

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

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(with thanks to Dr. Andy Narva)

Presented by
Indian Health Service (IHS)
Division of Diabetes

This Presentation

- Definitions
- CKD Data (good news for a change!)
- CKD Screening, Diagnosis and Monitoring:
 Estimated Glomerular Filtration Rate
 (**eGFR**) and Urine Albumin Creatinine Ratio
 (**UACR**)
- CKD Tools—and where to get them
- Case Studies

Diabetes and Kidneys

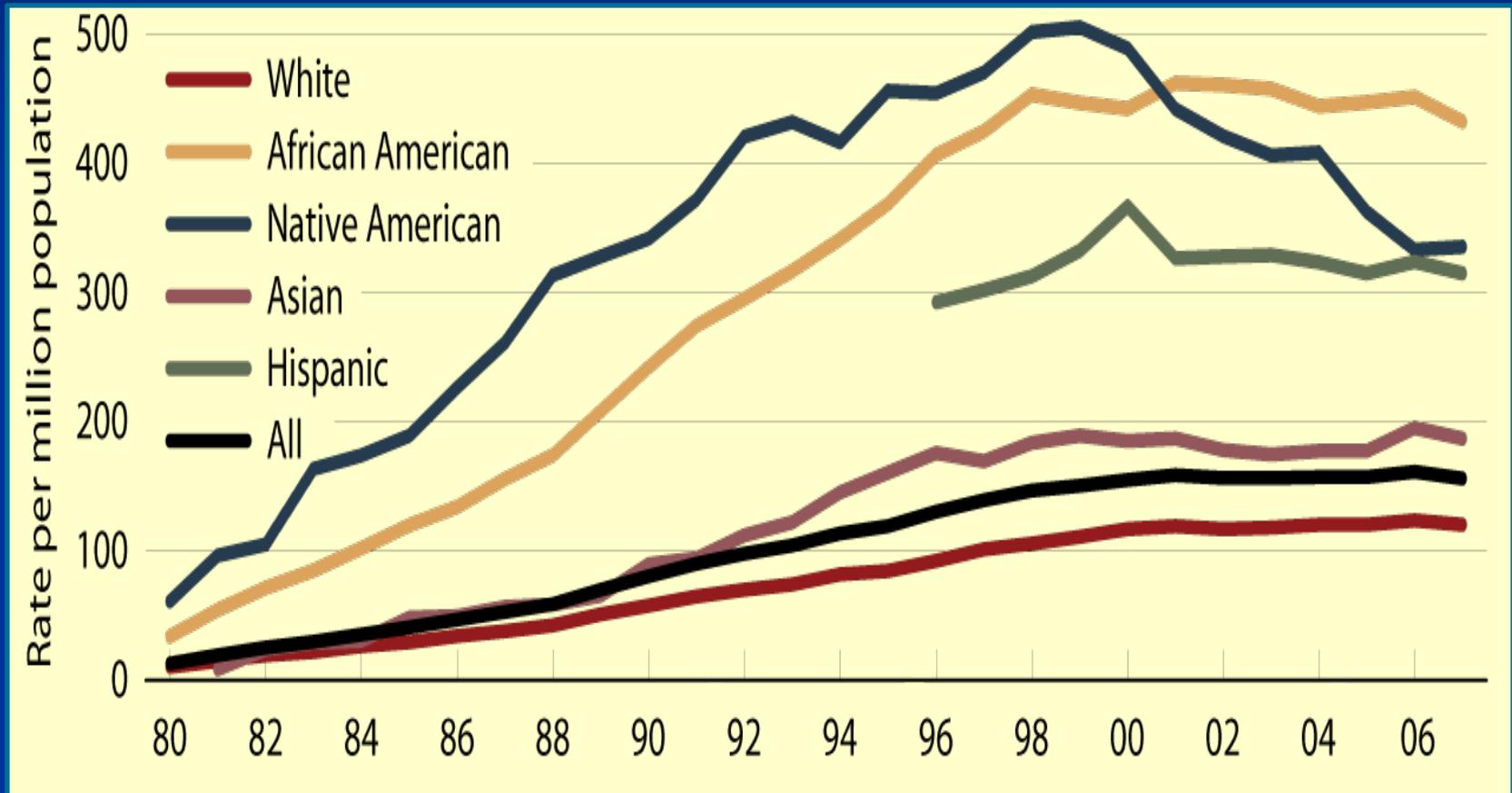
- Why are kidney function issues so important in diabetes care?
 - Diabetic nephropathy occurs in 20–40% of patients with diabetes.
 - It is the single leading cause of end-stage renal disease (ESRD) in the U.S

ADA Clinical Practice Recommendations 2011, Diabetes Care 2011;34: Supplement 1

Diabetes and Kidneys (Continued)

- What is the difference between CKD and diabetic nephropathy?
 - Often used interchangeably but there are some differences
 - Diabetic nephropathy: damage to the kidneys caused by diabetes
 - CKD has a clinical definition and may be caused by diabetes or by other diseases (or both!)
 - Both reflect damage to systemic vasculature as well as kidneys

Age-adjusted* rate of persons initiating therapy for ESRD with diabetes as the primary diagnosis, by race, United States, 1994–2006



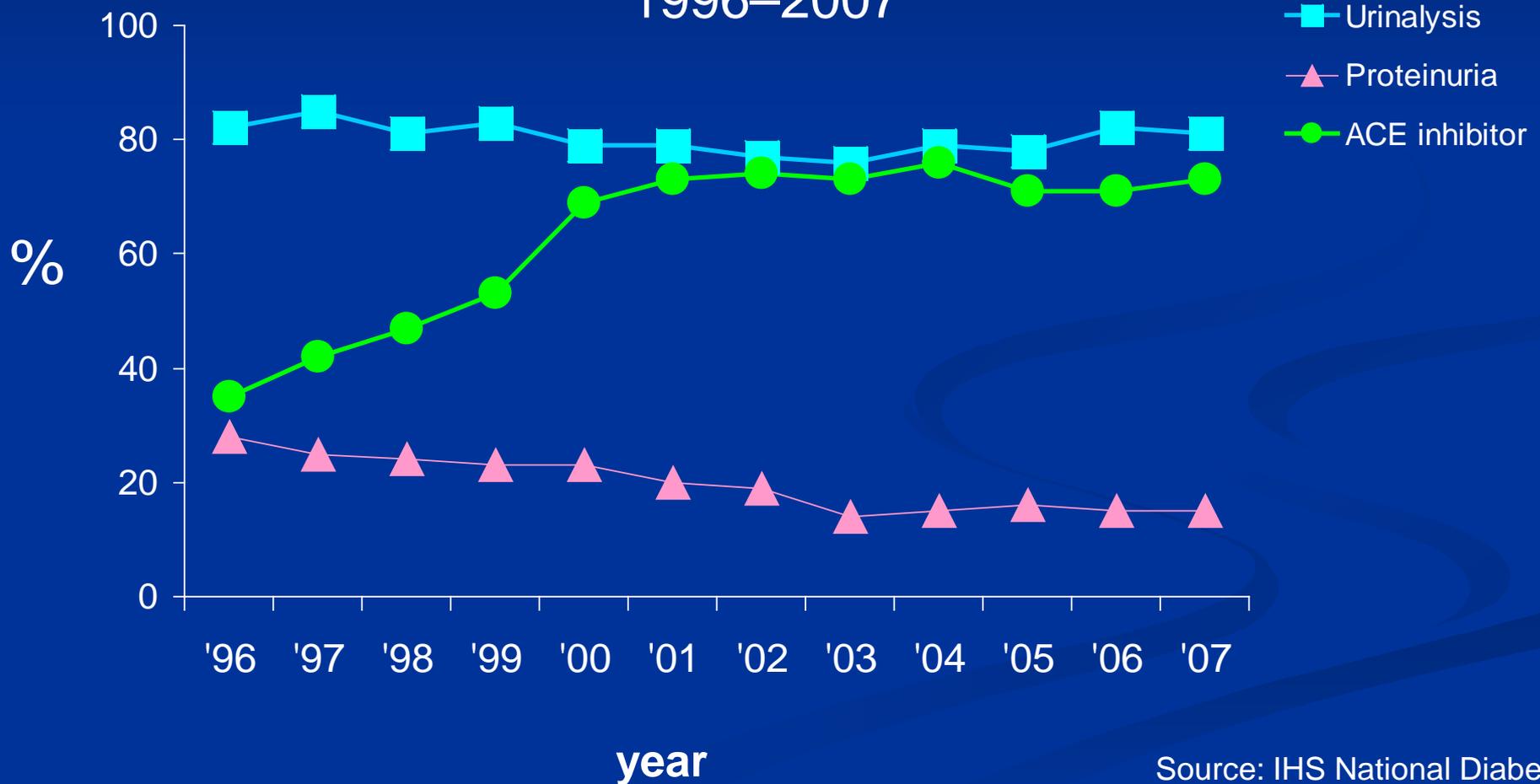
*Based on the 2000 US population

IHS Division of Diabetes

Source: CDC. Racial Differences in Trends of End-Stage Renal Disease, by Primary Diagnosis—US, 1994–2004. MMWR March 23, 2007 / 56(11);253-256

IHS Diabetes Care and Outcomes Audit

Kidney Disease 1996–2007



What is CKD?

CKD is at least three months (“chronic”) of *either*:

- Decreased kidney *function* (ability to filter the blood), *or*
- Evidence of kidney *damage* (e.g. protein in the urine)
 - Earliest indicator
- Monitoring the two together over time tell a lot about what diabetes and hypertension are doing to the kidneys, including where they’re heading and how fast they’re going there...

National Kidney Foundation (NKF)

Definition of CKD

- **Kidney Function.** Glomerular filtration rate (GFR) <60 mL/min/1.73 m² for ≥ 3 months with or without kidney damage
- *Or*
- **Kidney damage** for ≥ 3 months, with or without decreased GFR, manifested by either:
 - Pathologic abnormalities
 - Markers of kidney damage, i.e. **proteinuria**

Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m ²)
1	Kidney Damage with Normal or ↑ GFR	≥ 90
2	Kidney Damage with Mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney Failure	<15 or Dialysis

What is GFR?

- GFR is equal to the sum of the filtration rates in all of the functioning nephrons
- Estimation of the GFR gives a rough measure of the number of functioning nephrons
- GFR cannot be measured directly

What is GFR? (Extra Credit)

- Cardiac output = **6 L/min**
- x 20% of CO goes to kidneys = **1.2 L/min**
- x Plasma is 50% blood volume = **600 ml/min**
- x Filtration Fraction of 20% = ***120 ml/min***

eGFR

- Not the GFR. It's an estimated (eGFR).
 - Based on an equation, usually MDRD
 - Preferred over cockroft-gault in diabetes mellitus (DM)
 - Programmed into Resource and Patient Management System (RPMS) laboratory package
 - Not accurate for eGFRs >60
 - Should be reported as ">60"
 - Stages 1 & 2 CKD not clinically distinguishable (by current definition)
- Like all estimates of kidney function, it's based on creatinine:
 - Creatinine must be stable
 - Hospitalized patients
 - Affected by muscle mass
 - Body builders vs. little old ladies

Loss of Kidney Function in CKD

- Rate of GFR decline should be assessed to:
 - Predict the interval until the onset of kidney failure
 - Assess the effect of interventions to slow the GFR decline

So What About Proteinuria?

- **Albumin** is the primary protein excreted by kidneys damaged by diabetic nephropathy
 - “Proteinuria” and “Albuminuria” often used interchangeably
 - While the term is used in relation to some tests, there is no such thing as “microalbumin” (vs. microalbuminuria)
- It matters a lot:
 - How much albumin is being excreted
 - How fast it is rising
 - If an intervention manages to reduce it

Proteinuria—As Important As eGFR

- Community-based cohort study of 920,000 patients
- Risks of mortality (MI) progression to kidney failure associated with a given level of eGFR are independently elevated with higher levels of proteinuria
- Example: who's at higher risk?
 - Patient with eGFR >60 and UACR 400 mg/g= Stage 1
 - Patient with eGFR of 50 and UACR <30mg/g=Stage 3
 - The first patient has 2–10x higher risk than the second!

JAMA 2010;303(5):423-429

Proteinuria: Important in Screening, Diagnosing, and Treating CKD

- **Diagnosis:** ~40% of people with CKD are diagnosed based on urine albumin alone. Early marker of kidney damage (UACR ≥ 30 mg/g) due to diabetes, hypertension.
- **Prognosis:** Urine albumin is an important prognostic marker (especially in diabetic kidney disease) and may be used to monitor and guide therapy.
- **Marker for CHD:** marker of generalized endothelial dysfunction.
- A tool for **patient education** and self-management (like eGFR, A1C).

Proteinuria in Native Populations

- Patients with albuminuria:
 - Normal Glucose Tolerance (NGT): 8%
 - Impaired Glucose Tolerance (IGT): 15%
 - DM: 47%
- 18% of DM patients develop albuminuria within 4 years of DM onset
- DM patients 45–74 yrs old: prevalence 35–65%
- 50% of patients with macroalbuminuria progress to ESRD within 10 yrs

Diabetic Nephropathy in American Indians,
with a Special Emphasis on the Pima Indians
Current Diabetes Reports 2008;8:486-493

Proven Risk Factor for Chronic Heart Disease (CHD) in Native Populations

- **Strong Heart Study Calculator**
 - **Predicted Risk of CHD in 10 Years:**
 - Albuminuria, age, gender, Total Cholesterol (TC), Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), smoking, DM, Hypertension (HTN)—all CHD risk factors
 - Hazard ratios for macroalbuminuria:
 - Men: 2.11, Women: 2.69
 - Calculator uses UACR results—presence of either:
 - Microalbuminuria
 - Macroalbuminuria
 - <http://strongheart.ouhsc.edu/CHDcalculator/calculator.html>
Circulation 2006;113:2897–2905

**So for something so
important, we need a
really good test to
measure it!**

But which to choose??

Urine Protein Tests: Recipe for Confusion...

- Many different tests:
 - Some based on urine albumin, others on protein
 - Some quantitative, others semi-quantitative (test strips)
 - Some require timed urine collections (e.g. 24 hour, 4 hour, overnight), others spot samples
 - Some account for urine concentration, others don't
 - Some protocols call for one test for screening, others for diagnosis and monitoring
 - Most tests not standardized
- And many different names used for each of these tests!

'A test by any other name'... is confusing!

LOINC Codes for Urine Albumin Tests

12842-1	PROTEIN	MCNC	12H	UR	QN		
21482-5	PROTEIN	MCNC	24H	UR	QN		
26034-9	PROTEIN	MCNC	PT	UR	QN		
26801-1	PROTEIN	MRAT	12H	UR	QN		
2889-4	PROTEIN	MRAT	24H	UR	QN		
13801-6	PROTEIN/CREATININE	MCRT0	24H	UR	QN		
2890-2	PROTEIN/CREATININE	MCRT0	PT	UR	QN		
34366-5	PROTEIN/CREATININE	RATIO	PT	UR	QN		
40662-9	PROTEIN^RESTING	MRAT	12H	UR	QN		
40663-7	PROTEIN^UPRIGHT	MRAT	12H	UR	QN		
18373-1	PROTEIN	MRAT	6H	UR	QN		
20454-5	PROTEIN	ACNC	PT	UR	ORD	TEST STRIP	
27298-9	PROTEIN	ACNC	PT	UR	QN		
2887-8	PROTEIN	ACNC	PT	UR	ORD		
2888-6	PROTEIN	MCNC	PT	UR	QN		
32209-9	PROTEIN	ACNC	24H	UR	ORD	TEST STRIP	
32551-4	PROTEIN	MASS	XXX	UR	QN		
35663-4	PROTEIN	MCNC	XXX	UR	QN		
5804-0	PROTEIN	MCNC	PT	UR	QN	TEST STRIP	
40486-3	PROTEIN/CREATININE	RATIO	24H	UR	QN		
34535-5	MICROALBUMIN/CREATININE RATIO PANEL	-	PT	UR	QN		
14956-7	ALBUMIN	MRAT	24H	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
14957-5	ALBUMIN	MCNC	PT	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
1753-3	ALBUMIN	ACNC	PT	UR	ORD		
1754-1	ALBUMIN	MCNC	PT	UR	QN		
1755-8	ALBUMIN	MRAT	24H	UR	QN		
21059-1	ALBUMIN	MCNC	24H	UR	QN		
30003-8	ALBUMIN	MCNC	24H	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
43605-5	ALBUMIN	MCNC	4H	UR	QN	DETECTION LIMIT = 20 MG/L	
43606-3	ALBUMIN	MRAT	4H	UR	QN	DETECTION LIMIT = 20 MG/L	
43607-1	ALBUMIN	MRAT	12H	UR	QN	DETECTION LIMIT = 20 MG/L	
1757-4	ALBUMIN RENAL CLEARANCE	VRAT	24H	UR	QN		
13705-9	ALBUMIN/CREATININE	MCRT0	24H	UR	QN		PROTEIN..
14585-4	ALBUMIN/CREATININE	SCRTO	PT	UR	QN		PROTEIN..
14958-3	ALBUMIN/CREATININE	MCRT0	24H	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
14959-1	ALBUMIN/CREATININE	MCRT0	PT	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
30000-4	ALBUMIN/CREATININE	RATIO	PT	UR	QN	DETECTION LIMIT = 20 MG/L	MICROALE
30001-2	ALBUMIN/CREATININE	RATIO	PT	UR	QN	DETECTION LIMIT = 20 MG/L	TES MICROALE
32294-1	ALBUMIN/CREATININE	RATIO	PT	UR	QN		
44292-1	ALBUMIN/CREATININE	MCRT0	12H	UR	QN	DETECTION LIMIT = 20 MG/L	
9318-7	ALBUMIN/CREATININE	MCRT0	PT	UR	QN		

Spot UACR recommended
by: NKF, American Diabetes
Association, NIDDK/NIH

UACR

The ratio of albumin to creatinine in a spot urine specimen correlates closely to the total albumin excretion in 24 hours:

$$\frac{\text{Albumin (mg/dl)}}{\text{Creatinine (mg/dl)}} \approx \text{Albumin excretion in grams/24 hours}$$

However, generally expressed as mg albumin/g creatinine:

normoalbuminuria <30 mg/g

microalbuminuria 30-300 mg/g

macroalbuminuria >300 mg/g

Albuminuria is a “continuous risk variable” and the above terms will likely be replaced with a single term (e.g. urine albumin)

Why is UACR Recommended?

- Albumin is primary protein excreted in DM patients
- Most accurate, reproducible test
 - Quantitative (vs. semi-quantitative) test
 - Urine albumin assay being standardized, urine protein not standardizeable
 - Allows for early detection/monitoring of CKD (unlike tests that can't distinguish normal from microalbuminuria)
- Done on spot specimen any time of day
 - No need for timed specimens (e.g. 24 hr, 4 hr, overnight, first morning specimens, etc)
- Accounts for urine concentration using ratio to creatinine
 - Unlike albumin-only tests

What about POC albumin-to-creatinine ratio test strips?

- Per Clinitek's product information:
- “This product provides **semi-quantitative** results and can be used for **screening** samples for microalbuminuria; **positive results should be confirmed with quantitative methods for albumin.**”
 - Accuracy of 85% compared with UACR
- Whether to use Clinitek-type strips:
 - For screening (vs. monitoring CKD)
 - In remote clinical settings
 - Cost?

Urine Albumin Testing—IHS Cost

- ***In-house UACR*** \$2.30–\$9.10
Mean \$3.50
- Siemens Dimension, DCA 2000, Coulter DxC 600
- **POC option?: Yes (e.g. DCA)**
CLIA-waived?: No
- ***Send-out UACR*** \$6.31–\$10.00
Mean \$8.00
- Quest, LabCorps, RML—but ***may require a contract to get affordable prices***

Bert Tallant, Santa Fe Indian Hospital

UACR Results Prognostic and Should Guide Therapy

- Rate of rise as well as absolute value
 - Continuous variable (“micro” and “macro” arbitrary)
 - Extra credit: where did the 300mg cut-off come from?
- If intervene and decrease urine albumin, this is a real reduction in risk of progression
 - Most recent UACR is prognostic, even if previous test results were higher

Am J Kidney Dis 2008;51:759–766

UACR Works in Diabetic Kids, Too

- Pima Indian Youth
 - Cross-sectional and prospective study of youth +/- diabetes from 1982 to 2007
 - Elevated urine albumin in nondiabetic youth: infrequent and largely transient
 - *Diabetic* youth: frequent and largely persistent
 - “Microalbuminuria in youth with Type 2 diabetes strongly predicts progression to macroalbuminuria, which supports annual screening for albuminuria.”

Pediatrics 2010;125:e844–e851

But Youth Need A *Different* Equation To Calculate eGFR

- Adults: MDRD equation (programmed into RPMS)
- $GFR \text{ (mL/min/1.73 m}^2\text{)} = 175 \times (S_{cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if A.-A.})$
- For patients <18 yrs: use the Bedside Schwartz equation
 - $GFR \text{ (mL/min/1.73 m}^2\text{)} = (0.41 \times \text{Height}) / \text{Serum creatinine}$
 - Height in cm, Serum creatinine in mg/dL
 - National Kidney Disease Education Program (NKDEP) calculator:
http://www.nkdep.nih.gov/professionals/gfr_calculators/selecting.htm
 - NKF calculator:
http://www.kidney.org/professionals/kdoqi/gfr_calculatorPed.cfm

When *Not* to Screen for CKD

- eGFR
 - Any time serum creatinine not stable
 - Any acute medical condition
- UACR
 - As they may elevate urine albumin excretion, don't screen if:
 - Infection, fever, CHF, marked hyperglycemia, marked hypertension, or significant exercise within 24 hours

Urine Albumin Testing: What to Do?

- Sit down with laboratory manager, Clinical Applications Coordinator (CAC): figure out which tests are being done and how they're named.
- Be sure that laboratory performing (or sending out) UACR clearly names EHR and that results are in correct units (mg/g).
- Educate staff about UACR and make it the standard test at your facility for urine protein testing in patients with diabetes.

Nephrology Referral

- No predefined threshold
 - Depends on primary care provider and setting
- Situations to consider referral:
 - Unsure as to etiology of CKD (e.g. need a biopsy)
 - ***Not all CKD in diabetes is diabetic nephropathy!***
 - Rapid progression/significantly elevated urine albumin
 - Difficulty controlling complications
 - Usually by eGFR <30 (Stage 4)
 - Goal: educated patient who has chosen renal replacement option (including transplant) in advance and begins dialysis with mature fistula/graft (or ready for PD) calmly in the light of day with CKD complications controlled
 - Quality of care indicator

Bottom Line...

- eGFR and UACR are important tests for screening, diagnosing, and monitoring CKD in DM
 - Order at Type 2 diabetes diagnosis, then yearly
 - More often if changing rapidly, assessing interventions, and once CKD advanced
- CKD Dx= eGFR < 60 or UACR ≥ 30 mg/g for at least 3 months
 - 2 out of 3 UACR specimens ≥ 30 mg/g within 3–6 months
 - Microalbuminuria= 30–300 mg/g, macroalbuminuria >300 mg/g
- Just as important as testing is ***treating!***
 - **Blood Pressure** (goal <130/80)
 - Maximize ACEi/ARB
 - Glucose control
 - CVD risk: lipids, ASA as indicated, smoking cessation
 - Nephrology referral at Stage 4 CKD or sooner if:
 - CKD etiology unclear
 - Rapid decline in eGFR and/or increase in UACR
 - Difficulty managing any CKD issue

CKD Tools

And where to get them

NKDEP

- **NKDEP**

- Many excellent tools, videos, handouts, referral form
- NKDEP Director:
• Dr. Andy Narva
- Web site:
www.nkdep.nih.gov

The screenshot displays the NKDEP website interface. At the top, there is a navigation bar with the NKDEP logo and the text "National Kidney Disease Education Program". Below the logo, there are four small portrait photos of diverse individuals. The main navigation menu includes "Patients & Public", "Health Professionals", "Laboratory Professionals", "Resources", "News & Events", and "About NKDEP". A search bar is located below the menu with the text "SEARCH NKDEP:" and a "Go" button. A Facebook social media link is also present. The main content area is titled "Health Professionals" and features a "Chronic Kidney Disease (CKD) Overview" section. This section includes a definition of CKD, a list of risk factors, prevention tips, diagnostic methods, and treatment options. Below this, there is a "Tools & Resources" section with a list of various clinical tools and calculators. The "Clinical Practice Guidelines" section provides practical guidance for patient care. The "Educating Patients" section discusses the importance of patient education and offers resources like short web videos and patient education concepts. A "Statistics" section provides sources for data on kidney disease, and a "Related Links" section lists external resources. The footer contains site navigation links, a disclaimer, and logos for the U.S. Department of Health & Human Services, the National Institutes of Health, and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The two key markers for kidney disease are urine albumin and estimated glomerular filtration rate (eGFR). For patients with type 1 diabetes for 5 years or more or with type 2 diabetes, the American Diabetes Association and the National Kidney Disease Education Program (NKDEP) recommend that health care professionals:

- Assess urine albumin excretion yearly to diagnose and monitor kidney damage. More frequent monitoring may be indicated in patients with changing clinical status or after therapeutic interventions.
- Screen using a spot UACR. UACR estimates 24-hour urine albumin excretion. 24-hour collection and timed specimens are not necessary.

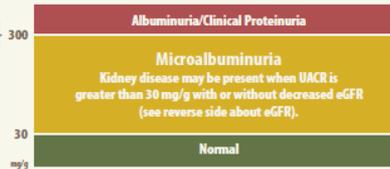
Reducing urine albumin to the normal or near-normal range may improve renal and cardiovascular prognoses.

$$\frac{\text{Urine albumin (mg/dL)}}{\text{Urine creatinine (g/dL)}} = \text{UACR in mg/g} \approx \text{Albumin excretion in mg/day}$$

UACR is a ratio between two measured substances. Unlike a dipstick test for albumin, it is unaffected by variation in urine concentration.

Interpreting UACR Results

Urine dipstick does not detect levels below 300 mg/g.



If kidney disease is detected, it should be addressed as part of a comprehensive approach to the treatment of diabetes.

For more information on UACR and kidney disease,

go to www.nkdep.nih.gov.

NKDEP, a program of the National Institutes of Health, aims to improve early detection of kidney disease, help identify persons at risk for progression to kidney failure, and promote interventions to slow progression of kidney disease.

NIDDK Publication No. 08-0286 • May 2008



The two key markers for kidney disease are eGFR and urine albumin.

The American Diabetes Association and the National Kidney Disease Education Program (NKDEP) recommend that health care professionals:

- Calculate eGFR from stable serum creatinine levels at least once a year in all patients with diabetes.
 - eGFR is more accurate than serum creatinine alone. Serum creatinine is affected by muscle mass, and related factors of age, sex, and race.
 - eGFR is not reliable for patients with normal kidney function, rapidly changing creatinine levels, or extremes in muscle mass and diet, e.g., very muscular or large people, cachectic people, and vegans.

See if your lab reports eGFR routinely or if you need to request it. GFR calculators are available on NKDEP's website at www.nkdep.nih.gov.

Interpreting eGFR Results

NKDEP recommends reporting values greater than or equal to 60 as "≥60," rather than numeric values. Exact values above 60 are not reliable.



If kidney disease is detected, it should be addressed as part of a comprehensive approach to the treatment of diabetes.

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NIDDK Publication No. 08-0286 • May 2008



IHS Division of Diabetes

- Web site: www.ihs.gov/MedicalPrograms/Diabetes
- CKD Quick Guide cards
- CKD online training (for CME/CE credit)
- “Advancements in Diabetes” Web seminars
 - Recordings available on Web site: two CKD sessions
- Algorithm cards:
 - CKD
 - Urine Protein Testing
 - CKD Complications
 - Other diabetes algorithms
 - Glucose Control, HTN, Lipids, Foot Care, Insulin, Neuropathic Pain
- Advances in Indian Health Conference
 - Diabetes track including CKD

Urine Albumin Screening and Monitoring in Type 2 DM

Albuminuria describes a condition in which urine contains an abnormal (high) amount of albumin. In people with Type 2 Diabetes, albumin is the primary protein excreted by the kidneys. Albuminuria is usually a marker of nephropathy and CVD. High levels and/or a rapid rise in urine albumin may be a sign of serious kidney disease. Not all kidney disease in people with diabetes is diabetic nephropathy; consider other causes of kidney damage.

The "gold standard" for kidney testing in people with diabetes = UACR and eGFR

Assessing Urine Albumin in Type 2 DM

1. **Screen:** Check UACR at diagnosis of Type 2 DM and yearly
2. **Diagnosis:** positive diagnosis albuminuria if UACR is greater than 30mg/g on 2 separate occasions
3. **Monitor:** Recheck UACR every year
More frequent monitoring may be needed in patients with changing clinical status or after therapeutic interventions. (Do not monitor urine albumin in dialysis patients)

When you should NOT screen for proteinuria:

Do not screen if symptoms of UTI or a UA that is positive for leukocytes, nitrite, or RBC. Address these issues first, then screen for urine protein once resolved
Causes of false positives include: strenuous exercise within 24 hours, infection, fever, CHF, marked hyperglycemia, pregnancy, marked hypertension, UTI, and hematuria.

Management of Albuminuria

The following strategies should be implemented to reduce albuminuria, prevent/slow nephropathy progression, and lower the risk of CVD:

Maximize ACE Inhibitor/ARB	BP Control
Stop smoking	Lipid Control
Protein restriction (later stages)	Glucose Control

Repeat UACR to monitor effectiveness of intervention; a decrease in urine albumin is therapeutically significant

Urine Albumin Tests

1. Urine Albumin: Creatinine Ratio (UACR)

- UACR measures Albumin excretion in: mg albumin/g creatinine
- Run on a spot urine sample; timed samples not necessary. This test accounts for variation in urine concentration
- Good at assessing any level of proteinuria
- Values can be used for screening, diagnosing, and monitoring interventions, for guiding therapy
- Requires lab analysis; Currently no CLIA waived POC test

The "gold standard" for urine albumin testing = UACR

Other urine protein tests

These tests are not recommended for assessing albuminuria

2. Urine Protein: Creatinine Ratio (UPCR)

- Not sensitive for early detection; not standardized

3. 24 hour urine collection for protein

- Labor intensive for patients and is difficult to get a complete and accurate sample; no more effective than simpler tests such as UACR for DM nephropathy

4. Microalbumin:Creatinine strips (e.g. Clinitek)

- Results may look like UACR (mg alb /g creatinine) but less accurate
- Local lab test names vary widely; Talk with your lab on how to order a UACR (and not a test strip).

5. Microalbumin strips (e.g. Micral)

- Less accurate; resulted as mg alb/L

6. UA dipstick

- Only detects higher levels of proteinuria (>300mg/g)
- Not precise and cannot be used to assess or monitor albuminuria in Type 2 Diabetes

This year's Diabetes Audit will still count any type of urine protein screening, but UACR is preferred

Albuminuria is a continuous variable, the terms "microalbuminuria" and "macroalbuminuria" are going out of use.

Since these terms are still used for ICD9 Coding:

Normal	= < 30mg/g
Microalbuminuria	= 30 - 300mg/g
Macroalbuminuria	= > 300mg/g

Type 2 Diabetes - Chronic Kidney Disease

CKD is eGFR < 60ml/min or kidney damage for ≥ 3 months (e.g. urine sediment, abnormal imaging, or proteinuria (UACR > 30mg/g = nl, 30-300 = micro, >300 = macro))

Stages of Chronic Kidney Disease (CKD)				
1	2	3	4	5
eGFR > 60	> 60	30-59	15-29	< 15 ml/min

Markers of progression: decreasing eGFR, increasing proteinuria, poor BP control

Workup of CKD to r/o non-diabetes causes

CMP, UA, UACR, Uric Acid, Phos, CBC, ANA, RF, C3, C4, HepB sAg, HepC Ab, dilated retinal exam, renal U/S, and if > 40 yo & UACR pos, SPEP and UPEP

Referrals

Nephrologist: Stage 4 or sooner if unsure of etiology or problems
Nutrition: Refer to RD for consult (protein, Na+, K+, PO4, fluids, saturated fat)

Managing Complications of CKD – Stages 3-5

Acidosis		
If CO2 < 22mmol/L	Start sodium bicarbonate 325-650mg (1-2 tabs) TID-QID	Goal: CO2 ≥ 22mmol/L
Anemia		
Check Hb at least yearly: Anemia = Hb <13.5 g/dL adult men, <12 g/dL adult women; r/o B12/folate deficiency, GI blood loss, other causes		
Baseline Labs: Ferritin, transferrin % sat, iron studies (Fe, % Sat, TIBC), CBC+diff		
Start oral iron therapy if ferritin/iron studies low		
Ferrous Sulfate (FeSO4) 325mg daily to TID		
Consider docusate 100mg BID to reduce constipation		
Monitor ferritin to avoid iron overload		
Consider IV iron or blood transfusion if needed		
Safety of erythropoiesis stimulating agents (ESA) unclear; reserve for patients on dialysis, pending renal transplant, or Hb < 9 with symptoms unresponsive to treatment above		
Blood Pressure		
Most effective CKD intervention: BP goal <130/80; continue ACEI/ARB (watch K+)		
Cardiovascular Disease (CVD)		
CVD: CKD increases CVD risk – patients on aspirin (if no contraindications)		
Achieve lipid targets, encourage tobacco cessation		
Diabetes		
Blood sugar control—as renal fxn declines pts' BGs often improve—titrate meds down as needed; Caution setting an A1c target <7% if advanced CKD or CVD		
D/C metformin when Creatinine >1.5 men or >1.4 women		
Peripheral Neuropathy: Foot ulcers common, check feet each visit, refer to shoe clinic		
Retinopathy: Ophth/retinal visits regularly		
Autonomic Neuropathy: Frequent BP fluctuations, including orthostatic symptoms.		

Type 2 Diabetes - Chronic Kidney Disease

Edema/Fluid Overload

Establish patient's dry wt; Titrate furosemide 20-240mg BID (diuresis lasts 6 hours-give AM & mid-day)

Metabolic Bone Disease

Evidence Based Phosphorus (PO₄): if >4.6 mg/dL, start binder (calcium); Refer to RD for dietary PO₄ restriction

Calcium (Ca): If <8.4, start/increase calcium supplementation; target: 8.4-9.5 mg/dL

If >10.2, correct causes (often 2^o meds, need to hold Ca and/or Vit D/calcitriol)

Consensus Opinion: if iPTH elevated, measure 25(OH) Vitamin D; if 25(OH)D >=30mg/mL, start calcitriol

If 25(OH) Vitamin D <30mg/mL, start ergocalciferol (Vitamin D2)

Follow Ca, PO₄, iPTH, and 25(OH)D (Vitamin D): if Ca or PO₄ above target or if iPTH below target, hold calcitriol and/or calcium

CKD Stage	eGFR	iPTH goal	PO ₄ Goal	Ca Goal	Ca goal Ca x PO ₄
3	30-59	35-70	2.7-4.6	8.4-9.5	< 55
4	15-29	70-110	2.7-4.6	8.4-9.5	< 55
5	< 15	150-300	3.5-5.4	8.4-9.5	< 55

Medication*	iPTH effect	PO ₄ effect	Ca effect	Comments
Phosphate Binders				
CaCO ₃ (Cyst-Cal or TUMS) 500-2000mg with meals	-	↓	↑	Use if Ca < 8.4; No more than 7g/d
Ca Acetate 1334-2863mg with meals	-	↓↓	↑	Use if Ca < 8.4 & PO ₄ > 5
Sevelamer (Renvelo) 800-1600mg TID	-	↓↓	-	Decrease PO ₄ , no effect on Ca, cost
Lanthanum 1500-3750mg/day w/meals	-	↓↓	↓	Decrease PO ₄ and Ca, cost
Aluminum 600-1200mg TID between meals & HS	-	↓↓	-	ONLY if PO ₄ > 7 and Ca x PO ₄ > 55, not more than 30 days (toxicity)
Vitamin D and Analogs				
Vit D2 (Ergocalciferol) 1.25-5mg daily	↓	-	↑↑	Use if Vit D < 30mg/ml
Calcitriol 0.25-1mcg daily or 0.5-3mcg TIW	↓	-	↑↑	Use only if Ca & PO ₄ in normal range
Doxercalciferol 1-3mcg daily or 10-20mcg TIW	↓	-	↑	Hold if Ca x PO ₄ > 55
Other				
Cinacalcet 30-180mg daily	↓	↓	↓↓	Do not use if Ca < 8.4

*Always include dietary phosphorous restriction

Drugs in *italics* are not on the IHS National Core Formulary

Lab Monitoring

Parameter	GFR > 60	GFR 30-59	GFR 15-29	GFR <15 not on Dialysis
Creatinine and eGFR	Annual	Each visit	Each visit	Each visit
UACR	Annual	Each visit	Each visit	Each visit
Hb	Annual	Q3mos	Q3mos	Q3mos
Fe, Transferrin Sat, Ferritin		Q3mos	Q3mos	Q3mos
Ca, PO ₄ and iPTH		At least annually	Q3mos	Q3mos

Monitor more often if values are worsening or on medications that affect these labs

Ref. KDOQI/NKF and UK Renal Assoc 4th Ed. Clinical Practice Guidelines for Complications of CKD
ADA Clinical Practice Recommendations 2010



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Quick Guides



CKD Overview

How To

Other Resources

Why is this important?

- Early CKD detection/treatment ↓'s development of kidney failure 30-70%.
- Screen, diagnose, monitor, treat CKD complications.
- Early preparation for kidney replacement therapy (transplant, dialysis) improves outcomes.

Quick Facts

- Screen all DM pts yearly:
 - Creatinine/eGFR (estimated Glomerular Filtration Rate).
 - UACR (Urine Albumin to Creatinine Ratio).
- Dx CKD: ≥ 3 mos duration of either:
 - **decreased function** - eGFR < 60 mL/min/1.73 m² or
 - **evidence of damage** - UACR ≥ 30 mg/g or other.
- BG & BP control (ACE inhibitor/ARB) ↓'s CKD progression.
- R/O non-DM potential causes of CKD.
- eGFR < 60 mL/min/1.73 m²: monitor/treat CKD complications:
 - Acidosis
 - Anemia
 - CVD
 - Edema/Fluid Overload
 - Metabolic Bone Disease
 - Uremia
- Monitor pts more closely if:
 - Amount of albuminuria is high (e.g. UACR >1000 mg/g) or
 - Rate of albuminuria increases rapidly.
 - Nephrology referral:
 - If unsure of cause of CKD (e.g. renal biopsy needed).
 - Difficulty controlling complications of CKD.
 - Usually once eGFR < 30 mL/min/1.73 m².
 - Rapid progression of CKD.



Algorithm Cards (1 of 2)
 (PDF, 33KB / DOC, 328KB)



Best Practice
 (PDF, 167KB)



Standards of Care
 (PDF, 234KB)



Important Resources

- [Quick Reference on UACR and eGFR](#) - Describes the two key markers for kidney disease, urine albumin and estimated glomerular filtration rate (eGFR).
- [Patient Education Videos](#) - Short videos demonstrating patient-provider interactions around common CKD questions. Topics include CKD and risk, treatment, testing and diagnosis, and dialysis and transplantation.





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CKD
Overview
How To
Other Resources

Screening and Diagnosis
Treating Complications

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Treating Complications

- Nephrology Referral:
 - If unsure of cause of CKD (e.g. renal biopsy needed).
 - Difficulty controlling complications of CKD.
 - Usually once eGFR < 30 mL/min/1.73 m².
 - Rapid progression of CKD.
 - Plan for kidney replacement (transplant, dialysis).
 - Goal: start dialysis using mature fistula or graft.
- Nutrition Referral: protein, phosphorus, sodium, potassium.
- Educate patient/family about CKD:
 - Progressive nature of CKD
 - Eventual need for renal replacement therapy
 - Protecting arm designated for fistula placement
 - Dialysis options (hemo, peritoneal)
- When eGFR < 60 mL/min/1.73 m²: monitor/treat CKD complications ([Type 2 DM and CKD Algorithm](#)):
 - Acidosis: Bicarbonate goal ≥ 22mmol/L
 - Anemia:
 - Monitor Hb.
 - Treat with Fe (PO or IV if needed) as appropriate.
 - Consider blood transfusion for significant anemia with Sx.
 - If Hb < 9 g/dL with Sx, not responding to above, consider Erythropoiesis-Stimulating Agent (ESA).
 - safety in nondialysis patients not clear, so restrict use:
 - Consider short term "rescue" ESA course.
 - If use ESA long-term to ↓ Sx, use low dose and aim to slowly ↑ Hb.
 - CVD: CKD further increases CVD risk:
 - Anti-platelet agent (e.g. ASA) if no contraindications
 - Achieve lipid targets
 - Tobacco cessation
 - Fluid Overload – diuretics as needed:
 - Thiazides while eGFR >30 ml/min.
 - Loop diuretics (e.g. furosemide) when eGFR < 30 ml/min.
 - Metabolic Bone Disease:
 - See [Type 2 DM and CKD Algorithm](#) for goals.
 - Control phosphorus, replace calcium.
 - Monitor iPTH, 25 (OH) Vitamin D; consider treatment.
 - Other issues:
 - Foot ulcers common in CKD pts: check feet each visit, refer to foot clinic.
 - Hypertension – goal still < 130/80, continue ACE Inhibitor/ARB (watch potassium).

Important Resources

- [CKD and Drug Dosing: Information for Providers](#) – Estimation of Kidney Function for Prescription Medication Dosage in Adults.
- [Consult Letter Template](#) – for nephrologists to facilitate communication with PCPs.
- [Patient Education Videos](#) – Short videos demonstrating patient-provider interactions around common CKD questions. Topics include dialysis and transplantation.



CKD Case Study #1

- 38-year-old woman diagnosed with Type 2 diabetes 5 yrs ago
 - Otherwise healthy, nonsmoker
- A1C 8.2%, blood pressure (BP) 138/82, lipids at target
 - Meds include low-dose ACEi
- On routine annual diabetes testing:
 - UACR 127 mg/g
 - eGFR >60
- What do you do?
 - Repeat UACR in three months to confirm diagnosis (micro)albuminuria
 - *Intervene*: increase ACEi/ lower BP, improve A1C and CVD risks
 - 6 months later: UACR 79 mg/g

CKD Case Study #2

- 42-year-old man diagnosed with diabetes 6 months ago
 - A1C 7.2%, BP 146/90, on max ACEi
 - eGFR >60, UACR 527 mg/g (2 months later: 617 mg/g)
 - Retinal exam: negative for retinopathy
- What do you do?
- Is this diabetic nephropathy??
 - Nephrology referral
 - Will need to be considered for kidney biopsy
 - And in the meantime,
 - Control BP
 - Control CVD risk factors

CKD Case Study #3

- 76-year-old man with diabetes x 24 years
 - eGFR 58, UACR 178 mg/g (stable over several years)
 - iPTH, Ca, Phos, Hgb normal
 - A1C 6.6%, Lipids: LDL 62, HDL 49, TG 140
 - BP 138/82; 6 months ago: orthostatic sx required lower BP meds
 - Retinal exam: minimal nonproliferative retinopathy
 - No edema, no known CVD, nonsmoker
 - Meds: statin, ASA, ARB, gabapentin, insulin
- What is this and what do you do with it?
 - Stage 3 CKD with microalbuminuria—relatively stable
 - Diabetic nephropathy with age-related ↓ in kidney function
 - Monitor eGFR/UACR regularly
 - Blood Pressure issues (“first, do no harm”)
 - Nephrology referral??

**Thank you
for participating in this
training**

Questions?

E-mail the IHS Division of Diabetes
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