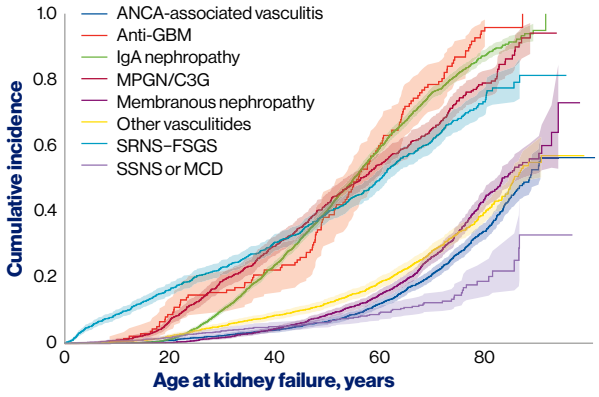
Estimated Glomerular Filtration Rate and Glomerular Diseases—The Clinical Utility of an Imperfect Biomarker

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]

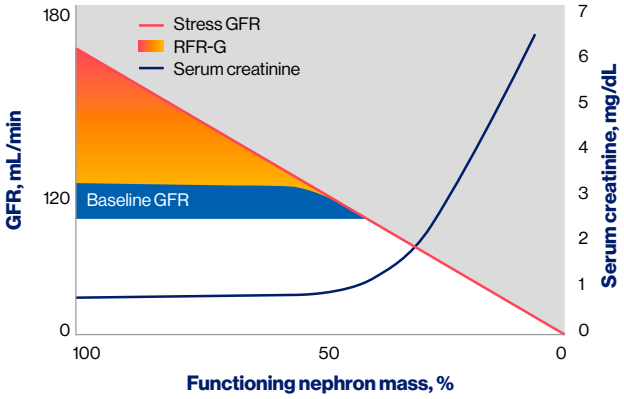
Incidence of kidney failure is significantly higher in patients with glomerular diseases than in those with other causes of CKD[1]

- Patients with glomerular diseases account for 25% of CKD cases worldwide[2]
- Early and accurate diagnosis is essential to try and slow progression and preserve the remaining nephron mass[2]
- Analyses of biomarkers, including eGFR, provide essential information for the diagnosis and prognosis of patients with glomerular diseases[2]

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]
- Only when the renal reserve is depleted does GFR begin to decline[3,4]
- When the GFR is >60 mL/min/1.73 m^2, serum creatinine may not be an accurate marker of renal function[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 masked[3-5]
- mGFR and renal reserve testing can be utilized to complement eGFR testing and detect earlier anomalies[3-7]
- Unlike eGFR, mGFR is not influenced by muscle mass, diet, or inflammation[6,8]

Relationship Between GFR and Serum Creatinine Changes



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RFR-G is the difference between maximum GFR and baseline GFR[4]

Serum creatinine levels begin to **elevate** only after **~50% of the nephron mass is lost**[3-5]

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; RFR-G, renal functional reserve-glomerular; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.

[a]Limitations include the fact that RaDaR reflects the clinical practice, ethnic, and genetic composition of the UK 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/day, 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.

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(4):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 September 26, 2025. 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 September 26, 2025. 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.

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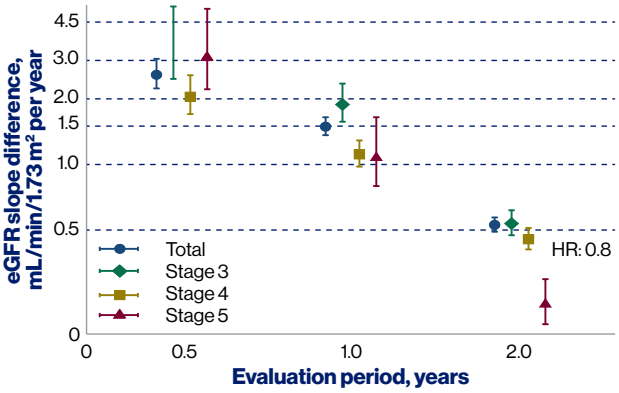
Enhancing the Clinical Value of eGFR Testing Through Continuous Assessments

Association Between Estimated Deceleration in eGFR Decline and Subsequent Kidney Failure With Replacement Therapy*



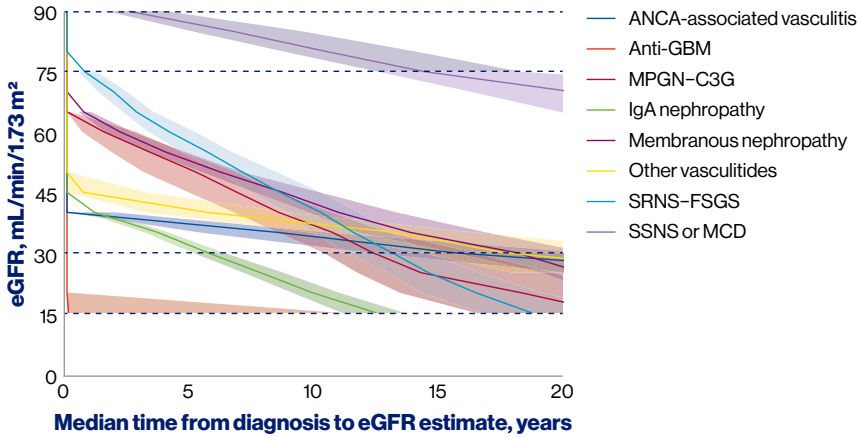
Adapted from Imaizumi T et al with permission.[1]

Assessing the trend of eGFR over time provides more accurate data than a single-point measurement[2,3]

- A minimum of 4 measurements over a period of 2 years is recommended[3]

- Multiple eGFR assessments are useful for prognostication, monitoring disease progression, and eGFR slope analysis[4-6]
- Trends in eGFR can be categorized into 3 patterns of progression[7,8]
  - Declining: ΔeGFR of ≤3 mL/min/1.73 m² per year
  - Stable: ΔeGFR of ±0.5 mL/min/1.73 m² per year
  - Improving: ΔeGFR of >0.5 mL/min/1.73 m² per year
- Recent research studying the use of the eGFR slope as a surrogate end point in kidney disease clinical trials showed that change in eGFR slope may help predict disease progression[1,9,10]
- Additionally, the eGFR slope can be used to distinguish between age-related decline vs CKD progression in patients with kidney diseases[11]
  - eGFR age-related decline is –0.8 mL/min/1.73 m² per year[4,5]

Kaplan-Meier Estimates of Median Time From Diagnosis to eGFR Value for Glomerular Kidney Diseases



Adapted from Wong K et al with permission.[12]

As disease progression varies among glomerular diseases, determining the eGFR slope is important to identify patients earlier

- Analysis of the eGFR[1,9,10]
  - Is an important consideration for the management of patients with glomerular diseases
  - Aligns with recent trends shifting toward frequent kidney function monitoring[4-6]

Continuous monitoring of eGFR and other biomarkers provides important information in patients with glomerular diseases, especially given they experience reduced eGFR levels at diagnosis

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; HR, hazard ratio; IgA, immunoglobulin A; MCD, minimal change disease; MPGN, membranoproliferative glomerulonephritis; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.

*This observational study did not examine changes after specific treatment interventions, nor did it compare eGFR slopes between different treatment arms. This study did not account for different treatment responses or acute and chronic effects of treatment. There was a limited sample size, and it included only Japanese CKD patients, of which the majority received care from board- certified nephrologists. Potential selection bias may have occurred by restricting the analysis to patients with eGFR measurements every 6 months and excluding those censored during the evaluation period. Another potential bias was eGFR measurement frequency, which may have been influenced by clinical circum- stances; however, the results were largely consistent across evaluation periods regardless of the measurement frequency.

References: 1. 1. Imaizumi T et al. *Clin Kidney J.* 2025 Jan 13;18(2):sfae398. **2.** Ali I et al. Biomark Insights. 2020:15:1177271920976146. doi: 10.1177/1177271920976146. **3.** National Institute of Diabetes and Digestive and Kidney Diseases. Accessed September 26, 2025. 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(4):S1-S276. **7.** KDIGO Working Group. Chapter 2: Definition, identification, and prediction of CKD progression. *Kidney Int.* 2013;3(1):63-72. **8.** Levey AS et al. *Am J Kidney Dis.* 2020;75(1):84-104. **9.** Robert A, Beggs J. Poster presented at: ISPOR US; May 5-8, 2024; Atlanta, GA. Poster CO129. **10.** Inker LA et al. *Nat Med.* 2023;29(7):1867-1876. **11.** Luyckx VA et al. *Nat Rev Nephrol.* 2022;18(3):171-183. **12.** Wong K et al. *Lancet*. 2024;403(10433):1279-1289.

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