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# New eGFR equations: Implications for cardiologists and racial inequities



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ABSTRACT

Recently, a new equation to predict estimated glomerular filtration rate (eGFR) that does not include a variable for race has been endorsed by professional organizations and increasingly adopted by clinical laboratories. We discuss the reasoning behind the development of the new equation, implications for cardiologists, and how the new eGFR equation could impact disparities in the cardiovascular care of these patients. Race, a social construct, is a poor proxy for biological variability. Clinical trials which recruit underrepresented minorities and advances in genomic medicine could accelerate the development of personalized medicine and help decrease inequalities in clinical outcomes.

Chronic kidney disease (CKD) is defined as the gradual loss of kidney function sustained for longer than three months. The kidney performs a myriad of functions, arguably the most important of which is the maintenance of homeostasis. The functional unit of the kidney is the nephron, which includes the glomerulus and the tubules. The glomerulus filters the blood to make an ultrafiltrate, the composition of which is finely tuned by tubular reabsorption and secretion of specific ions to maintain homeostasis. Additionally, the kidney has important synthetic functions, including vitamin D metabolism, erythropoietin synthesis and gluconeogenesis.

Belying the biological complexities, in clinical practice, kidney function is commonly assessed using serum creatinine to predict an estimated glomerular filtration rate, or eGFR. The most widely used formula to predict eGFR was the Modification of Diet in Renal Disease (MDRD) equation. While the MDRD equation fares well in most clinical situations, it is imprecise in patients with relatively preserved kidney function (generally those with an eGFR  $>60 \text{ ml/min/1.73 m}^2$ ). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was introduced in 2009 to overcome these limitations. In 2012, the CKD-EPI equation was modified to incorporate serum levels of cystatin C, a biomarker that is freely filtered and, unlike serum creatinine, is not affected by changes in muscle mass. However, both MDRD and the CKD-EPI equation included a race variable (Black individuals versus all other races) that increased a Black patient's eGFR by 21 %, and 16 % respectively [1], compared to the eGFR of a White patient of the same age, sex, and serum creatinine. This variable was included because these studies found that on average, Black participants had a slightly high creatinine for a given GFR. Recently, longstanding concerns about the misconceptions of race-based medicine have gained traction in discussions about the rationale for the inclusion of a Black race variable in eGFR equations. Critiques of race-based medicine highlight that race, a fluid socio-cultural construct rooted in racial hierarchies elaborated during the colonial era, is not a surrogate for biological differences, including genetics. The implications of utilizing race as a biological proxy are also fraught when considering individuals who identify as multi-racial or that the race of patients may be assumed by providers based on phenotype, as opposed to patients' self-reported race. Thus, race does not reflect clinically relevant genetic variance, regional and/or ethnic ancestry. Finally, the original studies from which the CKD-EPI and MDRD equations were derived from had several shortcomings in terms of the limited number of Black/African American participants (who also tended to have greater risk factors for CKD), a binary race variable which categorized participants as Black versus all other individuals and thus distinct from all everyone else, and disputed biological rationale for including race in the equation, that Black people had a higher muscle mass at baseline (and thus serum creatinine) [2–5]. However, the new CKD-EPI 2021 equation [6], endorsed by the American Society of Nephrology (ASN) and the National Kidney Foundation (NKF) does not include a race variable for Black patients, in contrast to the MDRD and earlier CKD-EPI equations. Much of the advocacy around changing eGFR calculation focused on the fact that the inclusion of the Black race variable in the prior CKD-EPI equation automatically increased a patients' eGFR without strong evidence of biological basis for these racial differences and the potential for delayed referral to

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nephrology and kidney transplantation [7]. For example, one study found increased transplant eligibility for Black patients when the race variable was removed from eGFR equations [8]. How these changes in eGFR might affect the cardiac evaluation and management of patients with CKD has been mostly overlooked. Here, we will outline the disparities in the cardiovascular care of patients with CKD and how recent changes in eGFR methodology could impact the care of these patients.

#### 1. Disparities in cardiovascular disease in patients with CKD

Cardiovascular disease (CVD) is one of the major complications of CKD and the leading cause of morbidity and mortality in these patients, with up to 50 % of all-cause mortality in CKD attributed to CVD complications [9] [10]. Unfortunately, there remain striking racial disparities in CKD and the CVD complications from it. Black Americans within the general population are exposed to higher risk of developing diabetes and hypertension, which are major risk factors for CKD. Black patients with CKD are less likely to have their blood pressure under control, which has implications for CKD progression [11]. Consistent with the higher prevalence of suboptimal treatment of hypertension, Black patients are at higher risk of developing left ventricular hypertrophy and other cardiomyopathies [12]. The increased risk of CVD is however not completely explained by the higher rates of common risk factors for CVD such as hypertension and diabetes in these patients. It is thought that the unique pathophysiology of CKD leads to factors such as increased oxidative stress, inflammation, endocrine, metabolic, and electrolyte abnormalities, and vascular calcification, all of which contribute to the excess cardiovascular risk in these patients.

The risk of CVD increases with worsening kidney function [9]. Black patients with CKD are more likely to develop or progress to advanced stage of CKD or end stage renal disease (ESRD) than White patients.

Unfortunately, despite the higher likelihood of advanced CKD, Black patients are less likely to be referred to nephrology and tend to be referred at later stages of CKD than White patients [13]. Further, disparities extend to renal transplantation, considered to be the gold standard treatment option for ESRD. Black patients are less likely to be referred to renal transplant evaluation compared to their White counterparts, more likely to receive an expanded donor criteria kidney [14] and wait longer for a transplant. The implementation of new eGFR equation can directly impact the assessment of kidney function. Of note, for deceased donor kidney transplant, prioritization often takes recipient wait time into account, and wait time can began to accrue once a patient's eGFR is <20 ml/min. The effects of the race coefficient in eGFR calculations potentially increases the time until Black patients' eGFR drops to the threshold. This bears important consideration because renal transplant has been shown to reduce CVD complications compared to patients on dialysis [15,16].

Despite the increased comorbidities, barriers to care, and suboptimal treatment, some retrospective cohort studies of dialysis patients have suggested that there exists a survival paradox. This survival paradox suggests Black/Hispanic patients on dialysis have a survival advantage compared to non-Hispanic White patients [17–19]. However, this 'survival paradox' was not readily apparent in patients with less advanced CKD, particularly those who were younger. In fact, in the Third National Health and Nutrition Examination Survey, a population-based survey of community-dwelling individuals that included 2892 patients with CKD, Black individuals with CKD who were younger than 65 years of age were 78 % more likely to die of CVD than White individuals with CKD. However, no differences were observed in those older than 65 years of age [20]. The Kidney Early Evaluation Program which included 10,560 participants with prevalent CKD found no decreased mortality in Asian and Hispanic individuals as compared to Black or White individuals

#### Table 1

Racial disparities in clinical outcomes associated with kidney disease.

First author	Year	Patient population	No of patients	Study type	Follow up time	Outcome
Frankenfield [33]	2003	Dialysis patients	8336	Retrospective cohort	1 year	Hispanics and non-Hispanic blacks had better survival. Similar mortality in older individuals and those with Diabetes
Murthy BV [17]	2005	Incident dialysis patients	100,618	Retrospective Observational cohort study	~3 years	Hispanic race was associated with lower mortality risks, though this was modified by race and co-morbidities
Robinson [18]	2006	Prevalent dialysis patients	6677	Prospective Observational Cohort	$\sim \! 10 \text{ years}$	Differences in outcomes by race were not significant and explained by co-morbidities and treatment characteristics.
Mehrotra [20]	2008	Community based cohort	14,611 2829 with CKD	Retrospective cohort Study	Mean 7.9 years	Higher risk of death in younger Black individuals with CKD, even when adjusted for CVD risk factors and CKD stage. Not apparent in individuals $\geq$ 65 years of age.
Kovesdy [34]	2009	Male Veterans with non-dialysis CKD	1243	Retrospective cohort	2.8 years	Lower unadjusted mortality in Black patients explained by case-mix
Jolly [21]	2011	Patients with CKD, not on dialysis, no history of prior renal transplant	19,205	Retrospective cohort study	2000–2008	Black patients had similar risk as Whites patients, Asian and Hispanic patients had lower mortality risk than White patients. American Indians/Alaska Natives had higher risk of death
Kucirka [35]	2011	Adult patients with ESRD	1,330,007	Observational cohort study	1995–2009	Black patients on dialysis had a lower risk of death overall, compared to white patents, but Black patients younger than 50 years have a higher risk of death.
Rhee [36]	2014	Adult patients on dialysis	130,909	Retrospective cohort study	2001–2009	Black patients had similar mortality as white patients in younger age group, but decreased mortality in older age group. Hispanic patients had lower mortality versus white patients at all ages. Black and Hispanic patients were less likely to undergo renal transplant versus white patients at all ages.
Lash [37]	2016	eGFR 20-70 ml/min	3785	Prospective cohort	6.6 years	No significant differences in atherosclerosis or heart failure outcomes by races
Ku [38]	2020	Patients with CKD enrolled in Chronic Renal Insufficiency Cohort, not on dialysis at time of enrollment	3288	Retrospective cohort study	Median 7.1 years	Black patients had a lower risk of death once on dialysis compared to white patients, but white patients on dialysis tended to have more severe comorbid conditions, suggesting that survival paradox may be due to Black patients with severe comorbid conditions not initiating dialysis

[21]. Other similar studies found no differences in mortality or even lower mortality in Black individuals. These studies are summarized in Table 1. These studies are confounded by age, socioeconomic status, cultural acclimatization, and ancestry. Thus, a fluid sociopolitical construct such as race might not be the best way to examine differences in biology or clinical outcomes. The use of race as a proxy for genetic or biological markers in precision medicine can widen disparities by denying medications that might have proven efficacy in improving clinical outcomes to some patients. Briefly, we describe the disparities in the workup and treatment of CVD in patients with CKD and how the widespread adoption of changes in assessment of eGFR might influence it.

#### 2. Disparities in investigation and treatment of CVD in CKD

Recognizing and treating CVD in CKD is often complicated. Patients with CKD are more likely to have 'atypical' clinical presentations that might be attributed to anemia or volume overload, complications that commonly accompany CKD. Stress tests for risk stratification often perform poorly in patients with CKD compared to the general population, as they are limited by abnormal basal electrocardiograms, chronotropic incompetence, and impaired vasodilatory ability. In the general population, Black patients undergo less frequent cardiac testing and risk stratification than White patients [22]. These racial disparities extend to those with CKD as well [23]. Individuals with CKD are offered inappropriately lower rates of angiography and revascularization [24]. Whether these disparities reflect the disproportionate representation of Black individuals in the CKD population is unclear. Racial disparities also extend to medical management of CVD in the general population. Patients other than of White race are less likely to be initiated on new glucose lowering medications such as SGLT2 inhibitors that have been shown to improve cardiovascular outcomes and slow progression of kidney disease in patients with CKD. Similarly, Black patients and those of Mexican descent with diabetes were less likely to be initiated on renin-angiotensin-aldosterone-system (RAAS) inhibitors, which are first line agents in diabetic kidney disease, or statins, as compared to White patients [25].

#### 3. Implications of new eGFR estimates

It is important to note that with adoption of the new race free CKD-EPI 2021 equation, measured eGFR will change. For the same serum creatinine level, the calculated eGFR will be lower in Black patients' while that of non-Black patients' will be higher. Furthermore, as health systems make the switch to CKD-EPI 2021 from prior race-based equations, providers may notice that Black patients' eGFR values drop. It will be important for providers to bear in mind the reason for this change and to think critically and carefully before making changes in management. It will also be important to educate patients on the reason behind the change in their eGFR.

When the potential drawbacks of moving away from race-based eGFR equations were being discussed, there were concerns that a lower eGFR in Black patients would make them ineligible for medications such as metformin or SGLT2 inhibitors, which have a beneficial effect on cardiovascular outcomes. However, it is important to remember that eGFR cut offs are arbitrary and estimates of GFR are imprecise. Moreover, renal function often fluctuates to some degree. In clinical practice, it is rare that we need more precise estimations of GFR. If needed, although not readily available and expensive, cystatin C based equations provide more reliable estimates of true GFR. Direct measurements of GFR using inulin or iohexol clearance are rarely available outside of research settings. Thus, we should be cautious about withholding medications which convincingly improve cardiovascular outcomes in patients whose eGFRs border recommended eGFR cutoffs, especially when the potential benefit is high. Likewise, it is important to not expeditiously stop these medications when observing a decline in eGFR, particularly with initiation of RAAS or SGLT2 inhibitors. These changes in eGFR reflect decreased intraglomerular hypertension secondary to decreased afferent artery dilation or vasodilation of the efferent artery. Decrease in eGFR up to 30 % is expected and identifies patients who are likely to benefit from these therapies. Worsening or more severe decreases in eGFR might reflect the presence of underlying bilateral renal artery stenosis and indicates need for cessation of therapy. Also, any equation to predict eGFR assumes steady state conditions and is not accurate when creatinine is rapidly changing as in acute kidney injury (AKI).

Another area of concerns is the use of contrast, such as iodinated contrasts with percutaneous coronary intervention and gadolinium with magnetic resonance imaging (MRI). Recent studies have suggested that the risks of contrast-associated AKI might be overstated in patients receiving intravenous contrast and contrast should not be withheld in the majority of such patients, particularly when the use of contrast might have a critical role in medical decision making. There are also studies examining PCI with lower contrast doses, indicating similar efficacy of procedures. Likewise, newer macrocylic or linear gadolinium-based contrast agents bind more tightly to gadolinium and theoretically should pose less risk of nephrogenic systemic fibrosis. Registry studies thus far have shown no evidence of nephrogenic fibrosis with these agents. However, given the long latent period and since initial symptoms are often overlooked, it behooves us to be prudent with the use of these agents. On the other hand, the use of iodinated and newer gadolinium based contrasts are safer than previously assumed and should not be withheld when it is important to clinical care.

The discussions of race and eGFR should also highlight some of the pitfalls of race-based hypertension treatment. Some studies have suggested that Black patients may have a lower renin profile and that RAAS inhibitors might be less effective in these patients [26]. As a result, at times anti-hypertensives relying on RAAS inhibition have not always been recommend as first line for Black patients, despite their renal protective properties of these medications and the higher risk of kidney disease in these patients. Furthermore, multiple guidelines recommend starting Black patients on a thiazide-type or calcium channel blocker over a RAAS inhibitor as initial antihypertensive treatment but recommend considering a RAAS inhibitor, calcium channel blocker or thiazide-type for other patient groups. Some researchers have even focused on the 'slave trade hypothesis' which postulated that lower renin in Black patients conferred a survival advantage during transatlantic passage. This theory has been heavily critiqued, and, as discussed before, relies on a misconception of race as a surrogate for to biology or ancestry [27]. Indeed, there is now evidence that RAAS inhibitors are effective in improving clinical outcomes in Black patient populations [28]. Further, most patients require two or more drugs to control blood given the significant benefits of RAAS inhibitors in reducing albuminuria, improving clinical outcomes and the pitfalls of race-based medicine, we caution against reflexively avoiding these medications in Black patients.

As highlighted in this piece, one of the important benefits of moving away from race-based equations that raise patients' eGFR for simply checking the "Black race" box is the potential for earlier referral to nephrology and renal transplantation. Black patients are less likely to be referred to transplant [29]. While there are no studies assessing the cardiovascular benefits of earlier nephrology referral, we do know that severity of CVD correlates with severity of CKD and that early nephrology referral as mortality benefits [30]. We might hope with earlier referral to nephrology and aggressive measures to slow CKD progression (especially with blood pressure and diabetes management), CVD complications may be mitigated.

#### 4. Conclusion

Race-based equations to measure eGFR have no clinical or biological validity. The CKD-EPI 2021equation has been endorsed by professional

organizations including the ASN, NKF and United States Pathology and Laboratory Society Leadership, and is expected to replace the current eGFR equations. The new equations will result in lower eGFR estimates for Black patients, which should prompt earlier referral to nephrology and renal transplantation. It is important that these changes not result in withholding therapy with RAAS or SGLT inhibitors in patients who could benefit from them. Recent developments in genomics might spur personalized medicine that is rooted in individual biological features rather than race, which is a heavily confounded sociopolitical construct, particularly when used for determining individual clinical risk profiles or population biology. Clinical trials incorporating genomics and the recruitment of diverse populations, including Black individuals who are underrepresented in such clinical trials [31,32], are urgently needed.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- JW Tsai JP Cerdeña WC Goedel WS Asch V Grubbs ML Mendu JS Kaufman. Evaluating the Impact and Rationale of Race-Specific Estimations of Kidney Function: Estimations From U.S. NHANES, 2015-2018.
- [2] D.W. Harsha, R.R. Frerichs, G.S. Berenson, Densitometry and anthropometry of black and white children, Hum. Biol. 50 (1978) 261–280.
- [3] V. Grubbs, Precision in GFR reporting: Let's stop playing the race card, Clin. J. Am. Soc. Nephrol. 15 (2020) 1201–1202.
- [4] J.E. Schutte, E.J. Townsend, J. Hugg, R.F. Shoup, R.M. Malina, C.G. Blomqvist, Density of lean body mass is greater in blacks than in whites, J. Appl. Physiol. Respir. Environ. Exerc. Physiol. 56 (1984) 1647–1649.
- [5] A.M. Silva, W. Shen, M. Heo, D. Gallagher, Z. Wang, L.B. Sardinha, S. B. Heymsfield, Ethnicity-related skeletal muscle differences across the lifespan, Am. J. Hum. Biol. 22 (2010) 76–82.
- [6] L.A. Inker, N.D. Eneanya, J. Coresh, et al., New creatinine- and cystatin C-based equations to estimate GFR without race, N. Engl. J. Med. 385 (2021) 1737–1749.
- [7] N.D. Eneanya, W. Yang, P.P. Reese, Reconsidering the consequences of using race to estimate kidney function, Jama 322 (2019) 113–114.
- [8] M.P. Hoenig, A. Mann, M. Pavlakis, Removal of the black race coefficient from the estimated glomerular filtration equation improves transplant eligibility for black patients at a single center, Clin. Transpl. 36 (2022), e14467.
- [9] G. Manjunath, H. Tighiouart, H. Ibrahim, et al., Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community, J. Am. Coll. Cardiol. 41 (2003) 47–55.
- [10] M.J. Sarnak, K. Amann, S. Bangalore, et al., Chronic kidney disease and coronary artery disease: JACC state-of-the-art review, J. Am. Coll. Cardiol. 74 (2019) 1823–1838.
- [11] C.D. Chu, N.R. Powe, C.E. McCulloch, et al., Trends in chronic kidney disease care in the US by race and ethnicity, 2012–2019, JAMA Netw. Open 4 (2021), e2127014.
- [12] F.S. Ahmad, X. Cai, K. Kunkel, et al., Racial/Ethnic differences in left ventricular structure and function in chronic kidney disease: the chronic renal insufficiency cohort, Am. J. Hypertens. 30 (2017) 822–829.
- [13] S. Prakash, R.A. Rodriguez, P.C. Austin, et al., Racial composition of residential areas associates with access to pre-ESRD nephrology care, J Am Soc Nephrol 21 (2010) 1192–1199.
- [14] R. Mohandas, M.J. Casey, R.L. Cook, et al., Racial and socioeconomic disparities in the allocation of expanded criteria donor kidneys, Clin. J. Am. Soc. Nephrol. 8 (2013) 2158–2164.
- [15] P.S. Rao, R.M. Merion, V.B. Ashby, et al., Renal transplantation in elderly patients older than 70 years of age: results from the scientific registry of transplant recipients, Transplantation 83 (2007) 1069–1074.

- [16] G.C. Oniscu, H. Brown, J.L. Forsythe, How great is the survival advantage of transplantation over dialysis in elderly patients? Nephrol. Dial. Transplant. 19 (2004) 945–951.
- [17] B.V.R. Murthy, D.A. Molony, A.G. Stack, Survival advantage of hispanic patients initiating dialysis in the United States is modified by race, J. Am. Soc. Nephrol. 16 (2005) 782.
- [18] B.M. Robinson, M.M. Joffe, R.L. Pisoni, et al., Revisiting survival differences by race and ethnicity among hemodialysis patients: the dialysis outcomes and practice patterns study, J. Am. Soc. Nephrol. 17 (2006) 2910.
- [19] C.M. Arce, B.A. Goldstein, A.A. Mitani, W.C. Winkelmayer, Trends in relative mortality between hispanic and non-hispanic whites initiating dialysis: a retrospective study of the US renal data system, Am. J. Kidney Dis. 62 (2013) 312–321.
- [20] R. Mehrotra, D. Kermah, L. Fried, et al., Racial differences in mortality among those with CKD, J Am Soc Nephrol 19 (2008) 1403–1410.
- [21] S.E. Jolly, N.R. Burrows, S.C. Chen, et al., Racial and ethnic differences in mortality among individuals with chronic kidney disease: results from the kidney early evaluation program (KEEP), Clin. J. Am. Soc. Nephrol. 6 (2011) 1858–1865.
- [22] M.B. Wenneker, A.M. Epstein, Racial inequalities in the use of procedures for patients with ischemic heart disease in Massachusetts, JAMA 26 (1989) 253–257.
- [23] C.A. Herzog, T. Natwick, S. Li, D.M. Charytan, Comparative utilization and temporal trends in cardiac stress testing in U.S. Medicare beneficiaries with and without chronic kidney disease, JACC Cardiovasc. Imaging 12 (2019) 1420–1426.
- [24] G.M. Chertow, S.L. Normand, B.J. McNeil, "Renalism": inappropriately low rates of coronary angiography in elderly individuals with renal insufficiency, J Am Soc Nephrol 15 (2004) 2462–2468.
- [25] M. Afkarian, L.R. Zelnick, Y.N. Hall, et al., Clinical manifestations of kidney disease among US adults with diabetes, 1988–2014, JAMA 316 (2016) 602–610.
- [26] B.J. Materson, D.J. Reda, W.C. Cushman, et al., Single-drug therapy for hypertension in men. A comparison of six antihypertensive agents with placebo. The Department of Veterans Affairs Cooperative Study Group on antihypertensive agents, N. Engl. J. Med. 328 (1993) 914–921.
- [27] P.D. Curtin, The slavery hypothesis for hypertension among african americans: the historical evidence, Am. J. Public Health 82 (1992) 1681–1686.
- [28] P. Vejakama, A. Ingsathit, G.J. McKay, et al., Treatment effects of renin-angiotensin aldosterone system blockade on kidney failure and mortality in chronic kidney disease patients, BMC Nephrol. 18 (2017) 342.
- [29] A.M. Epstein, J.Z. Ayanian, J.H. Keogh, et al., Racial disparities in access to renal transplantation-clinically appropriate or due to underuse or overuse? N. Engl. J. Med. 343 (2000) 1537–1544, 1532 p preceding 1537.
- [30] N.A. Smart, G. Dieberg, M. Ladhani, T. Titus, Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease, Cochrane Database Syst. Rev. (6) (2014), Cd007333.
- [31] L.T. Sullivan II, T. Randolph, P. Merrill, et al., Representation of black patients in randomized clinical trials of heart failure with reduced ejection fraction, Am. Heart J. 197 (2018) 43–52.
- [32] S.G. Coca, H.M. Krumholz, A.X. Garg, C.R. Parikh, Underrepresentation of renal disease in randomized controlled trials of cardiovascular disease, JAMA 296 (2006) 1377–1384.
- [33] D.L. Frankenfield, S.P. Ramirez, W.M. McClellan, et al., Differences in intermediate outcomes for asian and non-asian adult hemodialysis patients in the United States, Kidney Int. 64 (2003) 623–631.
- [34] C.P. Kovesdy, J.E. Anderson, S.F. Derose, K. Kalantar-Zadeh, Outcomes associated with race in males with nondialysis-dependent chronic kidney disease, Clin. J. Am. Soc. Nephrol. 4 (2009) 973–978.
- [35] L.M. Kucirka, M.E. Grams, J. Lessler, et al., Association of race and age with survival among patients undergoing dialysis, JAMA 306 (2011) 620–626.
- [36] C.M. Rhee, P. Lertdumrongluk, E. Streja, et al., Impact of age, race and ethnicity on dialysis patient survival and kidney transplantation disparities, Am. J. Nephrol. 39 (2014) 183–194.
- [37] J.P. Lash, A.C. Ricardo, J. Roy, et al., Race/Ethnicity and cardiovascular outcomes in adults with CKD: findings from the CRIC (Chronic renal insufficiency Cohort) and hispanic CRIC studies, Am. J. Kidney Dis. 68 (2016) 545–553.
- [38] E. Ku, W. Yang, C.E. McCulloch, et al., Race and mortality in CKD and dialysis: findings from the chronic renal insufficiency cohort (CRIC) study, Am. J. Kidney Dis. 75 (2020) 394–403.