% confidence interval, 4.0% to 7.2%) were reclassified to CKD Stage 3 after eliminating race adjustment (Table 3). Of the 1,156,935 Black individuals with CKD Stage 3, 6.3% (95% confidence interval, −2.7% to 15.4%) were reclassified to CKD Stage 4 after eliminating race adjustment.

Without race adjustment, 9.7% of Black adults in NHANES would be classified as having CKD Stage 3. Of these individuals, 45.0% would be classified as having CKD Stage 3 regardless of the use of race adjustment, whereas 55.0% would be newly classified as having CKD Stage 3 (Supplemental Figure 3).

CKD Prevalence and Reclassification in the VA

In the VA cohort, the mean (SD) eGFR was 80.0 (21.5) ml/min per 1.73 m² with the original CKD-EPI equation, and 78.0 (20.9) ml/min per 1.73 m² when race adjustment was eliminated. In the subset of veterans who were identified as Black race, the eGFR was 87.3 (23.3) with the original CKD-EPI equation, and 75.7 (20.8) with removal of race adjustment.
Supplemental Figure 2, Table 2). The overall estimated prevalence of CKD increased from 17.9% to 19.6%. Among those identified as Black race, the estimated prevalence of CKD increased from 12.4% to 21.6%. Change in estimated prevalence of eGFR category by age group, sex, and diabetes status is displayed in Figure 1.

Within the VA, 3,673,099 veterans (82.0%) had an eGFR $\geq 60$ ml/min per 1.73 m$^2$ using the original CKD-EPI equation, 687,034 (18.7%) of whom were identified as Black race. Among Black veterans, 71,805 were reclassified to CKD Stage 3 with removal of race adjustment (Table 3). Of 85,487 Black veterans with CKD Stage 4, 5444 (6.5%) were reclassified to CKD Stage 4 with removal of the race adjustment. Finally, 2735 (29.1%) of the 9409 Black veterans with CKD Stage 4 were reclassified to CKD Stage 5.

Within the VA, 19.4% of Black veterans would be classified as having CKD Stage 3, 52.7% of whom would be classified as such, regardless of race adjustment, and 47.3% of whom would be newly classified as having CKD Stage 3 (Supplemental Figure 3).

### Potential Effect on Prescription of Commonly Used Medications

There were 2452, 2372, 1560, 1216, 560, and 559 Black veterans with active prescriptions for metformin, gabapentin, tramadol, atenolol, rosuvastatin, and ciprofloxacins, respectively. The percentage of users potentially affected by changes in GFR estimation were highest for metformin, gabapentin, and ciprofloxacins (24.1%, 41.0%, and 33.5%, respectively), and 10.0% for tramadol, atenolol, and rosuvastatin (Figure 2).

### Effect on Kidney Failure Prognostication

Among the subset of veterans with a sustained eGFR $\geq 60$ ml/min per 1.73 m$^2$ on the basis of the CKD-EPI equation without race adjustment, 2.4% overall ($n=12,055$) and 3.8% of Black individuals ($n=3680$) progressed to kidney failure over 2 years. Among Black adults, the mean (SD) estimated 2-year risk of kidney failure increased from 2.7% (10.3) to 3.4% (11.5) when race adjustment was removed from CKD-EPI eGFR (Table 4). The c-statistic remained similar in the overall cohort (0.95) and increased marginally in the Black subgroup (0.96–0.97), when KFRE was computed with versus without race adjustment of eGFR. There was a marginal improvement in overall calibration as assessed by the Brier score without versus with race adjustment (Table 4). Plots of predicted versus observed risk demonstrated that both models overestimated kidney failure risk at levels of predicted risk <1%, and underestimated kidney failure risk among Black adults at levels of predicted risk $\geq$5%.

### Table 1. Cohort characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NHANES 2015–2016</th>
<th>VA 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weighted N*</td>
<td>Prevalence (%)</td>
</tr>
<tr>
<td>Overall</td>
<td>227,613,357</td>
<td>100%</td>
</tr>
<tr>
<td>Age, yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>5,417,116</td>
<td>2.4%</td>
</tr>
<tr>
<td>20–39</td>
<td>79,270,090</td>
<td>34.8%</td>
</tr>
<tr>
<td>40–59</td>
<td>80,553,129</td>
<td>35.4%</td>
</tr>
<tr>
<td>60–79</td>
<td>52,171,308</td>
<td>22.9%</td>
</tr>
<tr>
<td>80+</td>
<td>10,201,714</td>
<td>4.5%</td>
</tr>
<tr>
<td>Male</td>
<td>110,157,843</td>
<td>48.4%</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>145,590,488</td>
<td>64.0%</td>
</tr>
<tr>
<td>Black</td>
<td>24,898,373</td>
<td>10.9%</td>
</tr>
<tr>
<td>Multiple/Other</td>
<td>57,124,496</td>
<td>25.1%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>29,092,015</td>
<td>12.8%</td>
</tr>
<tr>
<td>Height, inches</td>
<td>66.2 (1.6)*</td>
<td>99.2%</td>
</tr>
<tr>
<td>Measured</td>
<td>225,845,734</td>
<td>0.8%</td>
</tr>
<tr>
<td>Weight, pounds</td>
<td>183.2 (47.7)*</td>
<td>99.1%</td>
</tr>
<tr>
<td>Measured</td>
<td>225,674,069</td>
<td>0.9%</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>29.3 (7.0)*</td>
<td>99.0%</td>
</tr>
<tr>
<td>Measured</td>
<td>225,449,410</td>
<td>1.0%</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.86 (0.3)</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
| Measured      | 227,613,357       | 100.0%  | 82.1 (347.5)* | 100%
| Urine ACR, mg/g | 34.9 (273.4)* | 98.8%   | 523,849  | 11.7% |
| Measured      | 224,969,918       | 1.2%    | 3,953,826| 88.3% |

BMI, body mass index.

*NHANES results estimated from statistical study weights.

bMean (SD).

(Supplemental Figure 2, Table 2). The overall estimated prevalence of CKD increased from 17.9% to 19.6%. Among those identified as Black race, the estimated prevalence of CKD increased from 12.4% to 21.6%. Change in estimated prevalence of eGFR category by age group, sex, and diabetes status is displayed in Figure 1.

Within the VA, 3,673,099 veterans (82.0%) had an eGFR $\geq 60$ ml/min per 1.73 m$^2$ using the original CKD-EPI equation, 687,034 (18.7%) of whom were identified as Black race. Among Black veterans, 71,805 were reclassified to CKD Stage 3 with removal of race adjustment (Table 3). Of 85,487 Black veterans with CKD Stage 3, 5444 (6.5%) were reclassified to CKD Stage 4 with removal of the race adjustment. Finally, 2735 (29.1%) of the 9409 Black veterans with CKD Stage 4 were reclassified to CKD Stage 5.

Within the VA, 19.4% of Black veterans would be classified as having CKD Stage 3, 52.7% of whom would be classified as such, regardless of race adjustment, and 47.3% of whom would be newly classified as having CKD Stage 3 (Supplemental Figure 3).
Table 2. Prevalence of eGFR category in the NHANES and VA with and without race adjustment of eGFR

<table>
<thead>
<tr>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Weighted N&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Weighted N&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Difference (%)</td>
</tr>
<tr>
<td>Overall Mean eGFR</td>
<td>143,745,115</td>
<td>70,351,461</td>
<td>373,160</td>
</tr>
<tr>
<td>eGFR ≥90</td>
<td>63.2 (59.1 to 67.2)</td>
<td>61.2 (57.9 to 64.6)</td>
<td>−1.9 (−2.8 to −1.9)</td>
</tr>
<tr>
<td>eGFR 60–89</td>
<td>30.9 (27.4 to 34.4)</td>
<td>32.2 (29.2 to 35.3)</td>
<td>1.3 (0.7 to 2.0)</td>
</tr>
<tr>
<td>eGFR 30–59</td>
<td>5.5 (4.5 to 6.6)</td>
<td>6.1 (5.2 to 7.0)</td>
<td>0.5 (0.2 to 0.9)</td>
</tr>
<tr>
<td>eGFR &lt;30</td>
<td>0.4 (0.3 to 0.5)</td>
<td>0.4 (0.3 to 0.5)</td>
<td>0.03 (−0.01 to 0.07)</td>
</tr>
<tr>
<td>Overall Black</td>
<td>104.5 (27.2)</td>
<td>90.2 (23.5)</td>
<td>73,996</td>
</tr>
<tr>
<td>eGFR ≥90</td>
<td>71.0 (66.7 to 75.3)</td>
<td>53.5 (49.4 to 57.6)</td>
<td>−17.5 (−20.2 to −14.7)</td>
</tr>
<tr>
<td>eGFR 60–89</td>
<td>23.8 (19.9 to 27.7)</td>
<td>36.0 (32.5 to 39.4)</td>
<td>12.2 (9.3 to 15.0)</td>
</tr>
<tr>
<td>eGFR 30–59</td>
<td>4.6 (3.2 to 6.1)</td>
<td>9.7 (8.0 to 11.3)</td>
<td>5.0 (3.5 to 6.5)</td>
</tr>
<tr>
<td>eGFR &lt;30</td>
<td>0.6 (0.1 to 1.0)</td>
<td>0.9 (0.3 to 1.4)</td>
<td>0.3 (−0.1 to 0.7)</td>
</tr>
</tbody>
</table>

Mean eGFR expressed as mean (SD). 95% CI, 95% confidence interval. ¹NHANES results estimated from statistical study weights. ²Confidence interval width ≤0.3.
Figure 1. Difference in prevalence of eGFR categories without versus with race adjustment in the NHANES 2015–2016 and Veterans’ Health Administration 2015 cohorts, by age group, sex, and diabetes mellitus status. A positive number indicates prevalence of eGFR category was higher without race adjustment, and a negative number indicates prevalence was lower without race adjustment.
(Figure 3). Visual inspection of the calibration plots suggested the KFRE model without race adjustment was better calibrated at levels of predicted risk $\leq 5\%$ and less well calibrated at levels of predicted risk below 1%. In the complete case analysis, discrimination of the KFRE among Black adults was slightly lower ($c$-statistic 0.91), and calibration was slightly better as compared with the multiple imputation analysis (Supplemental Table 2).

**DISCUSSION**

We found that removal of the adjustment for Black race from the CKD-EPI creatinine equation would double the prevalence of CKD in Black adults, resulting in a 0.6% absolute increase in the prevalence of CKD nationally and a 1.7% absolute increase in the prevalence of CKD in the VA population. Changes in estimated CKD prevalence were largest in older adults and persons with diabetes. The potential effect of changes in eGFR on medication dosing could affect a substantial number of Black adults, for example, up to 41% of gabapentin users and more than 25% of metformin and ciprofloxacin users. The discrimination of kidney failure risk prediction using GFR without race adjustment remained high, and calibration among Black adults was improved at higher levels of predicted risk.

Our study provides population-level estimates of the effect of removing race adjustment from the CKD-EPI creatinine eGFR equation. Although the NHANES and VA cohorts were quite different in their composition, the estimates overall and within subgroups were similar between the NHANES and VA. By quantifying the effect of changes in GFR estimation on medication prescribing and kidney failure prediction in a

<table>
<thead>
<tr>
<th>Table 3. Reclassification of CKD stage among black adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NHANES 2015–2016</strong></td>
</tr>
<tr>
<td>Race-adjusted CKD-EPI eGFR (in ml/min per 1.73 m$^2$)</td>
</tr>
<tr>
<td>$\geq 60$</td>
</tr>
<tr>
<td>30 $\leq$ eGFR $&lt; 60$</td>
</tr>
<tr>
<td>15 $\leq$ eGFR $&lt; 30$</td>
</tr>
</tbody>
</table>

$^a$NHANES results estimated from statistical study weights.

Figure 2. Number of Black adults with prescription in the following 90 days for common medications requiring dose adjustment for kidney function, and users potentially affected by change in eGFR. Dark-shaded bars represent veterans whose dose of medication would not be affected by removal of race adjustment from eGFR. Light-shaded bars represent the number of veterans whose eGFR without race adjustment crosses a dosing threshold. The figure above each bar represents the percentage of total medication users whose eGFR without race adjustment crosses a dosing threshold.
national cohort, our study adds to the findings recently reported by Ahmed et al. and Diao et al. Using an NHANES sample from 2001 to 2018, Diao et al. estimated that removing race adjustment of eGFR would result in an absolute increase in CKD prevalence of 3.5% among Black adults, and an increase of 1.2% for CKD Stage G3b and 0.3% for CKD Stage G4, consistent with our findings.

Although the inclusion of an adjustment for Black race in equations to estimate GFR may have improved their precision in study populations, the biologic underpinnings have not been well explained, raising concerns for misuse of race as a biologic variable and exacerbation of racial disparities in health care. The adjustment for Black race in the CKD-EPI creatinine equation is on the basis of the finding that individuals identified as Black had higher measured GFR compared with non-Black individuals of similar age, sex, and serum creatinine level. Whether muscle mass is the primary explanation for the observed differences remains unclear, because the addition of surrogates for muscle mass such as height and weight did not meaningfully attenuate the association between race and creatinine-based eGFR. Some studies have questioned the accuracy of the race adjustment factor in the CKD-EPI equation. Adjustment for Black race leads to an overestimation of kidney function in African populations, in young Black adults, and in Black individuals with early polycystic kidney disease; it may also underestimate the prevalence of CKD-related metabolic complications among Black individuals.

Estimation of GFR without race adjustment reclassifies a sizeable fraction of Black adults with CKD. Because the race-adjustment factor is constant and CKD prevalence is higher at earlier stages, its elimination leads to a larger effect on CKD prevalence at earlier versus more advanced stages. For example, prevalence of CKD stage G3 (eGFR 30–59 ml/min per 1.73 m²) increased by 5.0%, whereas prevalence of CKD stage G4 (eGFR 15–30 ml/min per 1.73 m²) increased by 0.3%. Consequently, the effects on individual patient care are likely to be experienced by a larger number of patients for clinical decisions at earlier stages of CKD.

We found these differences in GFR estimates could affect 6.0%–41.0% of Black adults using commonly prescribed medications, depending on the medication and GFR threshold for dose adjustment or discontinuation. Intermittently used chemotherapeutic agents and newer medications, such as sodium glucose cotransporter 2 inhibitors, would be similarly affected. If creatinine-based estimates of GFR without race adjustment systematically underestimate GFR in Black adults, adoption could result in under-dosing or withholding of beneficial medications, and inadvertently contribute to disparities in care. Although most dosing recommendations are on the basis of the Cockroft-Gault estimated creatinine clearance, in practice, clinicians and clinical decision-support algorithms substitute eGFR. Use of a confirmatory test, such as direct measurement of GFR or cystatin-c based estimation methods, has been proposed to dose drugs with a narrow therapeutic window or when creatinine-based estimates may lack

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### Table 4. Estimated 2-yr risk of kidney failure and accuracy of the KFRE in the Department of VA Health Care System with versus without race adjustment of eGFR

<table>
<thead>
<tr>
<th>Cohort</th>
<th>% (N) Progressing to Kidney Failure over 2 yr</th>
<th>eGFR with Race Adjustment</th>
<th>eGFR without Race Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KFRE (SD)</td>
<td>c-statistic</td>
<td>Brier Score</td>
</tr>
<tr>
<td>All CKD (n=495,959)</td>
<td>2.4% (12,055)</td>
<td>2.0%</td>
<td>0.954</td>
</tr>
<tr>
<td>Black patients (n=97,851)</td>
<td>3.8% (3680)</td>
<td>2.7%</td>
<td>0.959</td>
</tr>
<tr>
<td>White patients/other races</td>
<td>2.1% (8375)</td>
<td>1.8%</td>
<td>0.952</td>
</tr>
<tr>
<td>(n=398,108)</td>
<td>(6.6)</td>
<td>(0.950–0.955)</td>
<td></td>
</tr>
</tbody>
</table>

*P value for comparison of Brier score in models with versus without race adjustment of eGFR <0.0001.

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**Figure 3.** Calibration plots for original KFRE using eGFR with race adjustment (solid black line), and KFRE using eGFR without race adjustment (dashed black line) among Black adults in the VA cohort.
accuracy. Lack of widespread availability and long turn-around times limit the use of these strategies. Recalibration of the CKD-EPI equation is also under consideration, which would result in less-pronounced changes to CKD prevalence and smaller clinical effects than those estimated here.

One of the speculated harms of eliminating the adjustment for Black race is underestimation of the relation between reduced eGFR and the risk for progression to kidney failure, which in turn can affect the timing of specialty care referrals and planning for dialysis and transplantation. In the VA cohort, we found that both race-adjusted and non–race-adjusted equations underestimated risk of kidney failure among Black patients at higher levels of predicted risk, and that calibration of the KFRE improved at levels of predicted risk above 5% when eGFR was not adjusted for race. Conversely, calibration was poorer for the non–race-adjusted KFRE at levels of risk below 1%. Guidelines recommend the integration of predicted risk in the management of CKD. Improved calibration of the KFRE at lower levels of eGFR means that more Black adults would be correctly identified as high risk and meet proposed decision thresholds for vascular access and transplant referral, a 2-year risk >20%–40%. In contrast, poorer calibration at higher eGFR levels could lead to more nephrology referrals for low-risk Black adults.

The inclusion of race in GFR-estimating equations is premised on evidence of improved accuracy of these equations among Black patients with race adjustment. Assuming that eliminating race adjustment leads to a loss in accuracy among Black patients, our study provides empirical data on the implications of widespread adoption for both individual and public health. We focused on drug dosing and kidney failure predication because these clinical decisions affect patients at higher and lower levels of eGFR, respectively, illustrating trade-offs associated with removing race adjustment. Removal of race adjustment has the potential to affect other aspects of clinical management that we did not evaluate, such as eligibility for kidney donation, contrast administration for diagnostic imaging, waiting time for kidney transplantation, and eligibility for clinical trials. Ultimately, institutions and professional societies evaluating the use of race in GFR estimation are likely to consider many factors in addition to the equations’ accuracy and estimates of how many are helped or harmed by race adjustment, including the availability of confirmatory testing of eGFR, the historical misuse of race in medicine, and inequities in access to care.

Strengths and Limitations

NHANES is a nationally representative sample, thus the findings should be generalizable to the US adult population. We assessed potential clinical effects in VA, the largest healthcare system in the United States. We utilized prescription records rather than self-report to ascertain medication use, and we ascertained kidney failure with a national registry. Our study also has some limitations. Gold-standard measurement of GFR was not performed in NHANES, and reflective of clinical practice, was not available in most individuals in the VA cohort. Prevalence estimates of CKD were based on single measurements of eGFR, thus CKD prevalence is overestimated. We relied on self-reported race, which is the method used by laboratories to report eGFR, and did not evaluate ancestry. Fourth, the VA population is comprised mostly of males, which limits generalizability. Fifth, we did not evaluate medication use in NHANES, due to the small number of individuals available when the sample was restricted by race, eGFR, and specific medications. Sixth, our analysis assessed medication prescriptions and did not evaluate prescribed doses. Removal of race adjustment from the CKD-EPI eGFR equation without additional calibration would result in a near doubling of the estimated US prevalence of CKD among Black adults. Widespread implementation is likely to lead to sizeable changes in clinical care and population health strategies for Black adults.

DISCLOSURES

I.-C. Thomas, M. Kurella Tamura, and M.E. Montez-Rath are supported by HX002763 from the Department of Veterans Affairs. G.M. Chertow reports having consultancy agreements with Abeba, Amgen, Ardelyx, AstraZeneca, Baxter, Cricket, DiaMedica, Gilead, Miromatrix, Reata, Santilin, Unicycive, and Vertex; reports having an ownership interest in Ardelyx, CloudCath, Direct, OxNow, Eliaz Therapeutics, Outset, Physiowave, and PureCath; reports receiving research funding from National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and National Institute of Allergy and Infectious Diseases; reports being a scientific advisor or member of the Board of Directors of Satellite Healthcare, Co-Editor of Brenner & Rector’s The Kidney (Elsevier); and reports having other interests/relationships with data safety monitoring board service with NIDDK, Angion, Bayer, and ReCor. M. Kurella Tamura reports receiving honoraria from American Federation for Aging Research and reports being a scientific advisor or member of CJASN Editorial Board, Clin-Star Advisory Board, and Beeson External Advisory Committee. M.E. Montez-Rath reports receiving research funding from Sanofi. V. Duggal is an employee of Genentech, Inc. outside of submitted work, has an ownership interest in Roche Holding AG, and was supported by the Medical Informatics Fellowship at the Department of Veterans Affairs.

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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2020121780/-/
DCSupplemental

Supplemental Table 1. Kidney function dosing recommendations for common medications.

Supplemental Table 2. Estimated 2-year risk of kidney failure and accuracy of the Kidney Failure Risk Equation in the Department of Veterans Affairs Health Care System with versus without race adjustment of eGFR.

Supplemental Figure 1. Coefficient flow diagram.

Supplemental Figure 2. Histogram of eGFR distribution in NHANES and VA cohort with and without race adjustment of eGFR.

Supplemental Figure 3. Prevalence and number, in thousands, of CKD Stage 3 (eGFR 30–59 ml/min per 1.73 m²) among Black individuals in NHANES and VA cohorts using eGFR without race adjustment.

REFERENCES


2. Eneanya ND, Yang W, Reese PP: Reconsidering the consequences of using race to estimate kidney function. JAMA 320: 1539–1540, 2018


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Table 1. Kidney function dosing recommendations for common medications

Table 2. Estimated two-year risk of kidney failure and accuracy of the Kidney Failure Risk Equation in the Department of Veterans Affairs Health Care System with versus without Race Adjustment of eGFR in a complete case analysis

Figure 1. Cohort flow diagram

Figure 2. Histogram of eGFR distribution in NHANES and VA cohort with and without race adjustment of eGFR.

Figure 3. Prevalence and number, in thousands, of CKD Stage 3 (eGFR 30-59 mL/min/1.73 m²) among Black individuals in NHANES and VA cohorts using eGFR without race adjustment.
Supplemental Table 1. Kidney function dosing recommendations for common medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Level of kidney function at which dose reduction or discontinuation is recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Reduce dose and do not initiate when eGFR 30 to &lt;45 ml/min/1.73m² Discontinue when eGFR &lt;30 ml/min/1.73m²</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Reduce dose by 50% when eGFR &lt;50 ml/min/1.73m² Reduce dose by 75% when eGFR 15 to &lt;25 ml/min/1.73m² Reduce dose by 90% when eGFR &lt;15 ml/min/1.73m²</td>
</tr>
<tr>
<td>Atenolol</td>
<td>Maximum dose 50mg daily when eGFR &lt;35 ml/min/1.73m² Maximum dose 25mg daily when eGFR &lt;15 ml/min/1.73m²</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Maximum dose 10mg daily when eGFR &lt;30 ml/min/1.73m²</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Maximum dose 200mg daily when eGFR &lt;30 ml/min/1.73m², and dosing frequency increased to every twelve hours</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Maximum dose 250mg-500mg every twelve hours when eGFR &lt;50 ml/min/1.73m² Maximum dose 250mg-500mg every eighteen hours when eGFR &lt;30 ml/min/1.73m²</td>
</tr>
</tbody>
</table>
### Supplemental Table 2. Estimated two-year risk of kidney failure and accuracy of the Kidney Failure Risk Equation in the Department of Veterans Affairs Health Care System with versus without Race Adjustment of eGFR in a complete case analysis.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>% (N) progressing to kidney failure over two years</th>
<th>eGFR with Race Adjustment</th>
<th>eGFR without Race Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>KFRE (SD) c-statistic</td>
<td>Brier score</td>
</tr>
<tr>
<td></td>
<td></td>
<td>KFRE (SD) c-statistic</td>
<td>Brier score</td>
</tr>
<tr>
<td>All CKD (N=134,121)</td>
<td>2.1% (2,618)</td>
<td>1.7% (6.4) 0.8836 0.01489</td>
<td>1.9% (6.8) 0.8863 0.01488</td>
</tr>
<tr>
<td>Blacks (N=25,281)</td>
<td>2.8% (707)</td>
<td>2.0% (8.3) 0.9009 0.01877</td>
<td>2.7% (9.5) 0.9070 0.01872</td>
</tr>
<tr>
<td>White/Other races (N=108,840)</td>
<td>1.8% (1,921)</td>
<td>1.7% (5.9) 0.8782 0.01399</td>
<td>-</td>
</tr>
</tbody>
</table>

Abbreviations: CKD – chronic kidney disease, eGFR – estimated glomerular filtration rate, KFRE – kidney failure risk equation, SD – standard deviation
**Supplemental Figure 1.** Cohort flow diagram

4,578,287  
Adult Veterans with outpatient serum creatinine in 2015

Exclude
- 72,121 missing demographics
- 28,491 prior dialysis or transplant

4,477,675  
VA analytic cohort

Exclude
- 3,981,716 without a sustained eGFR <60 ml/min/1.73m$^2$

5385  
Adult NHANES participants with serum creatinine in 2015-2016

Exclude
- 16 prior dialysis

5,369  
NHANES analytic cohort

495,959  
VA cohort with CKD  
KFRE analytic cohort
Supplemental Figure 2. Histogram of eGFR distribution in NHANES (panel A) and VA cohort (panel B) with and without race adjustment of eGFR.

Panel A. Distribution of eGFR with and without Race adjustment among Black adults in NHANES.
Panel B. Distribution of GFR with or without Race adjustment among Black adults in VA
Supplemental Figure 3. Prevalence (Panel A) and number, in thousands (Panel B) of CKD Stage 3 (eGFR 30-59 mL/min/1.73 m$^2$) among Black individuals in NHANES and VA cohorts using eGFR without race adjustment.

Footnote: Blue bars represent the proportion of Black individuals who were classified as CKD Stage 3 with and without race adjustment. Orange bars represent the proportion of Black individuals who were classified as CKD Stage 3 only when using eGFR without race adjustment. Abbreviations: CKD – chronic kidney disease, eGFR – estimated glomerular filtration rate