

## Are the Creatinine-Based Equations Accurate to Estimate Glomerular Filtration Rate in African American Populations?

Pierre Delanaye,\* Christophe Mariat,<sup>†</sup> Nicolas Maillard,<sup>†</sup> Jean-Marie Krzesinski,\* and Etienne Cavalier<sup>‡</sup>

### Summary

Regarding the high prevalence of African American patients with ESRD, it is important to estimate the prevalence of early stages of chronic kidney disease in this specific population. Because serum creatinine concentration is dependent on muscular mass, an ethnic factor has to be applied to creatinine-based equations. Such ethnic factors have been proposed in the Modification of Diet in Renal Disease (MDRD) study equation and in the more recent Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations. This review analyzes how these correction factors have been developed and how they have, or have not, been validated in external populations. It will be demonstrated that the African American factor in the MDRD study equation is accurate in African American chronic kidney disease (CKD) patients. However, it will be shown that this factor is probably too high for subjects with a GFR of  $\geq 60$  ml/min per  $1.73 \text{ m}^2$ , leading to an underestimation of the prevalence of CKD in the global African American population. It will also be confirmed that this ethnic factor is not accurate in African (non-American) subjects. Lastly, the lack of true external validation of the new CKD-EPI equations will be discussed. Additional trials seem necessary in American African and African populations to better estimate GFR and apprehend the true prevalence of CKD in this population with a high renal risk.

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### Introduction

Measuring GFR is considered one of the classical ways, along with proteinuria, to assess kidney function (1). Because measuring GFR is relatively cumbersome, more “simple” biologic variables have been proposed. Among these variables, serum creatinine has been the most used for more than a century (2). However, we all know the limitations of this marker for estimating GFR. The most important limitation is linked to the fact that serum creatinine concentration is dependent not only on GFR but also on muscular mass. Because of this strong link to muscular mass, serum creatinine concentration and creatinine excretion will vary with ethnicity, gender, and age independently of any GFR changes (3–6). For this reason, several creatinine-based equations have been developed, including these last two variables to estimate GFR (7,8). From the same view, serum creatinine concentration will differ between ethnicities for the same GFR level because it is well known that African people proportionally have a larger muscular mass than Caucasian or Asian populations (9–11). At the same GFR, serum creatinine concentrations are higher in black populations not only because of higher muscular mass but also because creatinine tubular secretion could be a variable according to ethnicity (3–5). Moreover, in the black ethnicity, serum creatinine also reflects the risk of developing chronic kidney disease (CKD) (12).

Most of the former creatinine-based equations have been built from Caucasian populations and are thus logically inaccurate for estimating GFR in other ethnic populations (7). This is the case for the well known Cockcroft and Gault equation (3,7,13–15). In 1999, the Modification of Diet in Renal Disease (MDRD) study equation has been published and an ethnic correction factor has been proposed for African Americans (8). More recently, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation has been proposed with other ethnic factors (16,17). In this review article, we will describe how these African American ethnic factors have been developed and validated. We will only discuss ethnic factors and not “new” equations specifically built from the African American population because these equations, even if of interest, are used neither in clinical practice nor in clinical trials (13). The importance of an accurate ethnic factor correction is high, notably for epidemiologic trials on CKD prevalence (9,18–21). This last point must be underlined. Actually, compared with the general population, the proportion of African American ESRD patients in the United States is impressive (13,20,22,23). In the same way, African American subjects have a relatively higher risk of macroalbuminuria and of a longitudinal rise in creatinine (12). On the contrary, in the general population, the prevalence of stage 3 CKD is lower in African Americans than in Caucasians. This observation is a sort of an

Departments of  
\*Nephrology, Dialysis,  
Hypertension and  
Transplantation, and  
‡Clinical Chemistry,  
University of Liège,  
CHU Sart Tilman,  
Liège, Belgium; and  
†Department of  
Nephrology, Dialysis,  
Hypertension, and  
Transplantation,  
University Jean Monnet,  
Hopital Nord, Saint-  
Etienne, France

**Correspondence:** Pierre Delanaye, Service de Dialyse, B35, CHU Sart Tilman, 4000 Liège, Belgium. Phone: ++32-4-366-71-11; Fax: ++32-4-366-72-05; E-mail: pierre\_delanaye@yahoo.fr

“epidemiologic paradox” (16,20,21). We will discuss this paradox in the light of the performances of the creatinine-based equations in African American subjects.

### Derivation of Ethnic Coefficient in MDRD Study

The MDRD study equation has been derived from 1628 patients. Mean measured GFR in this cohort was  $39.8 \pm 21.2$  ml/min per  $1.73$  m<sup>2</sup>. Compared with Caucasians ( $n = 1304$ ), the sample of African Americans was relatively low (only 8% of the MDRD sample,  $n = 197$ ). The reference population was arbitrarily chosen to be the Caucasians. The African American ethnic factor should always be interpreted as a comparison between African Americans and Caucasians as opposed to some intrinsic characteristic of African Americans. Moreover, the mean GFR in African Americans was slightly but significantly higher compared with African Americans ( $39.2 \pm 20.8$  versus  $43.6 \pm 21.4$  ml/min per  $1.73$  m<sup>2</sup>). In the multiple regression models, black ethnicity was considered as a dichotomous variable and was an independent predictor of higher GFR. A 1.18 ethnic factor was thus proposed for African American populations in the six-variable MDRD study equation (including albumin and urea) (8). The abbreviated MDRD study equation was later published in an abstract form (24). The African American ethnic factor was thus calculated at 1.21, which was later confirmed in a full-text publication (25). Regarding the ethnic coefficient, the most important limitation of the original MDRD study is doubtless the limited African American sample. An external validation would have been necessary. It is also important to underline that most of subjects in the MDRD study are CKD patients. On the basis of these data, it is difficult to make a definitive conclusion regarding the performances of the ethnic factor according to the GFR levels. However, from Figure 1 in reference 8, it seems that if the relation of serum creatinine and GFR is different according to ethnicity, this difference is more important in low than in high GFR. Applying a “unique” ethnic factor to the all of the GFR range does not reflect this difference.

### Validation of Ethnic Coefficient in the African American Study of Hypertension and Kidney Disease and the Consortium for Radiologic Imaging Studies of Polycystic Disease

The African American Study of Hypertension and Kidney Disease (AASK) trial was doubtless the best study to validate the African American factor in the MDRD study

equation (13,15,26). Briefly, the AASK trial was designed to study the effect of different antihypertensive therapies on renal outcomes in African American CKD subjects (26). In the AASK study, the GFR was measured by an isotopic method; that is, urinary clearance of iothalamate and creatinine was measured at the Cleveland Laboratory with the CX3 Beckman method (13,15,27). These two last points are of importance because these reference and creatinine measurement methods are also used in the original MDRD study. The difference in reference methods or in creatinine calibration between trials can thus not explain potential differences in estimating GFR (28–30). In the same view, we know that performance of the MDRD study equation will strongly vary with the GFR range (28,31,32). The MDRD study equation is actually the most accurate in the low-GFR range (stage 3 and 4 CKD), but it underestimates GFR in higher GFR ranges (*i.e.*, in healthy subjects) (28,31,33). The mean GFR range in the AASK study, although statistically different, is comparable to the mean GFR in the MDRD study in terms of CKD staging (most subjects with stage 3 or 4 CKD) (Table 1). Age and body mass index are also statistically different in the MDRD and the AASK trials. As weight is not a variable in the MDRD study equation, difference in weight between AASK and MDRD populations will not directly influence the results. In the same way, difference in age (<5 years) is too small to greatly impact on global results. So, the main difference between the two populations is the ethnicity; all the patients are African American in AASK but only 8% in the MDRD study (8,13,15). In 2001, Lewis *et al.* published the performance of the MDRD study equation in the AASK population (13). In this article, the authors also proposed other original equations (Table 2). However, the performance of the original MDRD study equation was so high that the Lewis equations have never been used in clinical practice. Actually, the absolute median difference between estimated and measured GFR is 12% in the AASK study. This result is really excellent. Nevertheless, three criticisms can be made. First, the bias between measured and estimated GFR is pretty good, but we have less clear data regarding the precision (only  $r^2$  value is given) in the AASK population. However, precision is probably acceptable ( $r^2 = 0.819$ ). Second, in the Lewis study, only the six-variable MDRD study equation was tested (8). To the best of our knowledge, the abbreviated MDRD study equation (Table 2), which is now the most used and validated equation, has not been studied specifically in the AASK

**Table 1. Population characteristics in the AASK and in the MDRD study equation according to ethnicity (8,13)**

	MDRD (all)	MDRD AA	MDRD non-AA	AASK
Sample	1628	197	1431	1703
Age (years)	50.6	48.9	50.8	53.9
Gender (% women)	40	42.6	39.2	35.5
GFR (ml/min per $1.73$ m <sup>2</sup> )	39.8	43.6	39.2	56.9
BMI (kg/m <sup>2</sup> )	27	28.7	27	30.7
Weight (kg)	79.6	84.1	79.3	90.2
Serum creatinine (mg/dl)	2.3	2.21	1.9	2.15

BMI, body mass index; MDRD, Modification of Diet in Renal Disease; AA, African American; AASK, African American Study of Hypertension and Kidney Disease.

**Table 2. Creatinine-based equations developed in the AASK, MDRD, and CKD-EPI trials**

## Six-variable MDRD study equation

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 170 \times SCr \text{ (mg/dl)}^{-0.999} \times age^{-0.176} \times 0.762 \text{ (if woman)} \times BUN \text{ (mg/dl)}^{-0.170} \\ \times albumin^{+0.318} \times 1.18 \text{ for African American}$$

## Four-variable MDRD study equation

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 186 \times SCr \text{ (mg/dl)}^{-1.154} \times age^{-0.203} \times 0.742 \text{ (if woman)} \times 1.21 \text{ for African American}$$

## Six-variable AASK study equation

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 222 \times SCr \text{ (mg/dl)}^{-0.974} \times age^{-0.267} \times 0.757 \text{ (if woman)} \times BUN \text{ (mg/dl)}^{-0.108} \\ \times albumin^{+0.372}$$

## Four-variable AASK study equation

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 329 \times SCr \text{ (mg/dl)}^{-1.096} \times age^{-0.294} \times 0.736 \text{ (if woman)}$$

## Four-variable MDRD study equation (IDMS traceable)

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 175 \times SCr \text{ (mg/dl)}^{-1.154} \times age^{-0.203} \times 0.742 \text{ (if woman)} \times 1.21 \text{ for African American}$$

## CKD-EPI study equation

## African American female

serum creatinine &lt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 166 \times (SCr/0.7)^{-0.329} \times 0.993^{age}$$

serum creatinine &gt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 166 \times (SCr/0.7)^{-1.209} \times 0.993^{age}$$

## African American male

serum creatinine &lt;0.9 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 163 \times (SCr/0.9)^{-0.411} \times 0.993^{age}$$

serum creatinine &gt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 163 \times (SCr/0.9)^{-1.209} \times 0.993^{age}$$

## Caucasian female

serum creatinine &lt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 144 \times (SCr/0.7)^{-0.329} \times 0.993^{age}$$

serum creatinine &gt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 144 \times (SCr/0.7)^{-1.209} \times 0.993^{age}$$

## Caucasian male

serum creatinine &lt;0.9 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 141 \times (SCr/0.9)^{-0.411} \times 0.993^{age}$$

serum creatinine &gt;0.7 mg/dl

$$GFR \text{ (ml/min per } 1.73 \text{ m}^2) = 141 \times (SCr/0.9)^{-1.209} \times 0.993^{age}$$

SCr, serum creatinine; BUN, blood urea nitrogen; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; IDMS, Isotope Dilution Mass Spectrometry.

trial (24). The ethnic factors in the six- versus four-variable MDRD study equations are not strictly the same (1.18 versus 1.21, respectively). Anyway, we can admit that the effect of such a difference could be limited. Third, because the GFR range in the AASK study is comparable to the GFR range in the MDRD study equation, we have no direct proof of the accuracy of the ethnic factor in higher GFR ranges. We know that the relationship between serum creatinine and GFR is not the same in CKD compared with healthy Caucasian subjects (32,34). Combining the results of the MDRD and AASK studies (8,13), we also know that the relationship between creatinine and GFR is not the same between CKD Caucasian subjects and CKD African American subjects, which implies the ethnic correction. However, we have no direct proof of a significant difference in the GFR-creatinine relationship between healthy Caucasian subjects and healthy African American subjects even if we can reasonably presume it. More importantly, we do not really know if these two last differences are the same from a quantitative point of view. In other words, is the quantitative difference in muscular mass between CKD African Americans and Caucasians exactly the same as the difference in muscular mass between healthy African Americans and Caucasians? This is actually speculative, although applying the same ethnic factor in all of the GFR

range implies it is. If the absolute difference in muscular mass between Caucasian and African Americans (and thus in serum creatinine concentration) is higher in CKD subjects than in healthy patients, the ethnic factor of 1.21 would be too high in healthy African Americans and in GFR ranges near 60 ml/min per 1.73 m<sup>2</sup>. Such a difference in the relationship between GFR and creatinine in African Americans and non African Americans had already been shown in the original MDRD study (8) (Figure 1 in reference 8) and thereafter briefly suggested by Poggio (32). Likewise, the same observation has been previously made for the gender coefficient factor (35). Some data from the CRISP study (Consortium for Radiologic Imaging Studies of Polycystic Disease) could further support this notion (36). In this longitudinal study, 234 patients with autosomal dominant polycystic kidney disease (ADPKD) were followed for 4 years with one GFR measurement per year. Once again, serum creatinine measurement was adequately calibrated and GFR was measured by iothalamate urinary clearance. However, contrary to the MDRD and the AASK cohorts, the ADPKD subjects had measured GFR >60 ml/min per 1.73 m<sup>2</sup> (mean GFR of 95 ml/min per 1.73 m<sup>2</sup>). Among the 234 subjects, 24 (10%) were African Americans. The authors have studied association between predictor variables and measured GFR with the same mul-

tivariable regression model used in the MDRD study. The African American coefficient factor was determined at 1.04 in this limited cohort of patients in CKD stage 1 or 2. Still more interesting, this coefficient factor trends to increase in the 3 following years (1.08, 1.09, and 1.1 at 1, 2, and 3 years of follow-up, respectively), although the mean GFR cohort is declining. These two results argue for a different ethnic correction according to GFR levels and to a lower ethnic coefficient factor in higher GFR levels.

Let us now go back to the AASK study for a final comment about results regarding GFR estimation for patient follow-up (13). Actually, Lewis *et al.* have shown that estimating changes in renal function using creatinine-based equations (with their “own” AASK equations, not the MDRD study one) yielded the same conclusion about the efficiency of the interventions in the AASK trial than measured GFR by a reference method did (37). This last finding is fundamental and confirms that the African American ethnic factor is accurate in CKD African American subjects.

### Derivation and Validation of Ethnic Coefficient in CKD-EPI Studies

The CKD-EPI group includes data from different trials having interest in measuring and estimating GFR (16,17,33). This group developed new creatinine-based equations with more accuracy in high GFR levels, named the CKD-EPI equations. The first database includes 10 studies all using iothalamate clearance for measuring GFR. The global sample was 8254 participants divided randomly into two separate data sets for development ( $n = 5504$ ) and internal validation ( $n = 2750$ ). The second database was used as external validation ( $n = 3896$ ) and included studies with other reference methods for measuring GFR. All of the creatinine values used in these databases can be considered as Isotope Dilution Mass Spectrometry (IDMS) traceable (27). Compared with the MDRD study equation, there are significantly more healthy subjects in all of the databases, even if “healthy” subjects are actually organ donors, for the vast majority, which may be not representative of the general healthy population (38). In 2007, performance of the abbreviated MDRD study equation was described in the 5504 subjects from the development data set (8). Among these 5504 subjects, 1737 (32%) were considered as African Americans (8,16). Most of these African American subjects were actually coming from the AASK study ( $n = 1205$ , 69%) and most of them had a GFR  $<60$  ml/min per  $1.73 \text{ m}^2$  (8). In Table 3, we show the results of the MDRD study equation performance in the subgroup of

African American subjects. Performance of the MDRD study equation is comparable in global and for Caucasian and African American populations when the estimated GFR is  $<60$  ml/min per  $1.73 \text{ m}^2$ . However, difference appears in subjects with estimated GFR  $>60$  ml/min per  $1.73 \text{ m}^2$ . Indeed, although estimated GFR underestimates measured GFR in the overall population (and in all of the subgroups, except the transplanted patients), the bias is excellent in the African American population. Accuracy (defined as the percentage of subjects with an estimated GFR within 30% of measured GFR) in this African American subgroup is the best among other subpopulations (88%). Actually, the MDRD study equation logically underestimates GFR in healthy Caucasian subjects because MDRD was built from a Caucasian CKD population and the relationship between GFR and creatinine is not the same in CKD and healthy subjects (28,31). However, this underestimation is not seen in healthy African American subjects. One explanation could be that the unique ethnic factor corrects adequately for ethnicity in CKD but should be lower in healthy people. As we have suggested, the factor of 1.21 appears too high in healthy African Americans from an “ethnic” point of view, but, by chance, this overestimation also compensates for the underestimation linked to the GFR level. Actually, these “abnormally” good results for the MDRD study equation in healthy African American subjects argue for a different African American ethnic factor between CKD and healthy subjects.

The new CKD-EPI equation is sensed to be more accurate in healthy subjects and different “subformulas” have actually been developed according to the creatinine level (Table 2) (16,17). According to our hypothesis and because healthy subjects are well represented in the development data set, the African American ethnic factor in this new equation is lower than in the former MDRD study equation (1.159 versus 1.212) (Appendix Table 5 in reference 16). However, this ethnic factor is still similarly applied in CKD and healthy populations (16). It must also be underlined that the African American sample in the second data set (external validation) is relatively modest ( $n = 384$ , 10% of the external validation data set). Moreover, among these 384 black patients, 84 (22%) are European black patients (most coming from the Nephro-test cohort in France [31]), and it is plausible that the African American ethnic factor is not accurate in African European subjects. This topic is absolutely not discussed in the CKD-EPI articles. Definitive conclusions from the CKD-EPI trial (external validation) are thus eventually difficult to do regarding the African American subjects (39,40). A recent trial published by

**Table 3. Performance of the MDRD study equation according to ethnicity in the CKD-EPI group (33) (bias is median difference between estimated GFR and measured GFR)**

	Estimated GFR $<60$ ml/min per $1.73 \text{ m}^2$			Estimated GFR $>60$ ml/min per $1.73 \text{ m}^2$		
	Sample	Median Difference (%)	P30	Sample	Median Difference (%)	P30
Overall	2874	−3	82	2630	−8.7	84
Caucasian and other	1668	−2.3	82	1799	−11.7	83
African American	1085	−3.4	82	643	−0.2	88

P30, percentage of subjects with an estimated GFR within 30% of measured GFR.

the CKD-EPI group has studied a new equation including other ethnic distinctions (Hispanic, Native American, and Asian). This four-level race equation has little effect on the equation (see Table 3 in reference 17) and on its performance in African American people. Global accuracy of the two-level CKD-EPI equation is not different from the MDRD study equation in African Americans (accuracy within 30% is 82%), and the authors unfortunately do not give data according to the GFR level (over and below 60 ml/min per 1.73 m<sup>2</sup>) (17). This point is important, once again for epidemiologic implications. Actually, the prevalence of stage 3 CKD in the global population (National Health and Nutrition Examination Survey [NHANES] study) logically lowers in the global and Caucasian population using the CKD-EPI equation compared with the MDRD study equation (6.32% *versus* 7.8%, respectively, in the global population and 7.38% *versus* 9.24%, respectively, in Caucasians). However, it is questionable that the prevalence of stage 3 CKD in African Americans is, on the contrary, very comparable with the CKD-EPI and the MDRD study equations (4.83% *versus* 4.75%, respectively) (16). If our hypothesis that the MDRD study equation overestimates GFR (and thus underestimates CKD prevalence) in African Americans is correct, we have to conclude that this error is not, or is very little, improved by the CKD-EPI equations (see below for additional “epidemiologic arguments”).

### Validation of Ethnic Coefficient in African Population

The study published in 2008 by van Deventer *et al.* is of interest because they have analyzed 100 black South African people (14). For the first (and only) time, performance of the (four-variable) MDRD study equation was evaluated against a GFR reference method in African non-American people. This well designed study (adequate reference method and creatinine calibration) has shown that performances of the MDRD study equation were actually better (less overestimation) when the ethnic factor was not applied (median bias of 27% *versus* 5%, respectively). Compared with the MDRD study, the reference method for GFR measurement was different (plasma clearance of <sup>51</sup>Cr-EDTA), which could have flawed the results and explain some bias between studies. Moreover, the absence of a Caucasian group must also be underlined. However, this *a priori* surprising result could also be explained, at least in part, by the low socioeconomic level in black South Africans and the high percentage of HIV patients (20%) included in the South African trial. Both conditions will probably negatively influence the muscular mass, especially when compared to African Americans, thus leading to GFR overestimation by the MDRD study equation (14). This is also indirectly suggested by the difference in weight observed between the trials (mean weight of 69.5 kg in South Africans *versus* 84.1 kg in African Americans in the MDRD study) (8,14). The same results have also been found in Ghanaian populations even if GFR was only estimated by creatinine clearance (and not measured GFR) (11). From the same South African cohort, inaccuracy of the CKD-EPI study equation has also been recently demonstrated by the CKD-EPI group (31). The ethnic factors

proposed in the MDRD and CKD-EPI study equations do not seem to be applied worldwide in all people originating from Africa. Even in Africa, differences in muscular mass among northern, western, and eastern Africans will probably require different “ethnic” factors (14,41).

### Relevance to Research and Clinical Practice

The MDRD and the CKD-EPI study equations have improved and standardized GFR estimation in clinical practice. Because serum creatinine is the most important variable in these equations, it is clear that the ethnic factor must be taken into account. Improvements have certainly been made in this area. Therefore, the African-American ethnic factor of the MDRD study equation is certainly excellent to estimate GFR in CKD African-American populations. However, there are indirect but strong arguments suggesting this factor is too high for African-American subjects with GFR values near 60 ml/min per 1.73 m<sup>2</sup>. This “error” could actually improve the estimation of GFR in CKD stage 1 or 2 (compensation of two successive “errors”). However, in epidemiologic studies, this correction could lead to an underestimation of the prevalence of CKD in the African-American general population. Such an underestimation of CKD prevalence in African Americans has been recently suggested by Peralta *et al.* (20). These authors have shown that the lower prevalence of stage 3 CKD in African Americans compared with Caucasians could be due to creatinine-based equations and to ethnic coefficients. Actually, they have shown in the CARDIA (Coronary Artery Development in Young Adults) database that prevalence of stage 3 CKD is higher in Caucasians when the MDRD study equation is used, but that prevalence is the same in Caucasians and African Americans when the CKD-EPI is used. The CKD prevalence is even higher in African Americans if they used their own ethnic coefficient factor (*i.e.*, 1.12) (20). Moreover, we have to keep in mind that the MDRD study equation underestimates GFR (thereby overdiagnosing CKD) in Caucasian “healthy” subjects (31,32,42). Combining CKD underdiagnosis in African Americans and overdiagnosis in Caucasians could easily lead to misconception of CKD epidemiology in the United States and to the “epidemiologic paradox.” Using the CKD-EPI equation in the NHANES trial also confirms a higher prevalence of stage 3 CKD in Caucasians than in African Americans (7.38% *versus* 4.83%), even if the difference is lower than with the MDRD study equation (9.24% *versus* 4.75%), so the epidemiologic paradox persists. Peralta *et al.* finally stated in their article, “Current equations used to define CKD may systematically miss a high-risk group of blacks at a time in the disease course when interventions are crucial” (20). We fully agree with this assertion and we have added strong arguments to explain why.

In the same way, Foley *et al.* showed that, compared with Caucasians, African American subjects will present CKD-related metabolic complications (hypertension, anemia, hyperphosphoremia, and high uric acid levels) at higher estimated GFR in the NHANES III cohort (43). If our hypothesis regarding the respective performance of the MDRD study equation in healthy subjects according to ethnicity is correct, this higher rate of complication could be “artificial.” “True” GFR may be effectively compara-

ble when metabolic complications occur in both populations.

### Future Directions

Performances of the new CKD-EPI equations remain to be proven because the “African” sample in the external validation data set was too low. The external sample may also be inadequate because African Europeans are also included. Even if provocative, we could write that the MDRD study equation has been better validated in African Americans (especially in CKD African Americans) than the CKD-EPI equation. We have suggested that the underestimation of GFR among African Americans is offset by the race coefficient. However, this hypothesis should be tested in well designed clinical and epidemiologic studies. Lastly, the African American factor cannot be considered as an “African” factor because it is currently not accurate in African (and maybe in African European?) populations. Eventually, we need additional trials to better estimate GFR in African subjects. This is a necessary step to better assess the real prevalence of CKD in these populations in which prevention is preponderant in health politics because of low economic resources (11,44).

Lastly, new renal biomarkers (*e.g.*, cystatin C) could be of interest to estimate GFR in non-Caucasian subjects. Cystatin C has been shown to be less dependent on muscular mass compared with serum creatinine (45). In a population-based study (Multi-Ethnic Study of Atherosclerosis), Kramer showed no significant difference in mean cystatin C levels between African Americans and Caucasians, although serum creatinine strongly varies according to ethnicity (9). Stevens and the CKD-EPI group have shown that plasma cystatin C is very similar in African Americans and Caucasians after adjustment for GFR measurement (46). This is reflected in the cystatin-C-based equations proposed by the same authors in which the ethnic factor is much lower (*i.e.*, 1.06) compared with creatinine-based equations (47). However, more studies seem to be necessary to definitively favor cystatin C in clinical practice.

### Disclosures

None.

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