UK Kidney Association

The rationale for removing adjustment for ethnicity from eGFRcreatinine and recommendations for implementation of the change in practice.

The most commonly used diagnostic (laboratory) test to calculate kidney function is the estimated glomerular filtration rate (eGFR). This test is essential for the care of people with kidney disease. For people from black ethnic groups eGFRcreatinine is often calculated with an adjustment for their ethnicity. There is no ethnicity adjustment for patients from other racialised or ethnic groups.

There is increasing concern that the adjustment for ethnicity does not reflect the wide diversity within individuals of black ethnicity, with the adjustment based on outdated and unfounded biological assumptions for differences between ethnic groups at the expense of better understanding of social and ancestral determinants. Ethnicity and race are social constructs and do not match genetic categories as demonstrated by The Human Genome Project, which found more genetic diversity within racial groups than between them. Therefore, adjusting for black ethnicity/race assumes that all individuals self-identifying as black share the same ancestry. For some individuals of black ethnicity, adjustment for ethnicity could lead to an overestimation of their eGFR, and potential inequality in delivery of care.

In the 2021 NICE chronic kidney disease (CKD) guideline the recommendation to adjust for ethnicity, present in the 2014 version, has been removed. On review of the evidence, NICE agree that adjusting for ethnicity when calculating eGFR may not be valid or accurate.

As UK organisations representing kidney patients and healthcare professionals involved in the care of people with kidney disease, we support NICE and recommend that the adjustment for black ethnicity for eGFR be removed from UK practice. Further evidence is needed and there is concern by professionals and patients that adjustment may be a source of inaccuracy and potential inequity.

We advocate individualised interpretation of eGFR results. We recommend discussions with the patient so that they are supported to have a clear understanding of the potential inaccuracy of eGFR and what that means to them, leading to a shared decision on interpretation of eGFR and treatment choices for CKD.

We convened a working group to support these recommendations and to help address unmet need in kidney function testing, both in respect of the accuracy of kidney function tests and in improving understanding, communication, and use of eGFR and other kidney function tests to help improve the care of patients with kidney disease. We seek to work collaboratively with all stakeholders in furthering these aims.

Further details and recommendations

- Each day in the UK, laboratories carry out and report several hundred thousand kidney function tests. These tests are essential for the diagnosis, monitoring and care of patients with CKD and other long-term conditions, and acute illnesses.

- In clinical care, kidney function is recorded using the estimated eGFR. eGFR is calculated based on laboratory measurement of serum creatinine. Creatinine is a small molecule that is generated by muscles (and liver) and diet, and is cleared by the kidneys, predominantly through glomerular filtration, and to a lesser extent through tubular secretion, as well as through the gut. Our understanding about the different components of the physiology of creatinine and how this can vary between different people is limited.

- Estimating kidney function by eGFR from serum creatinine utilises assumptions concerning creatinine production. On average, creatinine production falls with age and is lower in women than men of a similar build, so correction factors for age and sex are used in the formulae used to calculate eGFR for an individual patient.

- eGFR can be misleading in people whose muscle mass (and therefore, creatinine production) is higher or lower than the assumed average for their age, sex, and body size. Creatinine production is higher in people with more muscle mass than usual (e.g. athletes, weight trainers) and lower in people with lower muscle mass than usual (e.g. people with severe illness, or people who have had an amputation). Higher creatinine production rates than expected lead to falsely low eGFR, and lower creatinine production rates to falsely high eGFR.

- Studies from which the formulae to calculate eGFR were derived were nearly all done in the USA and relied on simultaneous measurements of creatinine and measured GFR in a range of subjects. In these studies, it was also noted that creatinine generation rates were, on average, higher in people who self-identified as African-American. This observation led to the use of the 'correction factor' in the formula for people of black ethnic backgrounds, to correct the falsely low eGFR. Use of this correction factor was shown, in these studies, to improve the agreement between measured (true) GFR and eGFR.

- Many researchers previously assumed that higher creatinine production rates in African-American people reflected a genetic difference rather than being related to social and environmental factors affecting creatinine generation.

- When use of eGFR to measure kidney function was first introduced into the UK (and other countries), it was assumed that the same correction factor for people of black ethnicity and clinicians were advised to apply this correction factor to all 'black' patients, including people of African-Caribbean, African-American, and African heritage.

- Results of subsequent studies in the UK and other countries outside the USA have cast doubt on whether this correction factor is valid or necessary. No study has shown that creatinine production rates are higher in 'black' people in the UK or that the eGFR formula used for individuals from other racial or ethnic groups cause over-estimation of true GFR.

- Many institutions in Africa and in the USA no longer use adjustment for black ethnicity for eGFR due to concerns over accuracy and the inappropriate practice of 'race-based medicine', which is based on unfounded perceptions about biological differences between groups of people at the expense of better understanding social and ancestral determinants.

- People of black ethnicity in the UK with CKD are more at risk of kidney failure requiring transplantation or dialysis, and a higher proportion (two-fold) of people from a black ethnic background have kidney failure than people of white ethnicity. People of black ethnicity are also less likely to undergo kidney transplantation.

- Black people (and other racial and ethnic minorities) in the UK endure sustained inequalities in healthcare and experience worse health outcomes.

- Therefore, over-estimating kidney function in some people of black ethnicity may contribute to or amplify pre-existing inequalities. Assumptions based on self-reported ethnicity may be a source of inaccuracy across groups. Furthermore, national audit suggests that the ethnicity correction is not universally applied, even when ethnicity is known.

- **We recommend that this uncertainty about use of adjustment for eGFR for people from black ethnic backgrounds and the removal of the adjustment in clinical practice should be clearly communicated to all clinical and laboratory services, and, crucially, to patients.**

- **Until there is sufficient evidence, we advocate individualised interpretation of eGFR results including estimation of muscle mass, to ensure that the patient has a clear understanding of the potential inaccuracy of eGFR and what that means to them, supported by a shared decision on care plans.**

- **We believe that individualised clinical assessment of muscle mass will inform the patient and the clinician of the likelihood of under- or over-estimation of kidney function more reliably than blanket use of a correction factor based on a flawed construct.**

- **We recognise that there is a risk that this change could lead to new variation and inequality in care, for instance, people with high muscle mass (including some individuals racialised as black) could be falsely labelled as having kidney disease and prevented from receiving some drug treatments. We therefore recommend that where precision in GFR is required for an individual patient, for example around eGFR thresholds for cancer treatment or kidney donation, more accurate kidney function testing should be done through measured GFR. Again, care should be taken to explain this to the patient.**

- We recommend evaluation of the long-term impact of removal of ethnic adjustment for eGFR on health equity to ensure this change does not further exacerbate or introduce new, unforeseen inequalities.

- The gaps in evidence for eGFR in respect of ethnicity and all other relevant factors should be identified. These should be addressed through research, with implementation of clinically relevant findings in national guidance. This is supported by NICE.

- Future UK research into improving the accuracy of GFR estimation must ensure that ethnic minority groups are fully represented. The use of ethnic classifications in future equations should be avoided in favour of objective biological markers as a means of delivering better individualized care.