

# Combined Cystatin C and Creatinine eGFR Equation

Labcorp is proud to offer the CKD-EPI eGFR creatinine-cystatin C (eGFRcr-cys) calculation without race that has been shown to more accurately estimate measured GFR than equations using either the creatinine or cystatin C level alone.<sup>1</sup> The new eGFRcr-cys equation has smaller differences in bias between race groups than the corresponding eGFRcr equations, with less effect on prevalence estimates for CKD and GFR stages than the corresponding eGFRcr equations.<sup>2</sup>

## General eGFR questions

### 1. What is cystatin C? How is it used?

**A:** Cystatin C is a protein produced at a constant rate by all nucleated cells in the body and freely filtered by the kidneys. Cystatin C is considered to be a preferred marker to serum creatinine for estimating GFR. GFR can be estimated (eGFR) from serum cystatin C utilizing an equation that includes the age and gender of the patient. A cystatin C eGFR has advantages over creatinine eGFR in certain patient groups in whom muscle mass is abnormally high or low (for example, people who are elderly, malnourished or have quadriplegia). Serum creatinine levels may also be influenced by vegetarian and high protein diets and medications that block distal tubule secretion of creatinine. Blood levels of cystatin also equilibrate more quickly than creatinine. Therefore, serum cystatin C is more accurate than serum creatinine when kidney function is rapidly changing.<sup>3</sup>

### 2. Is cystatin C better than creatinine?

**A:** GFR calculations performed using cystatin C are independent of factors such as protein intake, muscle mass and race. This means that cystatin C testing can help provide an unbiased assessment of renal function, which can help with the diagnosis and management of chronic kidney disease (CKD).<sup>3</sup>

### 3. What are the advantages of measuring cystatin C in addition to creatinine?

**A:** Combining cystatin C and creatinine in the eGFR equation may improve the predictive capability of a creatinine-only based eGFR. The CKD-EPI eGFR creatinine cystatin C (eGFRcr-cys) calculation without race has been shown to more accurately estimate measured GFR than equations using either the creatinine or cystatin C level separately, leading to smaller differences from measured GFR between race groups.<sup>3</sup>

### 4. Should cystatin C be ordered for initial CKD assessment?

**A:** The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines recommends using serum creatinine and a GFR estimating equation for initial assessment of CKD. It suggests using additional tests (such as cystatin C) for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate. Confirmation of a decreased eGFR is warranted in specific circumstances where decisions depend on more accurate knowledge of the GFR, such as confirming a diagnosis of CKD, determining eligibility for kidney donation, or adjusting the dosage of toxic drugs that are excreted by the kidneys. The guidelines suggest measuring cystatin C in adults with eGFR creatinine 45–59 mL/min/1.73 m<sup>2</sup> who do not have markers of kidney damage if confirmation of CKD is required.<sup>4</sup> More recently, the National Kidney Foundation and American Society of Nephrology (NKF-ASN) Task Force recommended increased, routine, and timely use of cystatin C testing, especially to confirm eGFR in adults who are at risk or have CKD, because a combined equation using both creatinine and cystatin C typically provides the most accurate estimate of eGFR for most patients in ambulatory settings.<sup>1,5-6</sup>

### 5. Can cystatin C be measured from a urine sample?

**A:** Cystatin C measurement requires a blood sample.

### 6. Labcorp already offers a cystatin C testing. What is new?

**A:** In support of the NKF-ASN's Task Force recommendations on cystatin C utilization, Labcorp is offering three new panels containing eGFRcr-cys, one with the eGFR calculation alone and two in combination with recommended urine tests, to simplify the ordering process for diagnosing or confirming CKD. The combination of these tests along with the CKD-EPI eGFR creatinine-cystatin C (eGFRcr-cys) GFR calculation is new.

### 7. What are the new panels and what components do they include?

**A:** Below is a summary of the new panels.

- **eGFR Creatinine-Cystatin C Calculation [121022]:** includes creatinine, serum; cystatin C; eGFR creatinine-cystatin C calculation
- **eGFR Creatinine-Cystatin C Calculation With Albumin:Creatinine Ratio, Urine [121054]:** includes albumin, random urine; albumin:creatinine ratio; creatinine, serum; creatinine, urine; cystatin C; eGFR creatinine-cystatin C calculation
- **eGFR Creatinine-Cystatin C Calculation With Albumin:Creatinine-Protein:Creatinine Ratios, Urine [121065]:** includes albumin, random urine; albumin:creatinine ratio; creatinine, serum; creatinine, urine; cystatin C; eGFR creatinine-cystatin C calculation; protein, total; protein:creatinine ratio

### 8. Can the clinical use of cystatin C help address healthcare disparities?

**A:** The CKD-EPI eGFR creatinine cystatin C (eGFRcr-cys) calculation without race has been shown to more accurately estimate measured GFR than equations using either the creatinine or cystatin C level separately, leading to smaller differences from measured GFR between race groups.<sup>3</sup>

### 9. Do the new cystatin C panels use the eGFR equation without race?

**A:** Yes. The panels use the CKD-EPI eGFR creatinine-cystatin C (eGFRcr-cys) calculation without race.

### 10. When will Labcorp implement the new cystatin C panels and calculation?

**A:** The three new panels became orderable August 1, 2022.

## Clinical-related questions

### 1. Which is better for determining kidney damage, a creatinine-based eGFR or a cystatin-based eGFR?

**A:** The NKF-ASN Task Force reported that the combined cystatin C and creatinine eGFR equation is the most accurate when comparing with true (measured) GFR. Creatinine-only based eGFR remains a useful screening tool in general practice as it is available when patients undergo routine metabolic panel laboratory testing during annual physicals.

### 2. Can these panels be used instead of the Kidney Profile [140301] for screening for kidney disease?

**A:** Yes. The preferred screening profile when there is a clinical suspicion of CKD is **eGFR Creatinine-Cystatin C Calculation With Albumin:Creatinine-Protein:Creatinine Ratios, Urine [121065]**. However, when there is low pretest probability of CKD, screening using creatinine-only based eGFR equation is considered sufficient.

### 3. Will I need other tests besides eGFR to check for kidney disease?

**A:** The urine albumin and/or total protein to creatinine ratio (uACR and/or uPCR) test is recommended for measuring protein in the urine, a sign of kidney damage.

### 4. Can a cystatin C eGFR be used in place of a creatinine based eGFR?

**A:** Yes.

### 5. Which patient populations would benefit most from cystatin C testing, and how can providers determine which patients should be tested with cystatin C?

**A:** Patients who have variable muscle mass would benefit, including, children, elderly, athletes, amputees, malnourished individuals and patients with advanced liver or heart failure, and patients on vegetarian and high protein diets and medications that block distal tubule secretion. Cystatin C may also be used in patients who need confirmation of kidney function prior to kidney donation or for dose adjustments for certain medications that may be toxic to the kidneys.

### 6. Does this change any treatment?

**A:** Assessment of kidney function and treatment considerations will not be changed no matter what eGFR equation was used, but using the most accurate equation is always better for patient assessment and care.

### 7. What other factors do I need to consider for diagnosing CKD?

**A:** CKD is diagnosed and staged based on both eGFR results as well as other tests to assess kidney damage, most commonly the urine albumin to creatinine. The KDIGO guidelines definition of CKD is as follows: "CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health, and requires one of two criteria documented or inferred for >3 months: either GFR <60 mL/min/1.73 m<sup>2</sup> or markers of kidney damage, including albuminuria."<sup>4</sup>

## Reporting and code-change questions

**1. We currently use the partial reports feature; with the addition of the cystatin C and creatinine eGFR, will we see more partial reporting? What will we see? Can we turn this feature off for these new profiles?**

**A:** Depending on where your Labcorp testing facility is located, you may experience a 1-day delay for the cystatin C and the cystatin C-creatinine eGFR result. The report will provide results for all completed tests, and pending tests will be marked with “will follow” on the results report. If desired, you can request that the partial test feature be turned off for the new profile by contacting your local EDI team.

**2. What are the test numbers and result codes for the new profiles? Are there any new result codes?**

**A:** The following are the test numbers and result codes for the new panels. The only new result code is for the cystatin C-creatinine eGFR, which is result code number 121253.

Test No.	Test Name	Result Codes and Tests
121022	eGFR Creatinine-Cystatin C Calculation	001370 Creatinine
		121251 Cystatin C
		121253 GFR Cr-Cys calc
121054	eGFR Creatinine-Cystatin C Calculation With Albumin:Creatinine Ratio, Urine	001370 Creatinine
		121251 Cystatin C
		121253 GFR Cr-Cys calc
		140285 Albumin/Creatinine Ratio, Random Urine
121065	eGFR Creatinine-Cystatin C Calculation With Albumin:Creatinine-Protein:Creatinine Ratios, Urine	001370 Creatinine
		121251 Cystatin C
		121253 GFR Cr-Cys calc
		140285 Albumin/Creatinine Ratio, Random Urine
		003129 Protein and Creatinine, Random Urine

**3. What is the LOINC code for the creatinine-cystatin C eGFR?**

**A:** Visit the Test Menu at [www.labcorp.com](http://www.labcorp.com) for LOINC information.

## Reimbursement questions

**1. Is cystatin C covered by policies? What is allowable?**

**A:** While there is not a widespread policy around it, we are seeing that payors are covering it for CKD-related diagnostic codes, mainly stage 3A.

**2. What is cystatin C’s Medicare-covered indication?**

**A:** Cystatin C testing is medically reasonable and necessary when all of the following are met:

- In adults with eGFR<sub>creat</sub> 45–59 mL/min/1.73 m<sup>2</sup> (CKD stage 3A mildly to moderately decreased GFR) who do not have markers of kidney damage; **and**
- If confirmation is warranted; **and**
- When GFR estimates based on serum creatinine are thought to be inaccurate; **and**
- When decisions depend on a more accurate knowledge of the GFR, such as confirming a diagnosis of CKD, determining eligibility for kidney donation, or adjusting the dosage of toxic drugs that are excreted by the kidneys.

## EMR/EDI questions

**1. When will the compendium be available and how do I get it?**

**A:** The EDI notification letter indicating that the new panels are available was sent on August 1, 2022. If you would like a copy of the compendium, please contact your local EDI team for more details.

### References:

1. Delgado C, Baweja M, Crews DC, et al. A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. *Am J Kidney Dis.* 2022 Feb;79(2):268-288.e1.
2. Inker LA, Eneanya ND, Coresh J, et al. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race. *N Engl J Med.* 2021 Nov 4;385(19):1737-1749.
3. Inker LA, Titan S. Measurement and Estimation of GFR for Use in Clinical Practice: Core Curriculum 2021. *Am J Kidney Dis.* 2021 Nov;78(5):736-749. Epub 2021 Sep 11.
4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney International Supplements.* 2013;3:1-150. Accessed at [https://kdigo.org/wp-content/uploads/2017/02/KDIGO\\_2012\\_CKD\\_GL.pdf](https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf).
5. Shlipak MG, Inker LA, Coresh J. Serum Cystatin C for Estimation of GFR. *JAMA.* 2022 Aug 8; online ahead of print.
6. Gutiérrez OM, Sang Y, Grams ME, et al. Association of Estimated GFR Calculated Using Race-Free Equations With Kidney Failure and Mortality by Black vs Non-Black Race. *JAMA.* 2022 Jun 21;327(23):2306-2316.