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PRACTICE POINTER

Interpreting an estimated glomerular filtration rate (eGFR) in people of black ethnicities in the UK

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What you need to know

- More people of black African or black Caribbean ethnicity will meet criteria for chronic kidney disease (CKD) diagnosis when ethnicity adjustment for estimated glomerular filtration rate (eGFR) calculation is not used
- Classification and clinical coding of early CKD (including asymptomatic proteinuria) in primary care (including re-calculation of eGFR without adjustment) enables healthcare providers to systematically target interventions that aim to reduce cardiovascular events and progression to end stage kidney disease (ESKD)
- Measure albumin creatinine ratio in addition to eGFR to identify patients at highest risk of adverse events (cardiovascular disease and ESKD)

A 37 year old man attends his GP for a review of his blood pressure. He was born in the UK, and his parents are from Nigeria. He was last reviewed three years ago, soon after being diagnosed with essential hypertension, and had been given lifestyle advice and prescribed amlodipine 5 mg daily. An estimated glomerular filtration rate (eGFR) adjusted for ethnicity was 75 mL/min/1.73 m^2 (serum creatinine 114 µmol/L), and urinary albumin creatinine ratio (ACR) was 2 mg/mmol. His chronic kidney disease (CKD) classification was G2A1 (low risk of adverse outcomes).

Today, his blood pressure averaged 145/90 mm Hg across three readings. He has been taking 5 mg amlodipine regularly. His eGFR is calculated without an ethnicity adjustment to be 58 mL/min/1.73 m^2 (serum creatinine 140 µmol/L). Clinical examination is unremarkable. A urine dipstick analysis shows no blood and 2+protein, and a urinary ACR identifies progression to macroalbuminuria (37 mg/mmol). An ultrasound scan of the urinary tract, electrocardiogram, and prostate specific antigen (PSA) test are normal.

Chronic kidney disease (CKD) with proteinuria is a stronger predictor of cardiovascular events than diabetes, leading to significant morbidity and mortality.[1-3] There is substantial inequality in CKD outcomes and clinical coding for people of black, Asian, and minority ethnicities in the UK.[4] In August 2021, updated CKD guidelines from the National Institute for Health and Care Excellence (NICE) removed the recommendation for using an ethnicity adjustment for people of black African or black Caribbean ethnicity when calculating estimated glomerular filtration rate (eGFR).[5] Clinical implications for this change include more people of black ethnicity meeting the criteria for CKD.

In light of this change, we review a concise history of the development of eGFR equations, how these may have historically contributed to reduced diagnosis of CKD in people of black ethnicity and explore when further confirmatory tests may be needed to assess kidney function.

Background of estimated glomerular filtration rate (eGFR)

The true glomerular filtration rate (GFR) is the sum of the filtration of all the nephrons contained within the kidney, but measuring this in routine clinical practice would be invasive, costly, and time consuming. Estimating GFR using equations that include clinical factors such as age and sex and endogenous biomarkers (such as creatinine) are a feasible alternative, and, in most cases, adequate for estimating kidney function in patients who are stable (that is, in a physiologically steady state who are not acutely unwell).

Confirmatory tests are sometimes required—for example, when requiring a highly accurate measure of renal function (kidney transplant donor or for chemotherapy dosing) or when decreased renal function is unexplained or unexpected. A true measurement of GFR can be made using non-nuclear (iohexol) or radionuclide scanning with chromium-51-ethylenediamine tetraacetic acid (^{51}Cr-EDTA), diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) or iodine-125 iothalamate (^{125}I-iothalomate).

A measured GFR is not required for patients with an acute kidney injury in the context of an acute systemic illness. In this case eGFR is not reliable, and kidney function should be assessed through serum creatinine changes and urine output. An eGFR can be meaningfully repeated when the patient is not acutely unwell.

There are several formulae that can estimate GFR; the one recommended by NICE is the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation 2009,[6] which has replaced the Cockcroft-Gault Formula and the Modification of Diet in Renal Disease (MDRD) equation due to improved accuracy .[7] Both the MDRD and CKD-EPI equations were derived in the United States, and the rationale for the race based adjustment of eGFR was based on the observation that African American participants had relatively higher measured GFR for a given serum creatinine level than other population groups. This was assumed to be on the basis of higher muscle mass, although no causal association has been identified.

Unfortunately, the adjustment for African American ethnicity has been applied to many populations with African ancestry outside of the US without validation, including the prior recommendations by NICE to use these adjustments in the UK diaspora. However, recent findings from various studies have shown these adjustments overestimate GFR in the UK diaspora and in continental African populations.[8] To accommodate the findings of these studies, NICE published new guidelines for CKD in August 2021 and recommended clinicians no longer use ethnicity adjustment in eGFR equations,[5] in keeping with new recommendations by the National Kidney Foundation and American Society of Nephrology,[9] and welcomed by the UK Kidney Association.[10]

A new modified CKD-EPI 2021 equation to calculate eGFR has recently been developed from large cohorts in the US which does not include ethnicity adjustment, but it has not been validated in a UK population and is not currently recommended for clinical practice.[11]

Factors that do not affect kidney function but do affect eGFR

GFR estimation equations are limited by intra- and inter-patient variability in serum creatinine measurement, which may be affected by factors that affect the level of creatinine independently from GFR, such as muscle mass, nutrition, body size, and age (box 1).[13]

Box 1: Circumstances where eGFR may be inaccurate in any population

Scenarios where adjustment of eGFR, or confirmatory testing may be helpful include:

- Pregnancy—eGFR is overestimated due to hyperfiltration; look for change in trend and proteinuria
- Extremes of muscle mass—Including patients with amputations or muscle wasting, where the production of less creatinine may lead to an overestimation of eGFR; in this case consider cystatin-C eGFR equation, where using a different serum marker is likely to be more accurate
- Drugs that change handling of creatinine—For example, cimetidine, trimethoprim, pyrimethamine, and salicylates reduce the excretion of creatinine in the proximal tubule, leading to a reduced eGFR which is not reflective of a change in filtration[12]
- Acute illness and/or dehydration—eGFR may not capture true reduction in filtration rate in people in unstable states such as acute illness

GFR equations only provide an estimate of kidney function, and there is large variation in measured GFR for any given estimated GFR. For example, Shafi et al found that, for individuals with an eGFR of 60 mL/min/1.73 m^2, 95% of measured GFRs ranged from 36 to 87 mL/min/1.73 m^2.[14]

Inequality in CKD

The report *Kidney Health Inequalities in the UK*, commissioned by the charity Kidney Research UK, described people of black, Asian, and minority ethnicities to be five times more likely to be on dialysis.[4] Delayed treatment in all populations may be exacerbated due to the late development of symptomatic disease.[15] The UK CKD register and national CKD audit[16] have highlighted the important role of primary care in identifying and managing undiagnosed and early CKD. A study in south London looking at primary care records found that more than half of patients with CKD did not have the diagnosis entered on their medical record as a clinical code, and that these clinically uncoded patients were disproportionately living in areas of greater deprivation and/or ethnic minorities including those of black ethnicities.[17] Diagnosis, including adding diagnostic codes to health records, enables healthcare providers to target monitoring and interventions at a population level (see "Assessing CKD severity and prognosis" below and box 2).

Box 2: NICE (2021) guidelines for referring patients to renal services[5]

- A 5 year risk of needing renal replacement therapy of >5% (measured using the 4-variable Kidney Failure Risk Equation)
- A urinary albumin creatinine ratio (ACR) of ≥70 mg/mmol, unless known to be caused by diabetes and already appropriately treated
- An ACR >30 mg/mmol (ACR category A3) together with haematuria
- A sustained decrease in eGFR of ≥25% and a change in eGFR category within 12 months
- A sustained decrease in eGFR of ≥15 mL/min/1.73 m^2 per year
- Hypertension that remains poorly controlled (above the person's individual target) despite the use of at least four antihypertensive drugs at therapeutic doses
- Known or suspected rare or genetic causes of chronic kidney disease
- Suspected renal artery stenosis

Communicating disease classifications to patients

Explain the changes in how we measure kidney function to patients:

- Explain that estimating kidney function by a blood test is affected by how much muscle an individual has, and that previously we calculated kidney function for people of black African or black Caribbean heritage assuming they had a higher muscle mass which was dependent on data from the US
- For some people of black African or black Caribbean heritage, this meant that the test showed a better kidney function than they really had (up to 16% higher)
- We now do not adjust for skin colour, ethnicity, or race, but additional confirmatory tests (measured GFR or cystatin C eGFR equation) may be needed to confirm kidney function if important treatment decisions are affected
- No longer using ethnicity adjustment for eGFR equations may mean that an individual now meets the criteria for CKD when they did not before, but this will also mean that they can be offered further treatment and assessment to reduce progression of kidney disease and its complications.

Assessing CKD severity and prognosis

The most meaningful use of an eGFR is to stratify, manage, and communicate the risk of adverse events to a patient; in order to do this eGFR is combined with urinary ACR to calculate low, medium, or high risk of adverse outcomes (end stage kidney disease, cardiovascular outcomes, and death). This can be done through the KDIGO classification (Kidney Disease Improving Global Outcomes).[18] For patients with existing CKD, the combination of eGFR and urinary ACR can be used to risk stratify through the Kidney Failure Risk Equation (KFRE), which gives the risk of end stage kidney failure in the next two years and five years as a percentage.[19 20] The KFRE and KDIGO classification have now been incorporated in to NICE guidelines, which state that a decreased eGFR and an increased urinary ACR in combination multiply the risk of adverse outcomes.[5]

The low, moderate, high, and very high risk groups shown in table 1 and referred to in the KDIGO classification and NICE guidelines relate to adjusted relative risk calculated for all-cause mortality, cardiovascular mortality, kidney failure, acute kidney injury, and progressive CKD.[21] For example, someone with a CKD classification

of G3bA3 (such as in the case study) has a relative risk of cardiovascular mortality of 4.3 compared with a reference group with an ACR <10 mg/mmol and eGFR >105 mL/min/1.73 m^2.[18]

Table 1 | Classification of chronic kidney disease using estimated glomerular filtration rate (eGFR) and urinary albumin creatinine ratio (ACR). KDIGO classification combines GFR category (G1-5) and ACR category (A1-3)

	ACR category		
GFR category	A1: normal to mildly increased (<3 mg/mmol)	A2: moderately increased (3-30 mg/mmol)	A3: severely increased (>30 mg/mmol)
G1: normal and high (≥90 mL/min/1.73 m2)	Low risk. No CKD if there are no other markers of kidney damage	Moderate risk	High risk
G2: mild reduction related to normal range for a young adult (60-89 mL/min/1.73 m2)	Low risk. No CKD if there are no other markers of kidney damage	Moderate risk	High risk
G3a: mild to moderate reduction (45-59 mL/min/1.73 m2)	Moderate risk	High risk	Very high risk
G3b: moderate to severe reduction (30-44 mL/min/1.73 m2)	High risk	Very high risk	Very high risk
G4: severe reduction (15-29 mL/min/1.73 m2)	Very high risk	Very high risk	Very high risk
G5: kidney failure (<15 mL/min/1.73 m2)	Very high risk	Very high risk	Very high risk

Case outcome

After reassessment of the patient's eGFR without adjustment for ethnicity, his GP explained that he has chronic kidney disease with a code of G3bA3, which is associated with very high risk of adverse outcomes such as cardiovascular disease. This re-coding puts a clear focus on optimising his care to reduce progression of renal disease and cardiovascular risk. No confirmatory test was required, as risk criteria were met with raised ACR and a history of hypertension. Based on the Kidney Failure Risk Equation (KFRE), his risk of kidney failure in the next five years is 1.77% (considered low in patients with CKD 3).[22]

Recommended management of stage 3 CKD according to NICE guidelines includes optimal renin-angiotensin-aldosterone system (RAAS) blockade, optimisation of blood pressure control (<130/80 mm Hg for proteinuric CKD), initiation of a statin, and a sodium glucose co-transporter-2 (SGLT-2) inhibitor.[23]

Practical tips for GPs to improve recognition of CKD

- Check that your local laboratory is no longer reporting an adjustment factor for ethnicity and is using CKD-EPI 2009 equation with enzymatic assay for creatinine
- When seeing patients of black African or black Caribbean heritage ensure that their eGFR has been calculated without adjustment for ethnicity and that the CKD-EPI 2009 equation was used (this may require confirming with your local laboratory)
- If eGFR ethnicity adjustment has previously been performed, the care pathway of a patient of black African or black Caribbean heritage is likely to be affected by a 16% reduction in kidney function (that is, patients will have a new or more advanced diagnosis of CKD), and GPs must be prepared to discuss the changes in measurement
- Perform an ACR for all patients with diabetes and/or hypertension, all adults with an eGFR of ≤60 mL/min/1.73 m^2 if there is a strong suspicion of CKD, young people without diabetes but with a creatinine level above the reference range, and people with a family history of kidney disease or cardiovascular disease

A patient's perspective

Dee Moore

It is well documented that there exists a high level of mistrust from the members of the black community to medical professionals. In order to address the issue of mistrust the medical community must look within and be prepared to make changes. I believe that the removal of the ethnicity adjustment for the calculation of eGFR is a positive step forward in building trust in the management of care for patients of black Caribbean and black African heritage. I strongly believe that the care of each patient should be person-centred and personalised so that the care of each patient is led by their individual needs and not solely by their ethnicity.

For some patients this change will mean that they are newly diagnosed as having kidney disease, but this also now means that their disease has been identified earlier, meaning more can now be done to prevent further decline of their kidney function.

See also *Diary of a Kidney Warrior* podcast, episode 43

How patients were involved in the creation of this article

This article was reviewed and drafted in collaboration with a patient with kidney disease; Dee Moore gives her voice and a powerful message to clinicians about the nuances of communicating these changes to patients.

Education into practice

- How would you discuss a change in CKD classification from stage 2 to 3 due to removal of ethnicity adjustment with a patient?
- How many of your patients with hypertension have had albuminuria testing to allow adequate CKD coding? What are the barriers to albuminuria testing?
- What risk factors can be managed to reduce risk of CKD progression?

How this article was made

This article was written in collaboration with nephrologists, trainees, general practitioner, and academic researchers of relevant expertise. Sources are a combination of personal collections and Medline search (CKD-EPI, eGFR, ethnicity).

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