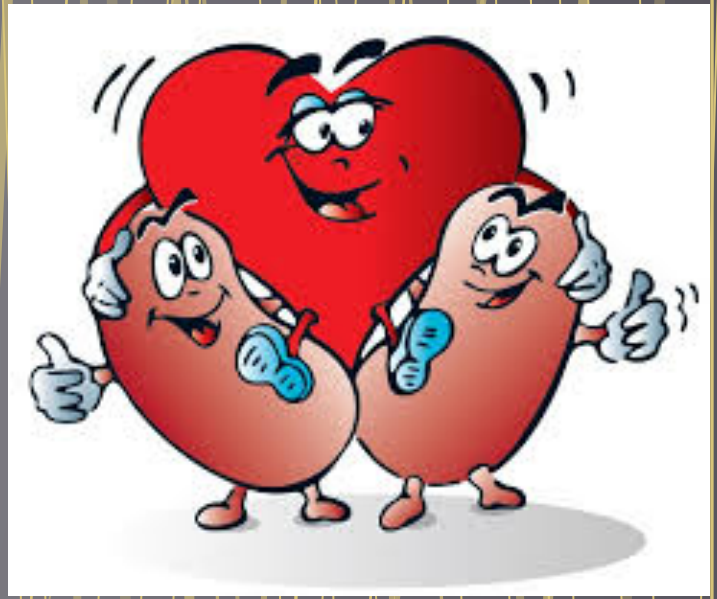
Going for the Gold!

Achieving best clinical outcomes for adults with CKD



Debra Hain, PhD, ARNP, ANP-BC, GNP-BC, FAANP
Associate Professor/Lead AGNP Faculty
Florida Atlantic University
Christine E Lynn College of Nursing
Nurse Practitioner, Cleveland Clinic Florida

Objectives

- Review incidence and prevalence of CKD
- Discuss risk factors for CKD
- Describe best evidence for nephrology/primary care co-management of CKD

Defining "Kidney Damage"

- Kidney damage for ≥ 3 months, defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either
  - Pathologic abnormalities, or
  - Markers of kidney damage, such as abnormalities of the blood or urine, or in imaging tests
  - GFR < 60 mL/min/1.73 m^2 for ≥ 3 months with or without kidney damage.

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Defining "Kidney Damage"

- Pathologic Abnormalities
  - **By Radiology (US, CT, MR, etc)--e.g.**
    - **Multiple cysts consistent with PKD**
    - **Extensive scarring**
    - **Small kidneys**
  - **By Histology--ie, renal biopsy**

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Defining CKD

- Markers of Kidney Damage
  - Proteinuria
  - Microalbuminuria
  - Hematuria (especially when seen with proteinuria)
    - Isolated hematuria has a long differential: infection, stone, malignancy, etc.
  - Casts (especially with cellular elements)

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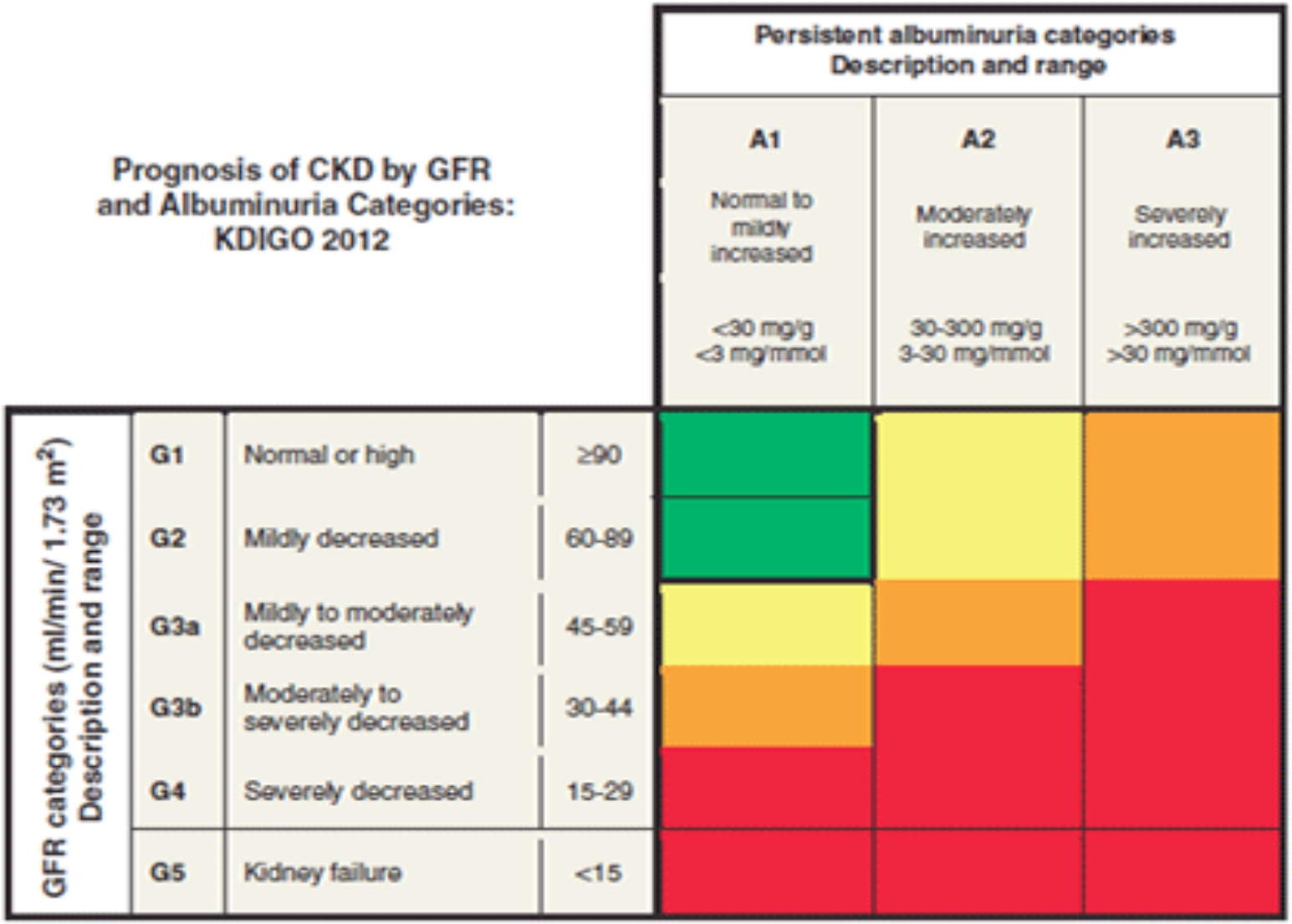
Stages of CKD

GFR Category	Description	GFR mL/min/1.73 m^2
G1	Normal or high	≥90
G2	Mildly decreased	60-89
G3a	Mildly to moderately decreased	45-59
G3b	Moderately to severely decreased	30-44
G4	Severely decreased	15-29
G5	Kidney failure	<15

Albuminuria Categories in CKD

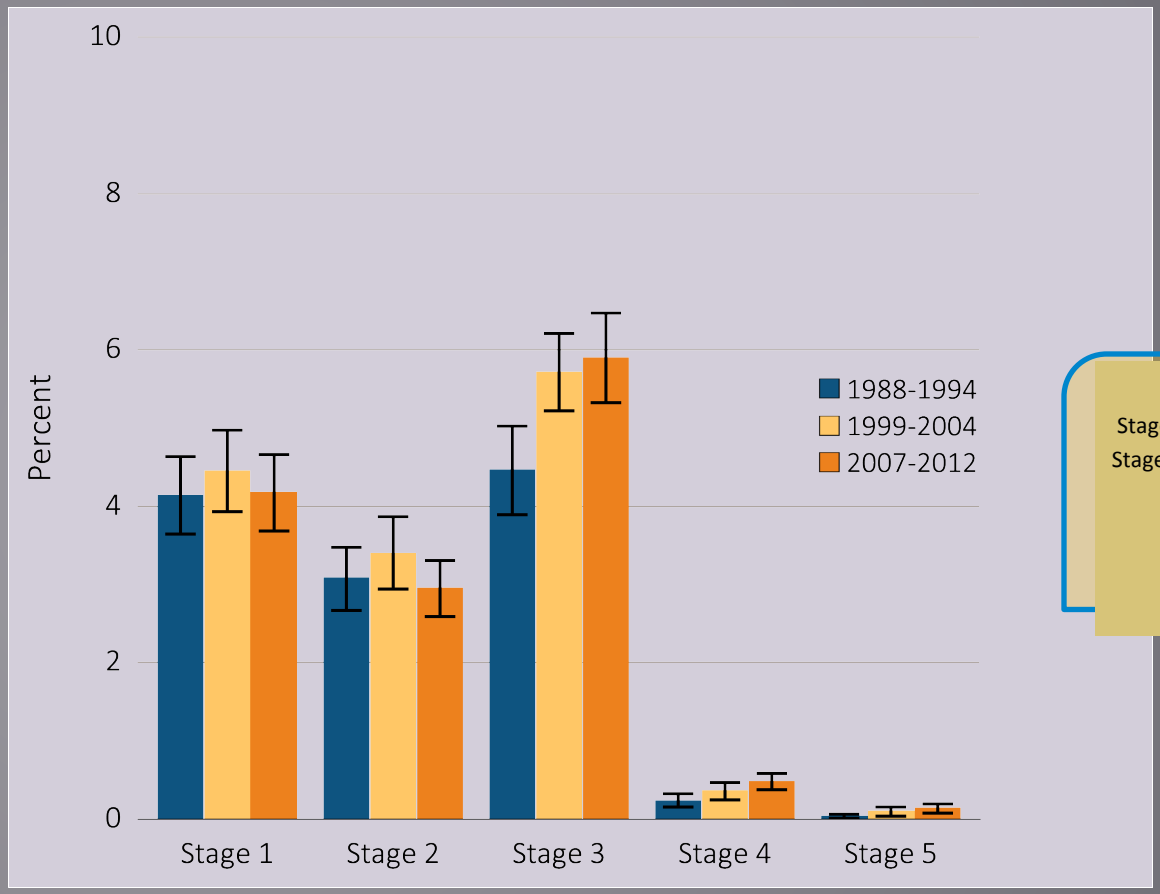
Category	AER (Mg/24 hrs)	ACR (mg/mmol) (mg/g)		Terms
A1	< 30	< 3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased *
A3	>300	>30	> 300	Severely increased **

Prognosis of CKD by GFR and albuminuria category



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

vol 1 Figure 1.1 Prevalence of CKD by stage among NHANES participants, 1988-2012



Stages of CKD – KDOQI 2002 Definitions

Stage 1: eGFR ≥ 90 ml/min/1.73m² and ACR ≥ 30 mg/g

Stage 2: eGFR 60-89 ml/min/1.73m² and ACR ≥ 30 mg/g

Stage 3: eGFR 30-59 ml/min/1.73m²

Stage 4: eGFR 15-29 ml/min/1.73m²

Stage 5: eGFR < 15 ml/min/1.73m²

Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2005–2012 participants age 20 & older. Whisker lines indicate 95% confidence intervals. Abbreviations: CKD, chronic kidney disease.

The patient with early stage CKD is 5 to 10 times more likely to die from a cardiovascular event than progress to ESRD

What can we do about it?

Foley RN, Murray AM, Li S, Herzog CA, McBean AM, Eggers PW, Collins AJ. Chronic kidney disease and the risk for cardiovascular disease, renal replacement, and death in the United States Medicare population, 1998 to 1999. J Am Soc Nephrol 2005; 16:489-95.

Primary Care Professionals: Critical to CKD Care

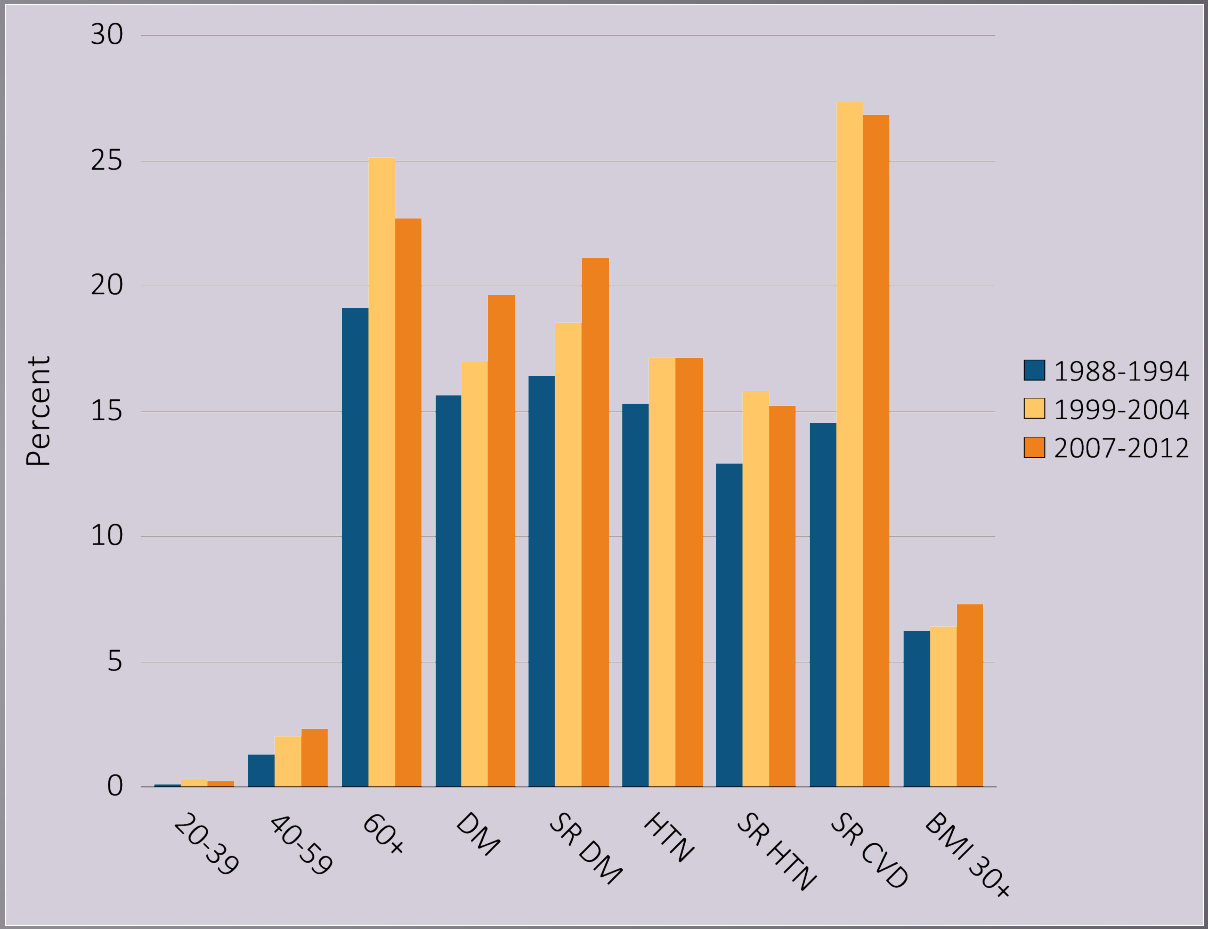
- Many of care issues overlap with those of diabetes and hypertension
- Identifying and intervening early lead to improve patient outcomes
  - Slowing progression and addressing CV risk factors
  - Co-manage with nephrology experts

The Key Issues in Managing CKD

- Identify those at risk
- Ensuring correct etiology
- Implementing appropriate therapy
- Monitoring patient
- Screening for CKD complications
- Educating patient

- Care coordination

vol 1 Figure 1.5 NHANES participants with eGFR <60 ml/min/1.73 m^2, by age & risk factor, 1998-2012



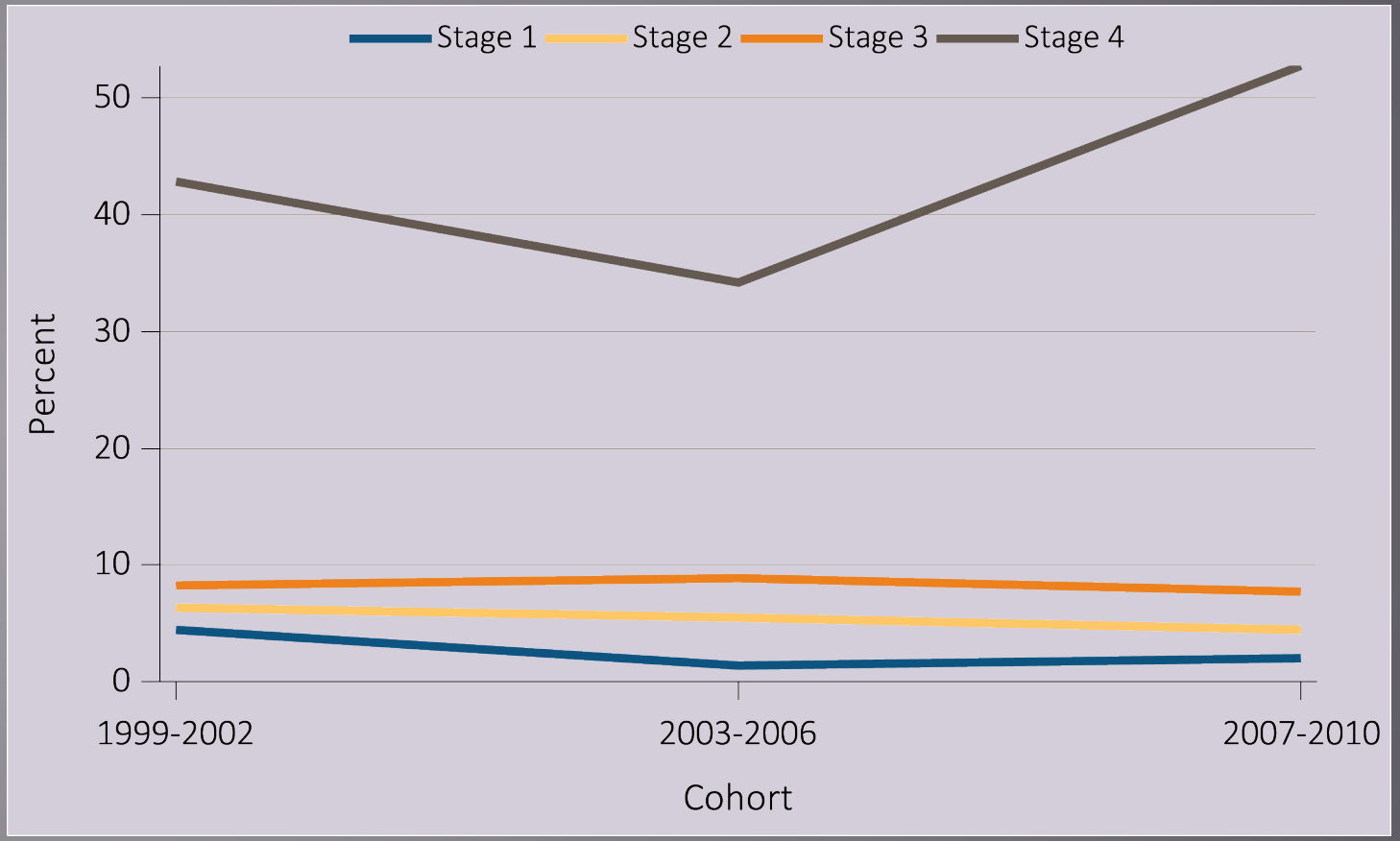
Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2007–2012 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Diabetes defined as HbA1c >7 percent, self-reported (SR), or currently taking glucose-lowering medications. Hypertension defined as BP ≥130/≥80 for those with diabetes or CKD, otherwise BP ≥140/≥90, or taking medication for hypertension. Abbreviations: ACR, urine albumin/creatinine ratio; BMI, body mass index; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HTN, hypertension; SR, self-reported.

vol 1 Table 1.3 Prevalence (%) of CKD in NHANES population within age, sex, race/ethnicity, & risk-factor categories, 1998-2012

	All CKD			eGFR <60 ml/min/1.73m²			ACR ≥30 mg/g		
	1988-1994	1999-2004	2007-2012	1988-1994	1999-2004	2007-2012	1988-1994	1999-2004	2007-2012
20-39	5.1	5.9	5.7	0.1	0.3	0.2	5.0	5.8	5.5
40-59	8.4	9.8	8.9	1.3	2.0	2.3	7.5	8.4	7.2
60+	32.2	37.5	33.2	19.1	25.1	22.7	18.0	20.1	17.7
Male	10.2	12.3	12.1	4.1	5.0	5.4	7.4	9.2	8.7
Female	14.2	15.7	15.1	5.6	7.2	7.6	10.2	10.3	9.6
Non-Hispanic White	12.3	14.0	13.9	5.5	7.0	7.6	8.2	8.9	8.4
Non-Hispanic Black/Af Am	14.5	14.9	15.9	4.1	5.0	6.2	12.7	12.4	12.3
Other	10.5	13.5	11.7	2.2	3.4	3.1	9.2	11.7	10.1
Diabetes	43.1	42.0	39.2	15.6	17.0	19.6	36.3	33.3	28.6
Self-reported diabetes	42.7	42.2	40.4	16.4	18.5	21.1	35.9	32.6	29.3
Hypertension	33.3	32.7	31.0	15.3	17.1	17.1	23.4	21.3	19.8
Self-reported hypertension	25.3	27.2	26.0	12.9	15.8	15.2	17.1	16.4	16.2
Self-reported cardiovascular disease	25.4	40.0	39.5	14.5	27.3	26.8	16.6	23.0	23.8
Obesity (BMI 30+)	16.6	16.8	16.6	6.2	6.4	7.3	12.3	12.6	11.5
All	12.0	14.0	13.6	4.9	6.2	6.5	8.8	9.8	9.2

Data source: National Health and Nutrition Examination Survey (NHANES), 1988-1994, 1999-2004 & 2007-2012 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Diabetes defined as HbA1c >7 percent, self-reported (SR), or currently taking glucose-lowering medications. Hypertension defined as BP ≥130/≥80 for those with diabetes or CKD, otherwise BP ≥140/≥90, or taking medication for hypertension. Values in Figure 1.12 cannot be directly compared to those in Table 1.3 due to different Survey cohorts. The table represents NHANES participants who are classified as hypertensive (measured/treated) but some of those are at target blood pressure. Abbreviations: ACR, urine albumin/creatinine ratio; BMI, body mass index; BP, blood pressure, CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

vol 1 Figure 1.11 NHANES participants with CKD aware of their kidney disease, 1999-2010

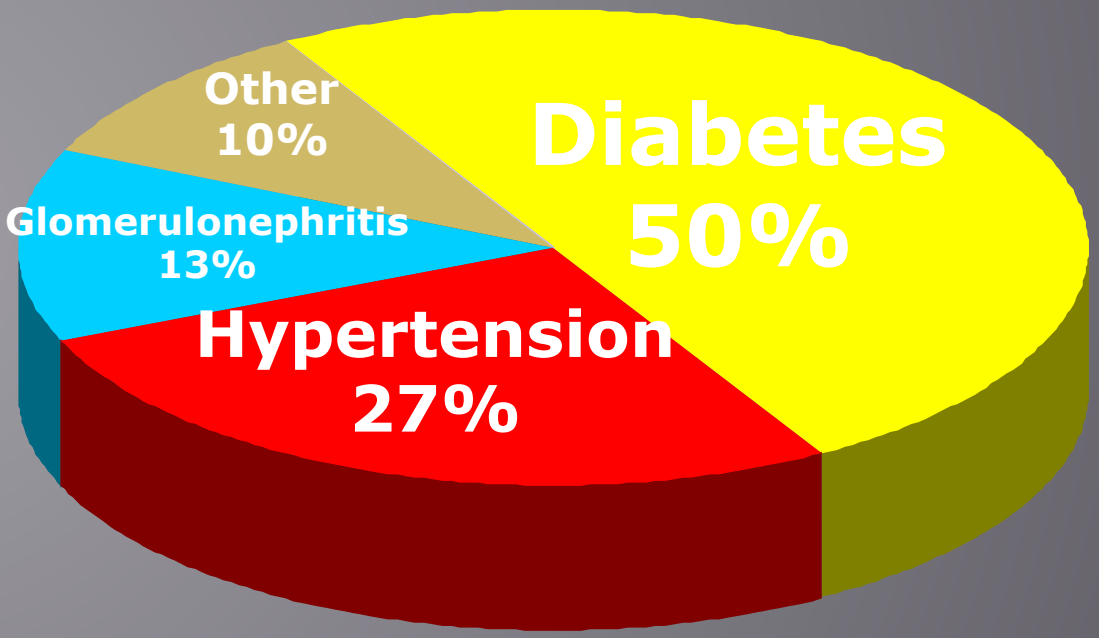


Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2007–2012 participants age 20 & older.
Abbreviations: CKD, chronic kidney disease.

What's the most common sign or symptom of early kidney disease?

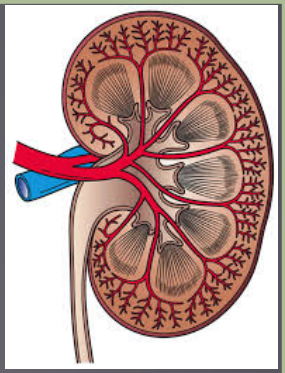
Asymptomatic

Primary Diagnoses for Patients Who Start Dialysis



United States Renal Data System (USRDS), 2000.

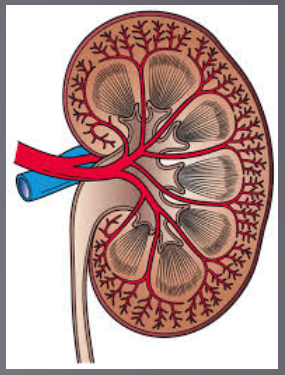
Risk Factors for CKD Early Detection



- Diabetes
- Hypertension
- Autoimmune Diseases
- Systemic Infections
- UTI
- Lower urinary tract obstruction
- Family history
- Recovery from AKI
- Reduction in kidney mass
- High-protein diet
- Atherosclerosis
- Obesity
- Exposure to nephrotoxic drugs
  - NSAIDS, Cox 2
  - Contrast dye

National Kidney Foundation, 2002.

Socio-demographic



- Aging
- Low income/education
- Racial-ethnic background
  - African American, Native American, Asian-American, Pacific Islander, Latin American, Hispanic)

KDIGO, 2012.

DECLINES IN KIDNEY FUNCTION WITH AGING (1 of 2)

Function	Mechanisms	Clinical significance
Glomerular filtration rate (GFR)	Numerous	↑ susceptibility to acute and chronic kidney disease
Sodium conservation	↓ in distal tubular sodium reabsorption, renin levels and activity, and aldosterone levels	↑ susceptibility to hyponatremia from salt loss caused by excessive diaphoresis, GI losses, etc
Sodium excretion	↓ in GFR and response to atrial natriuretic peptide	↑ percentage of nocturnal sodium load excretion contributing to nocturia, and susceptibility to hypernatremia

DECLINES IN KIDNEY FUNCTION WITH AGING (2 of 2)

Function	Mechanisms	Clinical significance
Renal concentrating capacity	↓ in tubular water transport in response to arginine vasopressin release	↓ response to hyperosmolar and volume-deprived conditions
Renal diluting capacity	Unclear; may be due to ↓ in GFR	↓ response to hyperosmolar and volume-overloaded conditions
Acid and ammonium excretion	↓ in GFR and renal mass	↑ susceptibility to metabolic acidosis

PRECIPITANTS OF OSMOLAR DISTURBANCES in Older Adults

- Decreased thirst sensation
- Impaired access to fluids and/or sodium
- Fluid and/or sodium loss from diarrhea, vomiting, diaphoresis
- Volume and pressure changes related to surgery
- Increased fluid intake
- Medications, especially diuretics (esp. thiazides) and NSAIDs
- Conditions and medications that cause SIADH
- Comorbidities, especially cardiac and hepatic dysfunction

Who should be screened?

- USPSTF does not recommend screening in asymptomatic adults unless have risk factors such as hypertension and diabetes
- American Diabetes Association recommends screening all individuals with diabetes
- Joint National Committee on Prevention, Detection, Evaluating, and Treatment of High Blood pressure recommends screening all those with hypertension

How should we screen?

Table 138. Clinical Evaluation of Patients at Increased Risk of Chronic Kidney Disease

All Patients
→ Measurement of blood pressure
→ Serum creatinine to estimate GFR
→ Protein-to-creatinine ratio or albumin-to-creatinine ratio in a first-morning or random untimed "spot" urine specimen
Examination of the urine sediment or dipstick for red blood cells and white blood cells
Selected Patients, Depending on Risk Factors
Utrasound imaging (for example, in patients with symptoms of urinary tract obstruction, infection or stone, or family history of polycystic kidney disease)
Serum electrolytes (sodium, potassium, chloride and bicarbonate)
Urinary concentration or dilution (specific gravity or osmolality)
Urinary acidification (pH)

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Serum Creatinine, CrCl, and eGFR--Nothing is Perfect!

- Serum Creatinine alone CAN NOT be used to accurately assess level of kidney function.
- Scr is a function of production (muscle mass) and excretion (both GFR and tubular secretion).
- Age, sex, and lean body mass have to be taken into account.
- Estimations of eGFR (MDRD equation) and CrCl (Cockcroft-Gault equation) were NOT developed in subjects with normal renal function or normal health.

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Factors Affecting Serum Creatinine Concentration

Increase	*Decrease*

• Kidney Disease
• Ketoacidosis
• Ingestion of cooked meat
• Drugs:
  • Trimethoprim
  • Cimetidine
  • Flucytosine
  • Some cephalosporins
	• Reduced Muscle Mass
	• Malnutrition

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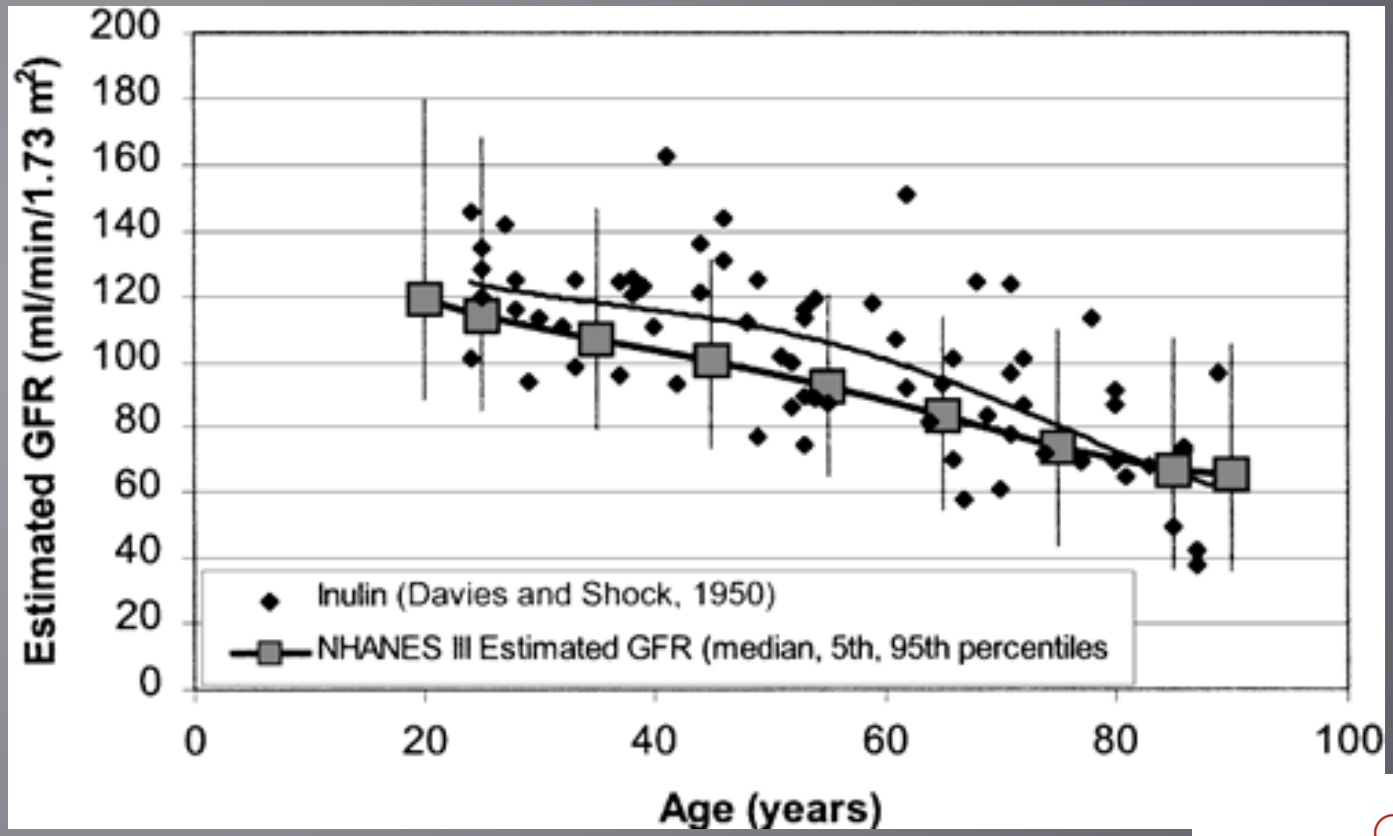
Remember….
GFR normally decreases with age!



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Improving Upon SCr Screening
Use Prediction Equation

Cockcroft-Gault (C-G) Method for Estimating Ccr

$$Ccr = \frac{(140 - \text{age [y]})(\text{body wt [kg]}) \times 0.85^{*})}{(72)(\text{SCr [mg/dL]})}$$

- **Example:**
  - **86-year-old woman, 66-kg body weight, 1.8 mg/dL SCr**
- **Formula result:**
  - **Ccr= 23 mL/min**

STAGE 4 SEVERE KIDNEY DISEASE

*** For women (x 1.0 for men)**

Cockcroft, 1976.

MDRD Equation

- Prediction based on age, gender, race and serum creatinine. Developed to follow GFR as part of the Modification of Diet in Renal Disease (MDRD) study. Validated.
- $GFR/1.73m^2 = 186 \times [P_{cr}]^{-1.154} \times [age]^{-0.203} \times [0.742 \text{ if female}] \times [1.212 \text{ if AfAm}]$

Limitations

- Not well validated in some populations
  - Age < 18 or > 70
  - GFR > 60 ml/min/1.73 m^2
  - Extreme body size
  - Severe malnutrition
  - Paraplegia or quadriplegia
  - Does not adjust for AC, Asian or Hispanic population

Limitations of Cockroft-Gault

- Originally formulated to calculate CrCl in patients without kidney disease
- Not widely validated in different populations
- Tends to overestimate GFR
- Equation uses weight, which results in inaccuracies at extremes of weight

Cockcroft-Gault vs. MDRD

- The MDRD equation estimates GFR.
  - eGFR is given per 1.73m^2 BSA
- The Cockcroft-Gault equation estimates CrCl.
  - CrCl is best used for drug dosing decisions--drug dosing is usually indexed to CrCl.

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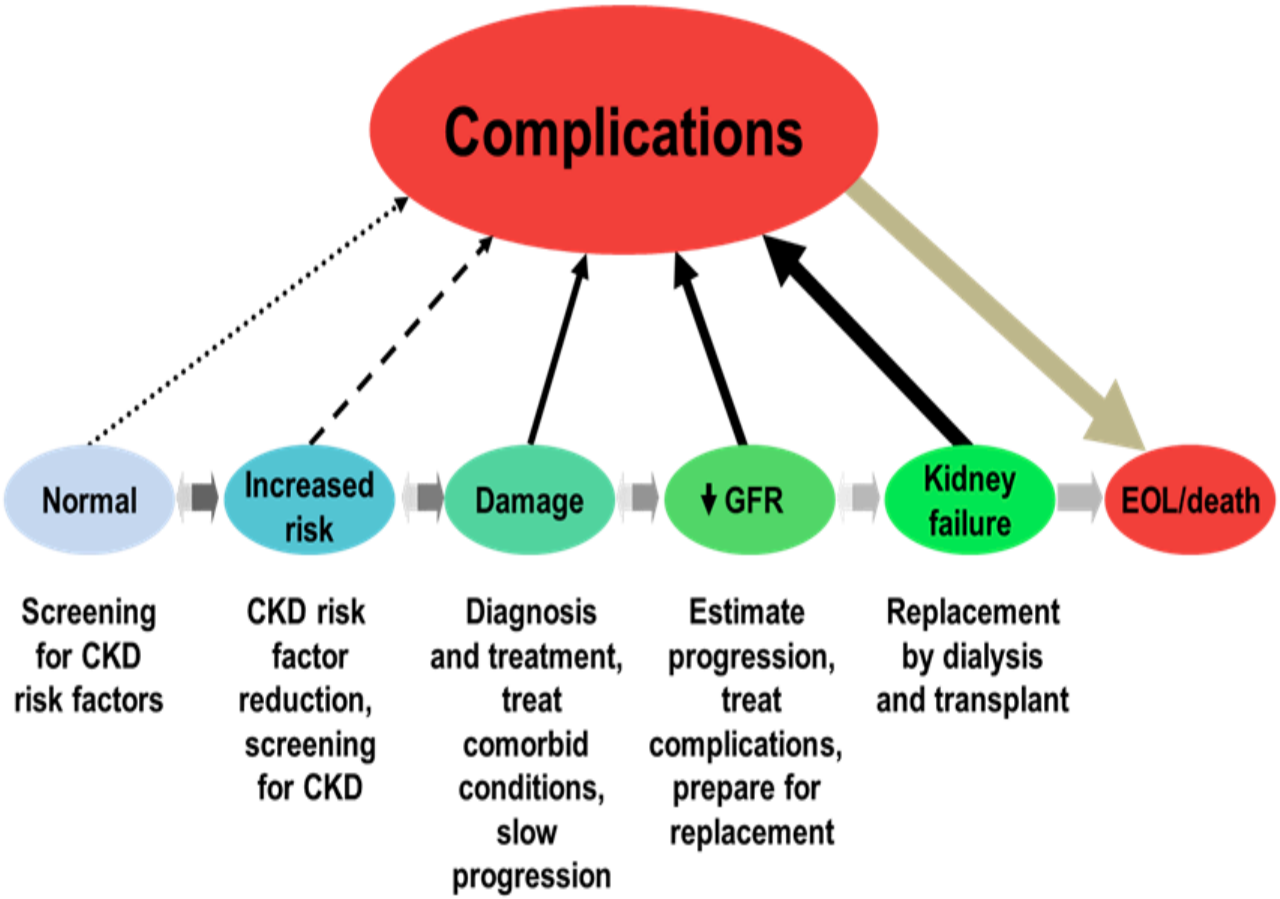
Conceptual Model of CKD



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Adapted with permission from the NKF. Levey AS, et. al. AJKD 2009; 53: S4-16.

Complications

- All people with CKD should be considered at risk for cardiovascular disease
  - As CKD progresses risk of experiencing ACS, stroke, heart failure, and sudden cardiac death increases
  - Albuminuria is associated with risk

Nontraditional Risk CVD

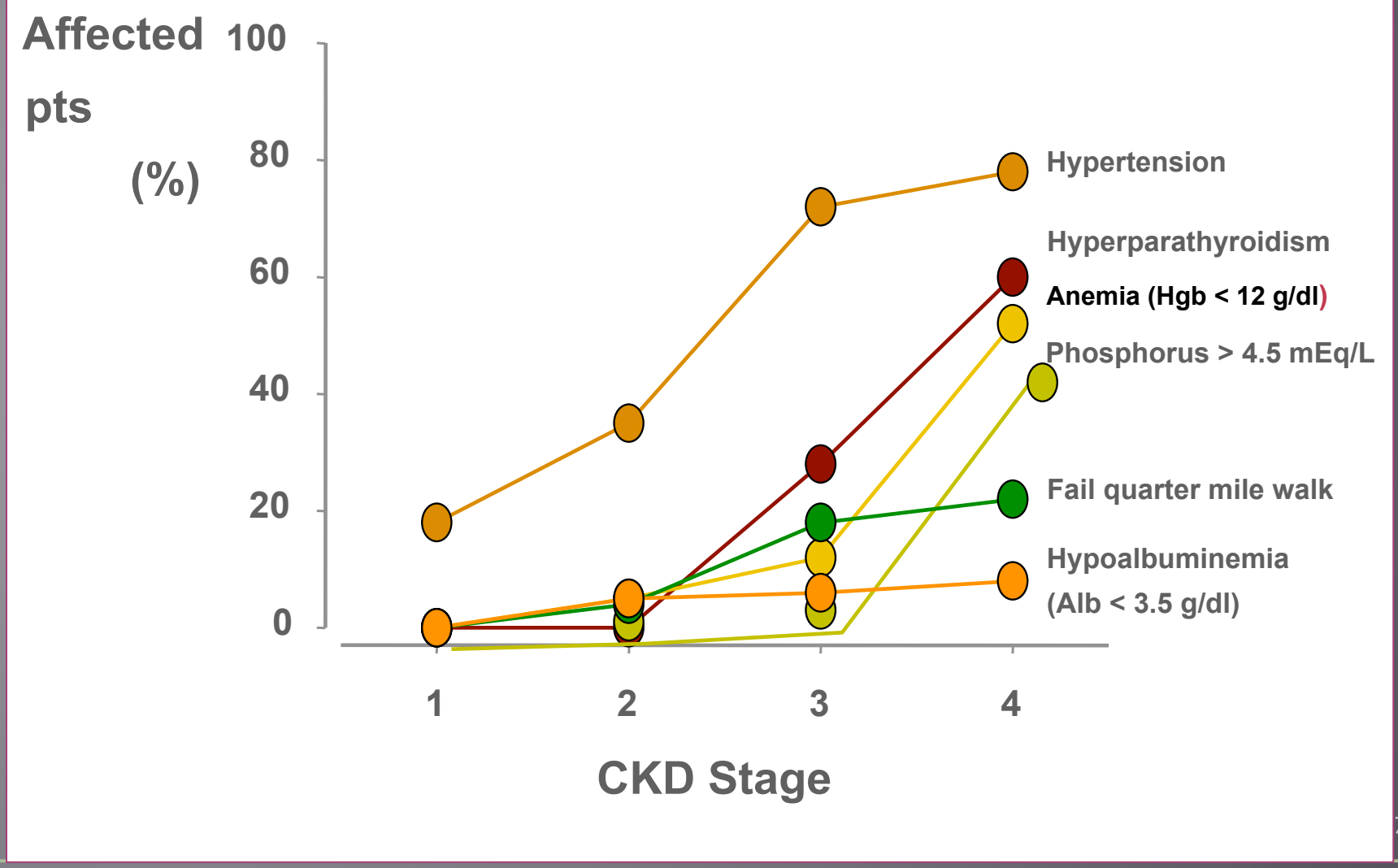
- Anemia
- Hyperhomocystinamia
- Abnormal calcium and phosphorus metabolism
- Oxidative injury
- Inflammation

Modification of Risk Factors

- Smoking cessation
- Exercise
- Weight reduction to optimal targets
- Lipid modification
- Glycemic control
- Optimal BP control <140/90 mm Hg or 130/80 mmHg depending on degree of albuminuria
- Correct anemia

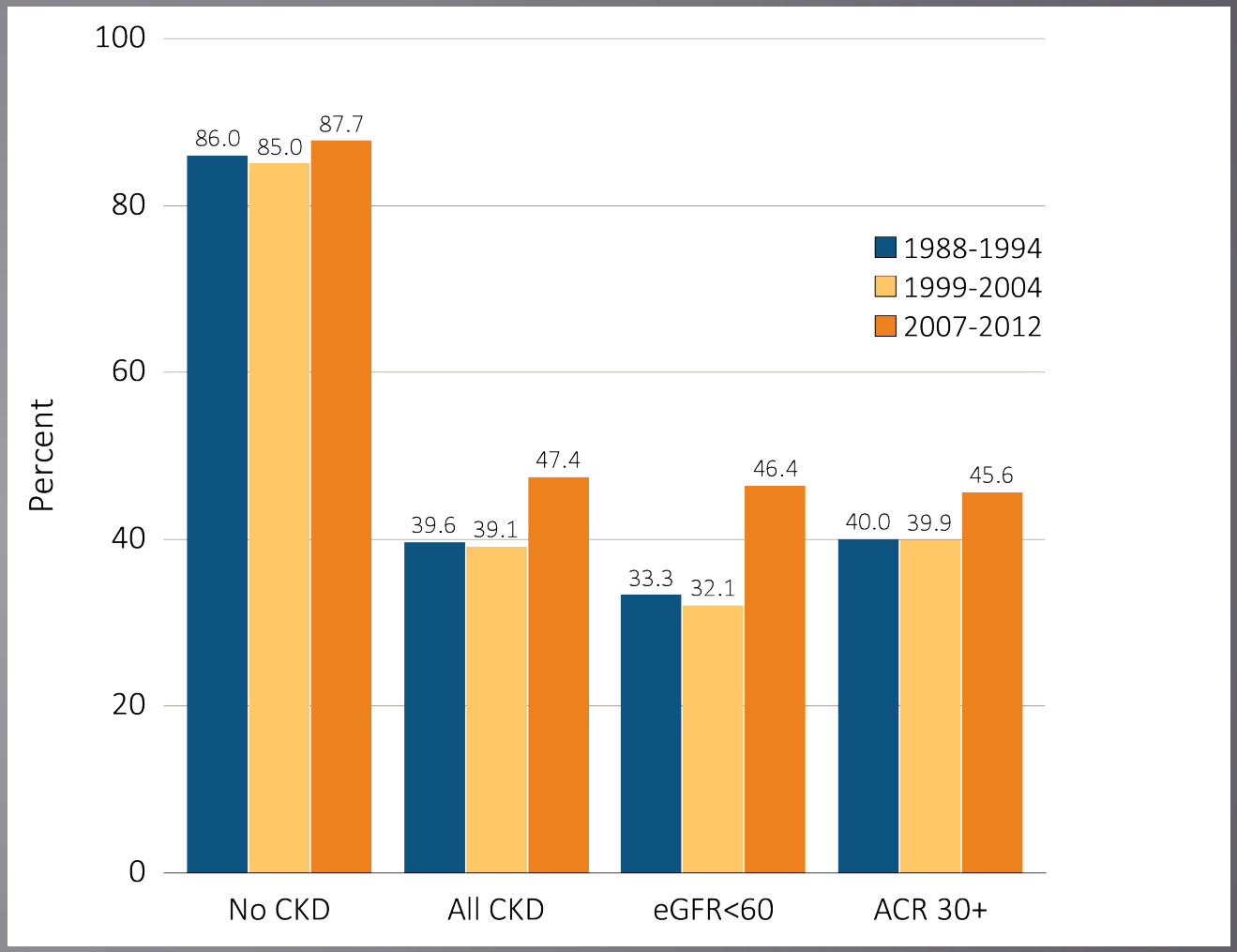
CKD Complications

Evolution and Acceleration by Stage



BP Control

vol 1 Figure 1.12 NHANES participants at target blood pressure, 1998-2012



Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2007–2012 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Figure represents all hypertensives plus those hypertensive participants that are at target blood pressure, probably due to medication. Abbreviations: ACR, urine albumin/creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Hypertension

- Leading cause of CV mortality and morbidity
  - If BP > 115/75 increased risk for every increase in 20 mmHg SBP and 10 mmHg in DBP
- Second leading cause of CKD in US
- HTN can be a consequence of CKD

Ambulatory BP monitoring and office measurement

- Office measurements can be variable
- Home BP monitoring can be stronger predictor of HTN and adherence to medication
- Ambulatory BP monitoring

Goal

- Individualize BP targets and agents according to coexistent CVD and other co-morbid conditions, presence or absence pf retinopathy (in CKD with diabetes) and tolerance of treatment
- Postural dizziness and check postural hypotension
- Tailor BP treatment regimens in elderly population with CKD

Lifestyle Modifications

- Weight reduction
  - Reduction in urinary protein excretion
- Salt reduction (< 2 grams per day)
  - Alterations in salt handing are most likely play key role in HTN in CKD
  - Some forms of CKD associated with salt wasting from the kidney
    - Higher risk of volume depletion
- Exercise (30 minutes 5 times a week)

Lifestyle Modifications

- Alcohol: limit to no more than 2 standard drinks per day
- Cigarette smoking and exposure to environmental tobacco
- Dietary supplements
  - Potassium supplementation has shown positive effects on BP
    - Risk of hyperkalemia
  - Magnesium
  - Fish oil

Optimizing BP

- Both diabetic and non-diabetic adults with CKD and urine albumin excretion < 30 mg/24 hours whose BP is consistently > 140 mmHg systolic or >90 mmHg diastolic treat with BP-lowering drugs to maintain a BP ≤ 140/90
  - Urine albumin ≥ 30 mg.24 hours BP goal is ≤130/80
  - Recommend ARB or ACE-I for diabetes with CKD with albumin excretion 30-300 mg/24 hours
    - > Urine albumin excretion > 300 mg/24 hours ARB or ACE-I regardless diabetes status

BP-Lowering Agents

- Most people with CKD require tow or more agents
- With the exception of ARBs or ACE-Is individuals with high levels of urinary albumin or protein excretion, no strong evidence supporting particular agent
- Tailor
  - Presence or absence of urinary protein
  - Co-morbidities
  - Concomitant medications
  - Adverse effects
  - Availability of agents

Renin-angiotensin-aldosterone system blockers

- Pivotal role in regulation of BP
- ACE-Is and ARBs
  - Block conversion of angiotensin I to angiotensin II and the degradation of bradykinin
  - Indicated if urinary albumin excretion is elevated
- Hyperkalemia
  - Dietary
  - Reduce dose
  - Switching fosinopril or trandolapril or adding potassium lowering agent

Monitoring GFR w/ BP meds

NKF-K/DOQI guidelines

Table 136. Recommended Intervals for Monitoring GFR According to Baseline GFR

	Baseline GFR (mL/min/1.73 m²)		
	GFR ≥60	GFR 30-59	GFR <30
After initiation or changes in dose of antihypertensive therapy	4-12 weeks	2-4 weeks	≤2 weeks
After blood pressure is at goal and dose is stable	6-12 months	3-6 months	1-3 months

GFR monitoring w/ ACE/ARB

NKF-K/DOQI guidelines

Table 137. Changes in Management Based on Magnitude of Early Decrease in GFR

	Early decrease in estimated GFR (%)			
	0-15%	15-30%	30-50%	>50%
Dosage adjustment for ACEI and ARB	None	None	Reduce	Discontinue
Recommended interval for monitoring GFR	As per GFR (previous table)	Once after 10-14 days. If repeat GFR remains within 15-30% of baseline value, resume monitoring schedule as per GFR (previous table)	Every 5-7 days until GFR is within 30% of baseline value	Every 5-7 days until GFR is within 15% of baseline value
Evaluate for causes of decreased GFR (including consideration of RAD, see Guideline 4)	No	No	Yes	Yes

ACE/ARB monitoring intervals

NKF-K/DOQI guidelines

Table 130. Summary of Recommended Intervals to Monitor for Side Effects of ACE Inhibitor or ARB Therapy after Blood Pressure Is at Goal and Dose Is Stable, According to Baseline Values

Baseline Value				
	SBP (mm Hg)	120-129	110-119	<110
	GFR (mL/min/1.73 m^2)	≥60	30-59	<30
	Early GFR Decline (%)	<15	<15	≥15
	Potassium (mEq/L)	≤4.5	4.6-5.0	>5.0
Interval (Months)		6-12	3-6	1-3

Clinicians are advised to evaluate each parameter and select the follow-up interval for the parameter that requires the earliest follow-up.

Aldosterone antagonists

- Spironlactone
  - Reduced dose (12.5 to 50 mg/day)
- Eplerenone, a mineralocorticoid receptor blocker with estrogen-like side effects has been develop
- Studies show benefit in patients with heart failure, including HF with MI
  - Risk hyperkalemia and reduction in GFR

Diuretics

- Salt and water retention are major factors contributing to high BP in CKD and to morbidity and mortality through systemic or pulmonary edema
- Thiazides: risk of hyperuricemia and hyperglycemia
- Loop diuretic
- Potassium-sparing

RECOGNIZING RENOVASCULAR DISEASE

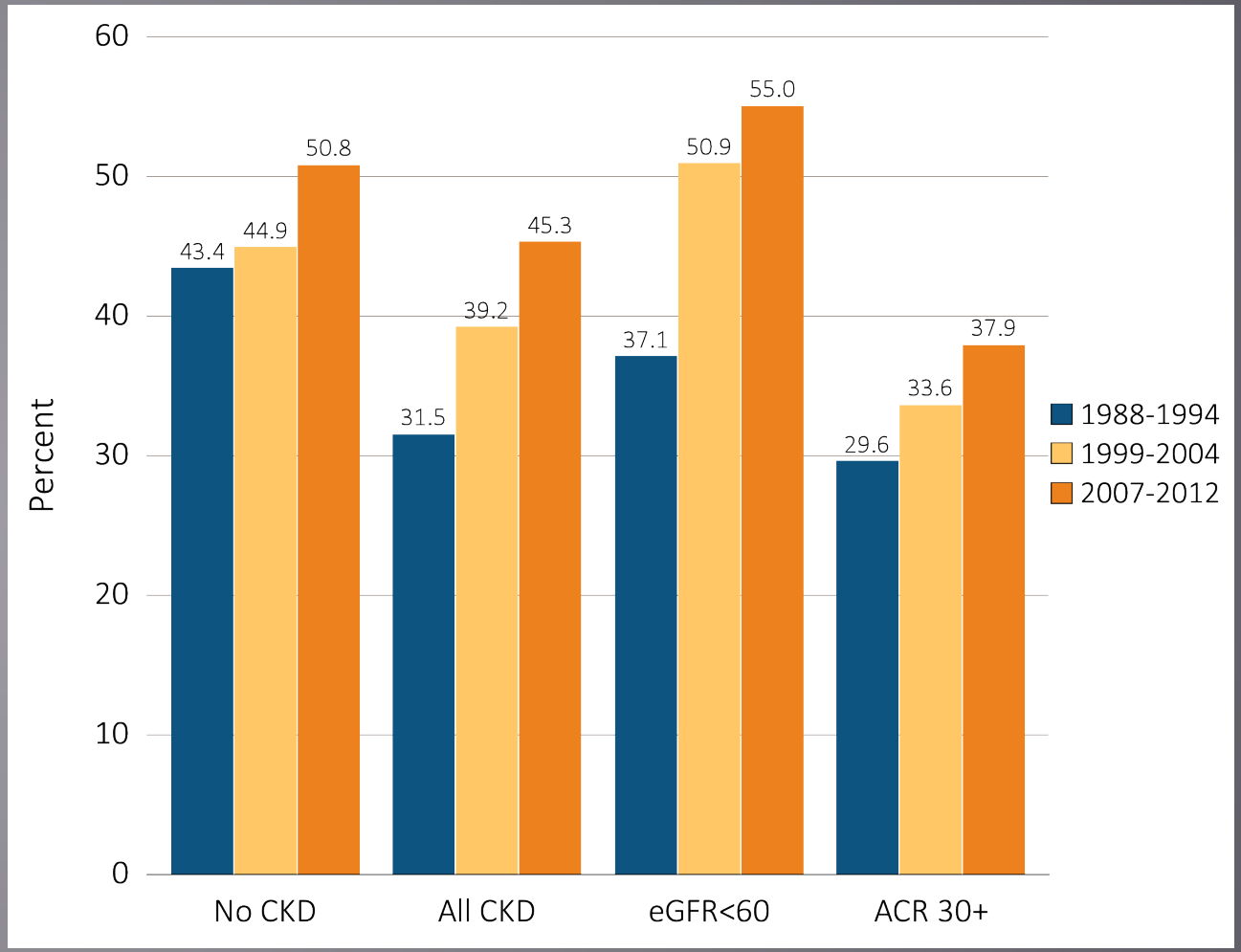
- Suspect renal artery stenosis in cases of:
  - New-onset diastolic hypertension (HTN)
  - HTN despite maximal doses of 3 antihypertensive agents
  - Abruptly worsening HTN that was previously stable
  - Azotemia induced by treatment with an ACE inhibitor or ARB
  - HTN accompanied by widespread vascular disease
- Diagnostic test options: renal artery duplex ultrasonography, CT angiography, or magnetic resonance angiography

TREATING RENOVASCULAR DISEASE

- Therapy is based on aggressive management of risk factors
  - Antihypertensive regimens should include angiotensin blockade
- Renovascular angioplasty ± stenting carries significant risks, particularly in patients with abdominal aortic atherosclerosis
  - Limit invasive procedures to patients in whom medical management has not controlled BP, those who develop heart failure, and those with progressive decline in renal function

Glycemic Control

vol 1 Figure 1.15 Diabetic NHANES participants with glycohemoglobin <7%, 1998-2012



Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2007–2012 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Figure represents all hypertensives plus those hypertensive participants that are at target blood pressure, probably due to medication. Abbreviations: ACR, urine albumin/creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Diabetic Kidney Disease

- Normoalbuminuria with elevated GFR-usually occurs within 5-10 years
  - Associated with glomerular and tubular hypertrophy and enlarged kidneys on ultrasound evaluation
  - Hyperfiltration –maladaptive and my be a risk factor for progression to CKD
- Microalbuminuria
- Macroalbuminuria

Glycemic Control

- NKF and Clinical Practice Guidelines for DM and CKD recommends target hemoglobin A1c of ~7.0% to prevent or delay the progression of microvascular complications of diabetes, including diabetic kidney disease

Other recommendations

- Not lower A1c below 7.0% for those at risk for hypoglycemia
  - Consider life expectancy and other co-morbidities and risk of hypoglycemia
  - A1c > 8% may be appropriate for some individuals
- More stringent A1c < 7.0% (< 6.5) for selected individuals without significant risk of hypoglycemia

Anemia

Anemia in CKD

Stage	GFR	% Anemia
1	≥ 90–120 mL/min/1.73 m^2	stage 1 and 2 about 26.7%
2	60–89 mL/min/1.73 m^2	
3	30–59 mL/min/1.73 m^2	41.6%
4	15–29 mL/min/1.73 m^2	53.6%
5	< 15 mL/min/1.73 m^2 or dialysis	75.5%

National Kidney Foundation. *Am J Kidney Dis*. 2002;39(suppl 1):S1-S266.

Risks Associated with Anemia

Increased morbidity

- Decreased mobility in community-dwelling
- Decreased quality of life
- Increased risk of fatigue, depression, dementia, delirium, hospitalization, and falls

Increased mortality

- Community-dwelling
- Nursing home residents
- Persons with preexisting heart or kidney disease
- Persons undergoing non-cardiac surgery

Bross, Soch, & Smith-Knuppel, 2010

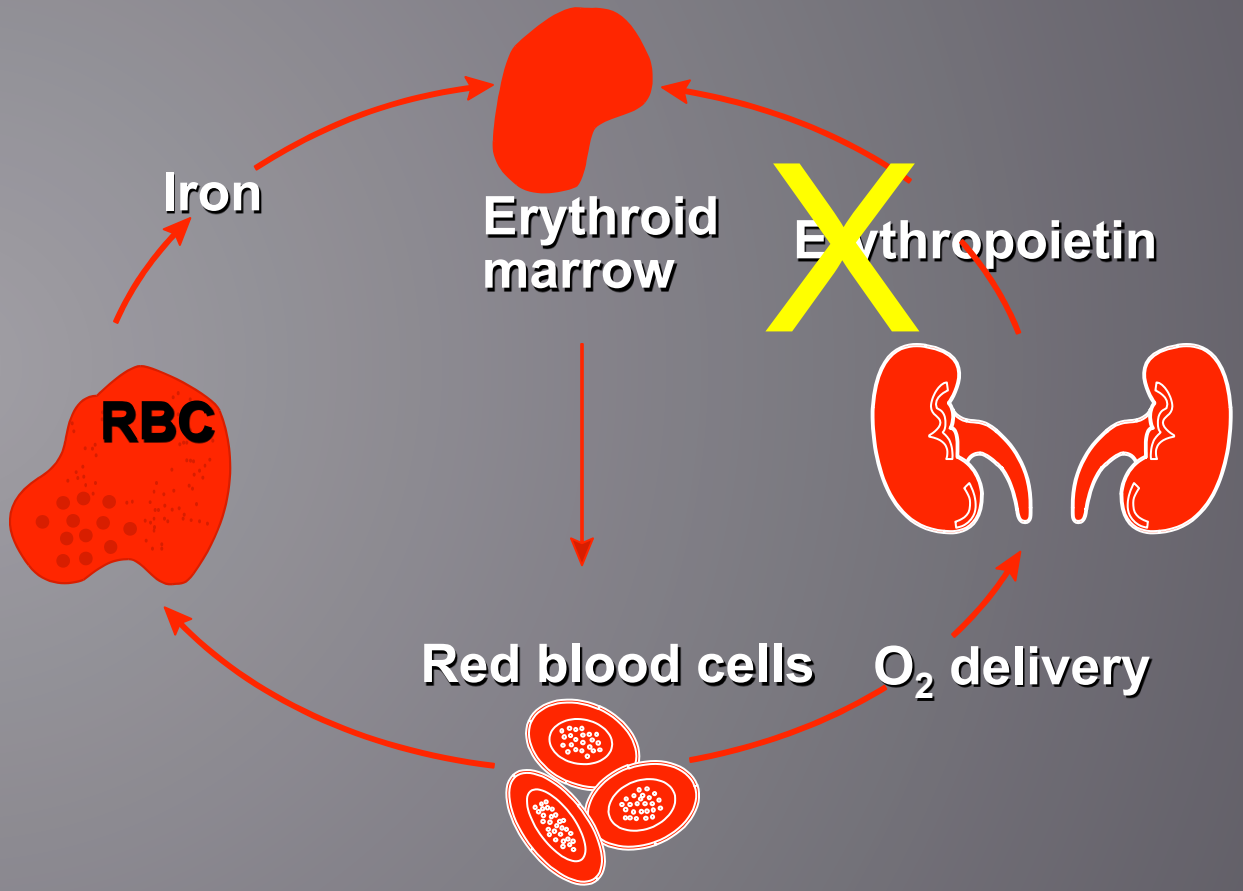
Factors Cause or Contribute to Anemia in CKD

- Insufficient production of endogenous erythropoietin
- Iron deficiency
- Acute and chronic inflammatory conditions
- Severe hyperparathyroidism
- Aluminum toxicity
- Folate deficiency
- Decreased survival of red blood cell

Erythropoietin

- Key regulator of erythropoiesis
- Kidney major site (90%) Liver (10%)
  - **Peritubular interstitial fibroblasts**
- Acts in the bone marrow to increase red blood cell mass
- Hypoxia is the major stimulus for EPO production

Erythropoiesis in CKD



Adapted from Hillman, 1998.

RE=reticuloendothelial

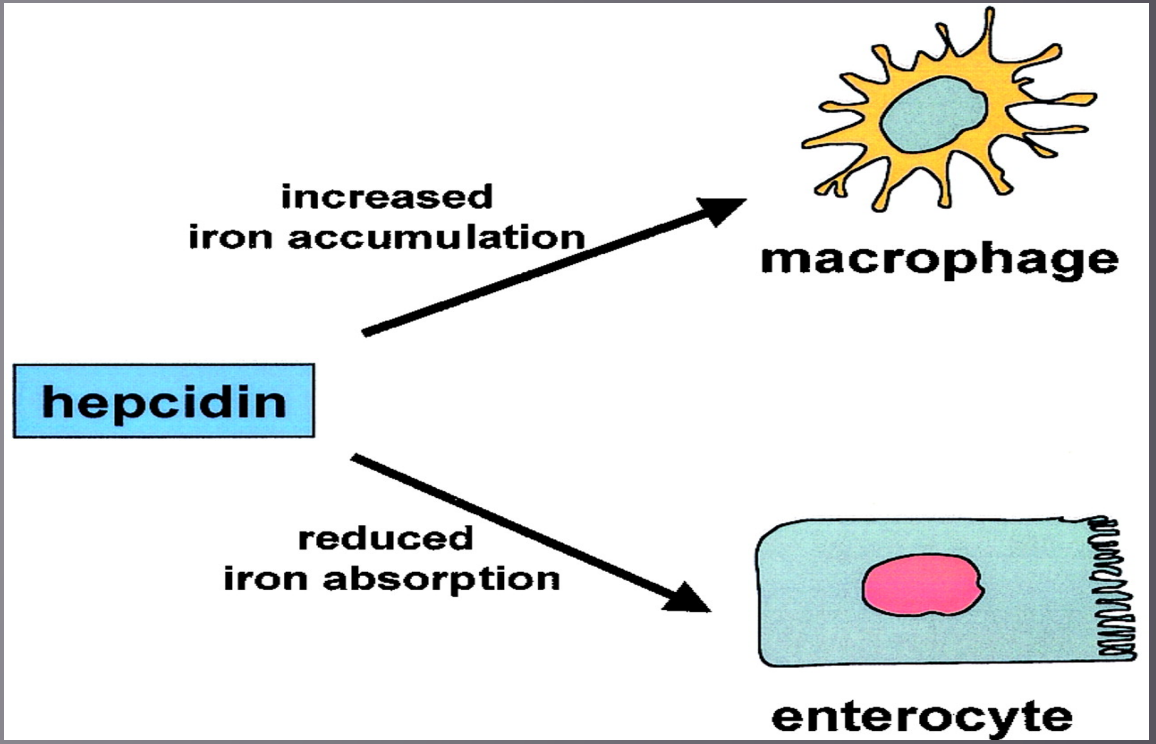
Decreased lifespan of RBC

- In people with CKD
  - 60-90 days (compared to 120 days in those without CKD)
- RBC trauma due to microvascular disease
- Resistance to oxidative stress

Circulating protein made by the liver, binds to ferroportin and internalizes it

Effectively limiting the iron absorption and release of iron from the RES

Hepcidin



Hepcidin increases when iron stores increase and during inflammation. Increased hepcidin during inflammation impairs the efficacy of oral iron to treat iron-deficiency anemia in people with CKD, especially those undergoing dialysis

Iron Deficiency in CKD

- Critical mineral for RBC production
  - Incorporated into heme at the erythroblast stage of red cell development
- Normal
  - Human body contains about 4-5 g of iron
  - 20-30% stored in hepatocytes and in macrophages
  - Health person absorbs 1-2 g from diet
- Negative iron balance
  - Increased iron losses
    - Blood loss
  - Reduced intestinal iron absorption in CKD

Specific to CKD

- Symptoms tend to occur when Hb < 10 g/dL and more severe at lower Hb
- Cardiac
  - Decreased myocardial oxygen delivery
    - Exacerbation of angina
  - Decreased peripheral oxygen delivery
    - Peripheral vasodilation, increased sympathetic nervous system activity, increased heart rate, stoke volume ultimately to LVH
  - LVH correlates to
    - Hospitalization and mortality

IV Iron

- Clinical trials have demonstrated that IV iron can at least partially bypass hepcidin-mediated iron blockade and treat iron-deficiency anemia in the setting of inflammation

Laboratory evaluation: KDIGO guidelines

- Patients with CKD and anemia regardless of the stage of CKD initial evaluation includes:
  - CBC including red cell indices, WBC with differential, and platelet, absolute reticulocyte count, serum ferritin, and transferrin saturation (TSAT) & vitamin B12 and folate
  - Anemia d/t insufficient erythropoietin stimulation is hypoproliferative and generally normocytic normochromic
  - Microcytic is suggestive of iron deficiency but can be seen in thalassemia
  - Macrocytic is suggestive of vitamin B12 or folate deficiency

Frequency of testing for anemia: Hb

- CKD without anemia
  - Stage 3 annually
  - Stage 4-5ND twice per year
- CKD with anemia
  - Stage 3-5ND every three months

KDIGO,2012

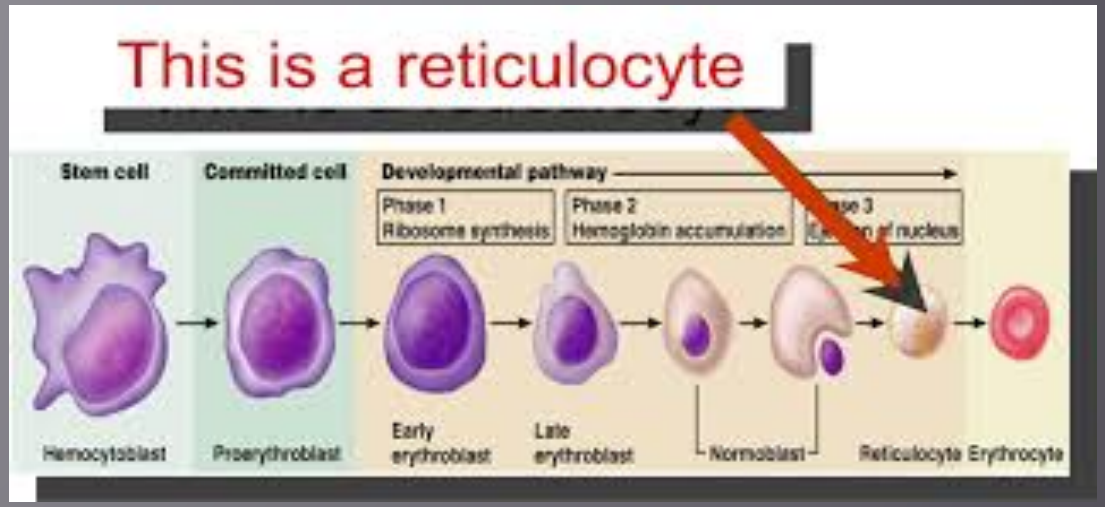
Lab Tests of Iron Deficiency of Increased Severity

	Normal	Fe deficiency without anemia	Fe deficiency with mild anemia	Fe deficiency with severe anemia
Serum iron	60-150	60-150	< 60	< 40
Iron binding capacity	300-360	300-390	350-400	> 410
Saturation	20-50	30	< 15	< 10
Hb	Nomal	Normal	9-12	6-7
Serum Ferritin	40-200	< 20	< 10	0-10

Source: Chmielewski at American Nephrology Nurses' Association 45th Symposium 2014

Reticulocytes

- Immature RBC
- Reticulocytes develop and mature in the red bone marrow
- Circulate for about a day in the blood stream before developing into mature RBC
- Normal 0.5 to 1.5%
- < 1%
  - Inadequate production
- >1%
  - Increased production



Available IV Formulations

Iron Name	Approved single dose administration	Comon off label use	Test dose
Iron dextran (INFeD)	100 mg over 30 minutes	1000 mg or more IV over 4 h	Yes, 25 mg; monitor 15-30 min
Iron dextran (Dexferrum)	100 mg over 30 minutes	1000 mg or more IV over 4 h	Yes, 25 mg monitor 15-30 minutes
Sodium ferric gluconate	125 mg IV push over 10 minutes	250 mg IV over 15 min	No
Iron Sucrose (Venofer)	200 mg IV over 2-5 min	300 mg IV over 1 h	No
Ferumoxytol (Feraheme)	510 mg IV over 1 min	Same dose as 15 min infusion	No
Ferric carboxymaltose (injectafer in US)	750 mg slow push or infusion over 15 min	None	No

Source: Larson & Coyne (2014) Update on IV iron choices, Current Opinion in Nephrology, 23(2), p. 188

Other

CALCIUM, PHOSPHORUS, AND BONE DISEASE IN CKD

- All patients with GFR < 60 should be regularly screened for calcium, phosphorus, and PTH abnormalities
- Maintain phosphorus concentrations between 2.7 and 4.6 mg/dL in patients with stage 3 or 4 CKD
  - Start dietary phosphorus restriction if PTH is increased, even if serum phosphorus is normal
  - Use phosphorus binders as soon as PTH starts to increase

NUTRITION AND CKD

- Dietary requirements for patients with CKD are complex
  - Intake of protein, phosphorus, and potassium all need to be controlled while maintaining adequate energy intake
- Once a patient reaches stage 4 CKD, an experienced renal dietician should be involved in the patient's nutritional management

Avoid NSAIDS

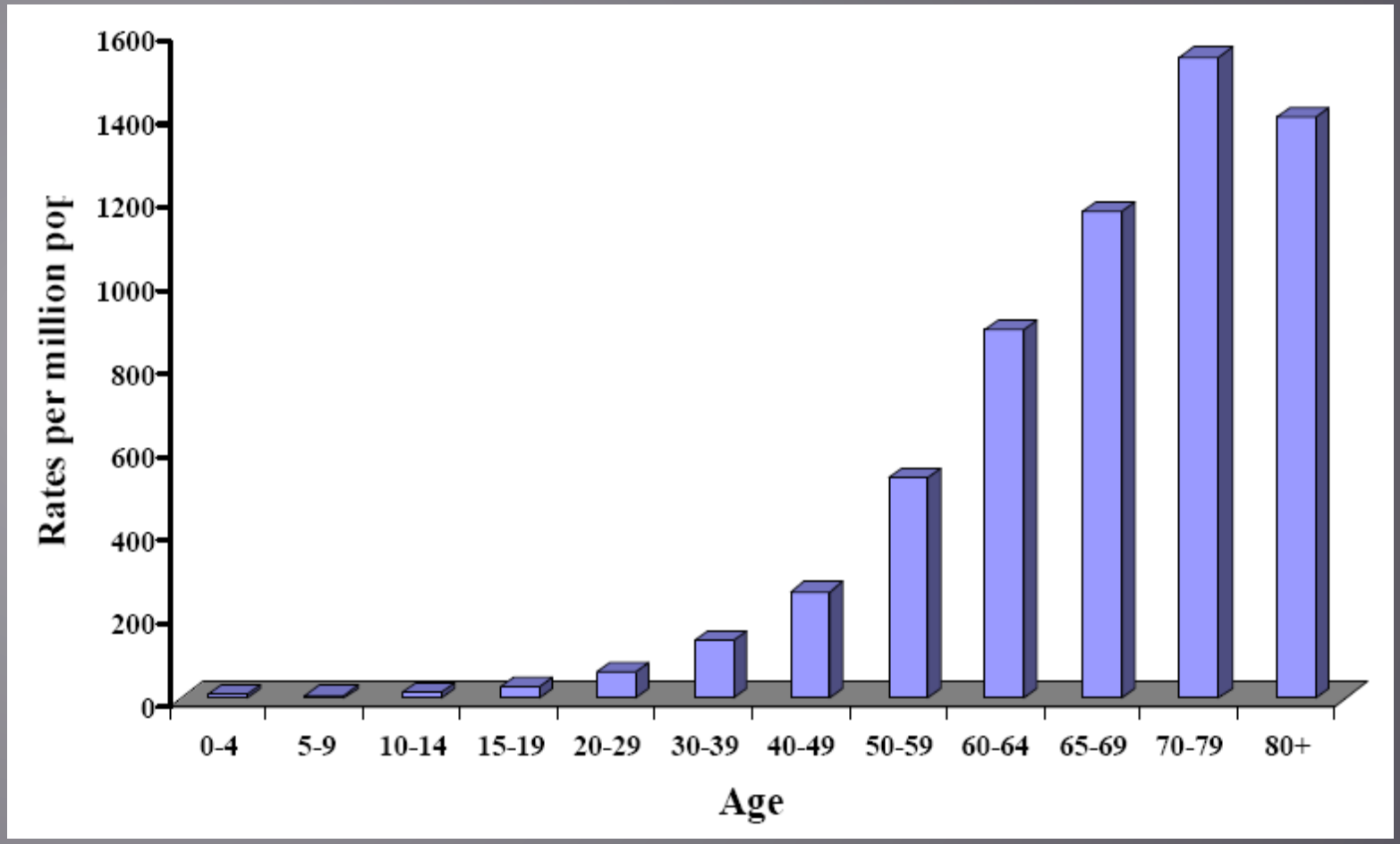
- When renal function normal NSAIDS have an insignificant effect on renal hemodynamics
- However when renal blood flow is compromised, compensatory afferent arteriolar vasodilation by prostaglandins plays a key role in maintaining glomerular perfusion
- NSAIDs block prostaglandins

ESKD

END-STAGE KIDNEY DISEASE

- End-stage kidney disease is that which requires dialysis or transplant for survival
- More than 55% of patients with ESKD are >60 yr
- Some of the increase in renal replacement therapy indicates greater willingness to offer treatment to older individuals, but much is related to increases in remaining life expectancy with attendant progression of CKD

ANNUAL INCIDENCE RATES OF TREATED ESKD



ESKD: DIALYSIS

- Age should not be the sole exclusion criterion
- Early referral to a nephrologist ensures adequate time for discussing options and for creating adequate access (creation of a native arteriovenous fistula can require up to 6 months)
- Hemodialysis and continuous ambulatory peritoneal dialysis appear to be equally effective in older adults, so the choice between them can be individualized
- Dialysis to patients with dementia is controversial

EFFECT OF DIALYSIS ON LIFE EXPECTANCY IN THE US

Age, yr	Remaining life expectancy, yr	
	Dialysis population	Nondialysis population
40–44	6.7–9.2	30.1–40.8
50–54	5.1–6.9	22.5–31.5
60–64	3.7–5.1	16.0–22.8
70–74	2.7–3.5	10.8–15.2
80–84	2.0–2.4	6.9–8.8

ESKD: KIDNEY TRANSPLANTATION

- As in younger patients, mortality rates in older patients with kidney transplants are considerably less than in those maintained on dialysis
- Older kidney recipients demonstrate lower acute rejection rates and lower incidence of chronic rejection and greater survival probability than patients remaining on dialysis, even when corrected for levels of comorbidity
- Older patients and their families should explore the option of transplantation as soon as the need for renal replacement therapy arises

ESKD: HOSPICE

- In almost half of cases, failure to thrive is the driving reason for withdrawal from dialysis
- Most people who withdraw from dialysis are >65 yr
- About 20% of the dialysis cohort withdraws in any given year
- Specialist such as geriatricians and AGNP have a unique role in educating nephrologists and patients about the value of hospice

Shared decision making

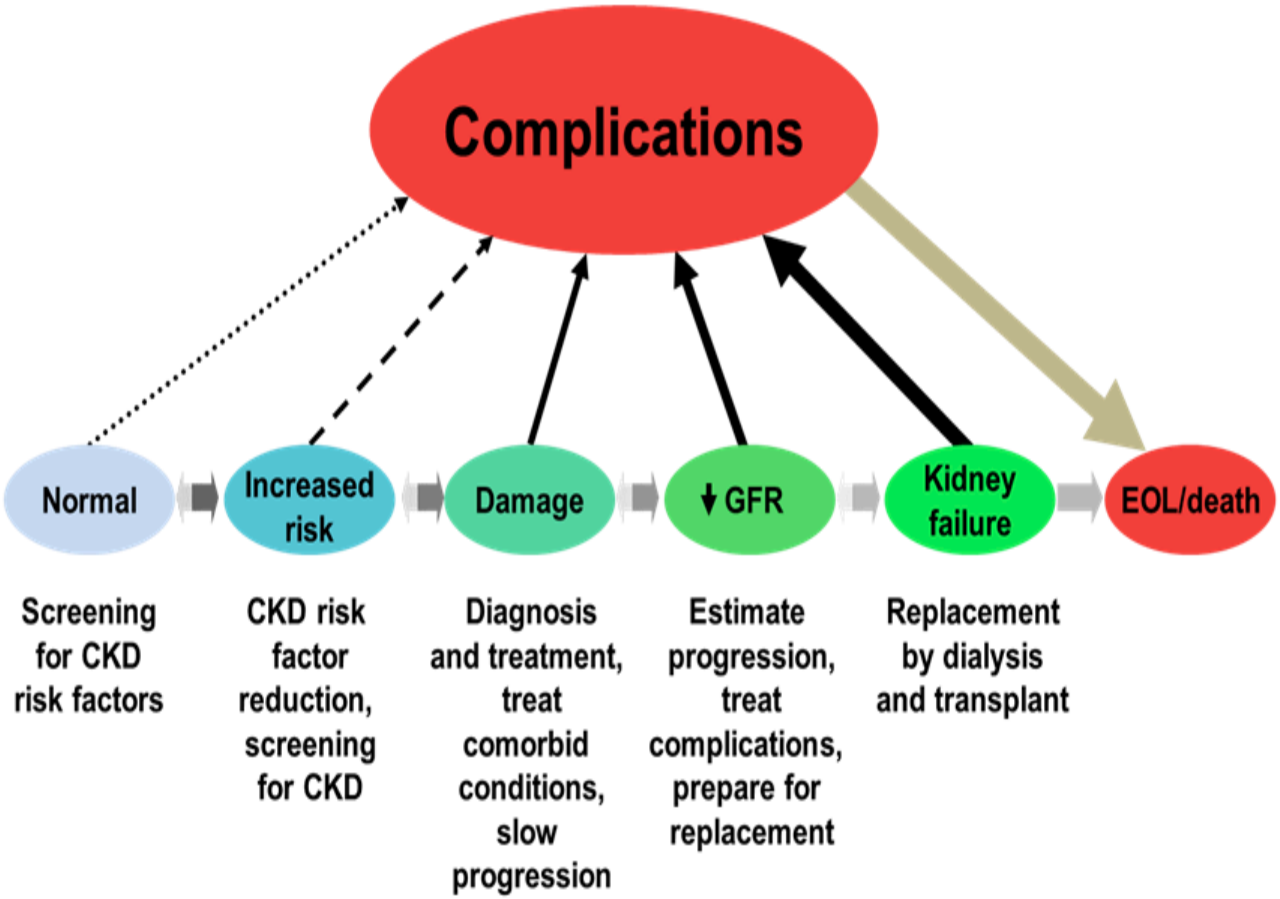
Medicare Educational Benefits

- Consult diabetic educator for Diabetes Self-Management
  - Annual diabetes self-management training is covered under Medicare Part B
- Consult dietician
  - MNT is a Medicare benefit for people with CKD before they receive kidney replacement therapy
- American Kidney Fund www.ckdeducation.org

When to refer

- AKI or abrupt sustained fall in GFR
- GFR < 30 ml/min.1.73m
- A consistent finding of albuminuria
- Progression of CKD
- CKD and HTN refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary KD
- Urinary red cell casts, RBC > 20 per high power filed sustained and not readily explained

Conceptual Model of CKD



National Kidney Foundation™

Adapted with permission from the NKF. Levey AS, et. al. AJKD 2009; 53: S4-16.

Thank you!