

Briefing Paper – The eGFR-C Study



Addition of cystatin C to standard laboratory testing improves accuracy of diagnosis and monitoring in chronic kidney disease

Executive summary

Chronic kidney disease (CKD) is diagnosed and monitored using glomerular filtration rate (GFR). In clinical practice, estimates of GFR based on serum creatinine concentration are commonly used but can be inaccurate. In England the Chronic Kidney Disease Epidemiology (CKD-EPI) creatinine equation is recommended for use.

Researchers from the eGFR-C study are advocating the addition of cystatin C to creatinine for estimating kidney function under conditions where improved accuracy aids clinical decision making and monitoring, including eligibility for treatments.

In a study funded by the National Institute for Health and Care Research, the eGFR-C investigators examined the utility of estimating equations for kidney function that included either a single biomarker (creatinine or cystatin C), or both biomarkers combined, to assess their accuracy against kidney function measured by a reference method (iohexol GFR). They found that combined biomarker equations offered improved accuracy and reduced negative bias at higher levels of kidney function. Combined equations performed equally well in different age, sex, albuminuria and body mass index categories.

The study also examined the longitudinal accuracy over 3 years of creatinine and cystatin C-based estimates of kidney function compared to the reference GFR method. Estimating equations based on both cystatin C and creatinine showed better agreement with changes in measured GFR than equations based on a single biomarker, though all equations underestimated GFR decline.

Study details

- Prospective, longitudinal, cohort study assessing the accuracy of kidney function estimated by glomerular filtration rate (GFR) equations versus measured GFR for monitoring kidney function in people with moderate CKD.
- 1167 adults aged ≥ 18 years (median age 67.5 years, 58.3% male, 86.9% white, 27.8% diabetes) with moderate CKD (estimated GFR 30-59 mL/min/1.73m²) from primary, secondary and tertiary care across six centres in England were recruited to the study.
- The accuracy of the widely used original kidney function estimating equations from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPIcreatinine, CKD-EPIcystatin, CKD-EPIcreatinine-cystatin), the remodelled 2021 versions of the CKD-EPI equations and the European Kidney Function Consortium equations (EKFCcreatinine, EKFCcystatin, and EKFCcreatinine-cystatin) were compared with iohexol measured GFR. Accuracy was expressed as P30 (percentage of estimates within 30% of measured GFR).
- After three years, 875 participants remained with measured and estimated GFR data recorded at study entry and exit. The ability of equations to monitor GFR over three years was assessed, with slope deviations from reference GFR within

± 3 mL/minute/1.73 m² per year indicating agreement. Ability of GFR-estimating equations to detect disease progression (i.e. a decline in measured GFR of >25% plus a progression in disease category) was determined.

Findings and recommendations

- Test calibration critically affected measurement of cystatin C, requiring a laboratory adjustment independent of the assay manufacturer.
- After recalibration of cystatin C, P30 values were 90.2% (CKD-EPIcreatinine), 89.5% (CKD-EPIcystatin), 94.9% (*CKD-EPIcreatinine-cystatin), 88.0% (CKD-EPI(2021)creatinine), 94.9% (*CKD-EPI(2021)creatinine-cystatin), 89.4% (EKFCcreatinine), 91.0% (EKFCcystatin), and 94.9% (*EKFCcreatinine-cystatin)(*all $p < 0.001$ compared to CKD-EPIcreatinine). Creatinine based equations showed varying bias depending on the GFR level; inclusion of cystatin C in the equations improved this effect. Differences in accuracy in age, sex, and GFR level subgroups varied by equation. Equations combining creatinine and cystatin performed equally across age, sex, diabetes status, albuminuria status, and body mass index categories.
- Median measured GFR (mL/minute/1.73 m²) decreased from 48.1 at baseline to 43.6 at 3-years. Median change in measured GFR exceeded median change in estimated GFR for all equations. All equations achieved agreement with change in measured GFR in >72.5% of participants. Dual biomarker equations showed better agreement with change in measured GFR (CKD-EPIcreatinine-cystatin 78.6%, CKD-EPI(2021)creatinine-cystatin 78.1%, EKFCcreatinine-cystatin 80.2%) than CKD-EPIcreatinine (73.1%)(all $p < 0.001$). Progression of kidney disease was observed in 139 (15.9%) individuals. All GFR equations had poor sensitivity (<54.1%) but good specificity (>90.4%) for identifying CKD progression.
- Although single biomarker GFR estimating equations had acceptable accuracy in a white population in England with moderate CKD, combined dual biomarker equations with both creatinine and cystatin C showed higher accuracy than either creatinine only or cystatin C only equations.
- Inclusion of cystatin C in GFR estimation may offer particular advantages in people with unusual muscle mass because of the relation of creatinine to muscle mass: these include people with amputated limbs, people with advanced malignancy, athletes, and body builders. Cystatin C may also be of benefit for estimating GFR in transgender people, where the assignment of sex can complicate estimation of GFR. Combined biomarker equations did not seem to be influenced by sex and may therefore offer advantages in this scenario.
- Underestimation of GFR decline by estimated GFR change requires further investigation. Equations including both creatinine and cystatin C more accurately monitored change in measured GFR compared to single biomarker equations.

Recommendations for Health Professionals

GFR estimating equations that incorporate both creatinine and cystatin C demonstrate improved accuracy compared to single biomarker equations, reduce negative bias at higher levels of GFR, and perform equally well across male and female, age, albuminuria, and body mass index categories.

Equations including both creatinine and cystatin C more accurately monitor change in measured GFR compared to single biomarker equations.

Increased uptake of combined biomarker equations in clinical practice could improve disease monitoring and potentially clinical care.

Strict attention should be paid to accuracy of assay calibration for cystatin C and its consistency over time: manufacturing tolerances may not be acceptable for clinical purposes.

What next?

- Increased uptake of combined biomarker equations in clinical practice could improve disease monitoring and potentially clinical care.
- Strict attention to standardisation of cystatin C assays for both clinical and research applications is of crucial importance.
- Further research is needed to determine the most accurate equation to use for estimating kidney function in people of black and South Asian origin and in other minority populations living in England.
- Estimating equations that include both creatinine and cystatin C display better agreement with measured GFR than single biomarker equations when monitoring GFR over time. Increased uptake of combined biomarker equations in clinical practice could improve disease monitoring and potentially clinical care.
- The use of cystatin C modestly increases the economic cost of managing CKD and proof of cost effectiveness is required.
- Updated clinical guidelines should consider the value of the improved accuracy of combined equations on clinical decision making (e.g. accuracy of chemotherapeutic prescriptions, eligibility for SGLT2 inhibitor treatment, preparation for pre-emptive transplantation and renal replacement therapy).

Further information:

Papers reporting the study findings can be accessed from:

BMJ Medicine 2026, <https://doi.org/10.1136/bmjmed-2025-001827> (Published 21 January 2026)

BMJ 2026; 392, <https://doi.org/10.1136/bmj-2025-085005> (Published 19 March 2026)

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