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Transforming Diabetes Care

Diabetic Kidney Disease:
Prevention, Detection and Treatment

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Polling Question - 1

What is your role as a healthcare provider?

a) Dietitian
b) Nurse
c) Nurse Practitioner
d) Pharmacist
e) Physician
f) Physician Assistant
g) Other

Polling Question - 2

What type of healthcare setting do you work in?

a) Health plan
b) Hospital
c) Outpatient specialty care
d) Pharmacy
e) Primary care
f) Other

Primary Care Providers-

The First Line of Defense Against Chronic Kidney Disease (CKD)

Primary care professionals provide

- Early diagnosis
- Early-stage CKD Treatment
- Patient education

Early detection of CKD

- Improves management
- Improves patient outcomes

CKD is part of primary care

CKD Risk Factors[1*]

Modifiable

- Diabetes
- Hypertension
- Acute kidney injury
- Frequent NSAID use

Non-Modifiable

- Family hx of
  - Kidney disease
  - Diabetes
  - Hypertension
- Age >60 (GFR normally declines with age)
- Race

*partial list

[1] Harjutsalo V., Groop PH. Advances in Chronic Kidney Disease. 2014;21(3): 260-266

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Diagnosing CKD ...

Changes clinician behavior

- Increased urinary albumin testing
- Increased appropriate use of ACEi or ARB
- Avoidance of NSAIDs
- Appropriate nephrology consultation

Results in significantly improved outcomes for patients with CKD 1-3[1-3]

[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.

Screening Tools: eGFR

- Best overall index of kidney function
- Normal GFR varies by
  - Age
  - Sex
  - Body mass
- **CKD-EPI** tool recommended to estimate GFR
- Other eGFR calculators
  - MDRD
  - Cockcroft-Gault
- Online eGFR calculator
  - https://www.kidney.org/professionals/kdoqi/gfr_calculator

Stage	Description	eGFR (mL/min/1.73 m²)
1	Kidney damage* with normal or increased eGFR	≥90
2	Kidney damage* with mildly decreased eGFR	60-89
3	Moderately decreased eGFR	30-59
4	Severely decreased eGFR	15-29
5	Kidney failure	<15 or dialysis

** Kidney damage is defined as UACR persistently ≥30 mg/g Cr or other abnormalities on pathological, urine, blood, or imaging tests. Adapted from Levey et al. (4).*

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eGFR, SCr Comparison

Age	Weight in lbs Height in Ft/in	Sex	Race	SCr mg/dl	eGFR ml/ min per CKD-EPI	eGFR Adj for BSA
25	285 6’	M	AA	1.6	68	97
49	180 5’4”	F	Hispanic	1.6	38	41
67	155 5’8”	M	Asian	1.6	44	46
92	98 5’1”	F	Caucasian	1.6	28	22

Polling Question - 3

How often do you screen people with diabetes for proteinuria?

a) Only if secondary indication is present
b) Annually
c) Semiannually
d) Quarterly
e) Every visit

Screening Tools: ACR

Urinary albumin-to-creatinine ratio (ACR)

- Albumin concentration in milligrams/creatinine concentration in grams
- Creatinine adjusts for varying urine concentrations
- More accurate results versus albumin alone
- Spot test; easy to collect
- First morning void preferable
- 24hr proteinuria test rarely necessary

Criteria for CKD Diagnosis

Abnormalities of kidney structure or function, present for >3 months, with implications for health

Either of the following must be present for >3 months:

- ACR >30 mg/g
- GFR <60 mL/min/1.73m2

Only 12% of people with diabetes with CKD 1-5 are diagnosed by their primary care provider[1]

[1] Szczech, Public Library of Science, Nov, 2014: 9(11).

CKD Heat Map

Risk for CKD Progression Based on eGFR and Albuminuria

Prognosis of CKD by GFR and Albuminuria Categories

GFR categories (mL/min/1.73m²) Description and range				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
	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			

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

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

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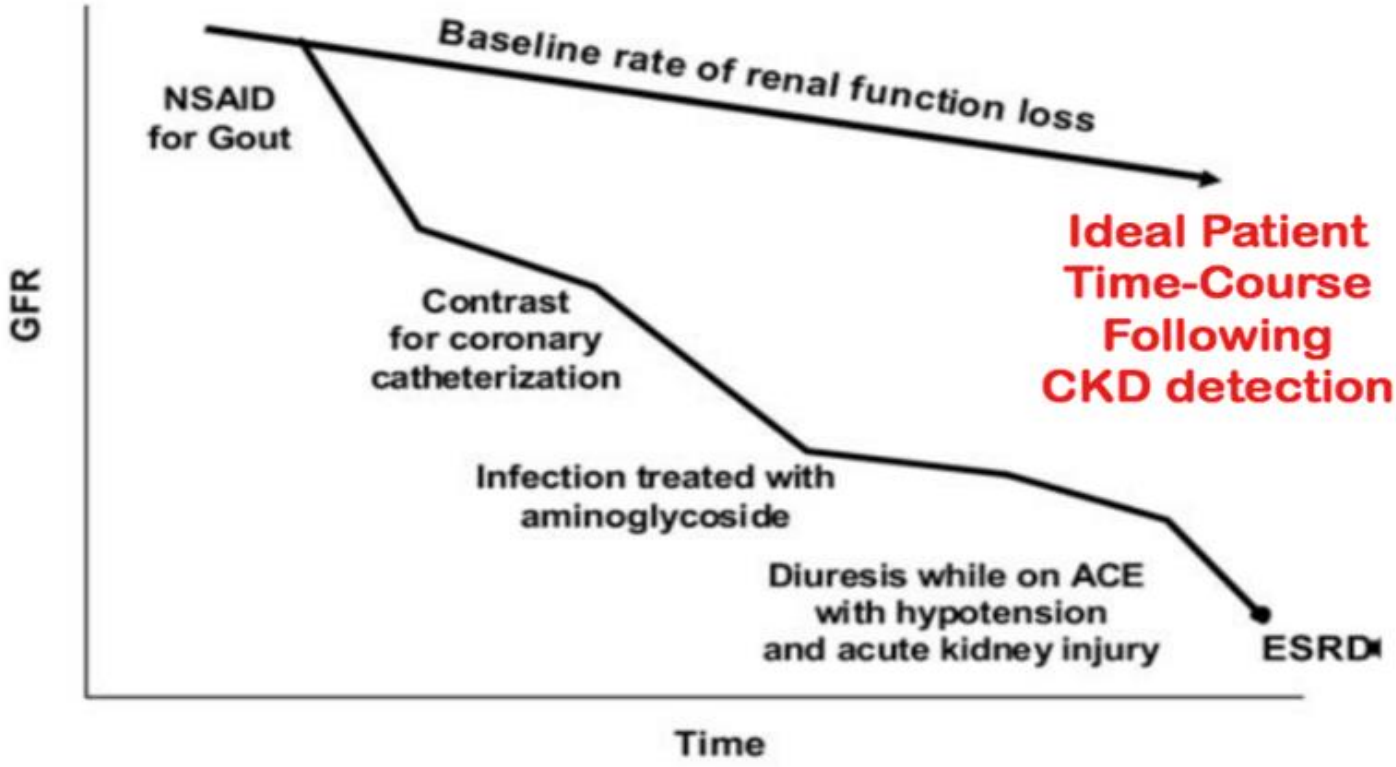
Opportunity for Primary Care Providers

to Impact CKD Progression



Improved diagnosis creates opportunity for strategic preservation of kidney function.

Fink et al. *Am J Kidney Dis.* 2009,53:681-668.

CKD Patient Safety Issues

Diagnostic tests

- Iodinated contrast media: AKI
- Gadolinium-based contrast: NSF
- Sodium Phosphate bowel preparations: AKI, CKD

CVD

- Missed diagnosis
- Improper management

Fluid management

- Hypotension/hypovolemia: AKI
- CHF exacerbation

AKI = acute kidney injury; CHF = congestive heart failure; NSF = nephrogenic systemic fibrosis.

Indications for Nephrology Referral

- Acute kidney injury or abrupt sustained fall in eGFR
- eGFR <30 mL/min/1.73m2 (eGFR categories G4-G5,/CKD 4-5)
- Persistent albuminuria (ACR >300 mg/g)*
- Atypical progression of CKD**
- Hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

*Significant albuminuria is defined as ACR ≥300 mg/g (≥30 mg/mmol) or AER ≥300 mg/24 hours, approximately equivalent to PCR ≥500 mg/g (≥50 mg/mmol) or PER ≥500 mg/24 hours
**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/1.73m2/year. KDOQI US Commentary on the 2012 KDIGO Evaluation and Management of CKD.

Blood Pressure and CKD Progression

Control of BP more important than exactly which agents are used

Avoidance of side-effects is important

With proteinuria

- Diuretic + ACEi or ARB

No proteinuria

- No clear drug preference
- ACEi or ARB ok to use

Slowing CKD Progression: ACEi/ARB

Check labs 2 weeks after initiation

- If less than 25% SCr increase, continue and monitor
- If more than 25% SCr increase, stop ACEi and evaluate for RAS

Continue until contraindication arises, no absolute eGFR cutoff

Better proteinuria suppression with low Na diet and diuretics

Avoid volume depletion

Polling Question - 4

Roughly what percentage of patients with diabetic nephropathy will progress to ESRD in spite of ideal medical management?

a) 10
b) 30
c) 50
d) 80

Blood Pressure Targets in CKD

Target blood pressure in non-dialysis CKD[1]

- ACR <30 mg/g: ≤140/90
- ACR 30-300 mg/g: ≤130/80*
- ACR >300 mg/g: ≤130/80

Individualize targets and agents by

- Age
- Coexistent CVD
- Other comorbidities

Avoid ACEi and ARB in combination[3,4]

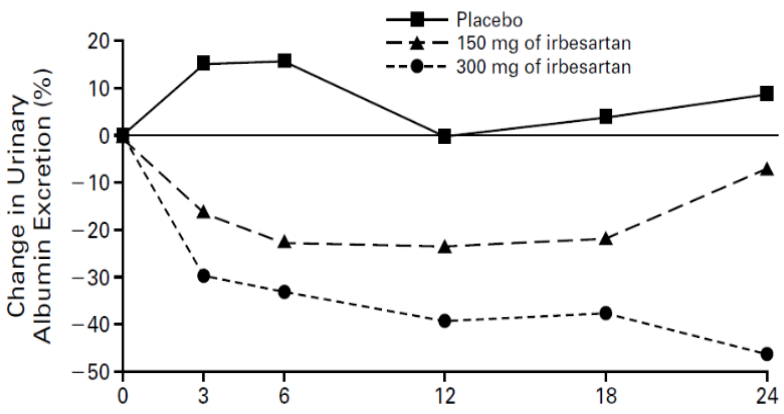
- Risk of adverse events
  - Impaired kidney function
  - Hyperkalemia

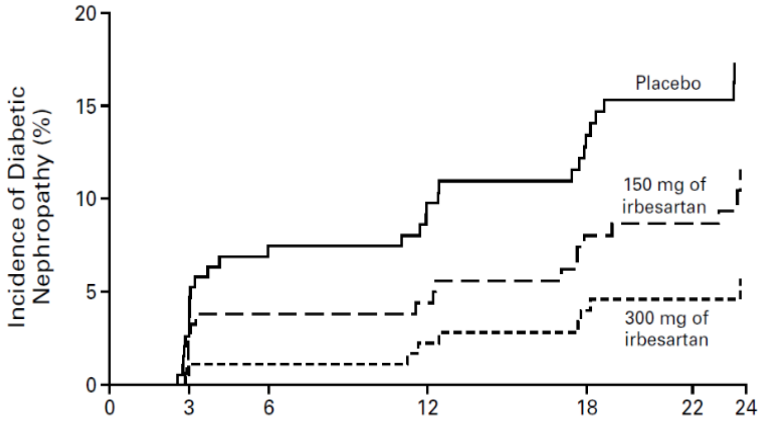
*Reasonable to select a goal of 140/90 mm Hg, especially for moderate albuminuria (ACR 30-300 mg/g).[2]

[1] Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. Kidney Int Suppl. (2012);2:341-342.
[2] KDOQI Commentary on KDIGO Blood Pressure Guidelines. Am J Kidney Dis. 2013;62:201-213.
[3] Kunz R, et al. Ann Intern Med. 2008;148:30-48.
[4] Mann J, et al. ONTARGET study. Lancet. 2008;372:547-553.

ARBs and Progression of Diabetic Nephropathy

- Most placebo-controlled studies in type 2 DM have been in patients with either moderate albuminuria (A2) or established nephropathy treated with ARB
- ARB and ACEi appear to be equivalent for moderate albuminuria (A2) and proteinuria reduction



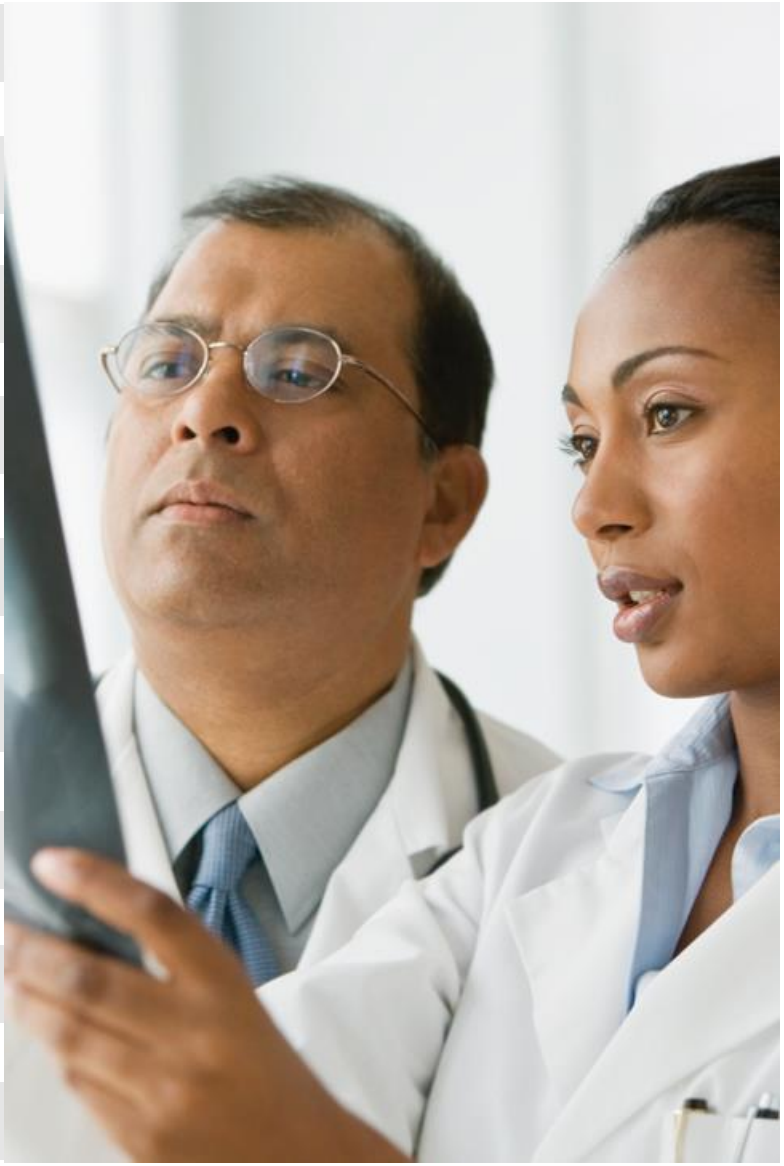


Parving HH, et al. *N Engl J Med.* 2001

Managing Hyperglycemia

- Hyperglycemia is a fundamental cause of vascular complications, including CKD
- Poor glycemic control has been associated with albuminuria in type 2 diabetes
- Risk of hypoglycemia increases as kidney function becomes impaired
- Declining kidney function may necessitate changes to diabetes medications and renally cleared drugs
- Target HbA1c ~7.0%[1]
  - Can be extended above 7.0% due to
    - Comorbidities
    - Limited life expectancy
    - Risk of hypoglycemia

[1] NKF KDOQI. Diabetes and CKD: 2012 Update. *Am J Kidney Dis*. 2012;60:850-856

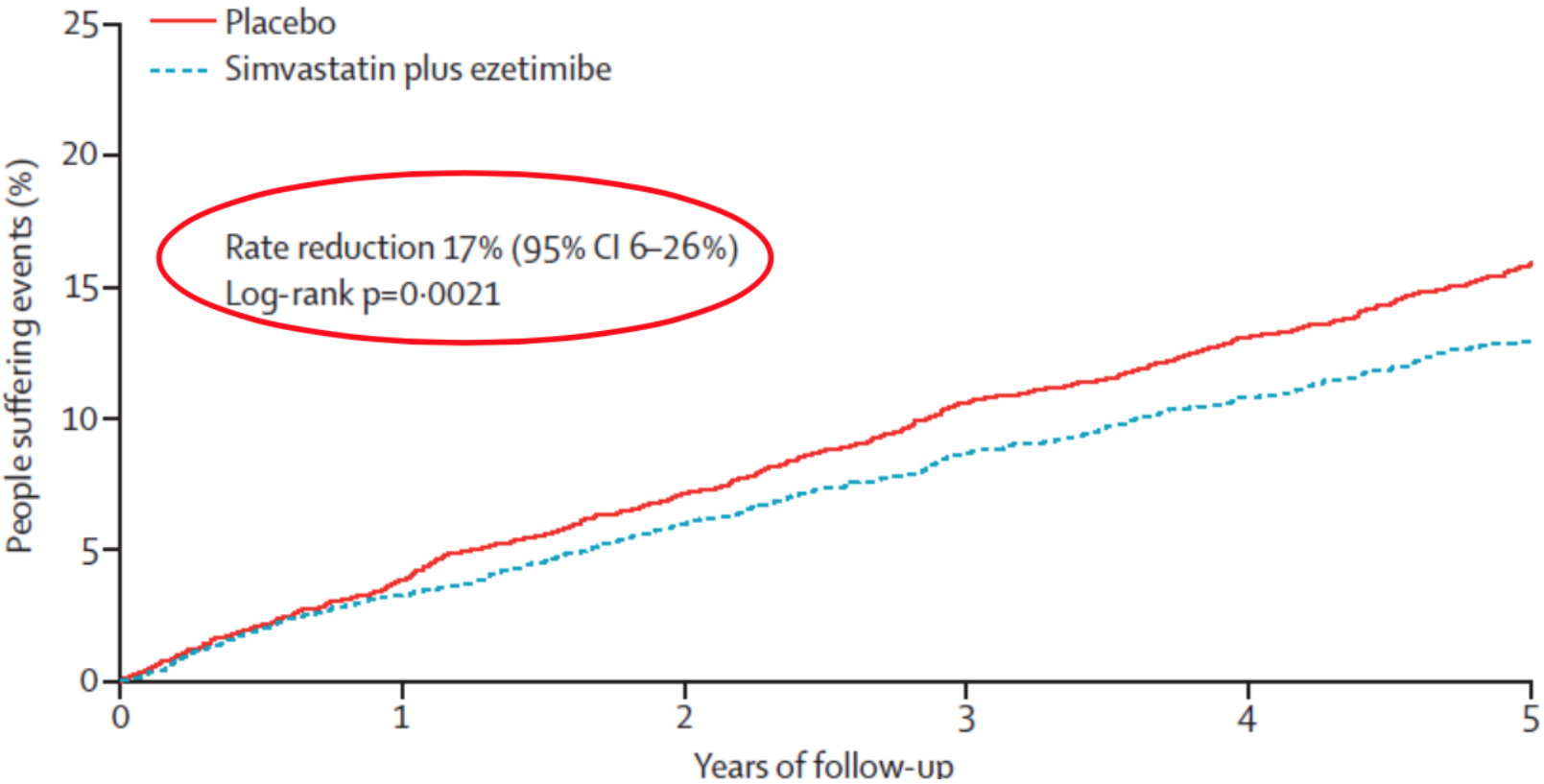


Lipid Disorders in CKD

- Use statin alone or statin + ezetimibe in adults >50 yrs with CKD 3-5(ND)
- Use statin alone in adults >50 yrs with CKD 1-2
- In adults <50 yrs use statin alone if history of known CAD, MI, DM, stroke
- Treat according to a “fire and forget” rather than “treat to target” strategy
- Treat CKD patients (non dialysis) with statins or statin/ezetimibe combinations without the need for follow up blood tests

Kidney Disease: Improving Global Outcomes (KDIGO) Lipid Work Group. Kidney Int Suppl. 2013;3:259-305.
http://kdigo.org/home/2013/11/04/kdigo-announces-publication-of- guideline-on-lipid-management/

Lipid Disorders in CKD



32% reduction in LDL associated with 17% reduction in primary outcome (nonfatal MI, coronary death, non-hemorrhagic stroke, arterial revascularization)

No reduction in CKD progression, overall or CAD mortality, other individual CAD end-points

Baigent C, et al. Study of Heart and Renal Protection (SHARP). Lancet. 2011;11:60739-60743.

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Vaccination in CKD

Annual influenza vaccine, unless contraindicated

Pneumococcal vaccine when eGFR <30 ml/min/1.73m2 and at high risk of pneumococcal infection

- Nephrotic syndrome
- Diabetes
- Receiving immunosuppression
- Revaccination within 5 years

Hepatitis B immunization when GFR <30 ml/min/1.73 m^2

- Confirm response with serological testing

Use of a live vaccine should consider the patient's immune status (e.g., immunosuppression)

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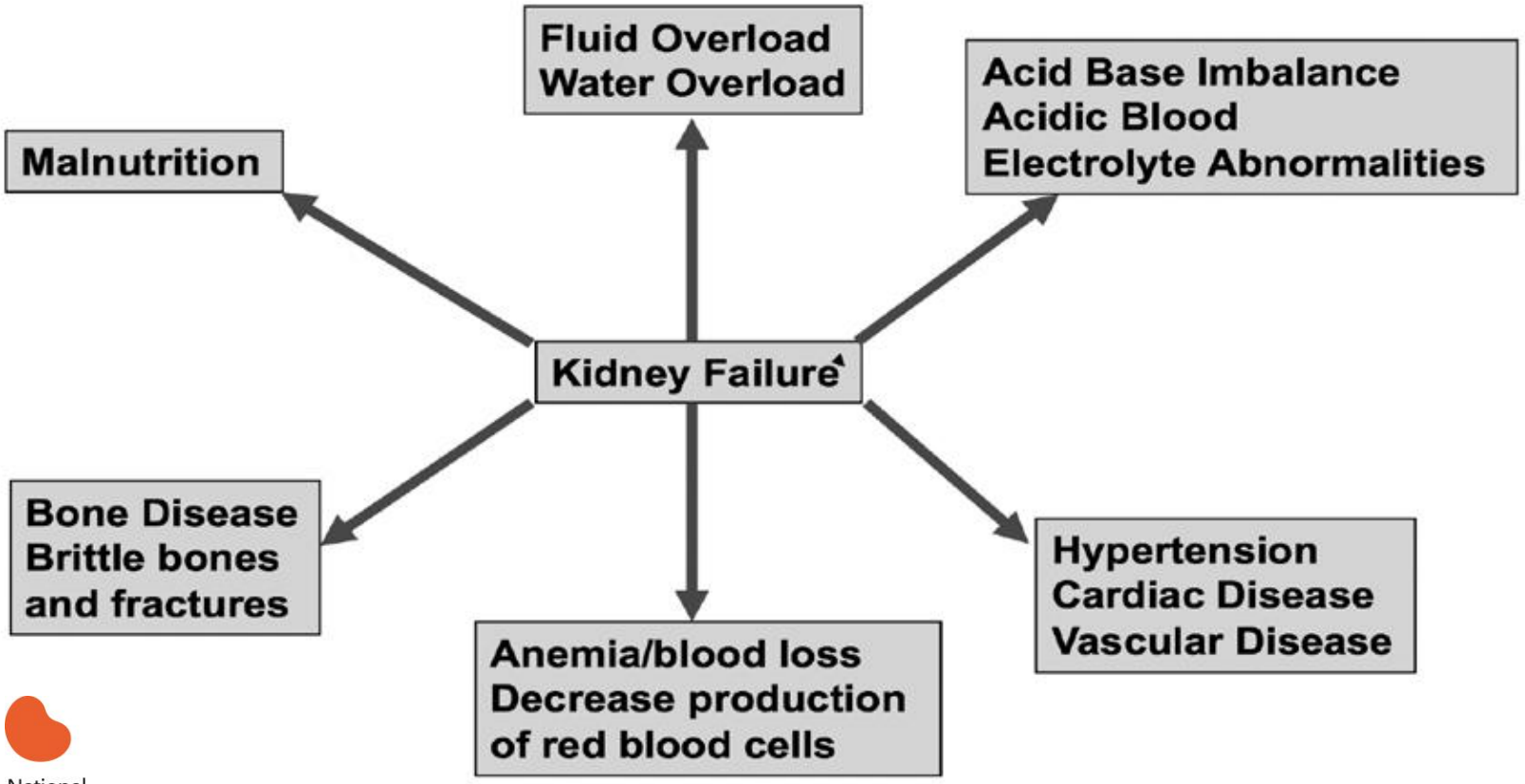
Complications of Kidney Failure

Start in Stage 3 and Progress



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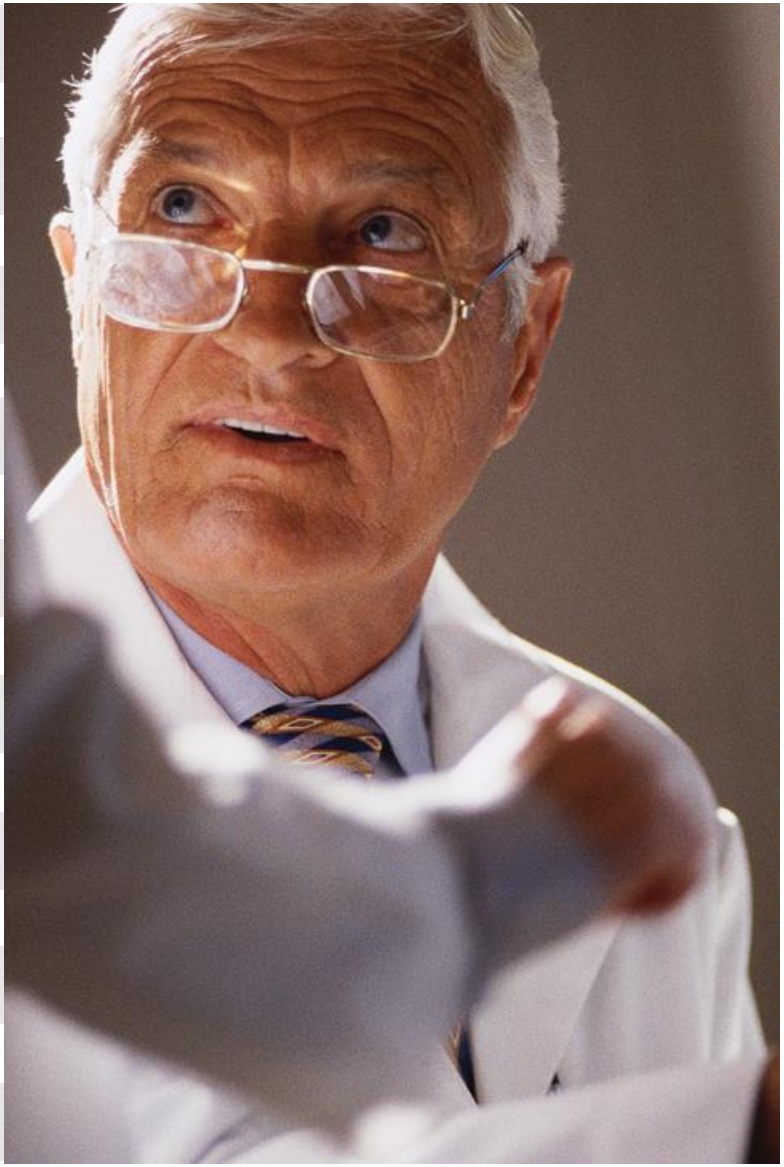
CKD 4-5 Management

Nephrogenic Anemia

- Erythropoetin Stimulating Agent (ESA)
- Iron supplement (PO or IV)
- Avoid transfusion for transplant candidates
  - If transfused use leukocyte filter to reduce HLA sensitization

CKD-MBD

- Vit D3 supplement
  - 2,000IU OTC cheaper and better absorbed than 50,000IU monthly D2 dosing
  - Limit dietary phosphorous
  - Phosphate binders
  - DEXA doesn't't predict fracture risk in CKD 3-5



CKD 4-5 Management

Metabolic Acidosis

- Becomes apparent at GFR <25-30 ml/min/1.73m^2
- More severe with higher protein intake
- Contributes to
  - Bone disease
  - Protein catabolism
  - CKD progression
- Correction of metabolic acidosis may
  - Slow CKD progression
  - Improve functional status[1,2]
- Target: Serum bicarbonate > 22 mmol/L
  - Start with 0.5-1 mEq/kg per day
    - Sodium bicarbonate tablets
    - Sodium citrate solution
    - Baking soda

[1] Mahajan, et al. Kidney Int. 2010;78:303-309.
[2] de Brito-Ashurst I, et al. J Am Soc Nephrol. 2009;20:2075-2084.

Hyperkalemia

- First try reduction of dietary potassium
- Stop NSAIDs, COX-2 inhibitors
- Stop potassium sparing diuretics (Aldactone)
- Stop or reduce beta blockers
- Avoid salt substitutes that contain potassium
- Stop or reduce ACEi/ARBs
- Add loop or thiazide diuretics
- Treat with laxatives
  - As effective as cation exchange resins

Summary of Diabetic CKD

Management Guidelines

eGFR (mL/min/1.73 m²)	Recommended Management
All patients	• Yearly measurement of UACR, serum Cr, potassium
45-60	• Referral to a nephrologist if possibility for nondiabetic kidney disease exists (duration of type 1 diabetes < 10 years, persistent albuminuria, abnormal findings on renal ultrasound, resistant hypertension, rapid fall in eGFR, or active urinary sediment on urine microscopic examination) • Consider the need for dose adjustment of medications • Monitory eGFR every 6 months • Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, and parathyroid hormone at least yearly • Assure vitamin D sufficiency • Vaccinate against Hep B virus • Referral for dietary counseling
30-44	• Monitor eGFR every 3 months • Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin, and weight every 3-6 months • Consider the need for dose adjustment of medications
<30	• Referral to a nephrologist

American Diabetes Association. *Microvascular complications and foot care. Sec10.* In Standards of Medical Care in Diabetes -2017. *Diabetes Care*. 2017;40(Suppl. 1):S88-S98

Considerations for CKD Management

in Older Adult

- More than 36 million adults are now over the age of 65, and~50% have two or more chronic diseases.[1]
- Management requires an individualized approach, with attention to unique considerations for older adults.
- Treatment of hypertension in older adults has been shown to reduce CV morbidity and mortality. However, older frail adults should be monitored for risk of hypotension.[2,3]
- Less stringent glycemic goals can be appropriate for older adults with other comorbidities, or those at higher risk for hypoglycemia.[4]
- Encourage advance care planning with patient and family. Undertake frank discussion on prognosis and treatment options.

[1] U.S. Census Bureau. Population by age and gender 2008. www.census.gov.
[2] Katz P, Gilbert J. Geriatrics and Aging. 2008;11:509-514.
[3] Aronow W. Clin Geriatr Med. 2008; 11(8):457-463.
[4] NKF KDOQI. Am J Kidney Dis. 2012 60:850-856.

Additional Online Resources for CKD Learning

- CDC's CKD Surveillance Project: http://nccd.cdc.gov/ckd
- National Kidney Disease Education Program (NKDEP): http://nkdep.nih.gov
- National Kidney Foundation: www.kidney.org
- United States Renal Data Service: www.usrds.org

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