## CKD in 2023



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

- Review the updated definition of CKD with removal of race modifiers for staging CKD 1-5
- 2) Discuss the causes, complications, and comorbidities of CKD
- Demonstrate peer reviewed, proven methods to prevent progression of CKD



## Kidney Disease Facts

30 million Americans have CKD
15% of the population
Most don't know it

**Every 5 minutes someone's kidneys fail** 

Between 2000-2019, there was a 41.8% increase in ESKD cases

More than 113,000 people are waiting for a kidney transplant

A program to increase testing/management for Am Indian population between 2000-2019, led to a less cases; saving Medicare \$520 million

## Kidney Disease Facts

In 2019, the cost of CKD Stage 1-5 was more than \$114 BILLION

Or 44% of the entire Medicare budget

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

saving Medicare \$520 million



## And it is growing.....

- CKD is the fastest growing chronic disease
- The rate of growth is highest in the 20-54 y/o!
- The incidence of CKD grew by 89%
- Death from CKD grew by 98%
- Disability from CKD grew 62%





## We are adapting and joining other societies

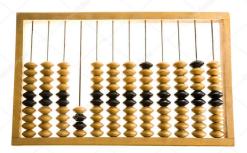
- In August 2020, the American Society of Nephrology and the NKF institute a Task Force to look into race-based issues in eGFR
- Along with the FDA, US weights and measures, the pathology society, researchers, patients and the transplant community, a new eGFR formula is released in Nov 2021
- In October 2022, *Diabetes Management in CKD* is published; ADA + KDIGO
- In February 2021, Hypertension Management in CKD is published
- In Oct 2021, NKF/ASN introduces a race-free eGFR calculator
- By the end of 2022, the new eGFR calculator adopted by medical community
- KDIGO announces new CKD update to be published in 2023

KDIGO Management of Diabetes in CKD 2020, KDIGO Management of HTN in CKD2021, ASN/NKF Race Task Force 2021, Consensus statement ADA/KDIGO DM in CKD 2022

## 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 (Black 1.2 modifier)
- Adjusted to age, gender, SCr, race in 2000 (Black 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 (Black 1.16x modifier)



of the N

A Unifying Approach for GFR Estimation: Recommendations

# Race in New eGFR calculator **CKD-EPI 2021**

consequences that do not



Recommend nat timely use of cy decision-makind



**Encourage and** endogenous filt racial and ethnic



The Task Force carefully review

Cynthia Delgado, Mukta Baweja, Deidra C. Crews, e Approach for GFR Estimation: Recommendations Force on Reassessing the Inclusion of Race in Dia AJKD DOI: 10.1053/j.ajkd.2021.08.003, JASN DOI: 1

Visual Graphic by Edgar Lerma, MD, FASN

National Kidney Foundation eGFR CALCULATORS

MOBILE APP





individuals.

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mation with new rventions to eliminate

e stakeholders and hese recommendations





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## What Changed in the Calculator?

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

eGFR = **141** x min (Scr/ $\kappa$ , 1)  $\alpha$  x max (Scr/ $\kappa$ , 1)<sup>-1.209</sup> x **0.993**<sup>Age</sup> x **1.018** [if female] x 1.159 [if black]

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

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

eGFR = **142** X min (Scr/k,1)  $\alpha$  X max (Scr/k,1) - 1.200 **0.9938**<sup>Age</sup> X **1.012** [if female]

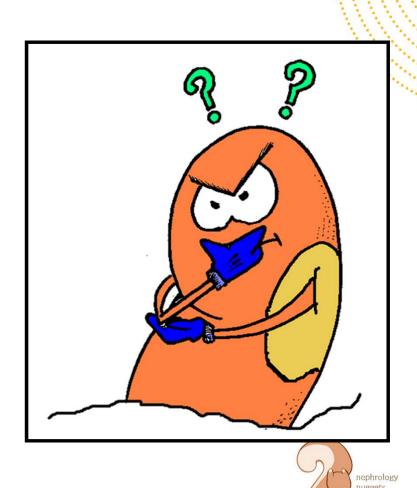
where Scr is serum creatinine, k is 0.7 for females and 0.9 males,  $\alpha$  is -0.241 for females and -0.302 for males, min indicates the minimum of Scr/k or 1, max indicates the maximum of Scr/k or 1

## Introduction of New Calculator

- February 28, 2022 All LabCorp moves to new calculator
  - Approx 51 million tests
- April 1, 2022 All VA labs move to new calculator
  - Largest integrated health system in the US
- July 11, 2022 All Quest labs move to new calculator
  - Approx 60 million tests
- July 2022 All transplant will be listed using the new
  - calculator
- August 2022 All large universities changed (Mayo, Stanford, Univ of AL, Harvard, Yale, etc)
- By the end of 2022, 80% of all labs were using the new race neutral calculator

So....who and how do we screen?

And why??



## 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, autoimmune...

Previous donor/Previous transplant

History of stones

History of cancer

History of oophorectomy

History of gout

Smoker (any type)

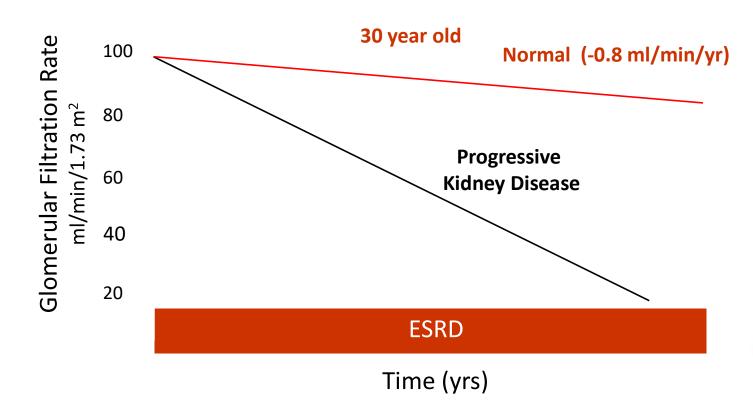
Soda drinkers

Moms who drank with pregnancy

**NACL** bingers

Almost any medical condition

## Normal Age Progression of Kidney Function







## Stages of CKD

Composite ranking for relative risks by GFR and albuminuria			Albuminuria stages, description and range (mg/g)					
			A1 Optimal and high-normal		A2 High	A3 Very high and nephrotic		
								(KDIGO 2009)
GFR stages, descrip- tion and range (ml/min per 1.73 m <sup>2</sup> )	G1	High and optimal	>105					
			90-104					
	G2	Mild	75-89					
			60-74					
	G3a	Mild- 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



#### Sadie

She reports she is 85 y/o, female, and she has diabetes **Labs:** eGFR 45ml/min

If you lose 1%/yr above the age of 30, 85-30 means 55 years of GFR loss

Or

100 (average perfect kidney function)-55 (years) or expected eGFR is **45ml/min**She is age appropriate but, will she progress?



## Albuminuria As Risk Factor

The relationship between magnitude of proteinuria reduction and the risk of ESRD: Results of the AASK study of kidney disease and hypertension Ach Intern Med 2001



The Progression of CKD: A 10year population-based study of the effects of gender and age. KI 2006



Combining GFR and albuminuria to classify CKD improves prediction of ESRD, JASN 2009



Changes in Albuminuria and subsequent risk of incident kidney disease, JASN 2017



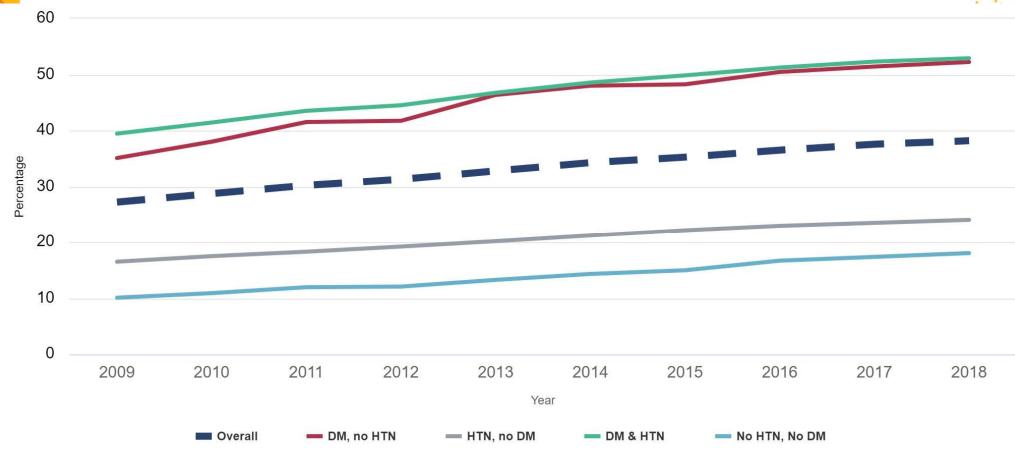
Changes in Albuminuria and the Risk of Major Clinical Outcomes in Diabetes: Results From ADVANCE-ON



Alberta Kidney Disease Network: Relation between kidney function, proteinuria, and adverse outcomes, JAMA 2010

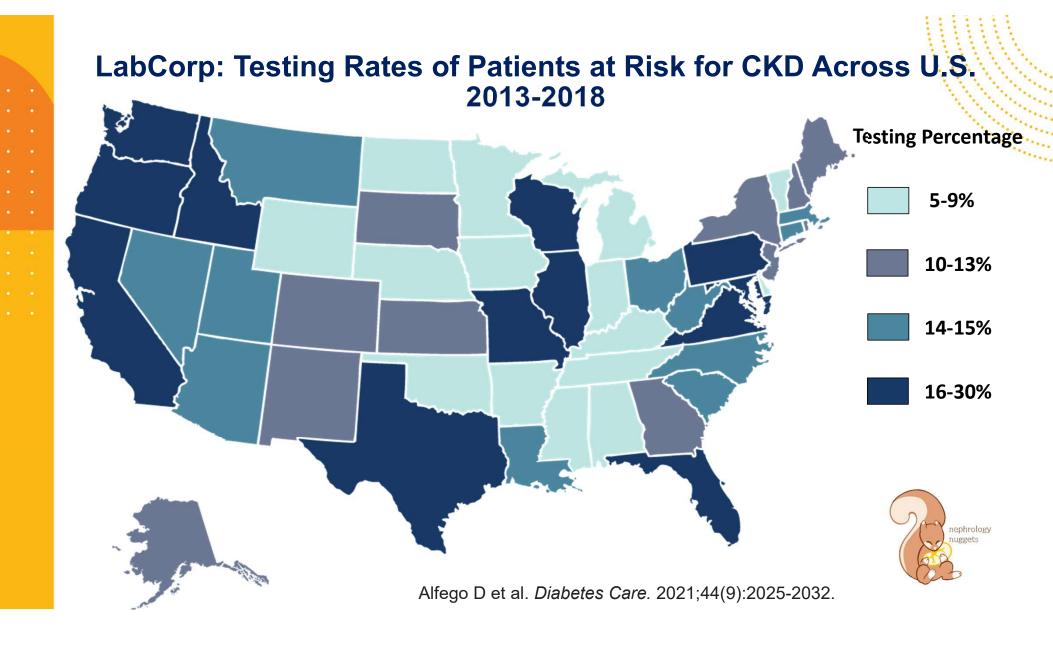


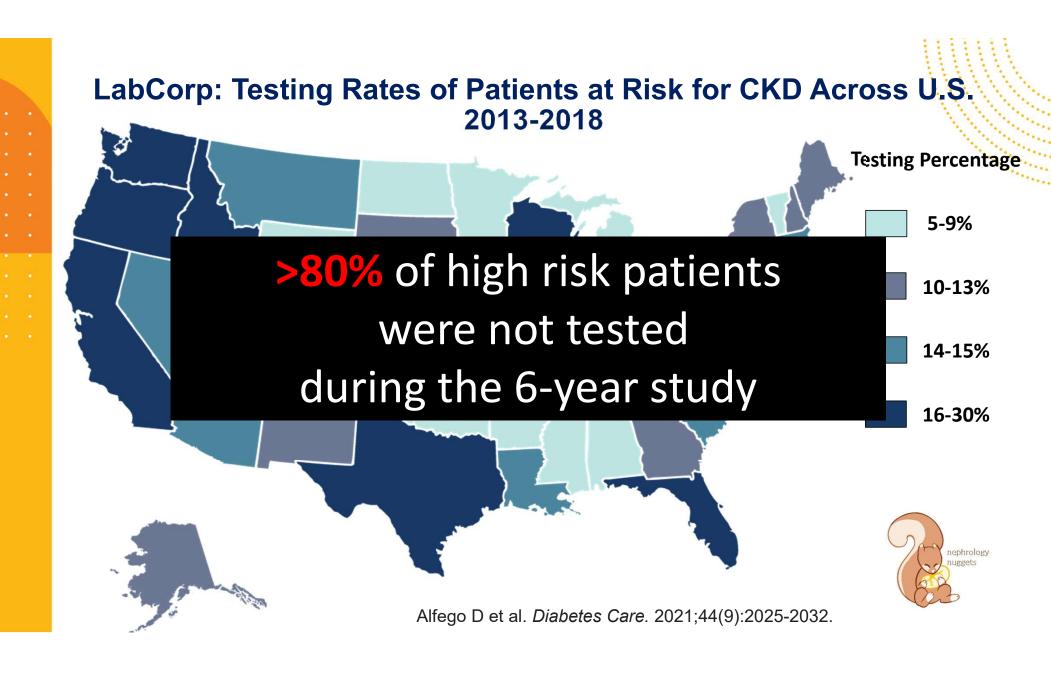
### Probability of urine albumin testing in at-risk Medicare patients



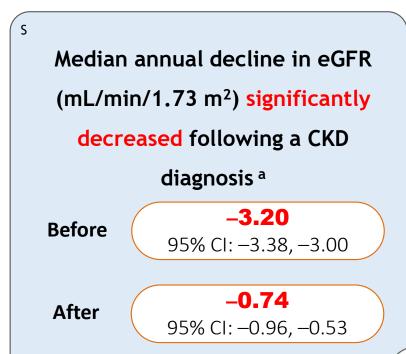
**USRDS 2020** 



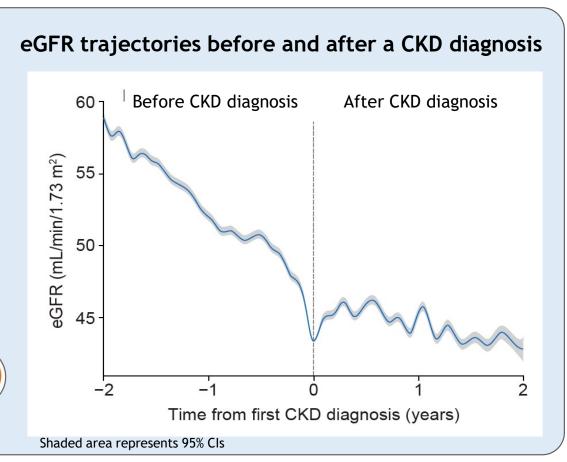




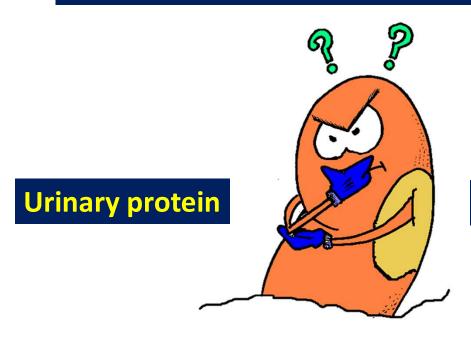
# REVEAL Trial: eGFR decline before and after a CKD Diagnosis



\*Springer Health presented ASN Nov 2022, Tangri N, et al. Adv Ther, Jan 2023



# Gold Standard: Urine albumin to creatinine ratio (UACR)



**Urine protein to creatinine ratio** 

Special Thanks to Scott and White of Temple TX for use of their kidney comic



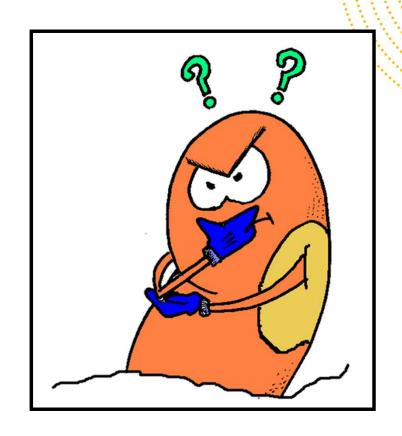
#### **Urine Pearls**

- UACR will be positive BEFORE eGFR drops
- Some labs (Quest, LabCorp) refer to a UACR as 'microalbuminuria'
- NKF has joined with Quest (Code: 39165, CPT: 82043; 82565; 82570) and LabCorp (Code: 140301, CPT: 82043; 82565; 82570) to roll out a 'Kidney Profile' that incorporates both the SCr + the UACR
- 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



So we know who has CKD
And we tested their urine

Now...how do we manage CKD in 2023?





## The Big 5

- 1) Hypertension
- 2) Diabetes
- 3) Obesity
- 4) Cardiovascular Disease
- 5) This and That (kind of defies categorization)





# Hypertension The most common comorbidity in CKD is HTN

If HTN doesn't cause your CKD, your CKD will cause HTN So what is the GOAL?

KDIGO 2021 HTN Management in CKD GUIDELINES:

Target SBP 120mm Hg
Use an automatic office cuff measurement
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	2-4mmgHg after 1 week

### **NACL** Restriction

Stage of Kidney Disease

= NACL clearance

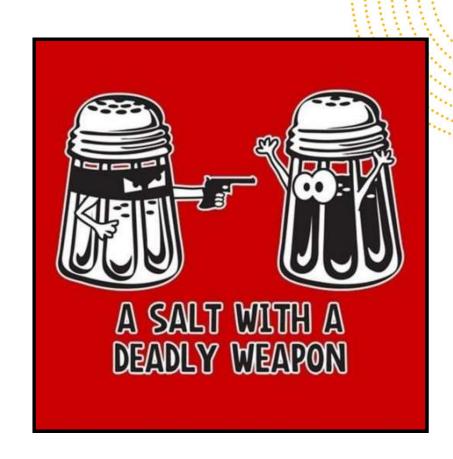
Most effective in

patients of color

#### **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





#### 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 when starting an ACEi/ARB?

Acceptable rise in SCr is 20-30%



## When do I stop an ACEi/ARB?

- If hyperkalemia cannot be controlled
  - Diet, education, medication



Continued use of ACEi/ARB with a GFR<30mm/min protected the heart WITHOUT an increase in ESRD\*

Stopping ACEi/ARB increased mortality and MACE endpoints by 11.9-13.6% with a <8% increase in ESRD in Stage 5 patients\*\*

Inc death rate due to CVD in those who had ACE/ARB stopped for hyperkalemia\*\*\*

<sup>\*</sup>Ass Between Renin-Angiotensin System Blockade Discontinuation and All-Cause Mortality Among Persons With Low Estimated Glomerular Filtration Rate, *JAMA Intern Med*, 2020
\*\*Stopping Renin-Angiotensin System Inhibitors in Patients with Advanced CKD and Risk of Adverse Outcomes: A Nationwide Study. JASN Feb 2021

<sup>\*\*\*</sup>Hyperkalemia-Related Discontinuation of Renin-Angiotensin-Aldosterone System Inhibitors and Clinical Outcomes in CKD: A Population-Based Cohort Study, AJKD 2022

## When do I stop an ACEi/ARB?

#### The STOP-ACEi trial

Multicenter UK <u>randomized</u> controlled trial of ACEi/ARB withdrawal in advanced kidney disease

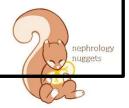
Enrollment completed June 2018, published Nov 2022

Trial time line 3 years

Do patients who stop ACEi/ARB have more cardiac events or more GFR loss??

Higher death rate from kidney AND cardiac endpoints
If you stop the ACEi/ARB



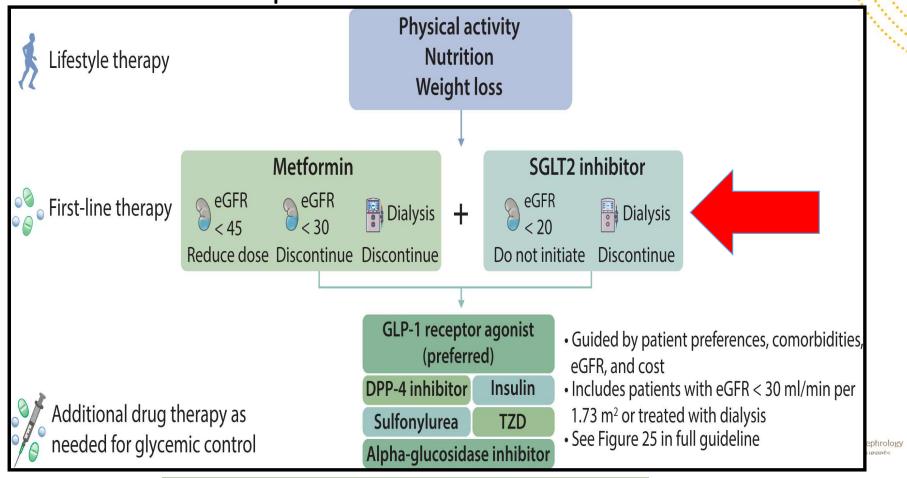


## Hypertension Pearls

- NACL restriction is just as effective as a medication
- 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
- Calcium channel blockers work VERY well in the AA population
- With cardiovascular disease...ACE/CCB>ACE/diuretic
- Thiazide diuretics do **NOT** work if the GFR<30ml/min
- NOTHING works if you cannot afford it

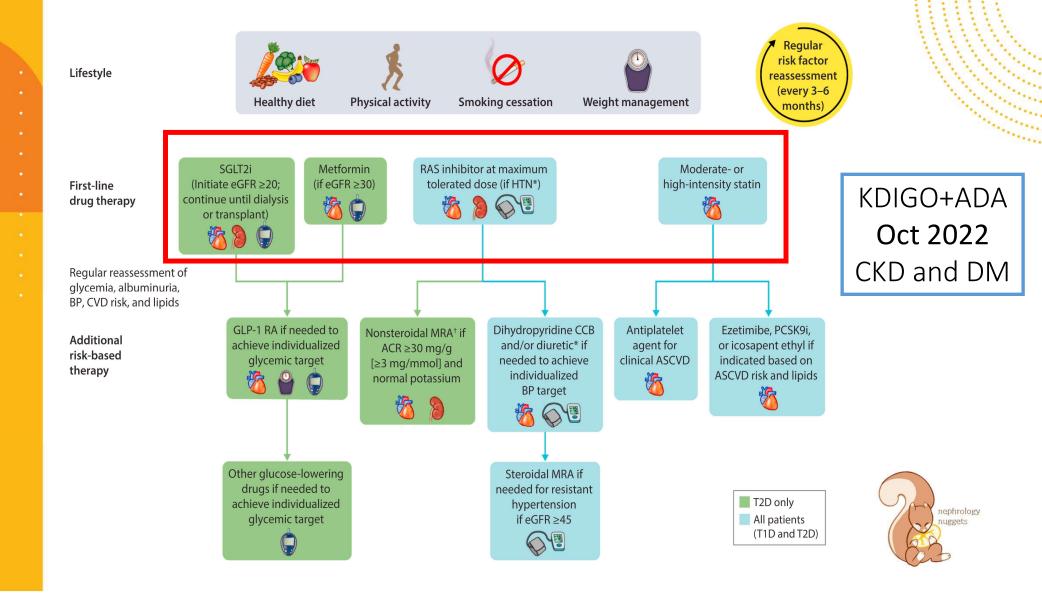


2022 KDIGO: Update for Diabetes Treatment in CKD



NOTE: Lower eGFR of 20 for starting SGLT2i





#### Comparison of the effects of three novel classes of glucose-lowering drugs on AKI risk in patients with or without type 2 diabetes





#### Electronic databases

Pubmed Embase Cochrane CENTRAL



Up to September 2020



2 independent reviewers

Event-driven CV or kidney outcome trials

n = 18 trials

n = 2 trials

(Patients with

(Patients with or Type 2 diabetes only) without Type 2 diabetes)



18 trials



156,690

Patients with Type 2 diabetes only



2051 AKI events Risk of AKI (vs placebo)



OR 0.76 (95% CI 0.66-0.88)

SGLT2 inhibitors



DPP-4 inhibitors OR 1.12

(95% CI 0.93-1.35)



GLP-1R agonists OR 0.96

(95% CI 0.83-1.11)

Risk of AKI (Comparisons between drugs)

SGLT2 inhibitors

VS DPP-4 **OR 0.68** (95% CI 0.54-0.86)

inhibitors

SGLT2 inhibitors

VS GLP1-R agonists OR 0.79

(95% CI 0.65-0.97)

Conclusion Current evidence indicates that SGLT2 inhibitors have a lower risk of AKI than both DPP-4 inhibitors and GLP-1RAs.

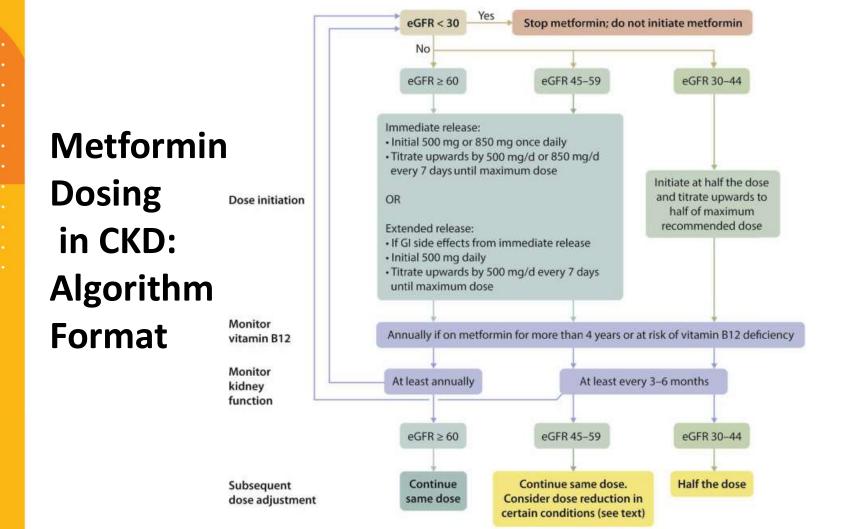
Min Zhao, Shusen Sun, Zhenguang Huang, et al. Network Meta-Analysis of Novel Glucose-Lowering Drugs on Risk of Acute Kidney Injury. CJASN doi: 10.2215/CJN.11220720. Visual Abstract by Edgar Lerma, MD, FASN

## 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
- No renal dosing needed
- 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





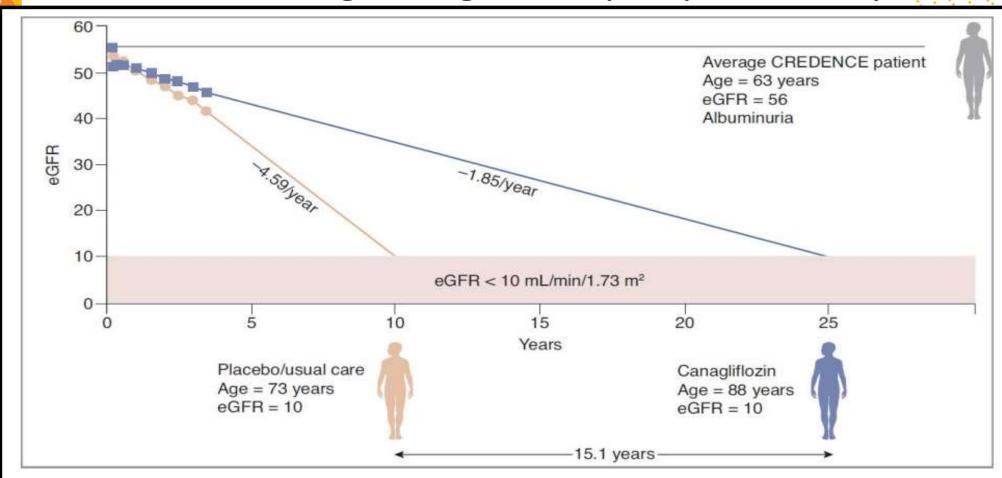
## MACE Endpoints for SGLT2i Trials

- 1<sup>St</sup> trial EMPA-REG with kidney as <u>secondary outcome</u>
   Protected against Nephropathy! 44% DECREASE in kidney endpoints
   Lowered albuminuria, slowed eGFR loss, lowered kidney/CV death
- CREDENCE enrolled <u>DKD patients for a primary endpoint trial</u>
   All had UACR>300mg/dL; Stopped early
   Lowered albuminuria, slowed eGFR loss, lowered kidney/CV death 43%
- DAPA CKD enrolled <u>CKD patients for primary endpoint trial</u>
   All had albuminuria but ½ did NOT have diabetes
   Lowered albuminuria, slowed eGFR loss, lowered kidney/CV death 41%
- EMPA-KIDNEY enrolled <u>CKD patients with and without albuminuria</u>
   Trial stopped early but all patients did better with SGLT2i
   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

## **CREDENCE: Using Canagliflozin postpones Dialysis**



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

## Tricks to Using SGLT2 inhibitors in CKD

- Initially treat with maximum dose of ACEi/ARB before adding SGLT2i
   SGLT2i can be used up to Stage 4 (20ml/min)
- If patient on loop diuretic, ½ the dose....

  (in trials, researcher choice: ½ number of daily doses or ½ 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

nephrolog

## Benefits of SGLT2i

#### Slows progression of CKD

- CREDENCE: if eGFR 56ml/min, UACR 927mg/dL-slow progression by 2.74ml/min/year
- DAPA-CKD: if eGFR 44ml/min, UACR 930mg/dL-slow progression by 1.8ml/min/year

#### Reduces albuminuria

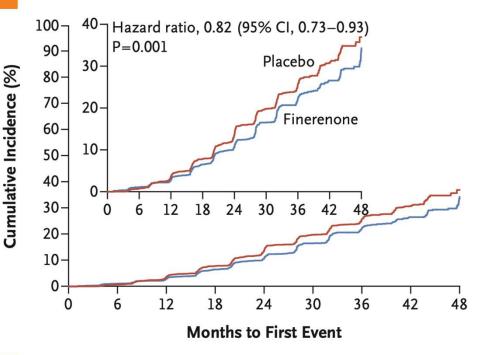
- 30-40% and this is on top of ACE/ARB
- SBP reduction
  - 4mm Hg
- Weight reduction
  - 5-6lb (if eGFR>45ml/min)
- Reduce A1C
  - 0.5-0.8% (if eGFR>45ml/min)
- Lower uric acid by 10%
  - A 50% lower risk of nephrolithiasis



Kristensen KB, et al. Diabetiologia 2021

## New Kid on the Block- Non-steroidal MRA Finerenone (Kerendia®)

#### **Primary Composite Outcome**



#### **Mechanism of Action**

Induces conformational change within the mineralocorticoid receptor Works to decrease inflammation?

#### FDA 7/9/21:

- 1) Reduce the risk of loss of kidney function
- 2) Reduce incidence of kidney failure
- 3) Reduce cardiovascular death
- 4) Reduce non-fatal heart attacks
- 5) Reduce hospitalization for heart failure in adults with CKD and T2DM

MRA-Mineralocorticoid Receptor Antagonists

Bakris GL, et al. N Engl J Med. 2020;383(23):2219-2229

## **Bariatric Surgery**

Large Kaiser group (714) over 3 years
44% minority, 77% female, 66% w/DM, 91% w/HTN
Surgical patients had nearly 10mL/min better
eGFRs at 3 years than non-surgical

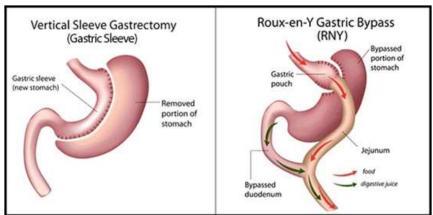


ANNALS OF SURGERY

Large Kaiser group (802) matched with those without gastric bypass surgery 79% females, BMI>40, +DM, HTN Surgical patients had a 79% lower 5-year risk of mortality

Bariatric surgery protects

kidney function + lowers death rate





Bariatric Surgery and Risk of Death in Persons With CKD, Ann Surg. 2022. eGFR Before/After Bariatric Surgery in CKD. Am J Kidney Dis. 2017

## Diabetes and Obesity Pearls

- Losing weight saves your kidneys
  - Studies show >7 year protection after bypass surgery (JASN 2018, 2144 patients)
- CKD diagnosis helps for Medicare coverage for Bariatric Surgery
- Some diabetic medications promote weight loss...Use them!
- 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

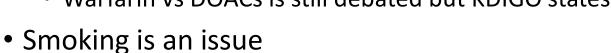




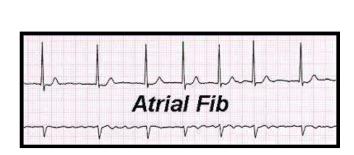
## Cardiovascular Disease (CVD)



- 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 NOACs



- Including vaping, marijuana and cigarette
  - Oral marijuana is safe in CKD
  - No studies on chewing tobacco



## KDIGO Guidelines for dosing in A Fib

CrCl (ml/min)	Apixaban* (Eliquis®)	Dabigatran (Pradaxa®)	Edoxaban** (Savaysa®, Lixiana®)	Rivaroxaban (Xarelto®)
>95	5mg bid	150mg bid	60mg qd^^	20mg qd
51-95	5mg bid	150mg bid	60mg qd	20mg qd
31-50	5mg bid (CrCl cut off 25ml/min)	150mg bid or 110mg bid^	30mg qd	15mg qd
15-30	2.5mg bid	Unknown	30mg qd could be considered	15mg qd could be considered
<15 not on dialysis	Unknown	Not recommended	Not recommended	Unknown
<15 on dialysis	Unknown	Not recommended	Not recommended	Unknown

## Hyperlipidemia

#### **CKD** = Heart Disease

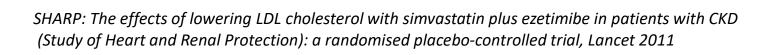


#### **SHARP Trial: Statins or statins + ezetimibe**

Fibrates are not recommended in CKD by KDIGO Debatable is effective in Stage 5/5D CKD

# Uremia affects LDL levels making them unreliable When you put a CKD patent on a Statin FIRE AND FORGET

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



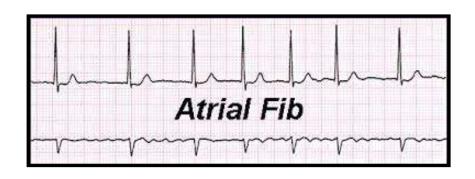


## Hyperlipidemia: KDIGO Guidelines

Statin	eGFR G1-G2		eGFR G3a-G5, including patients on dialysis or with a kidney transplant	
Lovastatin	GP (Genera	al public)	nd (not determined	
Fluvastatin	GP		80¹	
Atorvastatin	GP		<b>20</b> <sup>2</sup>	
Rosuvastatin (Inceased he	maturia) GP		10 <sup>3</sup>	
Simvastatin/Ezetmibe	GP		20/104	
Pravastatin	GP		40	
Simvastatin	GP		40	
Pitavastatin	GP		2	

#### **CVD Pearls**

- A CKD patient is more likely to die of CVD than via kidney fail
- 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 arrythmias
  - Mainly a fib
- All patients with CKD have heart disease

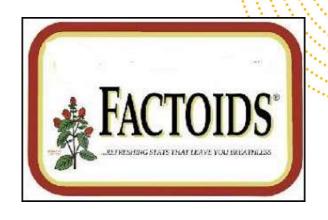






## This and That

- 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 cause CKD but very small risk
- As you lose kidney function, you are more likely to have a serious fall
- Untreated Hepatitis C will cause loss of GFR
- Gut and Dental disease are predictive of CKD





## The CKD Patient

- 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) Check for a fib, anemia, MBD, acidosis, consider birth control
- 10) Discuss concept of 'normal kidney eating' rather than 'diet'



nephrology

#### When to Refer

I always hear that your nephrology consultants complain about referrals...

We are overwhelmed but...

Start your referral with:

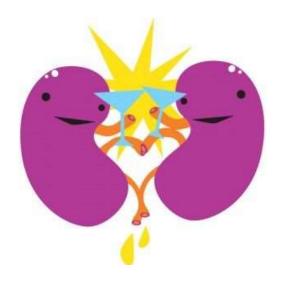
'Per KDIGO Guidelines,

I am referring this patient due to...'

- 1) Uncontrolled HTN
- 2) Stage 4 CKD (some places taking Stage 3a!)
- 3) eGFR dropped 25% in 6 months or
- 4) SCr increased 25% in 6 months
- 5) Patient request



# Thank you for helping us care for our CKD patients! We could not do it without you....



Kim Zuber, PAC aanpa1@yahoo.com



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