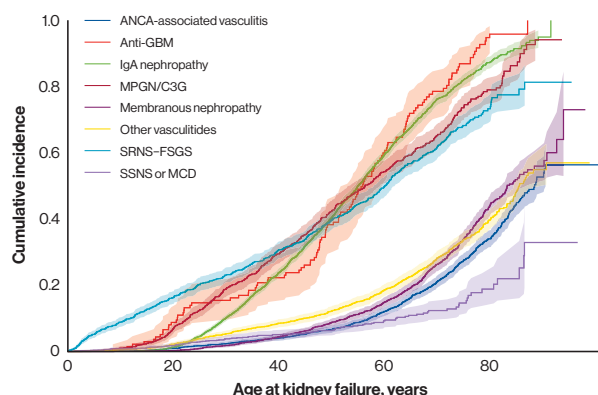


Estimated Glomerular Filtration Rate and Glomerular Diseases— Understanding an Imperfect Biomarker

Patients With Glomerular Diseases Have a Significant Risk of Progression to Kidney Failure

Kaplan-Meier Estimates of Cumulative Incidence of Kidney Failure for Glomerular Kidney Diseases^a



Adapted from Wong K et al with permission.¹

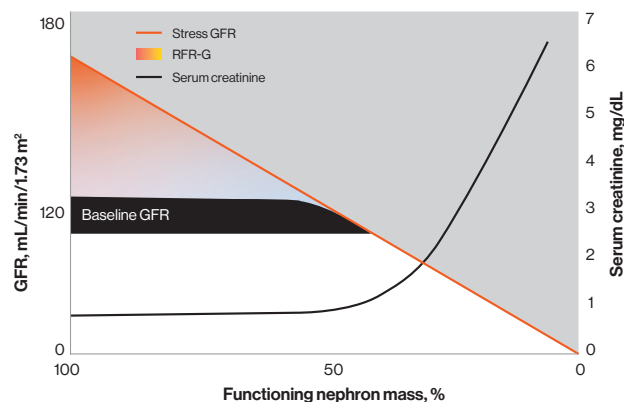
- Patients with glomerular diseases account for 25% of CKD cases worldwide²
- Early and accurate diagnosis is essential to try and slow progression and preserve the remaining nephron mass²
- Analyses of biomarkers, including eGFR, provide essential information for the diagnosis and prognosis of patients with glomerular diseases²

Incidence of kidney failure is significantly higher in patients with glomerular diseases than in those with other causes of CKD¹

Compensatory Kidney Mechanisms May Mask Signs of Kidney Damage, Including Delaying eGFR Decline

- Initial nephron loss is compensated by recruitment of the renal reserve, sustaining a healthy GFR^{3,4}
- Because eGFR tests cannot detect if GFR is being maintained due to utilization of the renal reserve, underlying kidney damage in the early stages of kidney disease may be masked³⁻⁵
- Only when the renal reserve is depleted does GFR begin to decline^{3,4}
- mGFR and renal reserve testing can be utilized to complement eGFR testing and detect earlier anomalies³⁻⁷
- Unlike eGFR, mGFR is not influenced by muscle mass, diet, or inflammation^{6,8}
- When the GFR is >60 mL/min/1.73 m², serum creatinine may not be an accurate marker of renal function⁴
 - Additional tests, such as cystatin C, may be performed in special circumstances when disturbances in creatinine generation are suspected^{2*}

Relationship Between GFR and Serum Creatinine Changes



Reprinted from Chawla LS et al with permission.⁴

RFR-G is the difference between maximum GFR and baseline GFR⁴
Serum creatinine levels begin to elevate only after ~50% of the nephron mass is lost³⁻⁵

eGFR testing is a vital step for the diagnosis of glomerular diseases and provides important prognostic and kidney functional status information. eGFR is a valuable but lagging biomarker for kidney function^{2-5,9}

ANCA, antineutrophil cytoplasmic antibody; C3G, complement 3 glomerulopathy; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; GFR, glomerular filtration rate; IgA, immunoglobulin A; MCD, minimal change disease; mGFR, measured glomerular filtration rate; MPGN, membranoproliferative glomerulonephritis; RaDaR, Rare Diseases Registry Program; RFR-G, renal functional reserve-glomerular; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.

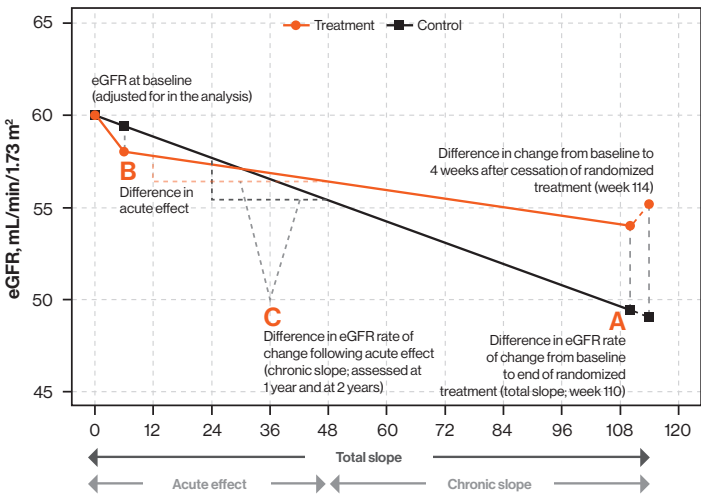
^aLimitations include the fact that RaDaR reflects the clinical practice, ethnic, and genetic composition of the United Kingdom and, hence, findings might not be generalizable to other settings; recruitment criteria for certain rare disease groups might favor ascertainment of patients with more severe disease (eg, IgA nephropathy included biopsy-confirmed diagnosis, proteinuria >0.5 g/d, or eGFR <60 mL/min/1.73 m² during disease course); and data for age at death are limited by length of follow-up and survivor bias. Additionally, most data are stratified by rare disease group, combining subcategories of patients, diagnoses, and treatments given. *Serum cystatin C as an alternative to serum creatinine has not been well validated in subjects with glomerulonephritis.²

References: 1. Wong K et al. *Lancet*. 2024;403(10433):1279-1289. 2. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. *Kidney Int*. 2021;100(4S):S1-S276. 3. Jufar AH et al. *Am J Physiol Regul Integr Comp Physiol*. 2020;319(6):R690-R702. 4. Chawla LS, Ronco C. *Kidney Int Rep*. 2016;1(1):57-63. 5. Fuhrman DY. *Crit Care Clin*. 2021;37(2):399-407. 6. National Kidney Foundation. Accessed July 2026. <https://www.kidney.org/kidney-topics/estimated-glomerular-filtration-rate-egfr> 7. National Institute of Diabetes and Digestive and Kidney Diseases. eGFR Equations for Adults. Accessed July 2026. <https://www.niddk.nih.gov/research-funding/research-programs/kidney-clinical-research-epidemiology/laboratory/glomerular-filtration-rate-equations/adults> 8. Levin A et al. *Kidney Int*. 2024;105(4):684-701. 9. Romagnani P et al. *Nat Rev Dis Primers*. 2025;11(1):8.



eGFR Testing Through Continuous Assessments

Hypothetical Conceptualization of eGFR Rate of Change¹



Adapted from Barratt J et al with permission.¹

- Assessing the trend of eGFR over time provides more accurate data than a single-point measurement, and can be useful for prognostication, monitoring disease progression, and eGFR slope analysis²⁻⁶
 - The rate of change of eGFR is typically estimated through repeated measurements over time^{1,7,8}
- Trends in eGFR slope can be categorized into 3 patterns of progression^{7,8}
 - Declining: Loss of ≥ 3 mL/min/1.73 m² per year
 - Stable: Minimal change of ± 0.5 mL/min/1.73 m² per year
 - Improving: Increase of >0.5 mL/min/1.73 m² per year
- Research studying the use of the eGFR slope in kidney disease showed that change in eGFR slope may help predict disease progression⁹⁻¹¹
 - eGFR age-related decline is -0.8 mL/min/1.73 m² per year^{4,5}

Different Ways to Measure eGFR Over Time

eGFR measurement	Definition
eGFR slope	The mean change in GFR over a prespecified time interval ¹²
Change from baseline to week X	The absolute change in eGFR from baseline to a prespecified week ¹
Time-weighted average eGFR	Measurement that weights recent values more heavily, ensuring more recent measurements have a greater influence on the result ¹³
Annualized total eGFR slope	Total rate of change in eGFR measured from baseline to end of follow-up, annualized over time and incorporating both acute and chronic effects ^{1,8,14,15}
A Total slope	Total rate of change in eGFR measured from baseline to the end of treatment period and incorporating both acute and chronic effects ^{1,15}
B Acute effect	Measures the initial short-term potential effect(s) of an intervention on eGFR ^{1,8,15}
C Chronic eGFR slope	The rate of decline of kidney function estimated after excluding the early treatment period (eg, first several weeks) to remove acute hemodynamic effects of the drug ^{1,8,15}

As patients with glomerular disease often experience reduced and declining eGFR levels at diagnosis, continuous monitoring of eGFR and other biomarkers provides important information⁶

eGFR, estimated glomerular filtration rate.
References: 1. Barratt J et al. *Kidney Int Rep.* 2019;4(11):1633-1637. 2. Ali I et al. *Biomark Insights.* 2020;15:1177271920976146. 3. National Institute of Diabetes and Digestive and Kidney Diseases. Accessed July 2026. <https://www.niddk.nih.gov/research-funding/research-programs/kidney-clinical-research-epidemiology/laboratory/glomerular-filtration-rate-equations/adults> 4. Jufar AH et al. *Am J Physiol Regul Integr Comp Physiol.* 2020;319(6):R690-R702. 5. Chawla LS, Ronco C. *Kidney Int Rep.* 2016;1(1):57-63. 6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. *Kidney Int.* 2021;100(4S):S1-S276. 7. KDIGO. *Kidney Int Suppl.* 2013;3(1):63-72. 8. Levey AS et al. *Am J Kidney Dis.* 2020;75(1):84-104. 9. Imaizumi T et al. *Clin Kidney J.* 2025;18(2):sfae398. 10. Robert A, Beggs J. Poster presented at: ISPOR US, May 5-8, 2024; Atlanta, GA. Poster CO129. 11. Inker LA et al. *Nat Med.* 2023;29(7):1867-1876. 12. European Medicines Agency. Accessed July 2026. https://www.ema.europa.eu/en/documents/qualification-opinion-grf-slope-validated-surrogate-endpoint-rct-ckd_en.pdf 13. Lafayette R et al. *Lancet.* 2023;402(10405):859-870. 14. Barratt J et al. *N Engl J Med.* 2026 Mar 29 [online ahead of print]. doi: 10.1056/NEJMoa2600743. 15. Heerspink HJL et al. *Kidney Int.* 2024;106(4):723-735.

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