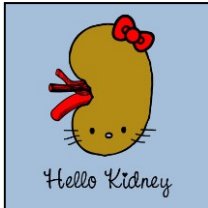


CKD in 2024 New KDIGO Guidelines



Kim Zuber, PAC
Executive Director
American Academy of Nephrology PAs
(AANPA)



Disclosures

I have no relevant relationships with ineligible companies to disclose within the past 24 months

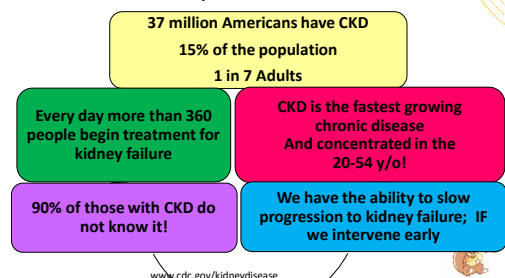


Objectives

- 1) Review the introduction of the race-neutral eGFR calculator
- 2) Discuss the causes, complications and comorbidities of CKD
- 3) Using the 2023 KDIGO CKD guidelines, demonstrate peer-reviewed proven methods to prevent progression of CKD



Kidney Disease Facts



Kidney Disease Facts

The cost of CKD Stage 1-5 is more than
\$130 BILLION
25% of the Medicare Budget

This is larger than the budget of the NIH
+ NASA + Homeland Security all added
together

How to Slow CKD Progression

- 1) Identify patients
 - A) Check SCr
 - B) Check UACR
- 2) Manage HTN
- 3) Manage DM
 - A) A1C < 7%
 - B) More importantly, no hypoglycemia
- 4) Manage Albuminuria
 - A) Decrease albuminuria by 30%
- 5) Protect the kidneys





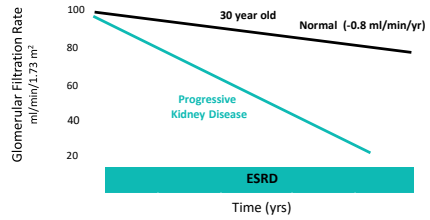
Stages of CKD

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)			Albuminuria stages, description and range (mg/g)				
			A1	A2	A3	A3	A3
GFR stages, description and range (mL/min per 1.73 m ²)	G1	High and optimal	>105	90-104	30-299	300-1999	>2000
			Optimal and high-normal	High	Very high and nephrotic		
	G2	Mild	75-89	60-74			
	G3a	Mid-moderate	45-59				
	G3b	Moderate-severe	30-44				
	G4	Severe	15-29				
G5	Kidney failure	<15					

KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of CKD, Kidney International, Jan 2013, Vol 3, Issue 1



Normal Age Progression of Kidney Function



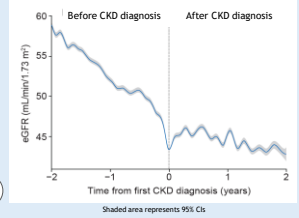
REVEAL Trial: eGFR decline before and after a CKD Diagnosis

Median annual decline in eGFR (mL/min/1.73 m²) significantly decreased following a CKD diagnosis *

Before: **-3.20**
95% CI: -3.38, -3.00

After: **-0.74**
95% CI: -0.96, -0.53

eGFR trajectories before and after a CKD diagnosis



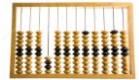
Tangri N, et al. Adv Ther, Jan 2023



eGFR Calculators for Kidney Function

1976 Cockcroft-Gault formula

- Compared 249 White hospitalized males with inulin vs calculator
- Requires age, gender, SCr, weight
- 15% less in females (never confirmed)
- Reports as CrCl, often in FDA package inserts



1999 Modification of Diet in Renal Disease (MDRD) formula

- Compared 1585 CKD patients with iothalamate vs calculator
- Requires age, gender, SCr, BUN, Albumin, race (Block 1.2 modifier)
- Adjusted to age, gender, SCr, race in 2000 (Block 1.2 modifier)

2012 CKD-EPI formula (on your present lab forms)

- Developed with input from large data bases at NIH (NHANES, AASK)
- Contains 'correction' for race (Block 1.16x modifier)



Race-neutral eGFR calculator

Recommendation #1

Recommend timely use of decision support tools to encourage endogenous racial and ethnic diversity.

Recommendation #2

Encourage endogenous racial and ethnic diversity.

Recommendation #3

Encourage endogenous racial and ethnic diversity.

National Kidney Foundation

eGFR CALCULATORS

MOBILE APP

ONLINE

of the **CKD-EPI creatinine** equation in all laboratories in the U.S. Fig. 1. Includes diversity in its development, its performance characteristics and potential impact on individuals.

rate increased, routine, and confirm eGFR in clinical practice.

estimation with new interventions to eliminate racial and ethnic disparities.

erse stakeholders and state these recommendations.

JASN AJKD

What Changed in the Calculator?

Old formula: CKD-EPI eGFRcr (CKD-EPI) (age, sex, race)

$$eGFR = 141 \times \min(Scr/k, 1)^\alpha \times \max(Scr/k, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

Where Scr is serum creatinine, k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/k or 1, and max indicates the maximum of Scr/k or 1

New formula: eGFRcr (CKD-EPI) refit without race variable

$$eGFR = 142 \times \min(Scr/k, 1)^\alpha \times \max(Scr/k, 1)^{-1.200} \times 0.993^{Age} \times 1.012 \text{ [if female]}$$

where Scr is serum creatinine, k is 0.7 for females and 0.9 males, α is -0.241 for females and -0.302 for males, min indicates the minimum of Scr/k or 1, max indicates the maximum of Scr/k or 1



How do I find CKD?

Go for the obvious!

- Elderly (60!!!!)
- Minority
- Hypertension/CVD
- Diabetes
- Family history
- Female
 - *Although less likely to go to ESRD!*
- On their medical history!

Go for the less obvious!

- Previous AKI
- Lupus, sarcoid, amyloid, gout, auto-immune...
- Previous donor/Previous transplant
- History of stones
- History of cancer
- History of oophorectomy
- History of gout
- Smoker (any type)
- Soda drinkers
- Moms who drank with pregnancy
- NAEL bingers
- Almost any medical condition



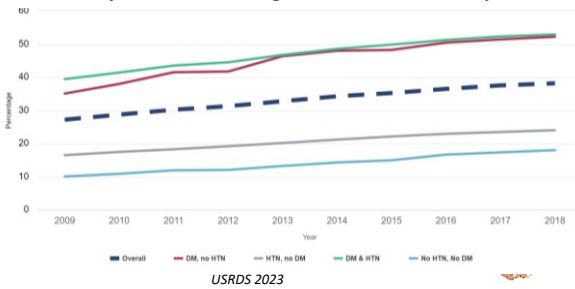
Sadie

She reports she is 85 y/o, female, she has diabetes

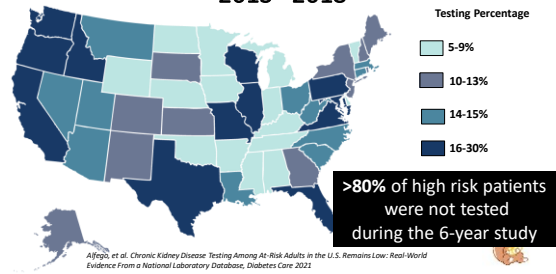
Labs: eGFR 45ml/min

If you lose 1ml/yr above the age of 30, 85-30 means 55 years of GFR loss
100 (average perfect kidney function)-55 (years) or expected eGFR is 45ml/min
Will she progress?

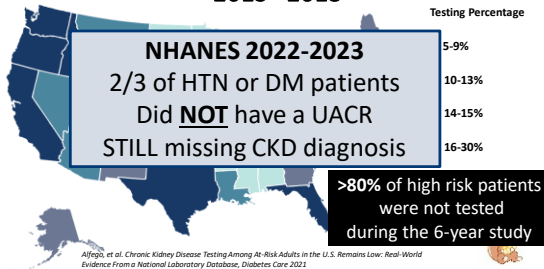
Probability of UACR testing in at-risk Medicare patients



LabCorp: Rates of Testing Patients with DM/HTN 2013 - 2018



LabCorp: Rates of Testing Patients with DM/HTN 2013 - 2018



What do I order?

Urinary albumin to creatinine ratio (UACR)

Urine protein to creatinine ratio (UPCR)



Urine Pearls

- Some labs (Quest, LabCorp) refer to a UACR as 'microalbuminuria'
- Order a UACR at least 1x/yr to monitor kidney function
 - For all patients with hypertension
 - For all patients with diabetes
 - For all patients with risk factors
 - Age >60 y/o is a risk factor
 - Home UACR tests!



How to Slow CKD Progression

- 1) Identify patients
 - A) Check SCr
 - B) Check UACR
- 2) Manage HTN
- 3) Manage DM
 - A) A1C < 7%
 - B) More importantly, no hypoglycemia
- 4) Manage Albuminuria
 - A) Decrease albuminuria by 30%
- 5) Protect the kidneys



Hypertension

The most common comorbidity in CKD is HTN



If HTN doesn't cause your CKD, your CKD will cause HTN

KDIGO HTN Goals:

- Target SBP 120mm Hg
- Use automatic office cuff X 3
- No DBP goal



Effectiveness of Lifestyle Changes

Modification	Example	Approx Reduction
Physical activity	Aerobic (brisk walking?) >30/day, most days	4-9mmHg
DASH eating plan	Low fat diet rich in fruits, vegetables	8-14mmHg
NACL restriction	Decrease to 2.4gm/day	2-8mm Hg
Moderate ETOH	1 drink/women, 2 drinks/men	2-4mmHg
Weight loss	BMI 18.5-25	5-20mmHg/10kg weight loss
Stress reduction	Practice modality	5mmHg
Quit smoking	Any which way	2-4mmHg after 1 week

NACL Restriction

Stage of Kidney Disease = NACL clearance

Tricks:

- Pork holidays
- No cooking w/NACL
- 'B' cooking



First Choice: ACEi/ARB

ACEi OR ARB:
First choice in Diabetes and/or CKD
 Even in the AA population
 Will decrease albuminuria....
 Use it even if there is no albuminuria
It doesn't matter ACEi vs ARB

- Only 1 or the other due to:
- inc risk of hyperkalemia
 - Hypotension
 - AKI/failure
 - no decrease in mortality



One or the other NOT BOTH!



Rose



74 y/o routine visit
PMH: PVD, HL, HTN
Meds: metoprolol, HCTZ, amlodipine, ASA, atorvastatin
PE: 168/98, home 150-160s
Labs: SCr 1.2mg/dL, UACR 30mg/dL, eGFR 56mm/min
 Add lisinopril for BP/UACR control

F/U labs 2 weeks later, **SCr 1.5mg/dL with K 5.2mEq/L**

What is an acceptable rise in SCr starting an ACEi/ARB?

Acceptable rise in SCr is 20-30%



When do I stop an ACEi/ARB?

The **STOP-ACEi** trial
 Multicenter UK **randomized** controlled trial of ACEi/ARB withdrawal in advanced kidney disease
 Trial ran 2018-2022
 Longer trail time due to pandemic
 Should we stop ACEi/ARB to try to save the kidneys???



Higher death rate from kidney endpoints if you stop the ACEi/ARB

Renin-Angiotensin System Inhibition in Advanced Chronic Kidney Disease, *NEJM*, Nov 2022



Hypertension Pearls



- NACL restriction is just as effective as medications
- Always tell a patient that it will take 3-4 meds for control; If it takes fewer, they think you are brilliant
- Start with **ACEi/ARB**, then diuretic (if possible)
- Consider an **SGLT2i** early in the process; It is a diuretic
- CCBs work **VERY** well but not specific for the kidneys
- With cardiovascular disease...**ACE/CCB**>ACE/diuretic
- Thiazide diuretics do **NOT** work if the eGFR<30ml/min
- **NOTHING works if you cannot afford it**

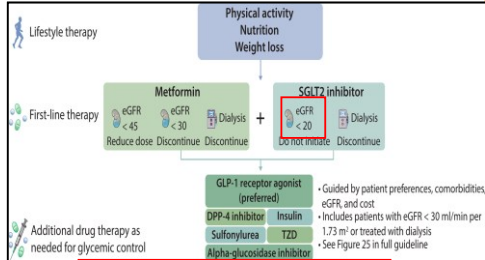


How to Slow CKD Progression

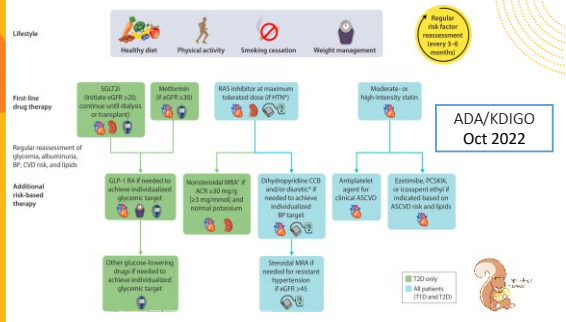
- 1) Identify patients
 - A) Check SCr
 - B) Check UACR
- 2) Manage HTN
- 3) **Manage DM**
 - A) **A1C < 7%**
 - B) **More importantly, no hypoglycemia**
- 4) Manage Albuminuria
 - A) Decrease albuminuria by 30%
- 5) Protect the kidneys



2022 KDIGO: Update for DM Treatment in CKD



NOTE: Lower eGFR of 20 for starting SGLT2i



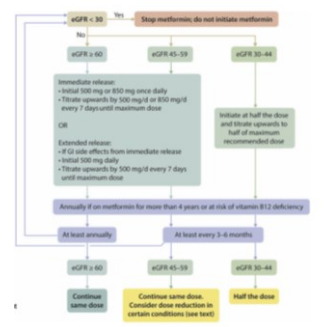
Kidney Specific Family Details: Metformin

- This should be the first medication for any DM patient
- Metformin is underutilized in DKD
- It is an older medications and therefore cheap
- Dosing is dependent of side effects (usually GI)
- Decreases CV risks which cause 70% of all CKD deaths
- Often will decrease cholesterol, triglycerides and weight



Therapeutic Considerations for Antihyperglycemic Agents in DKD CJASN May 2017

Metformin Dosing in CKD: Algorithm Format



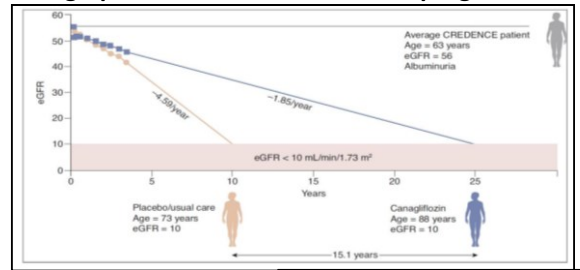
MACE Endpoints for SGLT2i Trials

- 1st trial **EMPA-REG** with kidney as secondary outcome Protected against Nephropathy! **44%** DECREASE in kidney endpoints Lowered albuminuria, slowed eGFR loss, lowered kidney/CV death
- **CREDESCENCE** enrolled DKD patients for a primary endpoint trial All had UACR>300mg/dL; Stopped early, **43%** DECREASE in kidney endpoints Lowered albuminuria, slowed eGFR loss
- **DAPA CKD** enrolled CKD patients for primary endpoint trial All had albuminuria but 1/2 did NOT have diabetes, **39%** DECREASE Lowered albuminuria, slowed eGFR loss, lowered kidney/CV death
- **EMPA-KIDNEY** enrolled CKD patients with and without albuminuria Trial stopped early but all patients did better with SGLT2i, **28%** DECREASE Those with more albuminuria showed best results



Wanner C, et al. NEJM 2019, Perkovic V, et al. NEJM 2019, Heerspink HJL, et al. NEJM 2020, The EMPA-KIDNEY Collaborative Group, NEJM Nov 2022

In graphic form; SGLT2i slows CKD progression



Perkovic V, et al. N Engl J Med. 2019;380:2295-2306

How to Slow CKD Progression

- 1) Identify patients
 - A) Check SCR
 - B) Check UACR
- 2) Manage HTN
- 3) Manage DM
 - A) A1C < 7%
 - B) More importantly, no hypoglycemia
- 4) Manage Albuminuria
 - A) Decrease albuminuria by 30%
- 5) Protect the kidneys



Practical Management Lessons for SGLT2i

- Initially treat with maximum dose of ACE/ARB before adding SGLT2i
SGLT2i can be used up down to an eGFR of 20ml/min
 - If patient on loop diuretic, 1/2 the dose...
(No difference if: 1/2 number of daily doses or 1/2 each dose)
 - Tell patient to increase fluid (water)
 - Monitor blood pressure; all SGLT2i are diuretics too!
 - There will be a drop in eGFR (inc in SCR) but take a deep breath, step away from EHR and ignore
 - The A1C may not decline by much as CKD progresses, however, reno/cardio protection occurs
 - SCR bump from RAAS is 4-6w but from SGLT2i is 4-6mo
- Even those with a bump in eGFR had better kidney outcomes**



Diet Pearls

- Losing weight saves your kidneys
 - Studies show >7 year protection after bypass surgery
- CKD diagnosis helps for Medicare coverage for Bariatric Surgery
- GLP trials** in analysis at this time; stopped early (Oct 2023) for good outcomes in CKD?!
- If you actually followed the diabetic, kidney, hypertensive, cardiovascular diet, you would only be allowed to eat cardboard
- Mediterranean diet is best, plant protein>animal protein
- High fruit and vegetables can cause hyperkalemia
 - Monitor K with any new diet changes (**and in Jan**)
- NACL holidays help with HTN and weight loss**



Association of Plant Protein Intake With Risk of Incident CKD: A UK Biobank Study

Study Design	Results		
Prospective cohort study N = 117,809 participants • eGFR ≥60 mL/min/1.73 m ² • UACR <30 mg/g • No history of CKD	Median follow-up: 9.9 years	Incident CKD N = 3,745 (3.2%)	
Web-based 24-hour recall questionnaire Dietary info collected between April 2009-June 2012	Plant protein intake (g/kg/day)	CKD Incidence (%)	Adjusted HR (95% CI)
	Q1: (<0.27)	1,151 (3.9%)	1.00 (REF)
	Q2: (≥0.27 and <0.35)	1,007 (3.4%)	0.90 (0.82-0.99)
	Q3: (≥0.35 and <0.46)	856 (2.9%)	0.83 (0.75-0.92)
	Q4: (≥0.46)	731 (2.5%)	0.82 (0.73-0.93)
	Per 0.1 g/kg/day increase		0.96 (0.93-0.99)

CONCLUSION: In this large, prospective cohort study, greater dietary plant protein intake was associated with a lower risk of incident CKD.

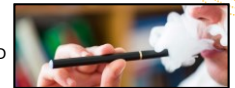
Ga Young Heo, Hee Byung Koh, Hyo Jeong Kim, et al
 @AJKDonline | DOI: 10.1053/j.ajkd.2023.05.007

How to Slow CKD Progression

- Identify patients
 - Check SCr
 - Check UACR
- Manage HTN
- Manage DM
 - A1C < 7%
 - More importantly, no hypoglycemia
- Manage Albuminuria
 - Decrease albuminuria by 30%
- Protect the kidneys**



Cardiovascular Disease (CVD)



- More than 70% of kidney patients die of CVD
- Statins are underutilized in CKD
- CKD patients are **2-3X** more likely to have atrial fibrillation
 - Take the time to listen with that stethoscope
 - Warfarin vs DOACs is still debated but **KDIGO states to use DOACs**
- Smoking is an issue
 - Including vaping, marijuana and cigarette
 - Oral marijuana is safe in CKD
 - No studies on chewing tobacco



Association between prescribed oral anticoagulants and AKI

Population-based cohort
 Ontario, Canada
 ≥ 66 years
 2009-2017
 Atrial Fibrillation
 n=20,683

Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
n=2269	n=2277	n=5363	n=5363	n=8383	n=8217
1.00	0.65	1.00	0.82	1.00	0.74
Ref	(0.43-0.79)	Ref	(0.70-0.96)	Ref	(0.64-0.85)

In subgroup analysis, the lower risk of AKI associated with each DOAC was consistent across each eGFR strata

The risk of AKI was significantly lower among users of each of the DOACs compared to warfarin users who had a percentage of INR 556.1%

Conclusion: DOACs were associated with a lower risk of AKI compared to warfarin.

Ziv Harel, Eric McArthur, Nivethika Jayakumar, et al. *The Risk of Acute Kidney Injury with Oral Anticoagulants in Elderly Adults with Atrial Fibrillation*. *CJASN* doi: 10.2215/CJN.09020421. Visual Abstract by Ediger Lemke, MD, FASN

KDIGO AND AHA Guidelines for dosing in A Fib

CrCl (ml/min)	Apixaban* (Eliquis®)	Dabigatran (Pradaxa®)	Edoxaban (Savaysa®, Lixiana®)	Rivaroxaban (Xarelto®)
Kidney excretion	27%	80%	50%	36%
>95	2.5 or 5mg bid	150mg bid	60mg qd (contraindicated AHA)	20mg qd
51-95	2.5 or 5mg bid	150mg bid	60mg qd	20mg qd
31-50	2.5 or 5mg bid (CrCl>25ml/min)	150mg bid or 110mg bid (KDIGO)	30mg qd	15mg qd
Pre-op holds	**Hold 48H pre-op	**Hold 96H pre-op	**Hold 48H pre-op	**Hold 48H pre-op
15-30	2.5mg bid	75mg bid (AHA)	30mg qd	15mg qd
<15 not on dialysis	2.5 or 5mg bid (AHA) Highest Safety* (KDIGO)	Not recommended	Not recommended	15mg qd (AHA)
<15 on dialysis	1.5 or 5mg bid (AHA) Highest Safety* (KDIGO)	Not recommended	Not recommended	15mg qd (AHA)

*Fu E. *Comparative Safety of warfarin or rivaroxaban vs apixaban in advanced CKD, AJKD, Oct 2023*, **KDIGO 2024 CKD guidelines

Decrease Smoking Rates



PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Kidney function and tobacco smoke exposure in US adolescents
(Pediatrics May 2013)

For current black smokers there is an 83% ↓ kidney function
19 cig/day = ↓ 75% kidney function
>20 cig/day = ↓ 97% kidney function
...worse with menthol cigarettes!
(J Am Heart Association, May 2016)



SMOKING or VAPING KILLS NEPHRONS
Marijuana is safe in CKD
As long as it is not smoked or vaped

Hyperlipidemia



CKD = Heart Disease

SHARP Trial: Statins or statins + ezetimibe

Rosuvastatin increases risks of AKI

Fibrates are not recommended in CKD by KDIGO

Uremia affects LDL levels making LDL levels unreliable

When you put a CKD patient on a Statin
FIRE AND FORGET

<http://kdigo.org/home/guidelines/lipids/>

SHARP: The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with CKD (Study of Heart and Renal Protection): a randomised placebo-controlled trial, Lancet 2011, Shin et al. Association of Rosuvastatin Use with Risk of Hematuria and Proteinuria, JASN 2022



Hyperlipidemia: KDIGO Guidelines

Recommended doses (mg/d) of statins in adults with CKD		
Statin	eGFR G1-G2	eGFR G3a-G5, including patients on dialysis or with a kidney transplant
Lovastatin	GP (General public)	nd (not determined)
Fluvastatin	GP	80 ¹
Atorvastatin	GP	20 ²
Rosuvastatin	GP	10 ³
Simvastatin/Ezetimibe	GP	20/10 ⁴
Pravastatin	GP	40
Simvastatin	GP	40
Pitavastatin	GP	2

CVD Pearls

- A CKD patient is more likely to die of CVD than kidney failure
- All CKD and DM patients should be on a statin
 - Add Vit D if leg cramps
 - **REAL** rhabdo from statins is <5%
- CKD patients are 2X more likely to have cardiac arrhythmias
 - Mainly a fib
- **All patients with CKD have heart disease**



This and That

- Drinking soda after exercise hurts the kidney
- Sleep (7h/night) is reno-protective
- Bilateral oophorectomy increases CKD risk
 - Increase 7.5% if premenopausal
- Increasing H2O does not help the kidneys
- Marijuana (oral) does not hurt the kidney and may be helpful in pain
- **ETOH is reno-protective**
- PPIs **DO NOT** cause CKD per Nov 2023 analysis
- As you lose kidney function, you are more likely to have a serious fall
- Untreated Hepatitis C will cause loss of eGFR
- Gut and Dental disease are predictive of CKD



Optimal Follow-up Guidelines for CKD Office visit + Labs



CKD Stage	Follow-up		
3A	6 months		
3B		3.2 months	
4			2 months

The CKD Patient

- 1) Stage by eGFR + UACR
- 2) Monitor UACR; it is predictive of progression
- 3) All CKD patients are cardiac patients
- 4) All patients should be on statins
- 5) All patients should be on RAAS; studies have shown best at higher doses but any dose is important
- 6) All patients should be considered for SGLT2i
- 7) Any patient with albuminuria should be on RAAS + SGLT2i
- 8) Labs 2x/yr for CKD 3a, quarterly for CKD 3b and q6wk for CKD 4, we follow CKD 5 monthly and CKD 5D weekly
- 9) Labs: CBC, A1C (as needed), CMP: Albumin, Ca, CO₂, SCr, Chloride, Glu, PO₄, K, Na, BUN, Vit D (+/-), UACR, Iron indices, Lipid levels, renal ultrasound (+/-)
- 10) Check for a fib, anemia, MBD, acidosis, **consider birth control**
- 11) Discuss concept of 'normal kidney eating' rather than 'diet'



The Magic Referral

I always hear that your nephrology consultants complain about referrals...
We are overwhelmed but...

Start your referral with:

'Per KDIGO Guidelines,

I am referring this patient due to...'

- 1) Uncontrolled HTN
- 2) Stage 4 CKD
- 3) eGFR dropped 25% in 6 months *or*
- 4) SCr increased 25% in 6 months
- 5) Patient request
- 6) Nephrotic range albuminuria or proteinuria



Thank you for helping us care for our CKD Patients!

THANK YOU



Kim Zuber, PAC aanpa1@yahoo.com



References

- 1) Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024;105(4S):S117–S314.
- 2) Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference: Trends and perspectives for improving quality of CKD care. *Kidney Int* (2023) 104, 888–903.
- 3) Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference: Managing the symptom burden associated with maintenance dialysis. *Kidney Int* (2023)
- 4) Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int.* 2021;99(3S):S1–S87.
- 5) Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* (2022)
- 6) United States Renal Data System. 2023 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2023.
- 7) Center for Disease Control and Prevention, Chronic Kidney Disease in the United States 2023 CKD fact sheet
- 8) Bhandari S, Mehta S, Khwaja A, Cleland JGF, et al for STOP ACEI Trial Investigators. Renin-Angiotensin System Inhibition in Advanced Chronic Kidney Disease. *N Engl J Med.* 2022 Dec 1;387(22):2021–2032.
- 9) The EMPA-KIDNEY Collaborative Group. Empagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med.* 2023.

