Guide to CKD Screening and Evaluation

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Disclosure

- **Alec Otteman, MD** has no financial relationships with commercial interest(s).

Learning Objectives

- Describe screening and evaluation methods for CKD based on the updated KDIGO guidelines

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Self Assessment Questions

- 1. Modifiable risk factors for CKD include:
  - o Diabetes
  - o Hypertension
  - o History of AKI
  - o Frequent NSAID use
  - o All of the above

- 2. NKF recommends the following calculator be used to estimate GFR for CKD staging:
  - o CKD-EPI
  - o MDRD
  - o Cockroft-Gault
  - o All of the above

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Primary Care Practitioners –
First Line of Defense Against CKD

- Primary care professionals can play a significant role in early diagnosis, treatment, and patient education

- A greater emphasis on detecting CKD, and managing it prior to referral, can improve patient outcomes

CKD is Part of Primary Care

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The Public Burden of CKD

CKD as a Public Health Issue

- 26 million American adults affected

- Prevalence is 11-13% of adult population in the US

- $42 billion in 2013

- 28% of Medicare budget in 2013, up from 6.9% in 1993

- Increases risk for all-cause mortality, CV mortality, kidney failure (ESRD), and other adverse outcomes.

- 6 fold increase in mortality rate with DM + CKD

- Disproportionately affects African Americans, Hispanics, Asians/Pacific Islander, American Indians

ESRD, end stage renal disease

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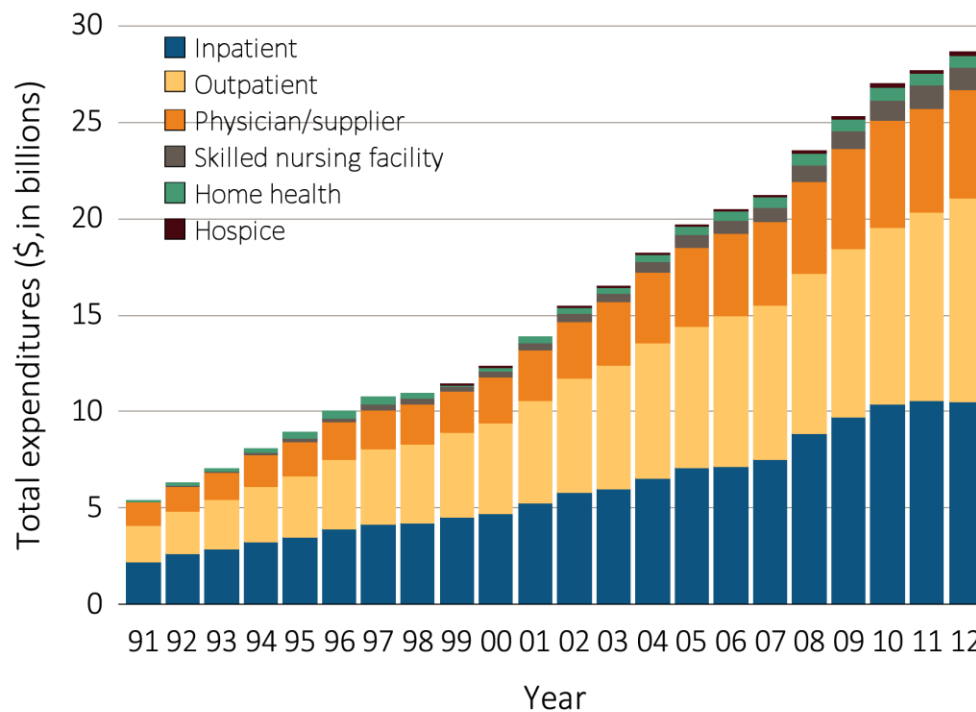
1. NKF Fact Sheets. http://www.kidney.org/news/newsroom/factsheets/FastFacts. Accessed Nov 5, 2014.
2. USRDS. www.usrds.org. Accessed Nov 5, 2014.
3. Coresh et al. *JAMA*. 2007. 298:2038-2047.

CKD-CVD-Diabetes Link: CKD is a Disease Multiplier
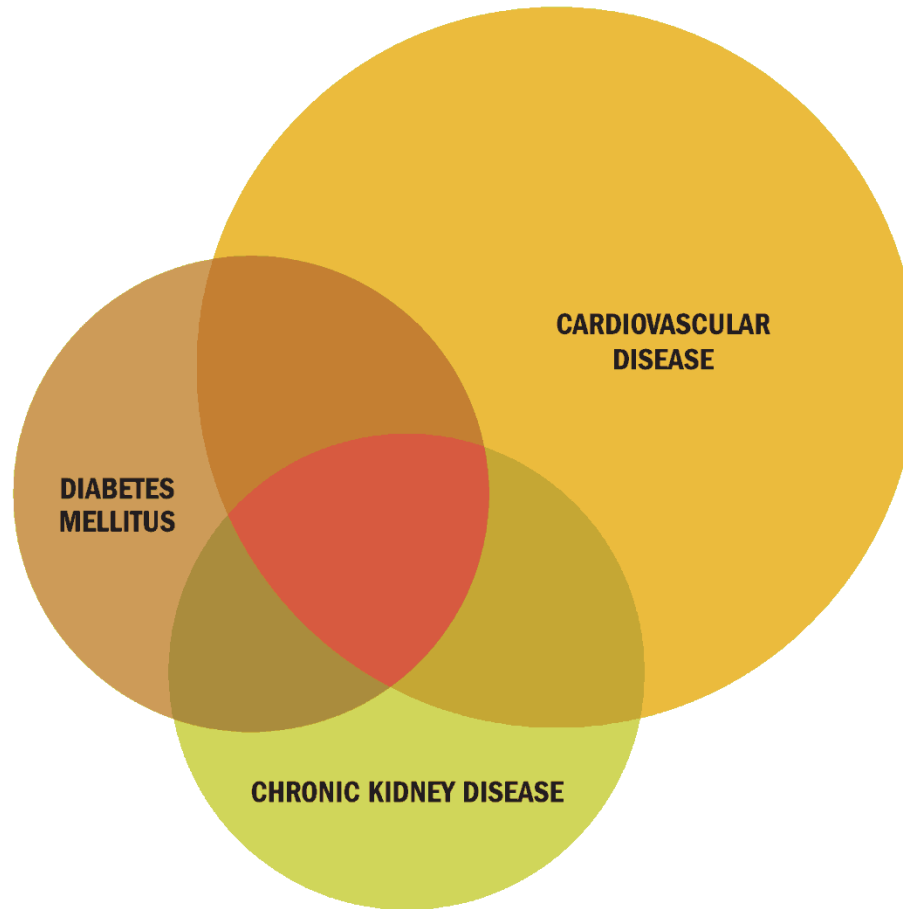
Total Medicare dollars spent on ESRD, by type of service

Preventing progression of CKD will help hold down costs as the treatment of kidney failure is expensive. ESRD requires some type of replacement therapy to maintain life.

USRDS ESRD Database. Total Medicare costs from claims data; includes all Medicare as primary payer claims as well as amounts paid by Medicare as secondary payer. USRDS ADR, 2014.

CKD Risk Factors*

Modifiable

- Diabetes
- Hypertension
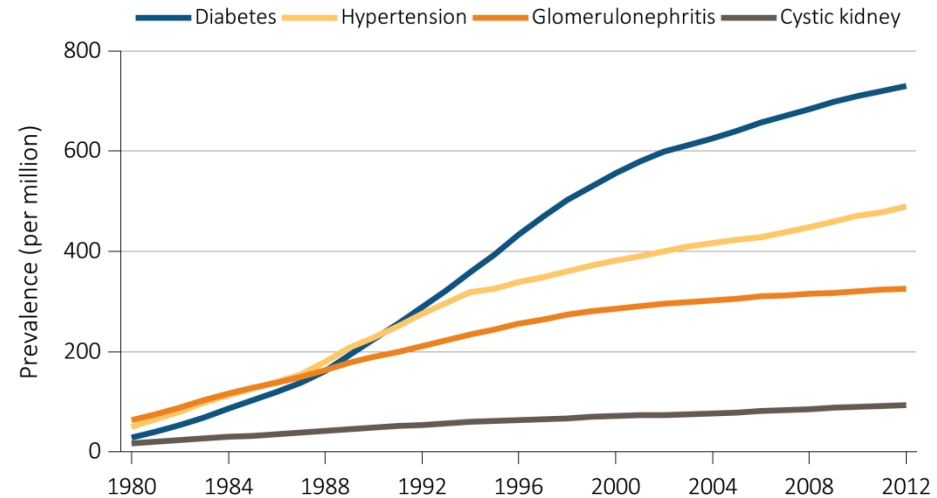- History of AKI
- Frequent NSAID use

Non-Modifiable

- Family history of kidney disease, diabetes, or hypertension
- Age (GFR seems to decline normally with age)
- Race/U.S. ethnic minority status

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*Partial list
AKI, acute kidney injury

Diabetes and hypertension are leading causes of kidney failure

(a) Prevalent Cases
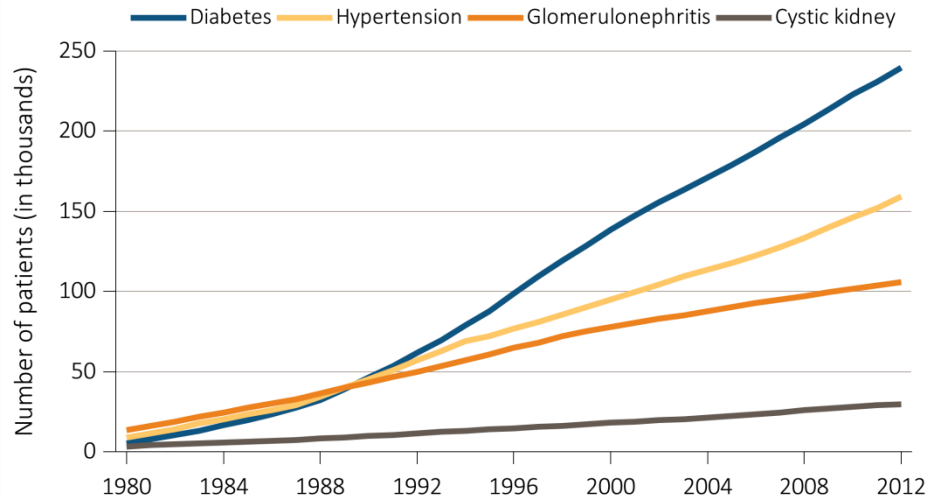
(b) Prevalence per million
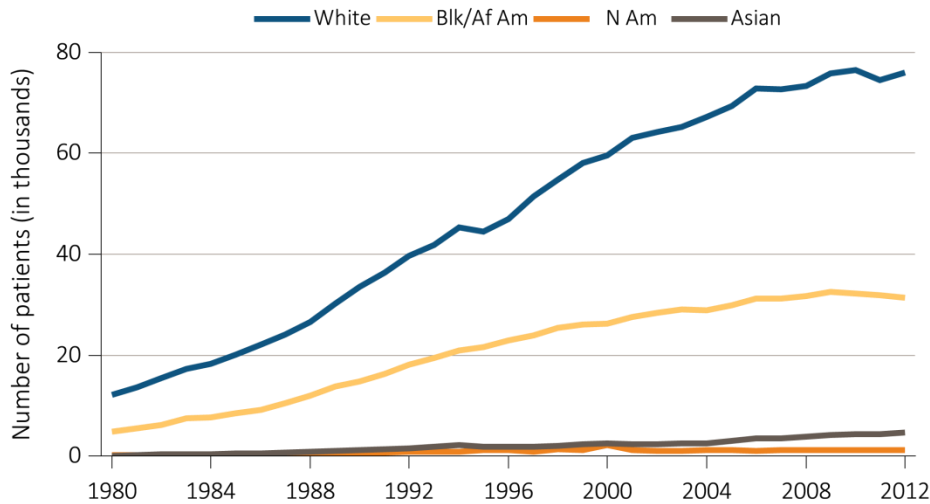

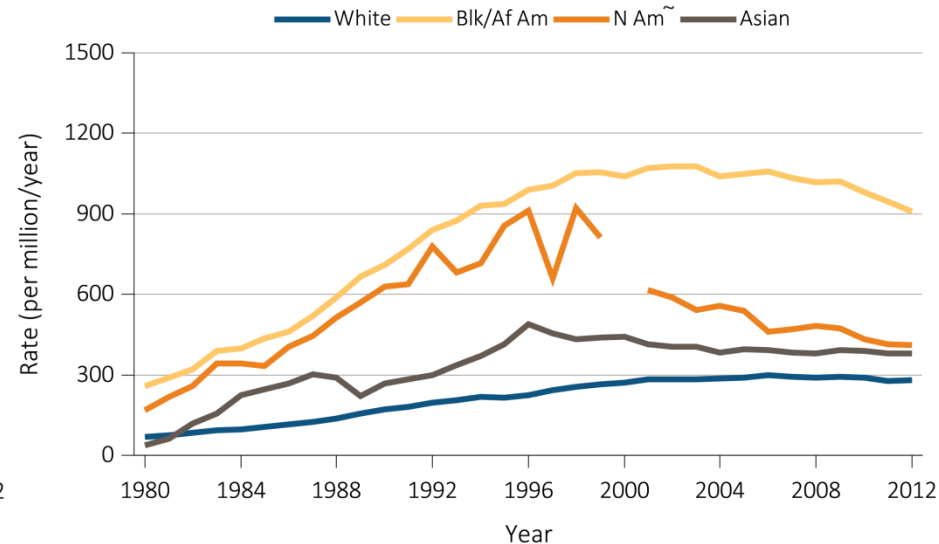**Trends in (a) prevalent ESRD cases and (b) adjusted* prevalence of ESRD, per million, by *primary cause of ESRD*, in the U.S. population, 1980-2012**

*Point prevalence on December 31 of each year; Adjusted for age, sex, and race, The standard population was the U.S. population in 2011 ESRD patients. ESRD, end stage renal disease. USRDS ADR, 2013.

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Incidence of ESRD Varies Widely by Race and Ethnicity

(a) Incident Cases

(b) Incidence Rates

Trends in (a) ESRD incident cases, in thousands, and (b) adjusted* ESRD incidence rate, per million/year, by race, in the U.S. population, 1980-2012

*Adjusted for age and sex; the standard population was the U.S. population in 2011. Panel b: ~Estimate shown is imprecise due to small sample size and may be unstable over time. The line for Native Americans has a discontinuity because of unreliable data for that year. Abbreviations: Af Am, African American; ESRD, end-stage renal disease; N Am, Native American. USRDS ADR 2014.

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Case Question 1

A 50-year-old Hispanic female was diagnosed with type 2 diabetes at age 30. She has taken medications as prescribed since diagnosis. The fact that she has confirmed diabetes puts this patient at:

A. Higher risk for kidney failure and CVD

B. Higher risk for kidney failure only

C. Higher risk for CVD only

D. None of the above

CKD Screening and Evaluation

Gaps in CKD Diagnosis

- 2014 Study
- Chart review of 466 primary care practices in the US in 2011-2012
- ~9300 type 2 diabetics identified
- 54.1% of patients had CKD
- 12.1% of these patients identified by PCP as having CKD

Szczech, Lynda A, et al. "Primary Care Detection of Chronic Kidney Disease in Adults with Type-2 Diabetes: The ADD-CKD Study (Awareness, Detection and Drug Therapy in Type-2 Diabetes and Chronic Kidney Disease)." *PLOS One – November* 2014.

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Gaps in CKD Diagnosis

CKD Screening in Primary Care
(% of patients)

Szczech, Lynda A, et al. "Primary Care Detection of Chronic Kidney Disease in Adults with Type-2 Diabetes: The ADD-CKD Study (Awareness, Detection and Drug Therapy in Type-2 Diabetes and Chronic Kidney Disease)." *PLOS One – November* 2014.

Improved Diagnosis...

Studies demonstrate that clinician behavior changes when CKD diagnosis improves. Significant improvements realized in:[1-3]

- Increased urinary albumin testing
- Increased appropriate use of ACEi or ARB
- Avoidance of NSAIDs prescribing among patients with low eGFR
- Appropriate nephrology consultation

1. Wei L, et al. *Kidney Int*. 2013;84:174-178.
2. Chan M, et al. *Am J Med*. 2007:120;1063-1070.
3. Fink J, et al. *Am J Kidney Dis*. 2009,53:681-668.

Steps to CKD Patient Care

1. Does the patient have CKD?
2. Assess GFR, albuminuria
3. Determine etiology
4. Assess for evidence of progression
5. Assess for associated complications
6. Patient education
7. Assess life expectancy and patient wishes for dialysis/transplantation

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Criteria for CKD

- Abnormalities of kidney structure or function, present for >3 months, with implications for health
- Either of the following must be present for >3 months:
  - GFR <60 mL/min/1.73 m^2
  - Albumin to Creatinine Ratio >30 mg/g
  - Markers of kidney damage (one or more)
    - Nephrotic syndrome
    - Nephritic syndrome
    - Tubular syndromes
    - Asymptomatic urinalysis abnormalities
    - Asymptomatic radiologic abnormalities
    - Hypertension due to kidney disease

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Case Question 2

A 42-year-old African American man with diabetic nephropathy and hypertension has a stable eGFR of 25 mL/min/1.73m^2. Observational Studies of Early as compared to Late Nephrology Referral have demonstrated which of the following?

A. Reduced 1-year Mortality

B. Increase in Mean Hospital Days

C. No change in serum albumin at the initiation of dialysis or kidney transplantation

D. Decrease in hematocrit at the initiation of dialysis or kidney transplantation

E. Delayed referral for kidney transplantation

Classification of CKD Based on GFR and Albuminuria Categories: "Heat Map"

Prognosis of CKD by GFR and Albuminuria Categories			Albuminuria categories Description and range		
			A1	**A2**	**A3**
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	**G1**	Normal or high	≥90		
	G2	Mildly decreased	60-90		
	G3a	Mildly to moderately decreased	45-59		
	G3b	Moderately to severely decreased	30-44		
	G4	Severely decreased	15-29		
	G5	Kidney failure	<15		

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.
KDIGO 2012

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Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppls.* 2013;3:1-150.

Screening Tools: eGFR

- Considered the best overall index of kidney function.

- Normal GFR varies according to age, sex, and body size, and declines with age.

- The NKF recommends using the CKD-EPI Creatinine Equation (2009) to estimate GFR. Other useful calculators related to kidney disease include MDRD and Cockroft Gault.

  - **Labs most commonly report out MDRD eGFR**

- GFR calculators are available online at www.kidney.org/professionals/KDOQI/gfr

  - Or go to www.kidney.org, mouse over "Professionals" and GFR equations are first on the list

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Summary of the MDRD Study and CKD-EPI Estimating Equations:
https://www.kidney.org/sites/default/files/docs/mdrd-study-and-ckd-epi-gfr-estimating-equations-summary-ta.pdf

Use These Equations Cautiously, if at all in ….

- Patients who have/are:
    - Poor nutrition/loss of muscle mass
    - Amputation
    - Chronic illness
    - Not African American or Caucasian
    - **Changing serum creatinine**
    - Obese
    - Young and the elderly

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eGFR, SCr Comparison

Age	Weight in lbs Height in Ft/in	Sex	Race	SCr mg/dl	eGFR ml/Min/1.73m^2 per CKD-EPI
25	285 6′	M	AA	1.6	68
49	180 5′4″	F	Hispanic	1.6	38
67	155 5′8″	M	Asian	1.6	44
92	98 5′1″	F	Caucasian	1.6	28

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Average Measured GFR by Age in People Without CKD

Age (Years)	Average Measured GFR (mL/min/1.73 m²)
20-29	116
30-39	107
40-49	99
50-59	93
60-69	85
70+	75

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Coresh J, et al. *Am J Kidney Dis.* 2003;41(1):1-12.

Decline in GFR with Aging

- GFR declines gradually with age, even in people without kidney disease.
- Appears to be substantial variation among individuals possibly related to initial nephron mass/number and other factors
- Reasons for decline are not fully understood
- Age-related decline in GFR was formerly considered part of normal aging
  - Decreased GFR in the elderly is an independent predictor of adverse outcomes, such as death and cardiovascular disease.
  - Decreased GFR in the elderly requires adjustment in drug dosages, as with other patients with CKD.

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Coresh J, et al. *Am J Kidney Dis.* 2003;41(1):1-12.

Other Changes in the Kidney with Aging

- Decrease in renal mass (mostly from cortex)
- Impaired sodium and potassium excretion and conservation
- Decreased concentrating and diluting capability
- Impaired excretion of acid loads
- Increased dependence on renal prostaglandins to maintain intrarenal perfusion (ie NSAIDs effect aging kidneys more)
- Increased susceptibility to contrast dye and ischemia
- Impaired recovery after insults

Taffet GE. Physiology of Aging. In: Geriatric Medicine: An Evidence-Based Approach, Cassel CK, Leipzig RM, Cohen HJ, et al (Eds), 4th Ed, Springer, New York, 2003.

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Assign GFR Category

GFR Categories in CKD			
Category	GFR	Terms	Clinical Presentations
G1	≥ 90	Normal or high	Markers of kidney damage (nephrotic syndrome, nephritic syndrome, tubular syndromes, urinary tract symptoms, asymptomatic urinalysis abnormalities, asymptomatic radiologic abnormalities, hypertension due to kidney disease)
G2	60-89	Mildly decreased*	
G3a	45-59	Mildly to moderately decreased	• Mild to severe complications: ○ Anemia ○ Mineral and bone disorder ▪ Elevated parathyroid hormone ○ Cardiovascular disease ▪ Hypertension ▪ Lipid abnormalities ○ Low serum albumin
G3b	30-44	Moderately to severely decreased	
G4	15-29	Severely decreased	
G5	< 15	Kidney failure	• Includes all of the above • Uremia
GFR = mL/min/1.73 m^2 *Relative to young adult level In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD. Refer to a nephrologist and prepare for kidney replacement therapy when GFR <30 mL/min/1.73m^2.			

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Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppls*. 2013;3:1-150.

Screening Tools: ACR

- Urinary albumin-to-creatinine ratio (ACR) is calculated by dividing albumin concentration in milligrams by creatinine concentration in grams.
  - Creatinine assists in adjusting albumin levels for varying urine concentrations, which allows for more accurate results versus albumin alone.
- Spot urine albumin-to-creatinine ratio for quantification of proteinuria
  - New guidelines classify albuminuria as mild, moderately or severely increased
- First morning void preferable
- 24hr urine test rarely necessary

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Assign Albuminuria Category

Albuminuria Categories in CKD		
Category	ACR (mg/g)	Terms
A1	< 30	Normal to mildly increased
A2	30-300	Moderately increased*
A3	> 300	Severely increased**
*Relative to young adult level. ACR 30-300 mg/g for > 3 months indicates CKD.		
**Including nephrotic syndrome (albumin excretion ACR > 2220 mg/g).		

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Classification of CKD Based on GFR and Albuminuria Categories: "Heat Map"

CKD is classified based on:
- **Cause (C)**
- **GFR (G)**
- **Albuminuria (A)**

				Albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR catagproes (ml/min/1.73 m² Description and range	G1	Normal or high	≥90	1 if CKD	Monitor 1	Refer* 2
	G2	Mildly decreased	60-90	1 if CKD	Monitor 1	Refer* 2
	G3a	Mildly to moderately decreased	45-59	Monitor 1	Monitor 2	Refer 3
	G3b	Moderately to severely decreased	30-44	Monitor 2	Monitor 3	Refer 3
	G3	Severely decreased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney failure	<15	Refer 4+	Refer 4+	Refer 4+

Colors: Represents the risk for progression, morbidity and mortality by color from best to worst. <u>Green</u>: low risk (if no other markers of kidney disease, no CKD); <u>Yellow</u>: moderately increased risk; <u>Orange</u>: high risk; <u>Red,</u> very high risk.

Numbers: Represent a recommendation for the number of times per year the patient should be monitored.

Refer: Indicates that nephrology referral and services are recommended.

*Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referral.

Adapted from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppls.* 2013;3:1-150.

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Classification of CKD

- This newer classification scheme puts more emphasis on proteinuria
- In practice, this is a significant factor in diagnosis and management of CKD
  - A low GFR with no proteinuria and slow progression probably requires less monitoring and could be followed by Primary Care
  - A relatively high GFR with heavy proteinuria is more concerning and should be referred more aggressively
- Also provides a helpful recommendation for how often to monitor patients

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Clinical Evaluation of CKD

Clinical Evaluation of Patients with CKD

- Blood pressure

- HbA1c

- Serum creatinine
  - Use a GFR estimating equation or clearance measurement; don't rely on serum creatinine concentration alone
  - Be attentive to changes in creatinine over time--even in "normal" range

- Urinalysis
  - Urine sediment

- Albuminuria/Proteinuria
  - Spot urine for protein/creatinine or albumin/creatinine ratio

- Electrolytes, blood glucose, CBC

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Clinical Evaluation of Patients with CKD

- Depending on stage: albumin, phosphate, calcium, vitamin D, iPTH
- Renal imaging
- Depending on age and PMHx
  - Light chain assay, serum or urine protein electrophoresis (SPEP, UPEP)
  - HIV, HCV, HBV tests
  - Complements, other serologies
    - limited role unless specific reason (e.g. systemic symptoms, hematuria)

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Indications for Nephrology Referral

- Acute kidney injury or abrupt sustained fall in GFR
- GFR <30 ml/min/1.73m^2 (GFR categories G4-G5)
- Persistent albuminuria (ACR > 300 mg/g)
- Atypical Progression of CKD[*]
- Urinary red cell casts, RBC more than 20 per HPF sustained and not readily explained
- Hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Anemia thought to be related to CKD
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

*Progression of CKD is defined as one or more of the following: 1) A decline in GFR category accompanied by a 25% or greater drop in eGFR from baseline; and/or 2) rapid progression of CKD defined as a sustained decline in eGFR of more than 5ml/min/1.73m^2/year. KDOQI US Commentary on the 2012 KDIGO Evaluation and Management of CKD

Observational Studies of Early vs. Late Nephrology Consultation

Table 36 | Outcomes of early versus late referral

Variable	Early referral mean (SD)	Late referral mean (SD)	P value
Overall mortality, %	11 (3)	23 (4)	< 0.0001
1-year mortality, %	13 (4)	29 (5)	0.028
Hospital length of stay, days	13.5 (2.2)	25.3 (3.8)	0.0007
Serum albumin at RRT start, g/dl [g/l]	3.62 (0.05) [36.2 (0.5)]	3.40 (0.03) [34.0 (0.3)]	0.001
Hematocrit at RRT start, %	30.54 (0.18)	29.71 (0.10)	0.013

Abbreviation: RRT, renal replacement therapy.

Adapted from Am J Med, Chan MR, Dall AT, Fletcher KE, et al[673] Outcomes in patients with chronic kidney disease referred late to nephrologists: a meta-analysis. 120: 1063-1070, 2007, with permission from Elsevier; accessed http://download.journals.elsevierhealth.com/pdfs/journals/0002-9343/PIIS000293430700664X.pdf

Chan M, et al. *Am J Med*. 2007;120:1063-1070.
http://download.journals.elsevierhealth.com/pdfs/journals/0002-9343/PIIS000293430700664X.pdf
KDIGO CKD Work Group. *Kidney Int Suppls*. 2013;3:1-150.

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Observational Studies of Early vs. Late Nephrology Consultation

- However there are no randomized trials of early versus late nephrology referral in the literature.

    - Interpreting the approximately 50 published observational studies that assessed the timing of nephrology referral is complicated by heterogeneity in study design and variable definitions of early referral.

- Greater choice of treatment options, including home hemodialysis, peritoneal dialysis and pre-emptive kidney transplantation, are associated with early initiation of nephrology services

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Case Question 3

All of the following adult patients should be referred for nephrology consultation, EXCEPT?

A. Initial visit: eGFR 26 & 3 months later: eGFR 28 (mL/min/1.73m^2)

B. Initial visit: eGFR 55, & 3 months later: eGFR 43 confirmed with repeat eGFR 45 (mL/min/1.73m^2)

C. Initial visit: ACR 450 (mg/g) & 3 months later: ACR 355 (mg/g) on both dates the eGFR > 60 mL/min/1.73m^2

D. Initial visit: eGFR > 60 & 3 months later: eGFR > 60 (mL/min/1.73m^2) with personal history of Autosomal Dominant Polycystic Kidney Disease.

E. Initial visit: eGFR 42 & 3 months later: eGFR 44 (mL/min/1.73m^2) on both dates the ACR < 30 mg/g.

Questions and Self-Assessment

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Take Home Points

- PCPs play an important role
- Identify risk factors
- Know patient's eGFR and albuminuria to help guide appropriate treatment strategies
- Partner and refer to specialist

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Self Assessment Questions

- 1. Modifiable risk factors for CKD include:
  - o Diabetes
  - o Hypertension
  - o History of AKI
  - o Frequent NSAID use
  - o <u>*All of the above*</u>
    - Rationale: Diabetes, hypertension, history of AKI, and frequent NSAID use can all damage the kidneys and are risk factors for CKD

- 2. NKF recommends the following calculator be used to estimate GFR for CKD staging:
  - o <u>*CKD-EPI*</u>
  - o MDRD
  - o Cockroft-Gault
  - o All of the above
    - Rationale: CKD-EPI is less biased than MDRD particularly at high GFRs and performs equally, or better compared to the MDRD equation in various age groups and all BMI groups (except those with a BMI <20) and is calibrated for the IDMS standardized creatinine available from all labs

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Questions and Answers

Additional Resources

- Centers for Disease Control and Prevention's CKD Surveillance Project: http://nccd.cdc.gov/ckd
- National Kidney Disease Education Program (NKDEP): http://nkdep.nih.gov
- National Kidney Foundation –CKD: A Global Public Health Crisis https://www.kidney.org/news/newsroom/nr/24
- NKF App: https://www.kidney.org/apps/screening-albuminaria-patients-diabetes
- GLOMERULAR FILTRATION RATE (GFR) Calculator
- https://www.kidney.org/professionals/kdoqi/gfr
- Kidney Disease Improving Global Outcomes (KDIGO) 2012 CKD Guidelines
- http://kdigo.org/home/
- The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI)™
- https://www.kidney.org/professionals/guidelines/guidelines_commentaries
- NKF Safety card for Patient Care: The chart summarizes cautionary safety recommendations for physicians when prescribing medications in people with CKD. https://www.kidney.org/sites/default/files/02-10-6793_IBE_Meds-ImagingStudiesRiskv10.pdf

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