Quest Diagnostics®

TOP 5

CKD questions white paper

1

In the context of kidney disease, what do **elevated serum creatinine** and **urine albumin** mean?

Introduction

Chronic kidney disease (CKD) affects 37 million people in the US.[1] While efforts have been made to prevent or delay disease progression, there's been very little progress over the last 3 decades.

That's why Quest Diagnostics is committed to supporting clinicians as they work with patients to achieve better CKD outcomes. Primary care physicians (PCPs) are on the front lines of CKD management, and our sales representatives and medical experts field many questions from them about CKD testing.

This white paper outlines the **top 5 questions PCPs ask about kidney disease testing and provides answers reviewed by our medical experts.** A recent study outlining PCPs' perceptions of barriers and facilitators to the optimal management of CKD provided additional insights.[1]

Meet our experts

Clinicians can rely on our medical experts for information about CKD test selection and results interpretation.

Harvey Kaufman, MD
Senior Medical Director

Lee Hillborne, MD
Senior Medical Director

Jeffrey Dlott, MD
Senior Medical Director, Diagnostic Services

Creatinine is a positively charged byproduct of muscle cells with an extremely low molecular weight of 0.11 kDa. Its positive charge and very small size allow it to move freely through the kidney's filtration barrier, which separates the glomerulus and bowman's capsule.

Albumin, on the other hand, is a negatively charged particle with a molecular weight of ~67 kDa. Its size combined with its negative charge prevent it from passing through the filtration barrier under normal circumstances.

In CKD, high blood pressure or direct damage to the filter caused by glycation or inflammation causes the filtration barrier to become dysfunctional, allowing albumin to be filtered out and into the urine.

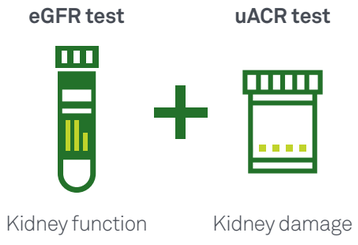
Over time, continued damage to the nephron—the functional unit of the kidney that filters blood on one end and transfers this filtrate to collecting ducts that lead to the bladder—results in its death. This reduces the filtering capacity of the kidneys. Since the kidneys are supposed to freely filter creatinine, the death of the kidney's nephrons manifests as increased serum creatinine levels.

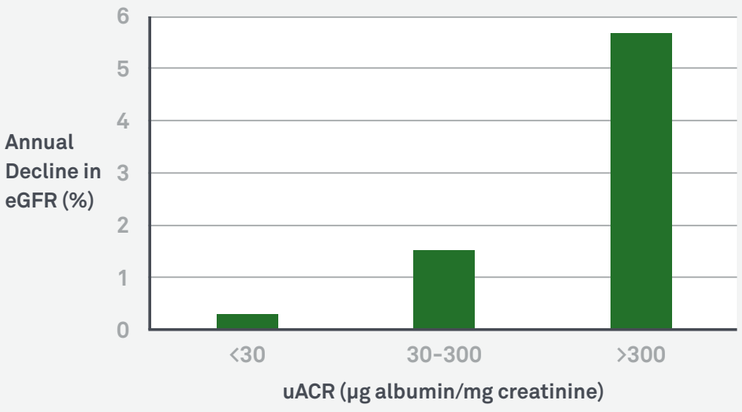
2

Why must **eGFR** and **uACR** be used together to diagnose and monitor CKD?

Serum creatinine with effective glomerular filtration rate (eGFR) defines the stage of CKD (kidney function). Urine albumin-creatinine ratio (uACR) indicates kidney damage.

Though many physicians often rely solely on eGFR testing, National Kidney Foundation guidelines recommend screening with both tests at least annually for all patients with diabetes, high blood pressure, prior kidney injury, a family history of CKD, or other risk factors.[2]





National Kidney Foundation guidelines recommend both eGFR and uACR testing to assess kidney function and damage.[2]

3

What does **elevated serum cystatin C** mean in the context of kidney disease?

Cystatin C is a positively charged protein with a low molecular weight of 13 kDa. Like creatinine, cystatin C is freely filtered by the glomeruli in the kidneys. High serum cystatin C levels suggest low glomerular filtration, indicative of CKD.

Whereas creatinine is primarily generated by muscle cells, cystatin C is generated by all nucleated cells. This means that it is less susceptible to bias due to above-average/below-average muscle mass, diet, or the use of certain supplements.[3]

eGFR based on cystatin C measurement can be used for confirmatory testing in specific circumstances when eGFR based on serum creatinine is less accurate such as with high or low muscle mass and when eGFRcreat is 45-59 mL/min/1.73m.[2]

4 What **complications** can occur as the kidneys fail?

The kidneys are responsible for many important bodily functions including blood pressure regulation, electrolyte regulation, stimulation of red blood cell production, acid-base balance, and stimulation of vitamin D absorption. As kidney function declines, these functions also deteriorate.

The National Kidney Foundation and Kidney Disease: Improving Global Outcomes (KDIGO) published evidence-based recommendations for testing for complications and comorbidities.[4]

KDIGO recommended CKD testing by stage[4]

1–2	3A	3B	4–5
If uACR ≥30 mg/g: • Lipid Panel annually • Hemoglobin A1C as needed to monitor glycemic control **If uACR <30 mg/g:** • Cystatin C to confirm CKD stage	• Lipid Panel annually • Hemoglobin A1C as needed to monitor glycemic control • Hemoglobin at least annually • Carbon dioxide at least once **If uACR ≥30 mg/g:** • Potassium, Serum, monitor for Hyperkalemia	• Lipid Panel annually • Hemoglobin A1C as needed to monitor glycemic control • Hemoglobin at least annually • Carbon dioxide at least once • Calcium at least once • Phosphate at least once • Parathyroid hormone at least once **If uACR ≥30 mg/g:** • Potassium, Serum, monitor for Hyperkalemia	• Lipid Panel annually • Hemoglobin A1C as needed to monitor glycemic control • Hemoglobin at least annually • Carbon dioxide at least once • Calcium at least once • Phosphate at least once • Parathyroid hormone at least once • Vitamin D, 25-Hydroxy, Total, at least once **If uACR ≥30 mg/g:** • Potassium, Serum, monitor for Hyperkalemia **Monitor anticoagulant therapy closely:** • Warfarin: Prothrombin time with INR • Low-molecular-weight Heparin: Anti-factor Xa

5 When should PCPs refer a patient to a **nephrologist**?

The KDIGO initiative published a useful risk map for determining when patients should be treated by their PCP versus referred to a nephrologist. This risk map emphasizes the importance of uACR testing—all patients with severely increased uACR should be referred to a nephrologist regardless of stage. In addition, patients with stage 4 CKD and beyond (eGFR <30) should be referred to nephrology.[5]

Nephrologists can use this information to help guide their next steps, from recommending lifestyle changes to modify cardiovascular risk factors, to prescribing medication.

Frequency of monitoring CKD based on risk of disease progression assessed using eGFR and uACR

CKD stage and eGFR range (mL/min/1.73 m²)			Albuminuria categories and ACR ranges (mg/g creatinine)		
			Normal to mildly increased <30	Moderately increased 30–300	Severely increased >300
	1 and 2	≥60	1	1	2,R
	3A	45–59	1,C	2	3,R
	3B	30–44	2	3	3,R
	4	15–29	3,R	3,R	≥4,R
	5	<15	≥4,R	≥4,R	≥4,R

- **Low risk:** monitor yearly if evidence of kidney damage (eg, indicated by imaging or biopsy). The NKDEP recommends that actual values above 60 mL/min/1.73m² be reported only as >60 due to variability near the upper limit of the reference range.
- **Moderately high risk:** monitor yearly
- **High risk:** monitor 2 times yearly
- **Very high risk:** monitor 3 times yearly
- **Very high risk:** monitor ≥4 times yearly

ACR=albumin-creatinine ratio; eGFR=estimated glomerular filtration rate; C=confirm using eGFR based on (1) cystatin C (test code 94588) or (2) creatinine plus cystatin C; **R=refer to specialist**

Powering chronic kidney disease prevention

These questions represent just some of the needs and concerns of PCPs with regard to the diagnosis and management of CKD and related testing. Additional support and insights can help PCPs and nephrologists work together to prevent or delay the progression of the disease for better patient outcomes.

Quest Diagnostics medical experts are here to help.
Visit **QuestDiagnostics.com/ChronicKidneyDisease** to learn more.

References

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