

## Screening and Monitoring of Chronic Kidney Disease (CKD) in Diabetes

## Frequently-Asked Questions

1. **Q:** Why are kidney function issues so important in diabetes care?

**A:** Diabetic nephropathy occurs in 20-40% of patients with diabetes. It is the single leading cause of end-stage renal disease (ESRD) in the U.S.

2. **Q:** What is the difference between “Chronic Kidney Disease” and “diabetic nephropathy”?

**A:** Diabetic nephropathy refers generally to the damage to the kidneys caused by diabetes. Chronic Kidney Disease (CKD) has a specific clinical definition (see below) and may be caused by diabetes or by other diseases.

3. **Q:** Why is it important to screen for CKD in people with diabetes?

**A:** In this high risk population, early CKD detection and treatment of the underlying risk factors reduce the development of kidney failure by 30-70%. Half of the patients with significantly increased urine albumin excretion (“macroalbuminuria”) will progress to ESRD within the next 10 years.

4. **Q:** How is CKD defined?

**A:** CKD is defined as  $\geq 3$  months duration of **either**:

- **Decreased kidney function:**  $eGFR < 60 \text{ mL/min/1.73 m}^2$
- **Evidence of kidney damage:** e.g.  $UACR \geq 30 \text{ mg/g}$ , abnormal kidney imaging or biopsy

eGFR = estimated Glomerular Filtration Rate

UACR = Urine Albumin-to-Creatinine Ratio

5. **Q:** What tests should be used to screen for and monitor CKD?

**A:** Given the definition of CKD above, it follows that the 2 tests which should be used together to give the best assessment of how the kidneys are doing are the **eGFR and UACR**. Both of these tests should be checked at diagnosis of type 2 diabetes and then annually thereafter. They should be checked more frequently if they are rising rapidly and as needed to assess the effect of therapeutic interventions. Once a patient has started dialysis, they no longer need to be checked.

**6. Q:** Staging of CKD is based only on eGFR, so why is urine albumin testing important?

**A:** Recent studies have made it clear that both kidney function (eGFR) and albuminuria are independent risk factors for progression to kidney failure. Also, albuminuria is often detected long before the eGFR drops below 60 mL/min/1.73 m<sup>2</sup>, thus allowing for earlier CKD diagnosis and intervention.

Further, albuminuria is a risk factor for coronary heart disease (CHD). Patients with CKD in even the earliest stages are at increased risk for subsequent CHD and their providers should intensify interventions that reduce those risks.

**7. Q:** Why is UACR the test of choice for evaluating proteinuria?

**A:** The American Diabetes Association, NIH/NIDDK, and the National Kidney Foundation (NKF) all recommend using the UACR. UACR has the following advantages over other urine protein tests:

- UACR is a quantitative test which is reliable for CKD screening, diagnosis, monitoring and clinical decision-making.
  - Even though the result from a semi-quantitative POC (point of care) test strip may look like a UACR result (mgScreening Monitoring CKD albumin/g creatinine), these strips should only be used for urine albumin *screening*, if used at all in the clinic setting. When the test strip indicates an elevated level of urine albumin, the result should be confirmed with a quantitative method (UACR). If the result is confirmed and persists for at least 3 months, the diagnosis of CKD is made. Thereafter, only UACRs should be used to monitor the patient's urine albumin excretion.
- UACR measures albumin, the major protein excreted in diabetic nephropathy
  - Urine albumin measurement and reporting is in the process of being standardized nationally so it will be even more accurate and reproducible.
- UACR accounts for urine concentration through the ratio to creatinine.
- UACR can reliably be done on a spot ("random") urine sample—there is no longer a routine need for 24-hour urine collections to assess proteinuria.

**8. Q:** Why is it important to have an accurate, quantified assessment of urine albumin?

**A:** Even mildly elevated urine albumin levels should prompt clinical interventions such as improving blood pressure control, starting or maximizing ACE inhibitors/ARBs, improving blood sugar control, and re-emphasizing smoking cessation. The UACR should then be rechecked to assess whether the intervention has succeeded in reducing the level of urine albumin—this is clinically significant as the most recent UACR result is the one that predicts that patient's future kidney status. Further, both the absolute amount as well as the "rate of rise" of urine albumin have clear prognostic value as well. Assessing this important indicator over time requires an accurate, quantified test.

**9. Q:** How are UACR results interpreted?

**A:** Urine albumin excretion is a continuous variable, meaning that there is increasing risk for every incremental increase in the result—there is no threshold above which risk abruptly changes. As such, the terms “microalbuminuria” and “macroalbuminuria” are no longer recommended.

Urine Albumin Excretion Categories:

- Normal = < 30mg/g
- Increased = ≥ 30mg/g

**10. Q:** Can UACR and eGFR be used in children with diabetes as well as in adults?

**A:** A recent NIH/NIDDK study in Pima Indians showed that UACR was useful in youth with diabetes and supported the same annual screening recommendation as in adults.

eGFR should be calculated using the MDRD equation for adult patients—this is the equation programmed into EHR laboratory packages. However, MDRD is not accurate in children—the Schwartz equation should be used for children; see the National Kidney Disease Education Program (NKDEP) website:

[http://www.nkdep.nih.gov/professionals/gfr\\_calculators/selecting.htm](http://www.nkdep.nih.gov/professionals/gfr_calculators/selecting.htm)

as well as the National Kidney Foundation calculator:

[http://www.kidney.org/professionals/kdoqi/gfr\\_calculatorPed.cfm](http://www.kidney.org/professionals/kdoqi/gfr_calculatorPed.cfm)

**11. Q:** What options are available for a clinic to provide the UACR test?

**A:** UACR can be done in any CLIA-certified laboratory, including those at many Indian Health sites. There is a POC option available but it is not CLIA-waived. If a site doesn't have the capability to provide UACR in-house, the test can be done at whatever reference laboratory is used. Since prices charged by these labs vary widely, it is often cost-effective for sites to establish a contract pricing agreement with their reference lab, either on their own or in collaboration with other sites. In addition to cost considerations, performing UACR in-house is advantageous in terms of something very important to busy clinics: turn-around time for providers to receive the test results. Diabetes providers should talk with their facility's laboratory supervisor to determine the most efficient and cost-effective way to provide UACR testing. It is also important to make sure that UACR is clearly and correctly listed in the local electronic health record's lab orders.

**12. Q:** This is a change from the tests we have used in the past to screen for and monitor CKD. What urine protein tests are accepted for the Diabetes Audit?

**A:** The only test accepted in the Diabetes Audit is the UACR. The same is true for the IHS GPRA measure on nephropathy assessment.

## References and Resources

American Diabetes Association. Clinical Practice Recommendations 2014. *Diabetes Care* 2014;37:Supplement 1.

Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010, published online May 18, 2010, doi:10.1016/S0140-6736(10)60748-9.

Di Angelantonio E, Chowdhury R, Sarwar N, Aspelund T, Danesh J, Gudnason V. Chronic kidney disease and risk of major cardiovascular disease and non-vascular mortality: prospective population based cohort study. *BMJ* 2010;341:c4986 doi:10.1136/bmj.c4986

Hammelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, Wiebe N, Tonelli M. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA* 2010;303(5):423-429.

Indian Health Service, Division of Diabetes of Diabetes Treatment and Prevention website resources on CKD:

<http://www.ihs.gov/MedicalPrograms/Diabetes/index.cfm?module=toolsCKDQuickGuides>

<http://www.ihs.gov/MedicalPrograms/Diabetes/index.cfm?module=trainingSeminars>

Kim NH, Pavkov ME, Knowler WC, Hanson RL, Weil EJ, Curtis JM, Bennett PH, Nelson RG. Predictive value of albuminuria in American Indian youth with or without type 2 diabetes. *Pediatrics* 2010, doi:10.1542/peds.2009-1230

National Kidney Disease Education Program website:

<http://www.nkdep.nih.gov/professionals/index.htm>

National Kidney Foundation website: <http://www.kidney.org/professionals>

Pakov ME, Kowler WC, Hanson RL, Nelson RG. Diabetic nephropathy in American Indians, with a special emphasis on the Pima Indians. *Current Diabetes Reports* 2008;8:486-493.