

UKKA Patient Safety Alert: Lack of standardisation of kidney function measurement across the United Kingdom

The UKKA estimated Glomerular Filtration Rate (eGFR) Working Group

The UKKA eGFR working group recommend:

- All UK laboratories should use the enzymatic method for the measurement of serum creatinine concentration.
- All UK laboratories should use the CKD-EPI 2009 equation without ethnicity coefficient for the calculation of estimated glomerular filtration rate (eGFR).
- CKD-EPI 2021 “ethnicity-neutral” equation should NOT be introduced until further validation in a UK cohort.
- All Trusts and laboratories should report the method of creatinine (e.g. Enzymatic) and the specific eGFR equation (e.g. CKD-EPI 2009) used alongside these results.
- Development of “UKKA GFR Champions” at tertiary nephrology centres to work with local Trusts, nephrology teams and laboratories; With the aim to assist with the implementation of these and future recommendations, and to strengthen the collaboration between laboratory and nephrology services.

Background and rationale

Early and precise diagnosis of chronic kidney disease (CKD) is crucial to prevent disease progression, manage cardiovascular risk and determine thresholds for renal function dependent medication use. Evaluation of disease severity is necessary to facilitate planning for advanced kidney care. Current assessment of CKD is based on estimated glomerular filtration rate (eGFR) using creatinine-based equations. Serum creatinine is predominantly produced by skeletal muscle and is freely filtered by the kidneys. Limitations of creatinine as a marker of kidney function include influences of muscle mass, extremes of age, diet and medications.

Creatinine is usually measured using one of two main methods (enzymatic and modified Jaffe). The enzymatic method is now preferred as it has less interference and is more accurate at lower concentrations of creatinine (i.e. higher glomerular filtration rate). There are multiple equations to calculate estimated glomerular filtration rate (eGFR) using creatinine, age and sex. The use of ethnicity adjustment factors has been shown to overestimate GFR in people identifying as Black in the UK and are not recommended.¹

The current National Institute for Health and Care Excellence (NICE) August 2021 CKD guideline recommends laboratories using the **enzymatic serum creatinine assay** and the **CKD Epidemiology Collaboration (CKD-EPI) 2009 equation without an ethnicity coefficient** to calculate eGFR.^{2,3} A new CKD-EPI ‘ethnicity-neutral’ 2021 equation has been developed; However, this has not yet been validated in the United Kingdom and is not recommended for use.⁴

The UK National External Quality Assessment Services 2022 audit reported:

- 31% of laboratory analysers measuring serum creatinine (respondents, N= 485) still use the modified Jaffe method
- 32% use the Modification of Diet in Renal Disease (MDRD) equation
- 15% use the ethnicity co-efficient⁵

The use of inappropriate eGFR equations and/or analysis of serum creatinine by the modified Jaffe method can lead to clinically significant inaccuracy in GFR estimation, which can impact timing of diagnosis, CKD staging and prescribing practice. However, the committee recognizes that prescribing of certain medications, such as direct oral anticoagulants (DOACs), remain dependent on creatinine clearance thresholds rather than eGFR.

Acknowledgements

This safety alert has been co-developed, reviewed and endorsed by the UK Kidney Association Glomerular Filtration Rate Working Group, the UK Kidney Association Patient Safety Committee, the Association for Clinical Biochemistry and Laboratory Medicine, the UK Renal Pharmacy Group, and the UK National External Quality Assessment Services.

References

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- 2 National Institute for Health and Care Excellence. Chronic kidney disease: assessment and management. NICE guideline NG203. 2021. <https://www.nice.org.uk/guidance/ng203> (accessed 4 May 2022)
- 3 Levey AS, Stevens LA, Schmid CH, *et al.* A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–12.
- 4 Inker LA, Eneanya ND, Coresh J, *et al.* New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race. *New England Journal of Medicine*. 2021;385:1737–49.
- 5 Marrington R, MacKenzie F. Variation of eGFR reporting and CKD equations used in the United Kingdom. *Annals of Clinical Biochemistry: International Journal of Laboratory Medicine*. 2023;60:328–38.