Brigham and Women's Hospital
Founding Member, Mass General Brigham

Chronic Kidney Disease

Harish Seethapathy, MD
Assistant Physician, MGH
Division of Nephrology, Department of Medicine
Mass General Brigham
Assistant Professor of Medicine
Harvard Medical School

Harish Seethapathy, MD

Medical School: Madras Medical College

Residency: Rochester General Hospital

Nephrology Fellowship: Mass General Brigham/HMS

Assistant Professor of Medicine at HMS
Clinical focus: Glomerular disease, onconephrology

DISCLOSURES

Please state any/all financial disclosures for past 24 months.

Scientific Advisory Board: Vera Therapeutics, Travere Therapeutics

Learning Objectives

Discuss the definition, diagnosis and prevalence of CKD

Discuss strategies to reduce progression of CKD

Clinical Case

75-Year-Old Male Patient with Type 2 Diabetes & Hypertension

Patient Profile

Age
75 Years Old

History
T2DM (8 Years)
Hypertension

Primary Concern
Renal Function & BP Control

Clinical Metrics

- Serum Creatinine (SCr)
  1.5 mg/dL
- Renal Function (eGFR)
  53 mL/min
- Blood Pressure Range
  140 - 150 mmHg
- Glycemic Control (HbA1c)
  7.4%

Current Medications

Lisinopril
ACE Inhibitor (HTN/Kidney)

Metformin
Oral Hypoglycemic (T2DM)

Hydrochlorothiazide
Thiazide Diuretic (HTN)

ASA (Aspirin)
Antiplatelet (CVD Prophylaxis)

Lab Values

Urinalysis & Albuminuria Assessment

Urinalysis (UA)

Protein Status

Trace Protein

No Hematuria

Albumin-to-Creatinine Ratio (UACR)

Quantitative Assessment

60 mg/g

An elevated UACR of 60 mg/g confirms the presence of **Microalbuminuria** (defined as 30–300 mg/g).

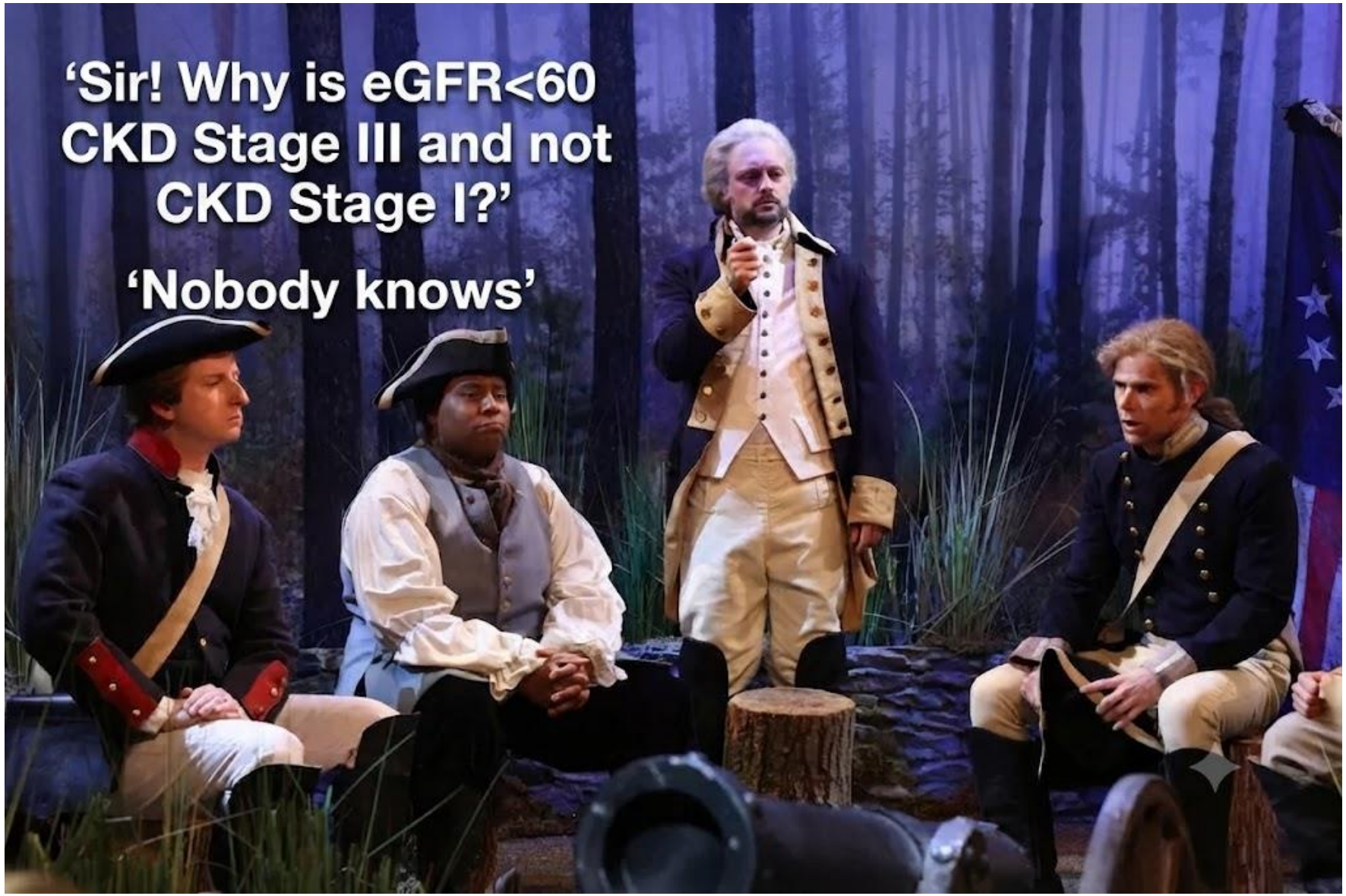
Does he have kidney disease?

Does he need to worry about it?

What are his next steps?

CKD Definition

Criteria for CKD (either of the following present for at least 3 months)	
Decreased GFR	GFR <60 ml/min/1.73m^2
Kidney Damage	Albuminuria (ACR ≥ 30mg/g) Structural Abnormalities found on imaging Electrolyte disorder attributable to abnormal tubular function Glomerular hematuria and other urine sediment abnormalities History of Kidney Transplantation Abnormalities detected by histology


‘Sir! Why is eGFR<60 CKD Stage III and not CKD Stage I?’
‘Nobody knows’

KDIGO 2024

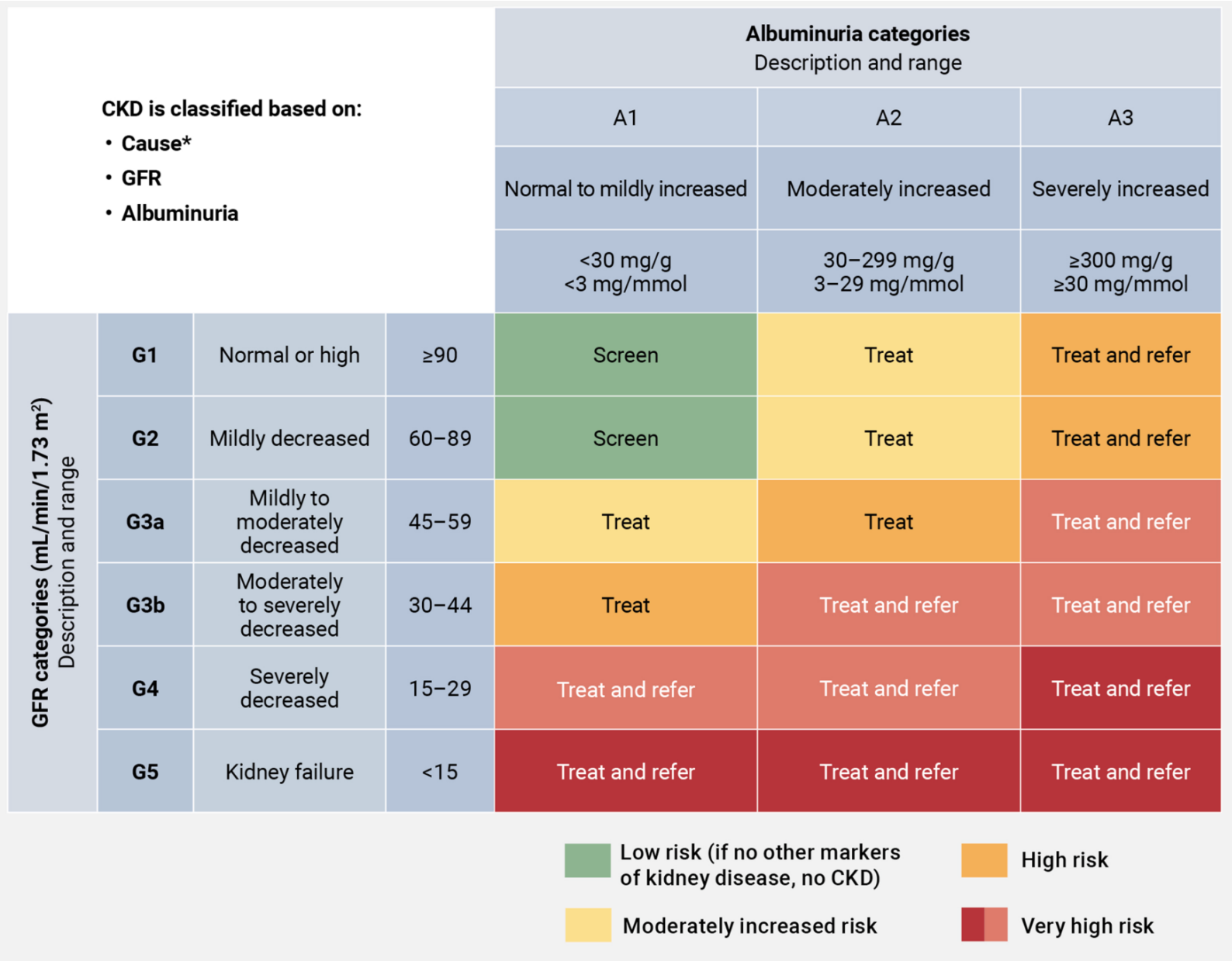
CKD is defined as abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health. CKD is classified based on Cause, Glomerular filtration rate (GFR) category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA.

KDIGO: Prognosis of CKD by GFR and albuminuria categories

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 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. GFR, glomerular filtration rate.

KDIGO 2024



CKD is classified based on: • Cause* • GFR • Albuminuria				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen	Treat	Treat and refer
	G2	Mildly decreased	60–89	Screen	Treat	Treat and refer
	G3a	Mildly to moderately decreased	45–59	Treat	Treat	Treat and refer
	G3b	Moderately to severely decreased	30–44	Treat	Treat and refer	Treat and refer
	G4	Severely decreased	15–29	Treat and refer	Treat and refer	Treat and refer
	G5	Kidney failure	<15	Treat and refer	Treat and refer	Treat and refer

Low risk (if no other markers of kidney disease, no CKD)
High risk
Moderately increased risk
Very high risk

KDIGO 2024

Age <65	ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+
	All-cause mortality			
105+	0.99	1.2	1.5	2.4
90–104	ref	1.3	1.5	2.5
60–89	1.2	1.6	2.0	2.9
45–59	2.1	2.7	2.9	4.5
30–44	2.7	3.8	4.2	5.6
<30	5.2	4.0	7.1	8.6

Age 65+	ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+
	All-cause mortality			
105+	1.2	1.4	1.9	3.5
90–104	ref	1.2	1.4	2.0
60–89	1.2	1.5	1.8	2.3
45–59	1.6	2.0	2.4	2.9
30–44	2.0	2.4	3.2	4.1
<30	3.4	4.1	5.1	6.5

Proteinuria alone (normal GFR) = 2-3.5 times higher mortality

GFR <60 (no proteinuria) = 2-5 times higher mortality

Proteinuria + GFR<60 = 3-9 times higher mortality

KDIGO 2024

Higher risk for what else?

Heart Failure, Afib, CV Mortality

Stroke, PAD

Hospitalizations

Decreased Fertility, Pregnancy Complications

Cystatin C

Cystatin C is produced by all nucleated cells; it is a lysosomal proteinase inhibitor
It is a sensitive and accurate biomarker of kidney function:
CKD-EPI Creatinine-Cystatin Equation (2021)

Clinical circumstances where Cystatin C is useful:

1.In patients with muscular atrophy, or significant chronic illness like heart failure, or cirrhosis.

2.To confirm or refute an initial diagnosis of chronic kidney disease (eGFR <60 ml/min/1.73 m^2).

3.When making medication dosing changes based on eGFR (especially hospitalized patients).

4.When patients with progressive CKD require clinical decision making that is contingent on an eGFR threshold. eg: transplant referral, dialysis modality choice, and dialysis vascular access planning.

5.When evaluating a patient as a potential kidney donor.

Take home point 1

Dx of CKD involves measurement of both GFR as well as UACR

$$\text{UACR} \quad \frac{\text{concentration of albumin}}{\text{concentration of creatinine}}$$

UACR ~ 50% of UPCR

Reported as mg/g or g/g (No unit)

Risk Factors for CKD

Clinical Factors	Diabetes	Autoimmune Disease
	Hypertension	Systemic Infections
	Urinary Tract Infections	Urinary Stones
	Urinary Tract Obstruction	Neoplasia
	Family History of CKD	Recovery from AKI
	Low birth Weight	Exposure to nephrotoxins
Sociodemographic Factors	Older Age	Low income/education
	Chemical and Environmental Exposures	Ethnic Minority Status (African American, American Indian, Hispanic or Pacific Islander

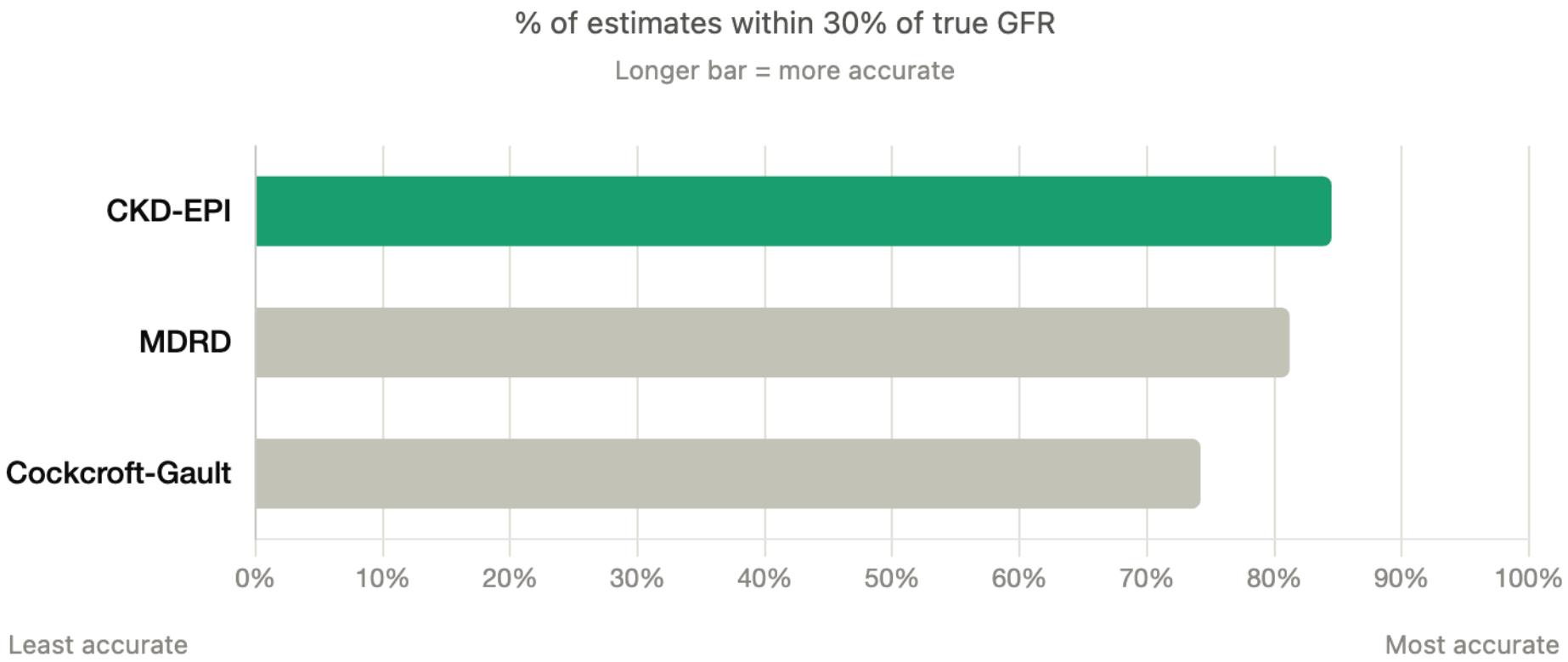
GFR Measurement and Estimation

Method	Description	Advantages	Potential Limitations
Measured GFR	•Urinary clearance of an exogenous or endogenous filtration marker. •Plasma clearance of an exogenous filtration marker.	•Accurate (gold standard methods)	•Inconvenient to patients •Expensive •Not suitable for population-based screening
Estimated GFR	•Equations based on serum levels of filtration markers (creatinine/cystatin C)	•Suitable for population screening •Rapid result (single measurement) •Inexpensive	•Non-GFR determinants of marker concentrations •Assay variation •Inaccurate particularly in non-steady state situations (AKI)

Comparison of eGFR equations

Equation	Best Used For	Primary Limitations
CKD-EPI (2021)	General population screening and staging; currently the clinical standard.	Can still overestimate kidney function, especially in specific populations.
MDRD	Patients with known CKD (GFR <60 mL/min/1.73m^2).	Often underestimates normal or near-normal kidney function; less accurate above 60 mL/min.
Cockcroft-Gault	Historically for drug dosing.	Less accurate than newer equations; highly sensitive to body weight/mass fluctuations.
eGFRcr-cys	Most accurate; combines creatinine and cystatin C.	Requires both markers; less commonly available in standard panels.

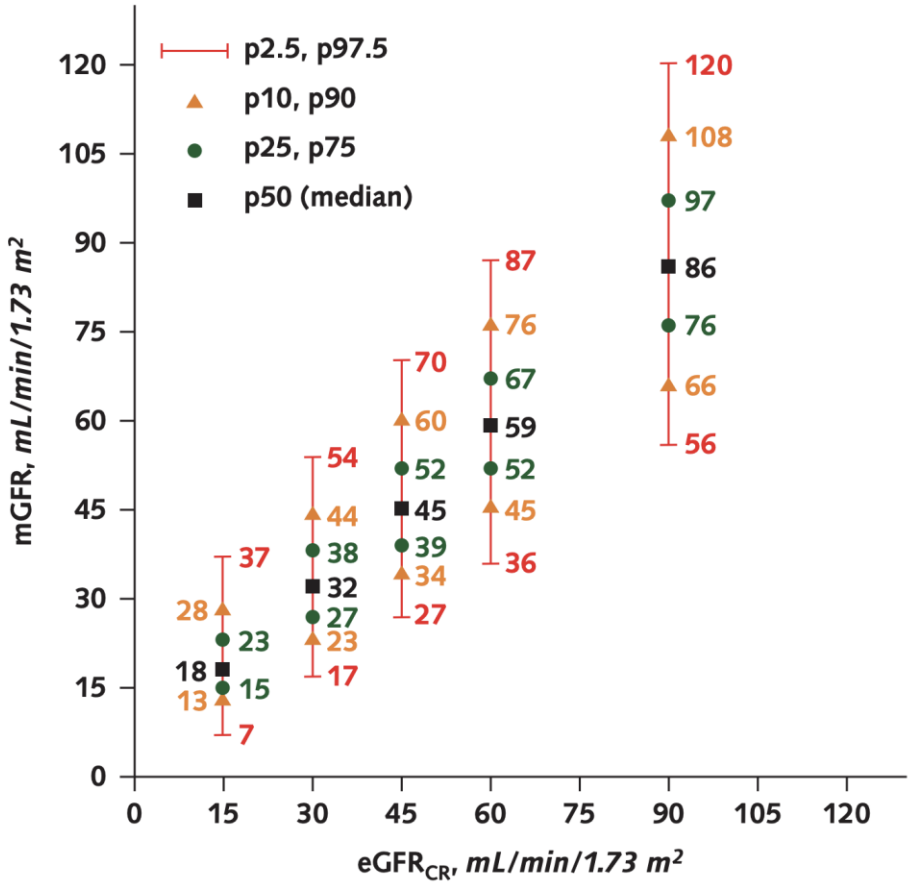
Accuracy of GFR equations



Michels, CJASN, 2010

Accuracy of eGFR in Individuals

- Wide variability
- eGFR was never designed for individual-level decision-making.
- Wide range of values for individuals at a given eGFR
- No improvement with $eGFR_{cys}$
- Likely should be reported as a range rather than a single number



Shafi et al, Ann Int Med 2022

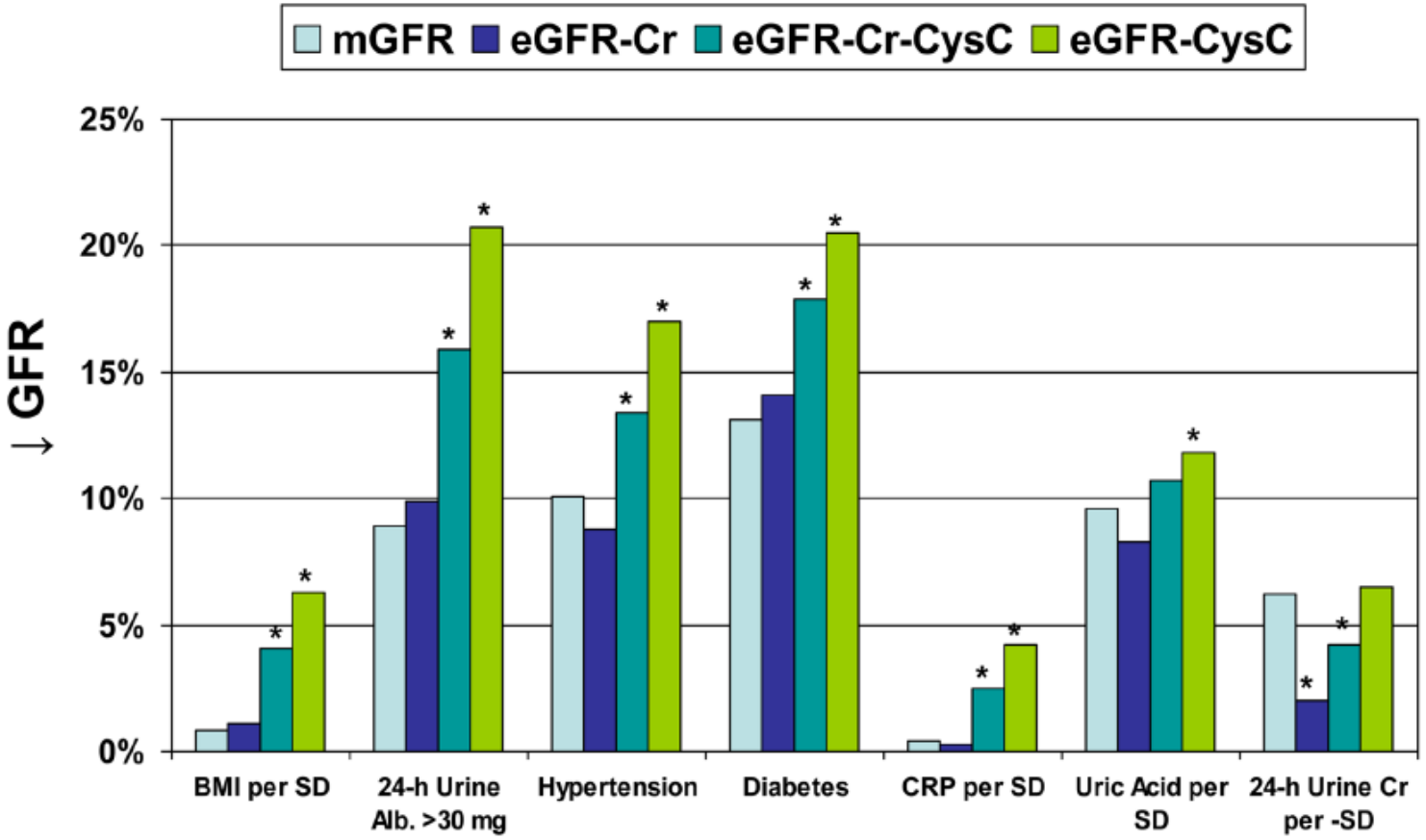
What does this mean?

Measured GFR (True GFR) = 60 mL/min

CKD-EPI eGFR is between 42-78 for 85% of individuals

In 15%....

Cystatin C



Rule et al, *Kid Int 2013*

Take home point 2

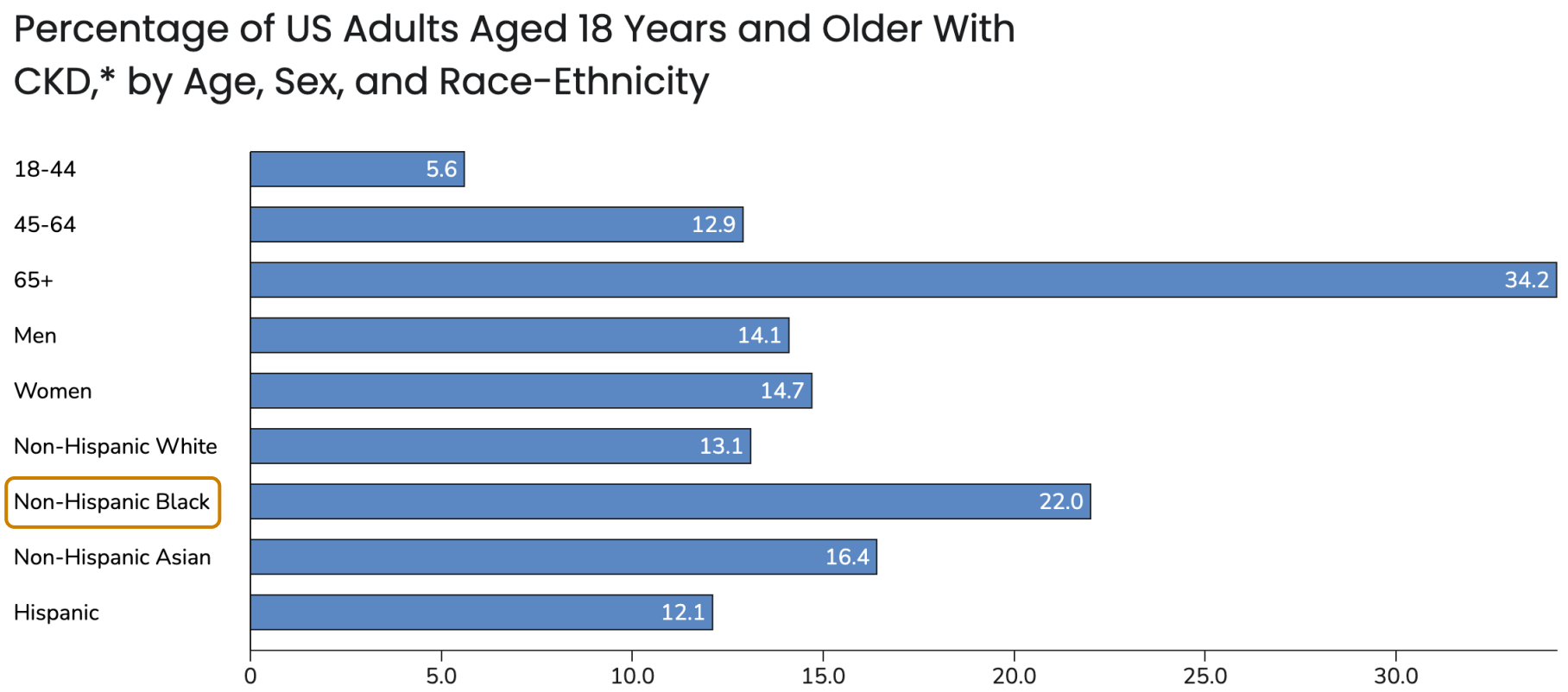
Current GFR equations are flawed

Combined CysC-Cr GFR is the practical standard

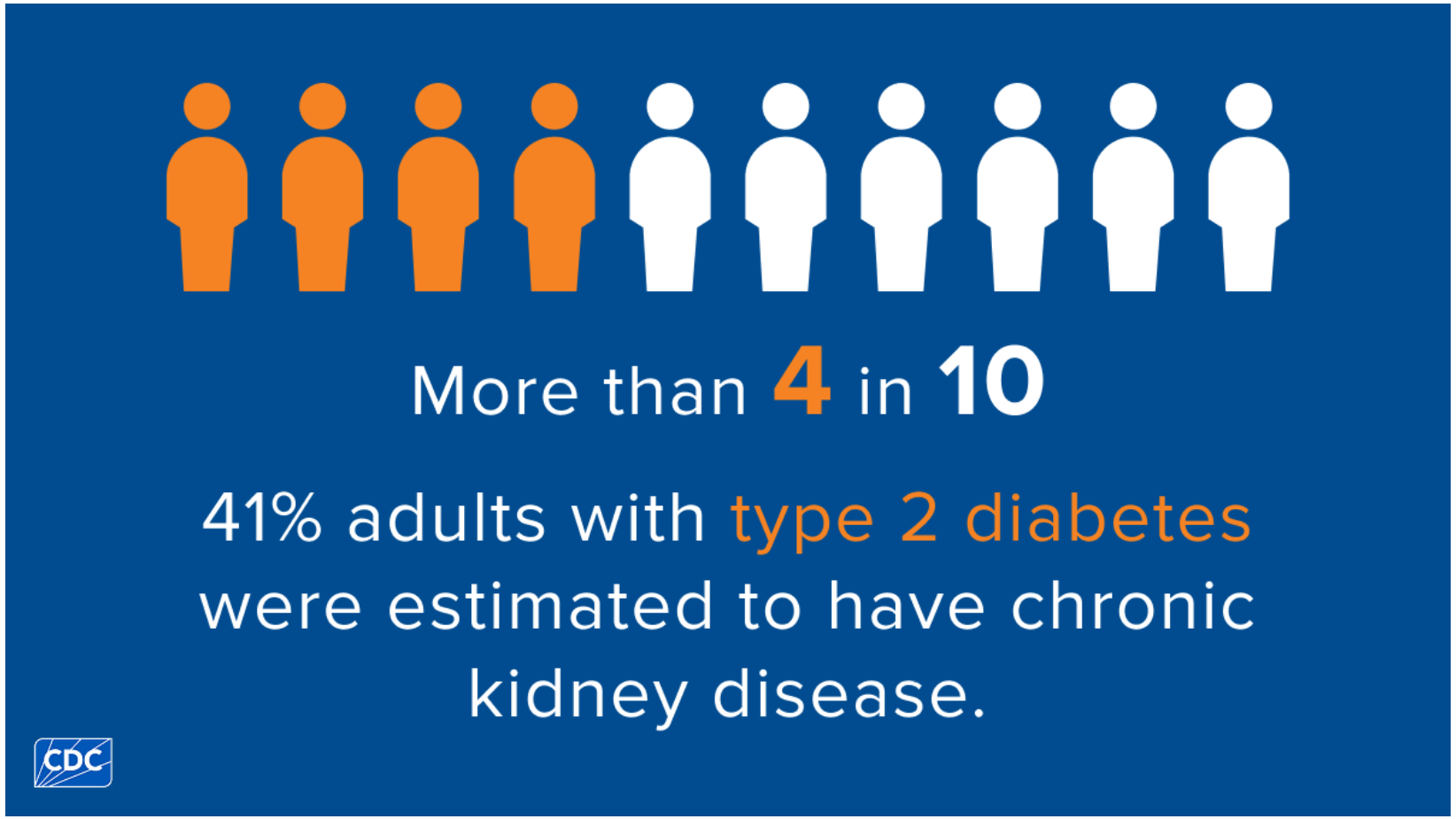
Important to use CysC and measured GFR in certain patients

How common is CKD?

Prevalence of CKD in US Adults

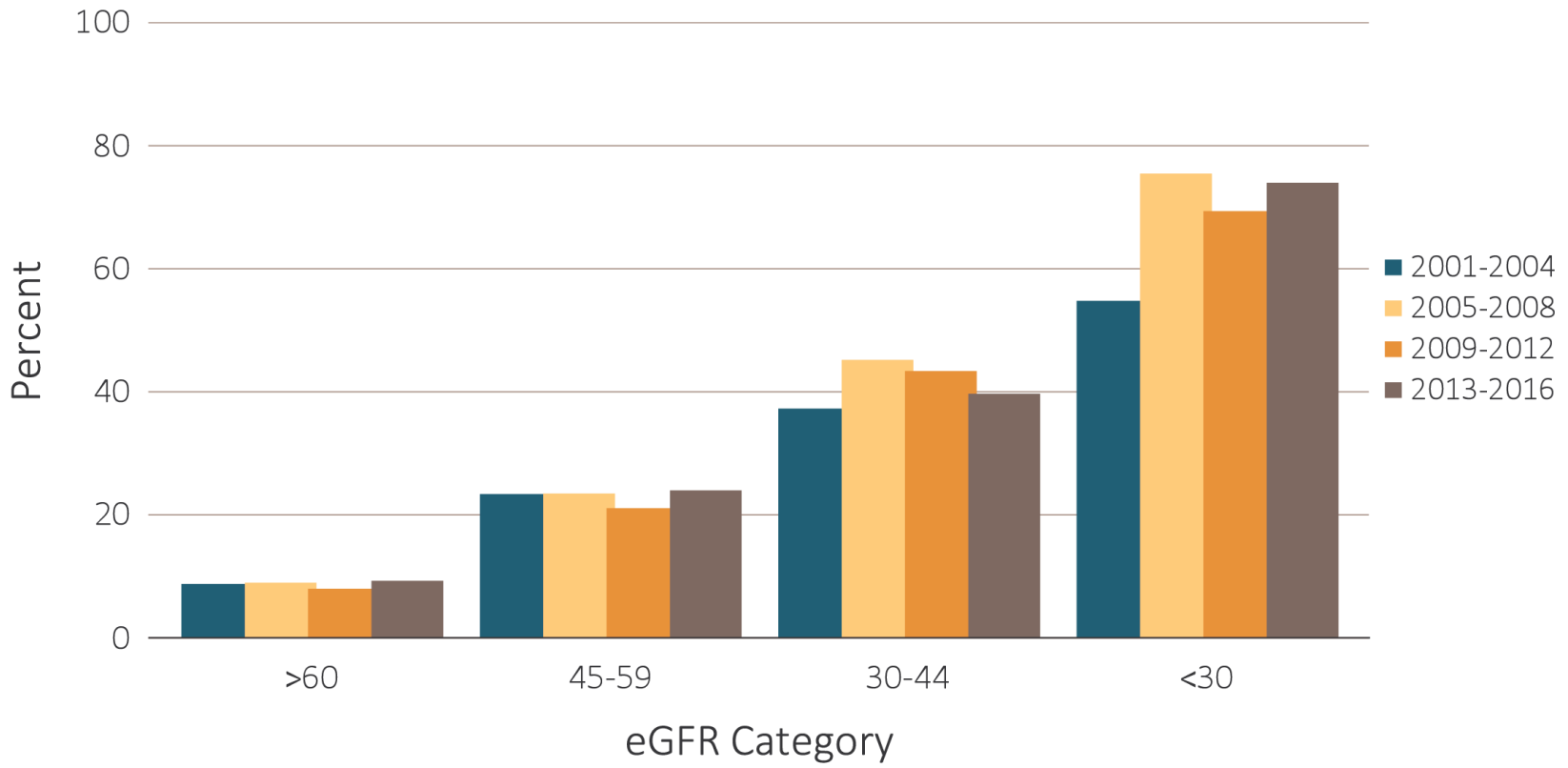


NHANES 2021-2023


More than 4 in 10
41% adults with type 2 diabetes were estimated to have chronic kidney disease.
CDC

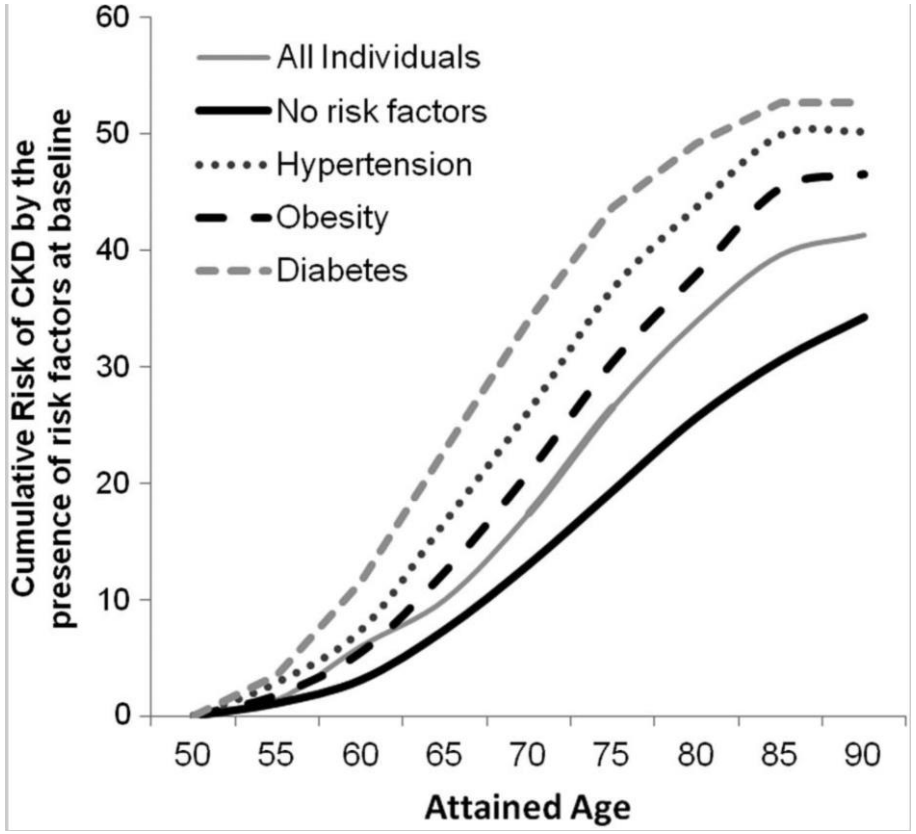
CDC

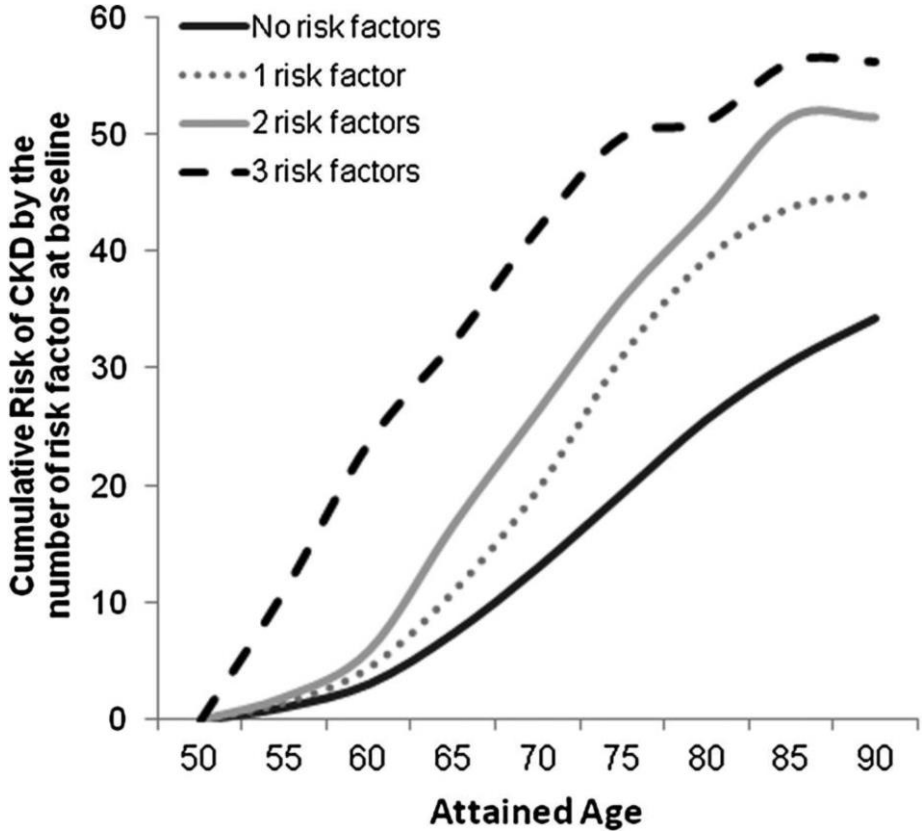
Prevalence of albuminuria by CKD category



Annual Report, *USRDS 2018*

Residual Lifetime Risk of CKD





McMahon et al, *NDT 2017*

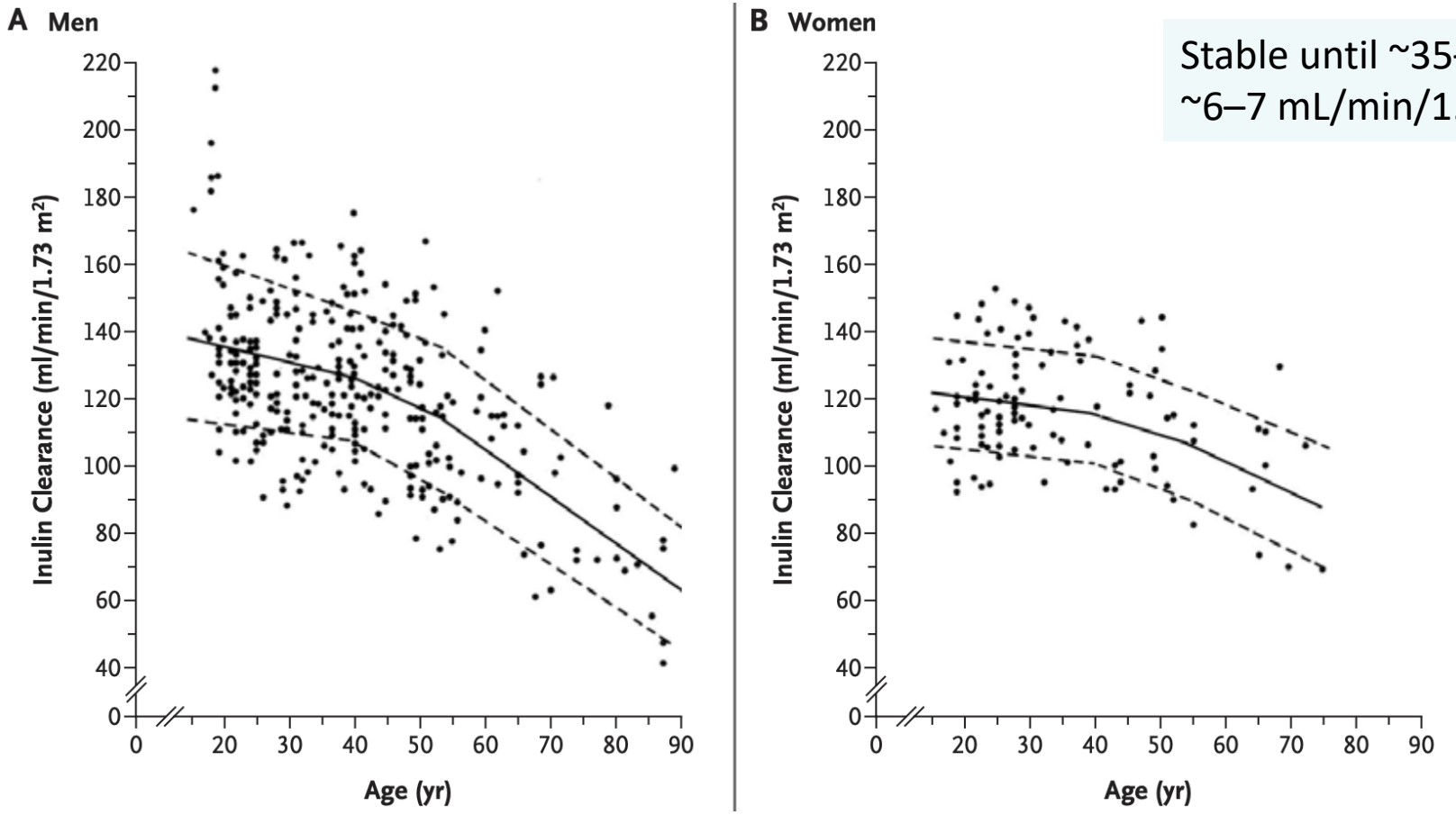
What does this mean?

13.5% of Medicare beneficiaries have CKD = 25% of spending

Annual Per-person spend
(Medicare A, B and D)

Twice as that of those without CKD

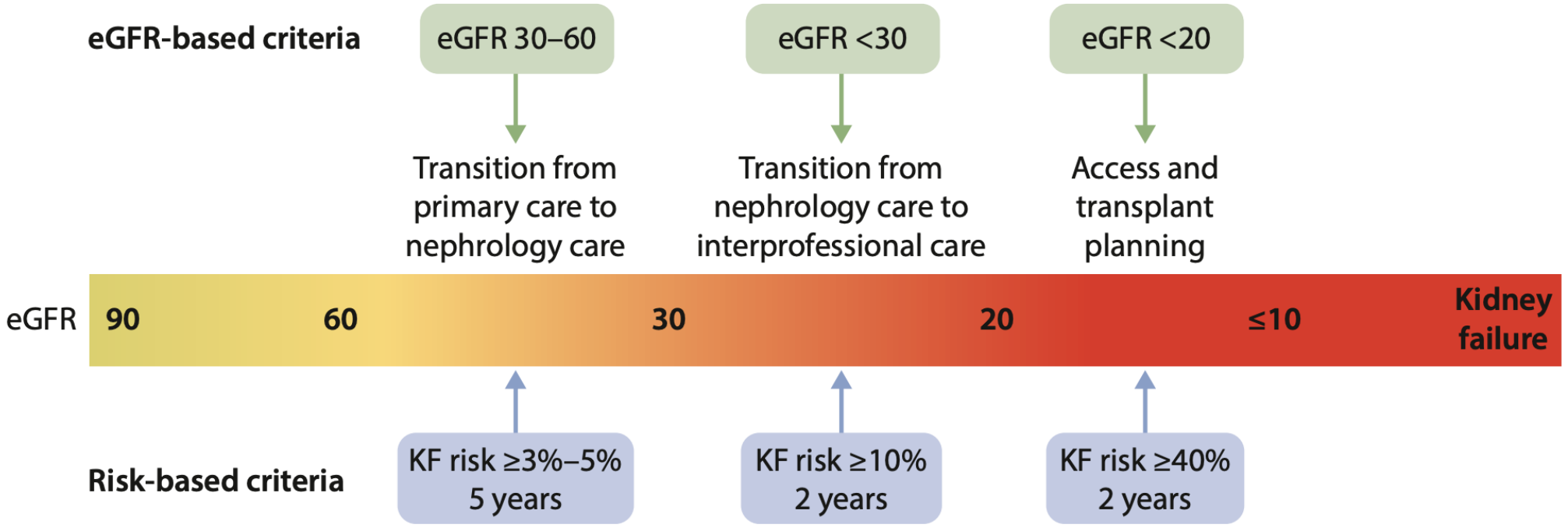
Increasing Prevalence of ?CKD with Age



Stable until ~35–40, then declines ~6–7 mL/min/1.73m² per decade

Wesson et al, *Physiology of the Human Kidney 1969*

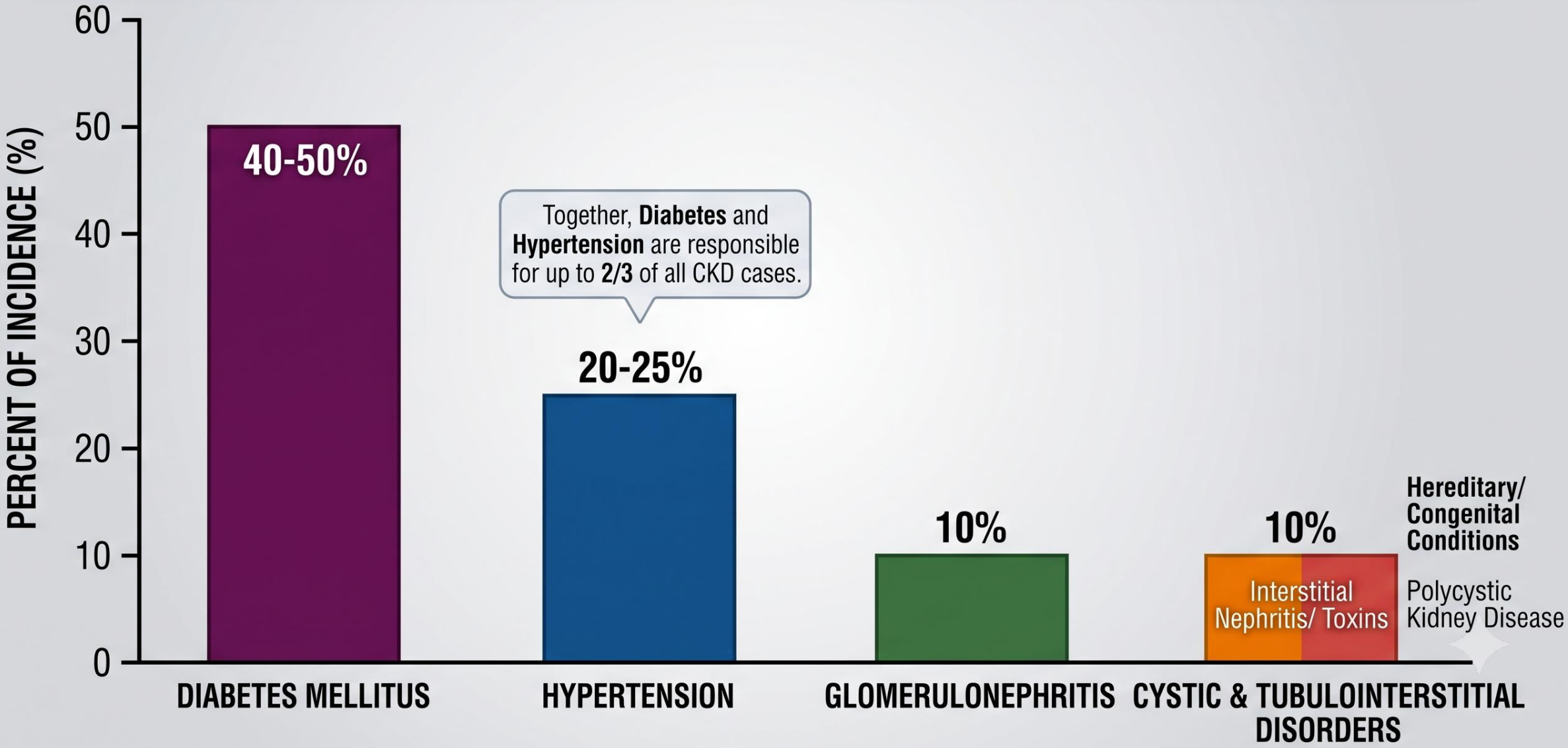
Referral to Nephrology



KDIGO, 2024

What causes CKD?

GLOBAL CKD CAUSE INCIDENCE (Estimates)



Data: Based on generalized global health estimates and nephrology guidelines.

Clinical Case

A 34-year-old African American man presents for a routine health evaluation.

He has no significant past medical history and takes no medications.

Blood pressure is 138/86 mmHg.

Laboratory studies reveal:

- Serum creatinine: 1.4 mg/dL (eGFR ~65 mL/min/1.73m² by CKD-EPI 2021)
- Urinalysis: 2+ proteinuria, no hematuria, no casts
- Spot urine albumin-to-creatinine ratio: 850 mg/g
- Hemoglobin A1c: 5.4%
- Fasting glucose: 88 mg/dL
- Renal ultrasound: normal-sized kidneys, no hydronephrosis or masses

Clinical Case

He reports a strong family history of kidney failure requiring dialysis — his mother, a maternal uncle, and a maternal grandfather all developed end-stage renal disease in their 40s–50s, none of whom had a documented history of diabetes. He has no history of NSAID use, illicit drug use, or recurrent infections.

Which of the following is the most appropriate next diagnostic test?

A) 24-hour urine protein collection

B) dsDNA, ANA and complement levels

C) Renal biopsy

D) Genetic testing

E) Hemoglobin electrophoresis

Clinical Case

Answer: D) Genetic Testing

Other choices:

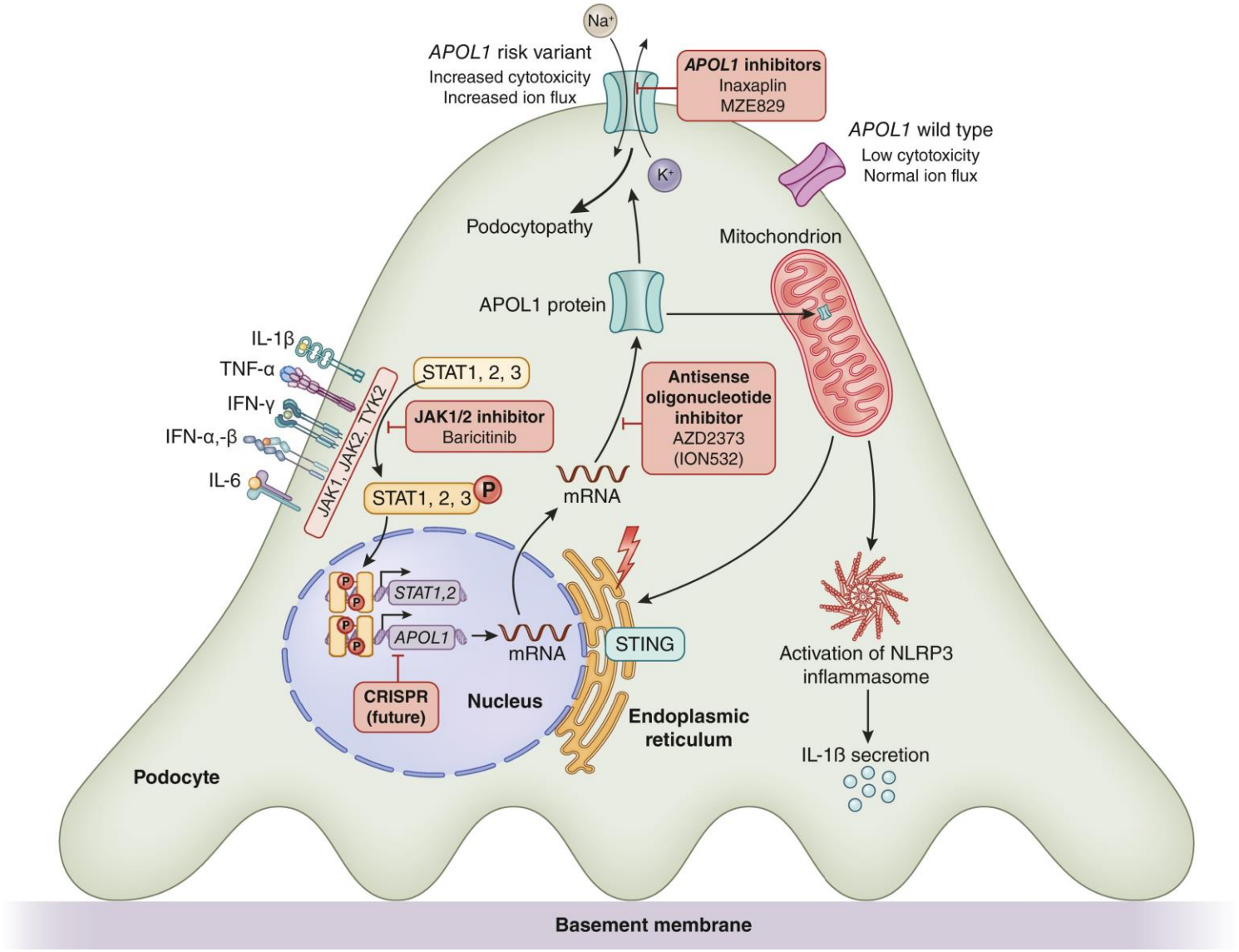
A) 24-hour urine protein collection – reasonable in Paraprotein mediated disease, Lupus etc.

B) dsDNA, ANA and complement levels – Lupus/connective tissue disorder associated GN

C) Renal biopsy – reasonable if genetic testing does not yield answers

E) Hemoglobin electrophoresis – Sickle cell disease (no other clues)

ApoL1



Ojo, KI, 2025

ApoL1 disease

Table 2. Association of *APOL1* Risk Alleles and Genotypes with CKD.*

APOL1 Genotypes	Odds Ratio (95% CI)	
	Unadjusted	Adjusted†
2 *APOL1* risk alleles vs. <2	1.34 (1.21–1.49)	1.25 (1.11–1.40)
G0/G1 vs. G0/G0	1.16 (1.03–1.31)	1.19 (1.04–1.35)
G0/G2 vs. G0/G0	1.18 (1.01–1.38)	1.19 (1.00–1.41)
G0/G1 and G0/G2 vs. G0/G0	1.17 (1.05–1.30)	1.18 (1.04–1.33)
G1/G1 vs. G0/G0	1.46 (1.26–1.69)	1.37 (1.16–1.61)
G1/G2 vs. G0/G0	1.40 (1.18–1.65)	1.34 (1.12–1.61)
G2/G2 vs. G0/G0	2.25 (1.52–3.34)	2.05 (1.35–3.13)

Monoallelic APOL1 variants

18% higher odds of CKD

61% higher odds of FSGS

Biallelic APOL1 variants

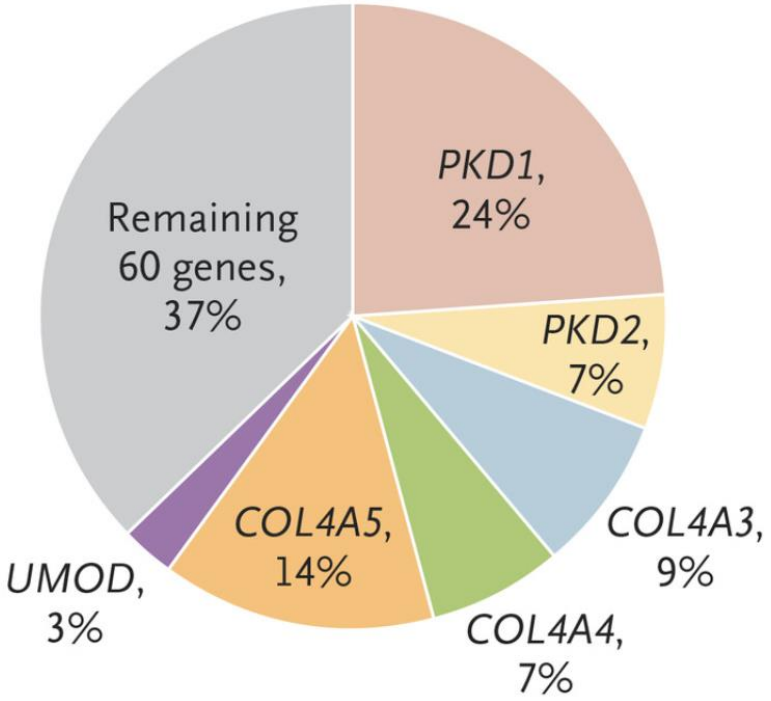
25% higher odds of CKD

84% higher odds of focal segmental glomerulosclerosis

Ulasi, NEJM, 2025

CKD of ‘unknown’ etiology

Diagnostic Utility of Exome Sequencing for Kidney Disease



3315 patients with CKD

~10% had a genetic cause

Groopman, NEJM, 2019

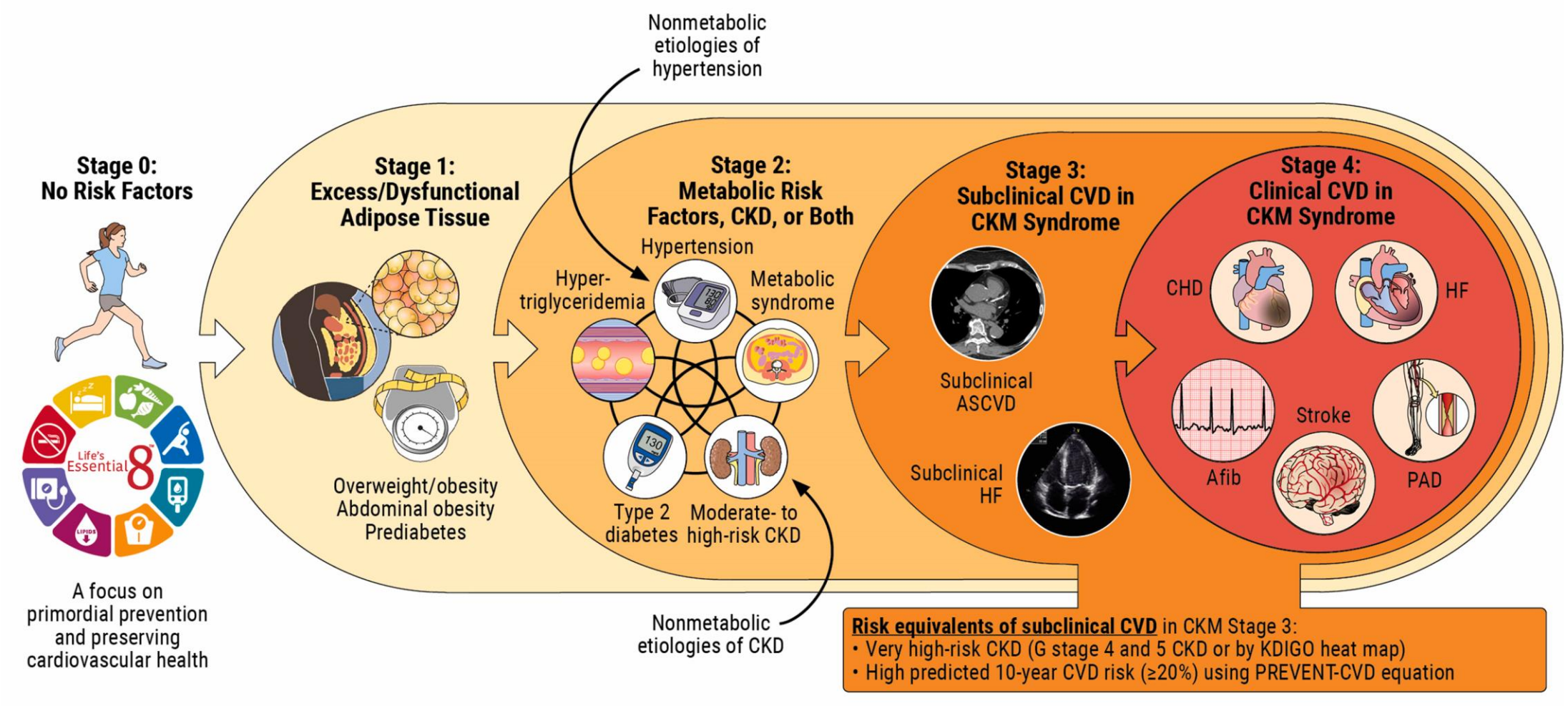
DKD Stages

25-30% are non-albuminuric

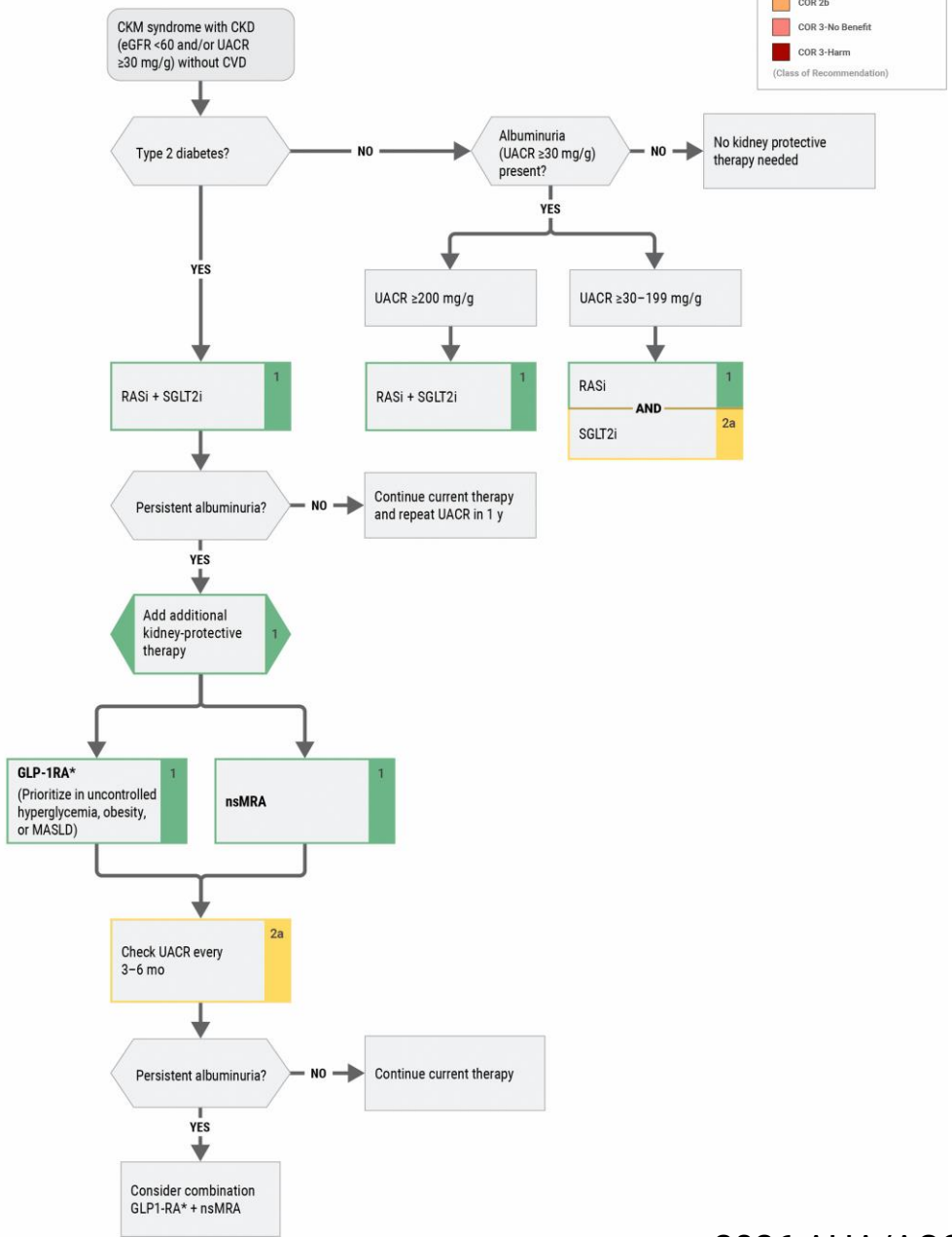
Stages	Clinical Features	Timing QUITE VARIABLE
Stage 1: Early hyperfiltration and hypertrophy	ACR <30 mg/g Cr **Increased GFR**	Onset of DM
Stage 2: Morphologic lesions without clinical disease signs	ACR <30 **Normal GFR**	0-5 years
Stage 3: Moderately increased albuminuria	**ACR 30-300 mg/g** **Cr and GFR starting to decline**	5-10 years
Stage 4: Overt nephropathy (Severely increased albuminuria and CKD)	**ACR >300 mg/g** **PCR >500 mg/g** **GFR < 60 ml/min**	>10 years
Stage 5: ESRD	On dialysis or transplanted	>15 years

How do we prevent CKD progression?

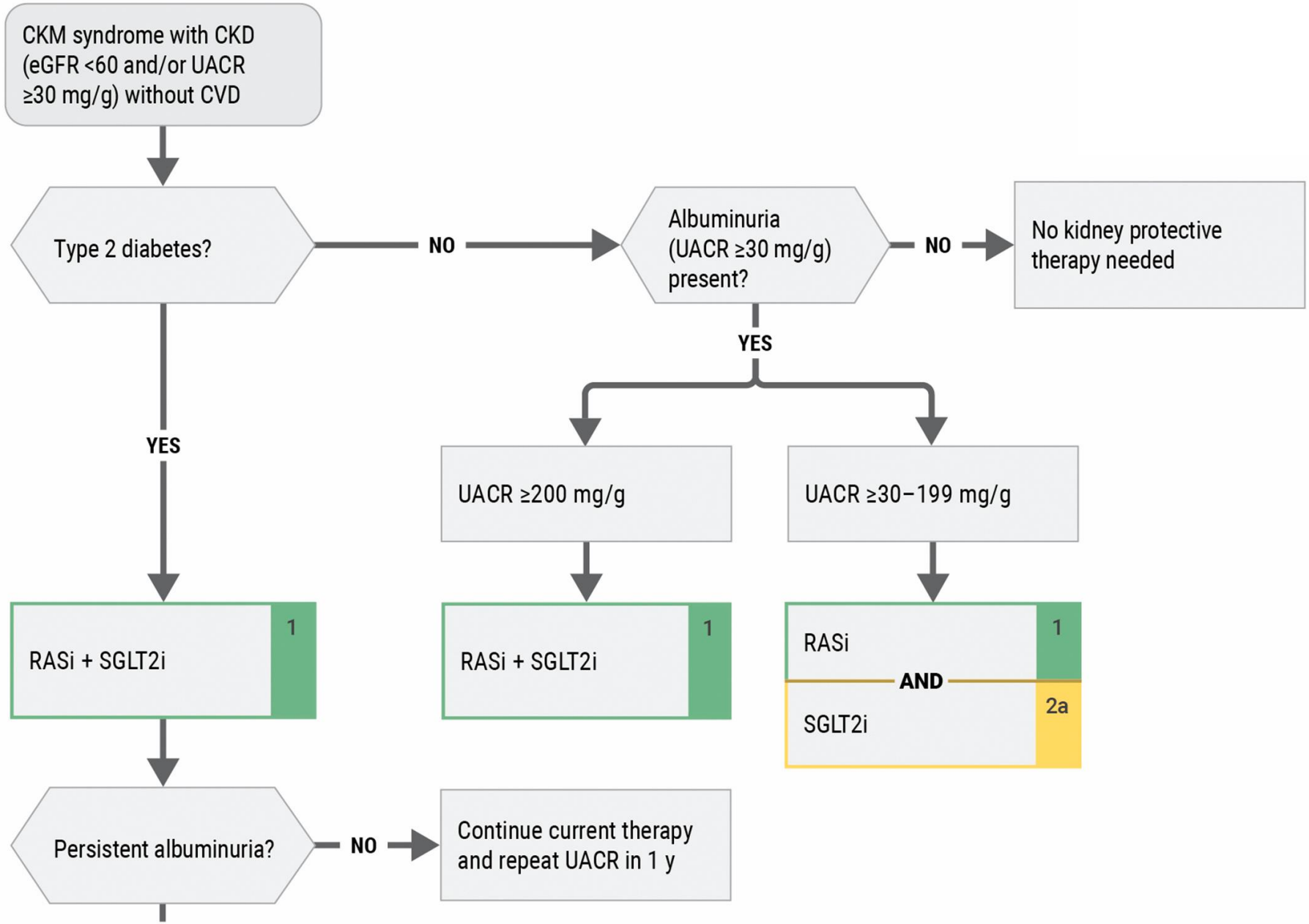
2026 AHA/ACC/ADA/ASN Guideline for CKM

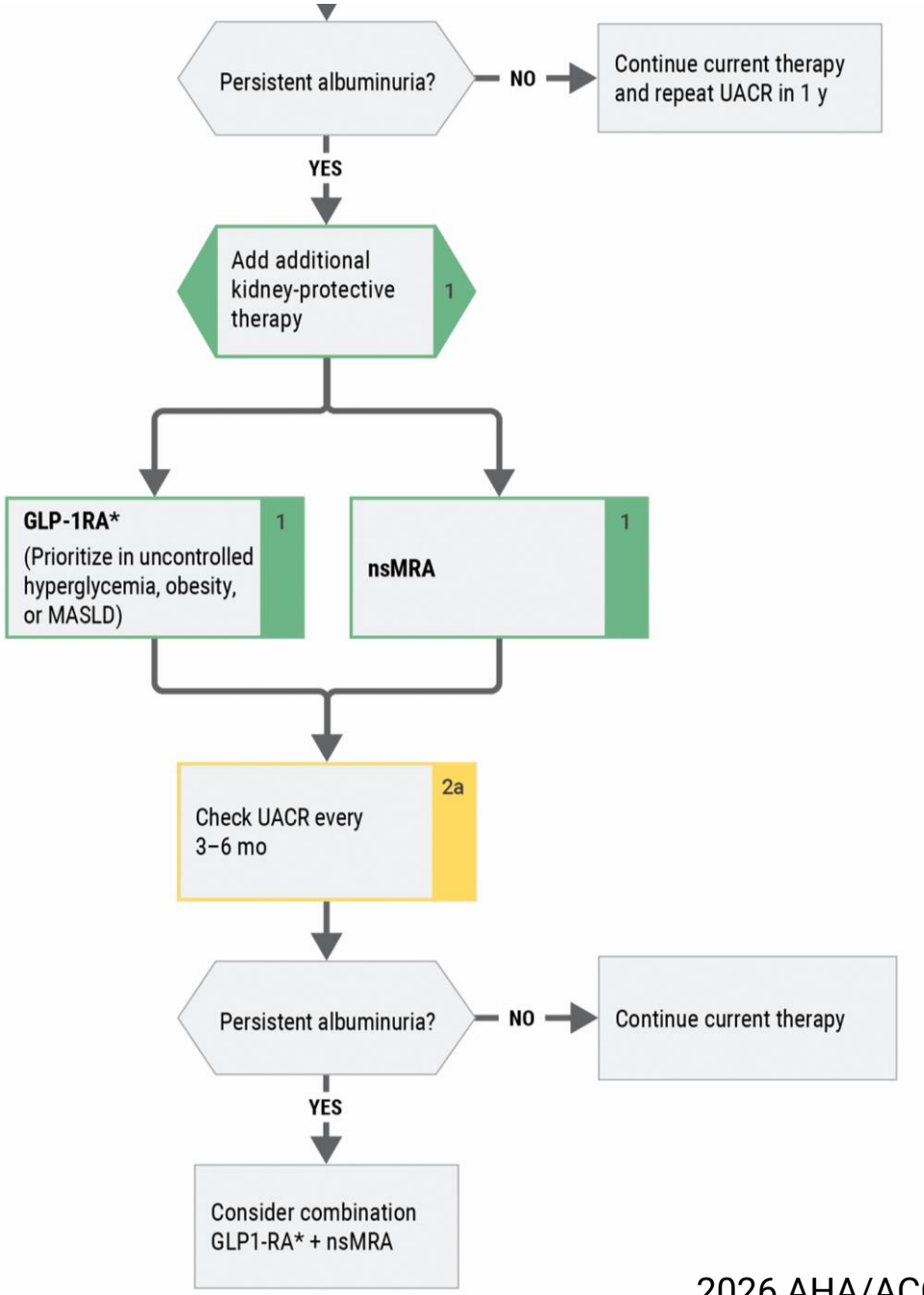


Management of CKD in CKM Syndrome Stages 2–3

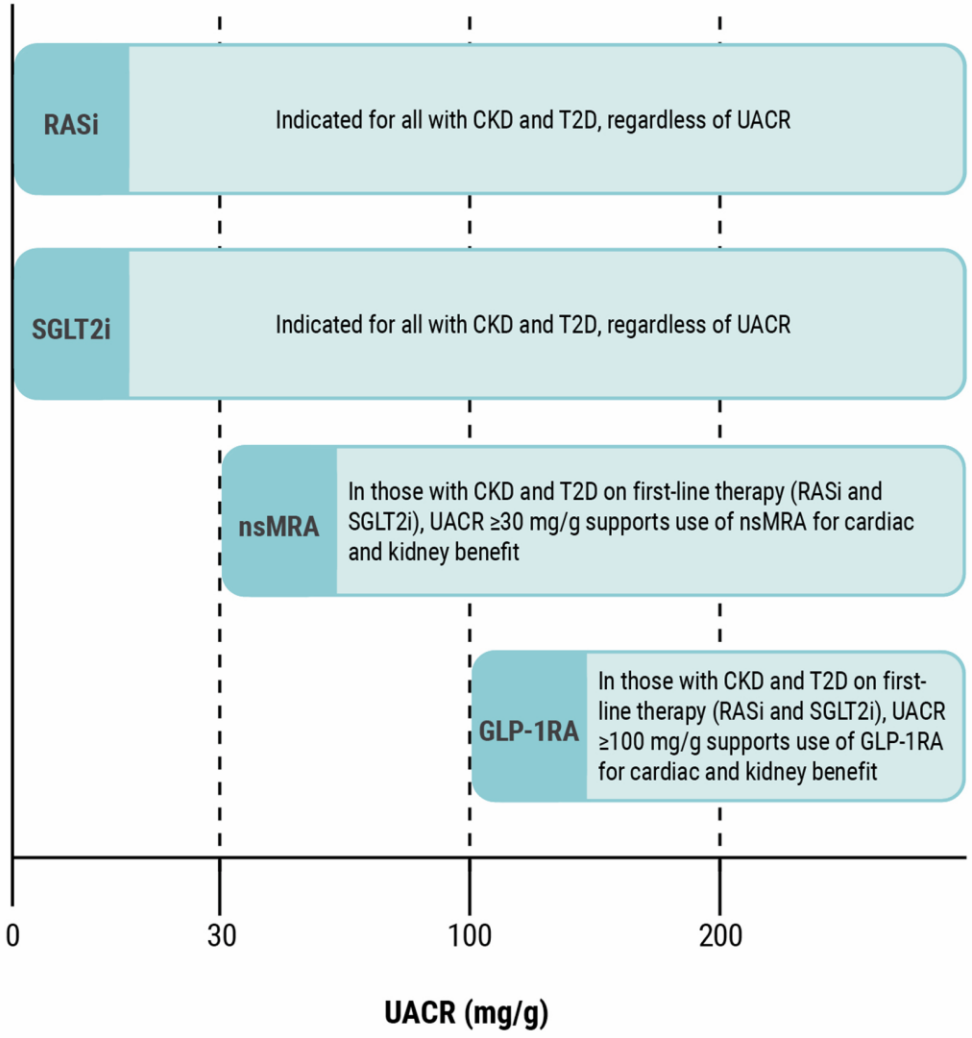


2026 AHA/ACC/ADA/ASN Guideline for CKM

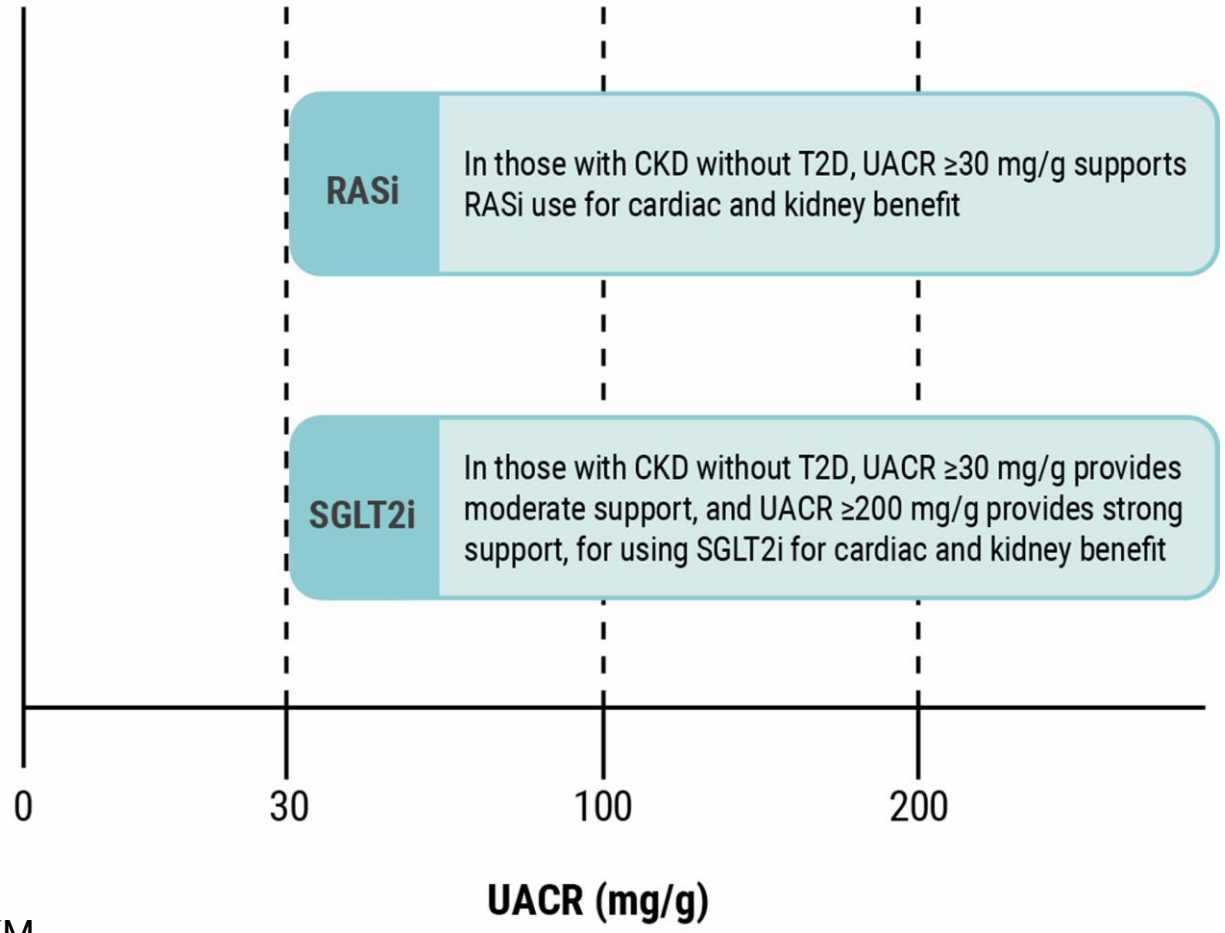

CKM syndrome with CKD (eGFR <60 and/or UACR ≥30 mg/g) without CVD
Type 2 diabetes?
NO
Albuminuria (UACR ≥30 mg/g) present?
NO
No kidney protective therapy needed
YES
YES
UACR ≥200 mg/g
UACR ≥30–199 mg/g
RASi + SGLT2i
1
RASi + SGLT2i
1
RASi
1
AND
SGLT2i
2a
Persistent albuminuria?
NO
Continue current therapy and repeat UACR in 1 y


Persistent albuminuria?
NO
Continue current therapy and repeat UACR in 1 y
YES
Add additional kidney-protective therapy
1
GLP-1RA*
(Prioritize in uncontrolled hyperglycemia, obesity, or MASLD)
1
nsMRA
1
Check UACR every 3–6 mo
2a
Persistent albuminuria?
NO
Continue current therapy
YES
Consider combination GLP1-RA* + nsMRA

Cardiovascular and Kidney Protective Therapies in CKD With Type 2 Diabetes Using UACR



Cardiovascular and Kidney Protective Therapies in CKD Without Type 2 Diabetes Using UACR



Stage IV CKM: ASCVD + CKD

Manage CKM Syndrome Guided by Patient Risk Profile

For Patients With Obesity

- **In HFpEF,** initiate GLP-1–based therapy to improve functional capacity, symptoms, and HF outcomes
- **In HFpEF**, consider exercise training and caloric deficit diet to improve functional capacity
- **In HFrEF**, benefits of weight reduction and initiation of GLP-1–based therapies are uncertain

For Patients With T2D

- In HF, prioritize SGLT2i as first-line in cardioprotective glucose lowering
- In HFpEF and other CKM risk factors, consider addition of GLP-1–based therapy to improve symptoms and reduce CKM-related adverse outcomes

For Patients With CKD

- In HF and eGFR ≥30, use ARNI/ACEi/ARB to improve HF and kidney outcomes
- In HF and eGFR ≥20, use SGLT2i to improve HF and kidney outcomes
- In HFmrEF/HFpEF, T2D, eGFR ≥25, and UACR ≥30 mg/g, consider finerenone to improve HF and kidney outcomes

Clinical Case

A 64-year-old man with type 2 diabetes, hypertension, and a history of myocardial infarction is found to have an eGFR of 26 mL/min/1.73m² (KDIGO CKD stage 4) and a UACR of 18 mg/g. He is already on an ACE inhibitor and a statin. Which of the following is the most appropriate next addition to his regimen?

A) Add a nonsteroidal mineralocorticoid receptor antagonist (nsMRA)

B) Add an SGLT2 inhibitor

C) Add a GLP-1 receptor agonist

D) No additional pharmacotherapy is indicated since he does not have albuminuria

Clinical Case

Answer B:

Add a SGLT2i

Other choices:

nsMRA – no albuminuria

GLP1a – not automatic with CVD, no history of obesity mentioned

Take home points 3

Drug-specific eGFR initiation thresholds

RASi ≥30 mL/min/1.73 m^2,

SGLT2i ≥20 mL/min/1.73 m^2

Finerenone ≥25 mL/min/1.73 m^2.

Continue until tolerated/dialysis

Things ‘around’ CKD

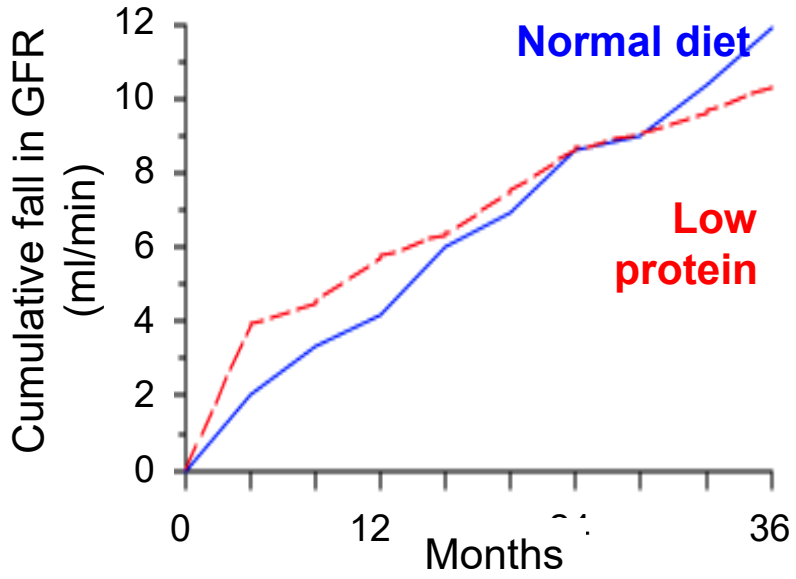
Complications develop early in CKD

Table 27 | Prevalence of CKD complications by GFR category*

Complication	GFR category (ml/min/1.73 m^2)				
	> 90	60-89	45-59	30-44	< 30
Anemia	4.0%	4.7%	12.3%	22.7%	51.5%
Hypertension	18.3%	41.0%	71.8%	78.3%	82.1%
25(OH) Vit D deficiency	14.1%	9.1%	10.7%		27.7%
Acidosis	11.2%	8.4%	9.4%	18.1%	31.5%
Hyperphosphatemia	7.2%	7.4%	9.2%	9.3%	23.0%
Hypoalbuminemia	1.0%	1.3%	2.8%	9.0%	7.5%
Hyperparathyroidism	5.5%	9.4%	23.0%	44.0%	72.5%

Reproduced from KDIGO CKD Guidelines 2012

Dietary Protein Restriction in CKD



MDRD study
585 patients with nondiabetic CKD
Mean GFR = 39
Randomized to 1.3 or 0.58 g/kg (achieved 0.6-0.8) protein per day
Little or no overall benefit

Conclusions:

- Dietary protein restriction *may* protect against the progression of CKD in humans by reducing intra-glomerular pressure
- Benefits of dietary protein restriction to 0.6-0.8 g/kg per day on CKD progression **is controversial**
- At best, a small reduction in the rate of GFR decline can be observed with low protein diet

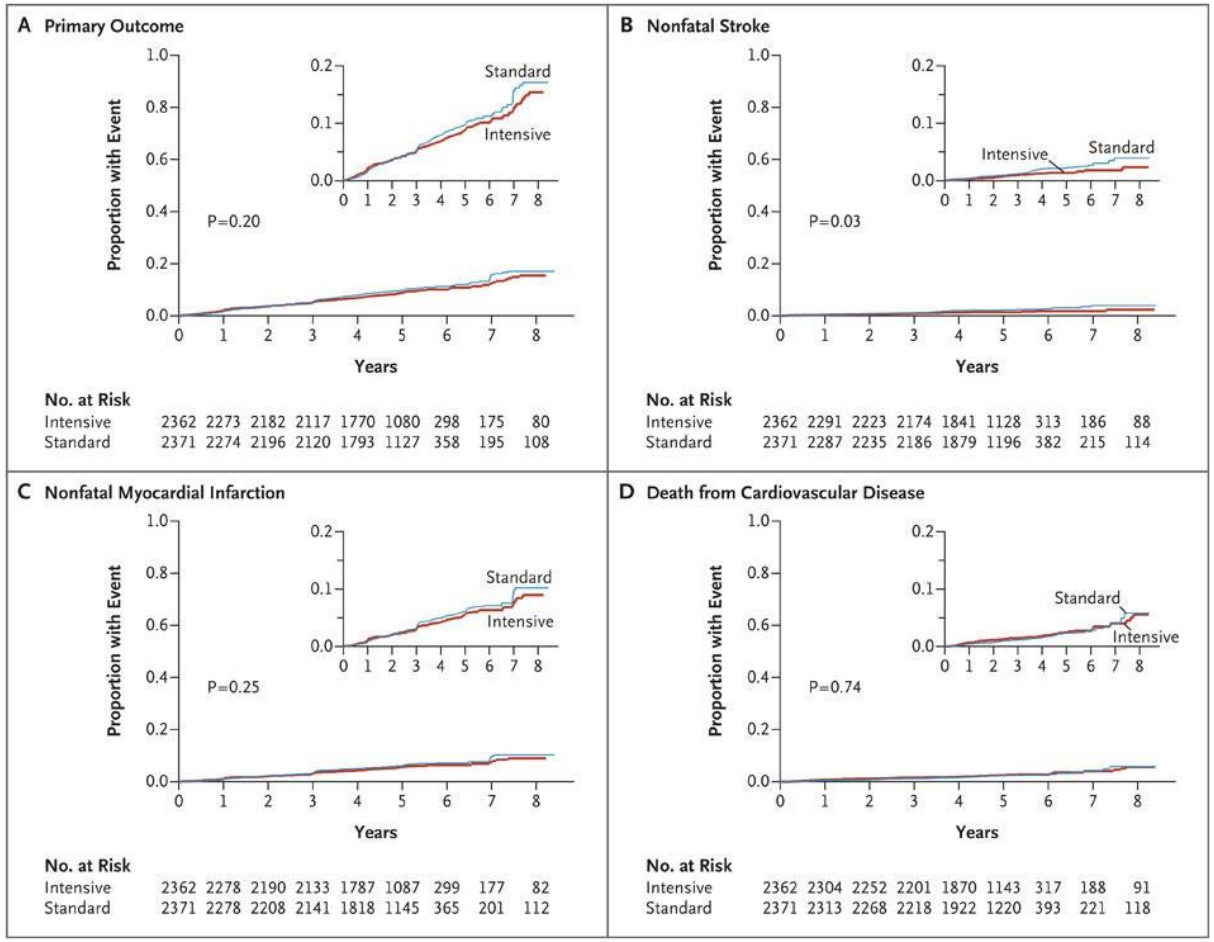
Plant based Diet in CKD

Study (N); study design	CKD stage or GFR	Intervention (follow-up)	Outcome
CRIC[467] (N = 2403); observational	20–70 ml/min per 1.73 m^2	High DASH vs. low DASH (14 yr)	CKD progression: HR: 0.83; 95% CI: 0.69–0.99 Mortality: HR: 0.75; 95% CI: 0.62–0.90
NHANES[468] (N = 1110); observational	30–59 ml/min per 1.73 m^2	DASH by quintiles (7.8 yr)	Kidney failure relative hazard (RH) compared with quintile 5: quintile 1: RH: 1.7; 95% CI: 1.1–2.7; quintile 2: RH: 2.2; 95% CI: 1.1–4.1
CORDIOPREV[466] (N = 53); RCT	<60 ml/min per 1.73 m^2	Mediterranean diet vs. low-fat diet (5 yr)	Decline in GFR −3.72 ml/min per 1.73 m^2 vs. −5.4 ml/min per 1.73 m^2, $P = 0.03$
CKD QLD[469] (N = 145); observational	CKD G3–G4	High vegetable and nut intake (median 36 mo)	Composite all-cause mortality, kidney failure, or doubling of SCr: HR: 0.61, 95% CI: 0.39–0.94
REGARDS[470] (N = 3972); observational	<60 ml/min per 1.73 m^2	Plant-based diet (6 yr)	All-cause mortality: HR: 0.77; 95% CI: 0.61–0.97
NHANES III[465] (N = 5346); observational	<60 ml/min per 1.73 m^2	Increasing plant-to-protein ratio (8.4 yr)	All-cause mortality for every 33% increase: HR: 0.77, 95% CI: 0.61–0.96
Longitudinal study of aging women[464] (N = 1374); observational	Baseline 65.6 ± 13.1 ml/min per 1.73 m^2	Higher vs. lower intake of plant-based protein (10 yr)	Each 10 g higher intake of plant-based protein reduced a decline in GFR by 0.12 ml/min per 1.73 m^2 per year

Blood pressure and CKD progression

ACCORD – no CV benefit for intense BP control (<120 vs <140) in T2DM

Reduction in albuminuria but no reduction in ESRD (underpowered)



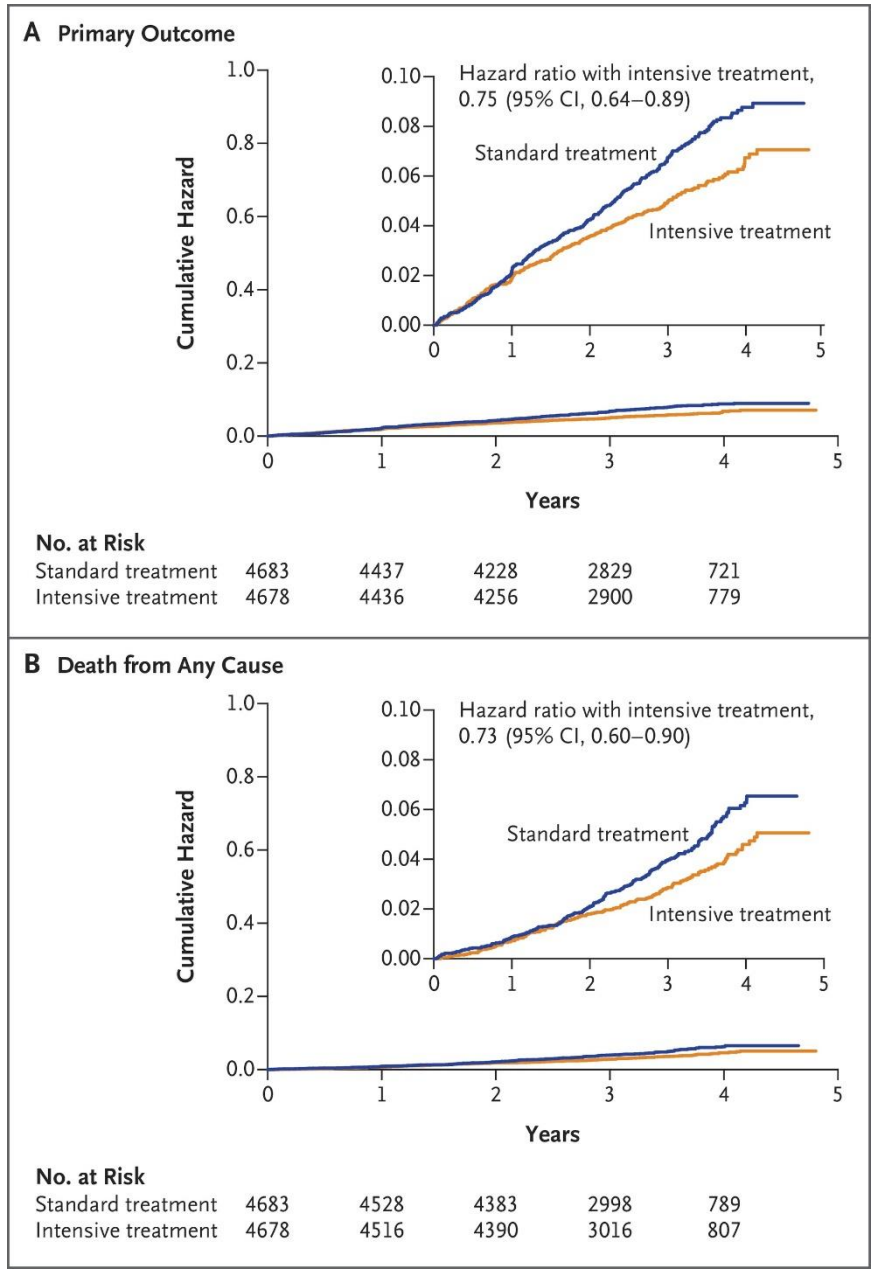
ACCORD Study Group, NEJM 2008

Blood pressure and CKD progression

Previous guidelines suggested higher BP targets in non-proteinuric CKD

SPRINT has changed this – now all high-risk patients should have a lower BP target to reduce CV risk

No effect on CKD progression
Increased risk of AKI in patients with CKD



SPRINT NEJM 2015

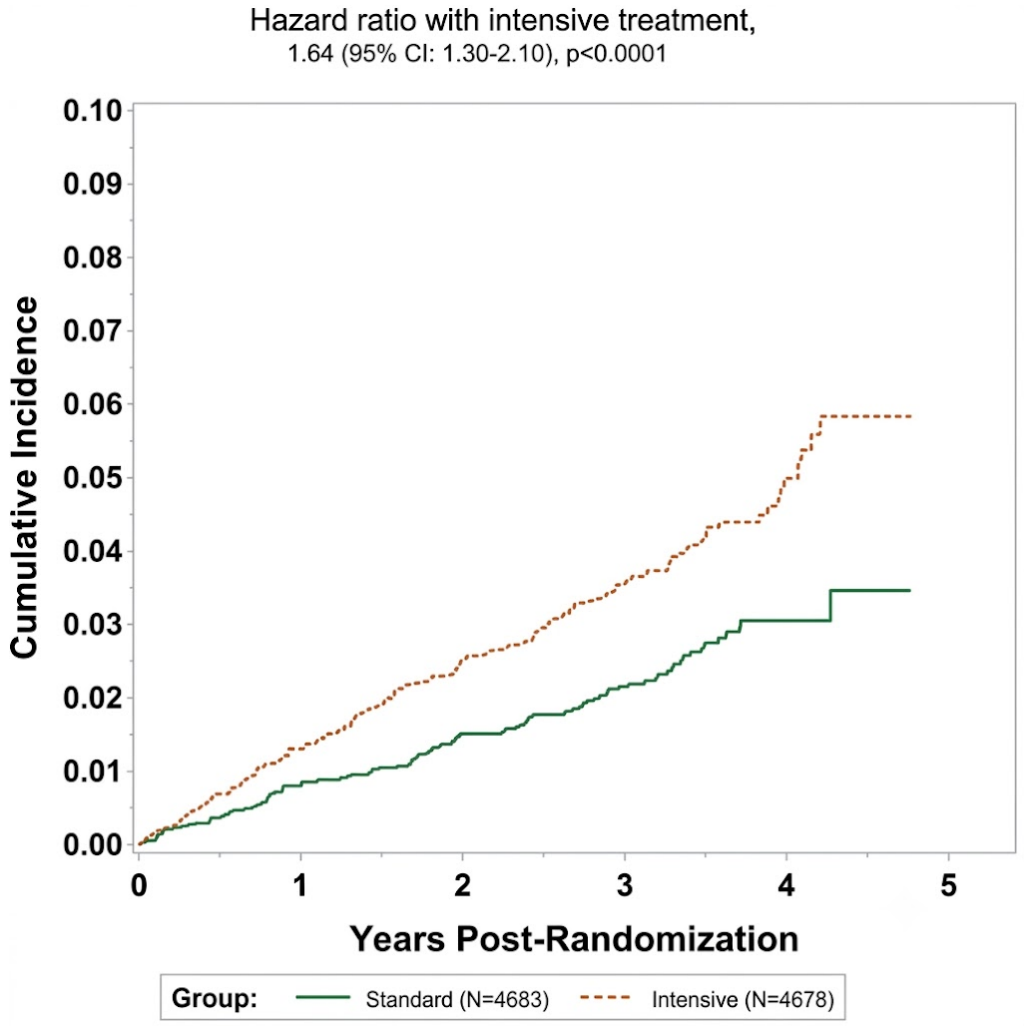
Risk of AKI with intensive BP control

Post-hoc analysis of SPRINT
Increased risk of AKI with intensive BP control

Most cases were mild and returned to baseline

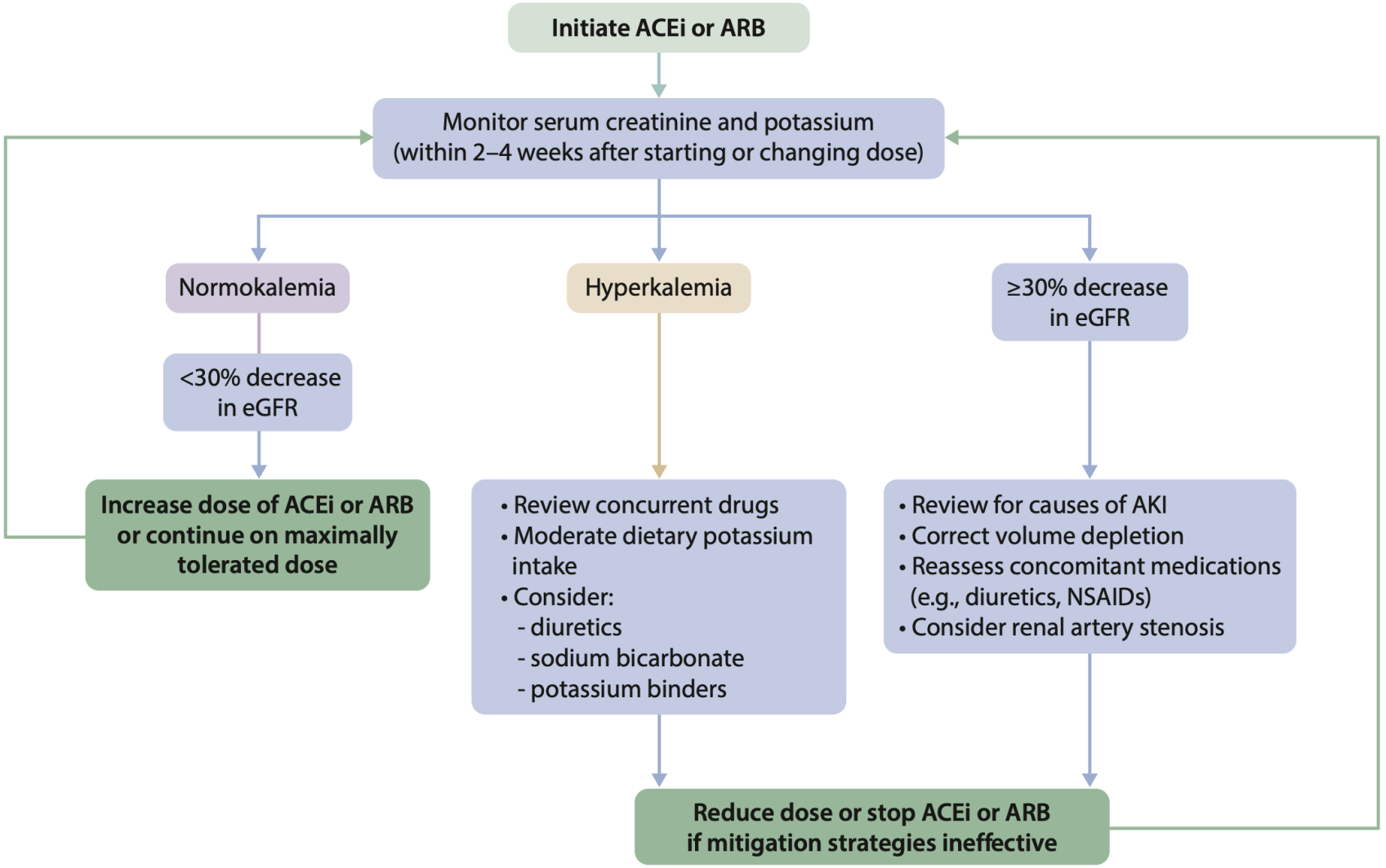
Subsequent analysis suggests higher CV risk in this group

Unclear if proteinuria modifies this effect



Reproduced from Rocco et al, AJKD 2018

RASi


Initiate ACEi or ARB
Monitor serum creatinine and potassium (within 2–4 weeks after starting or changing dose)
Normokalemia
Hyperkalemia
≥30% decrease in eGFR
<30% decrease in eGFR
Increase dose of ACEi or ARB or continue on maximally tolerated dose
• Review concurrent drugs
• Moderate dietary potassium intake
• Consider:
- diuretics
- sodium bicarbonate
- potassium binders
• Review for causes of AKI
• Correct volume depletion
• Reassess concomitant medications (e.g., diuretics, NSAIDs)
• Consider renal artery stenosis
Reduce dose or stop ACEi or ARB if mitigation strategies ineffective

BP Drug choices

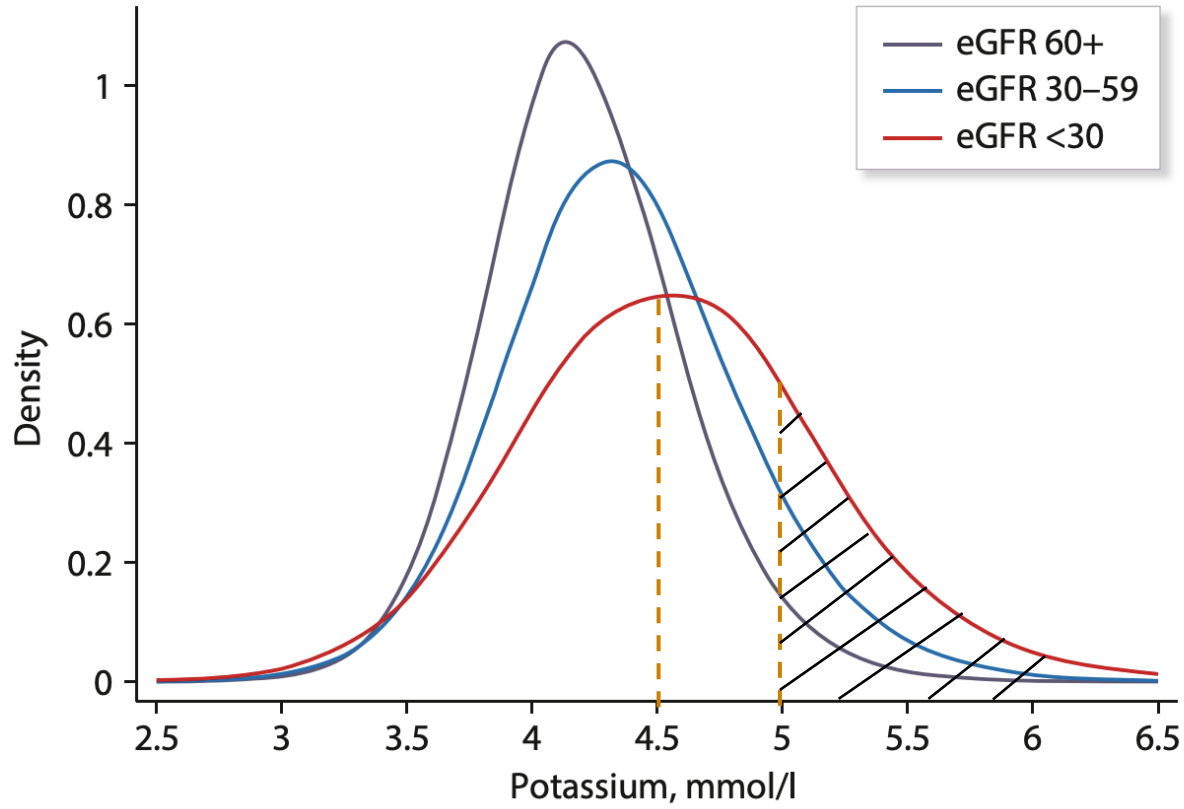
1. RAS blocker (ACEi or ARB)
2. Add CCB **or** thiazide
3. Add the third class (so all three together) if BP still uncontrolled

*BB with cardiac history (Coreg > metoprolol)

*Test for primary hyperaldosteronism

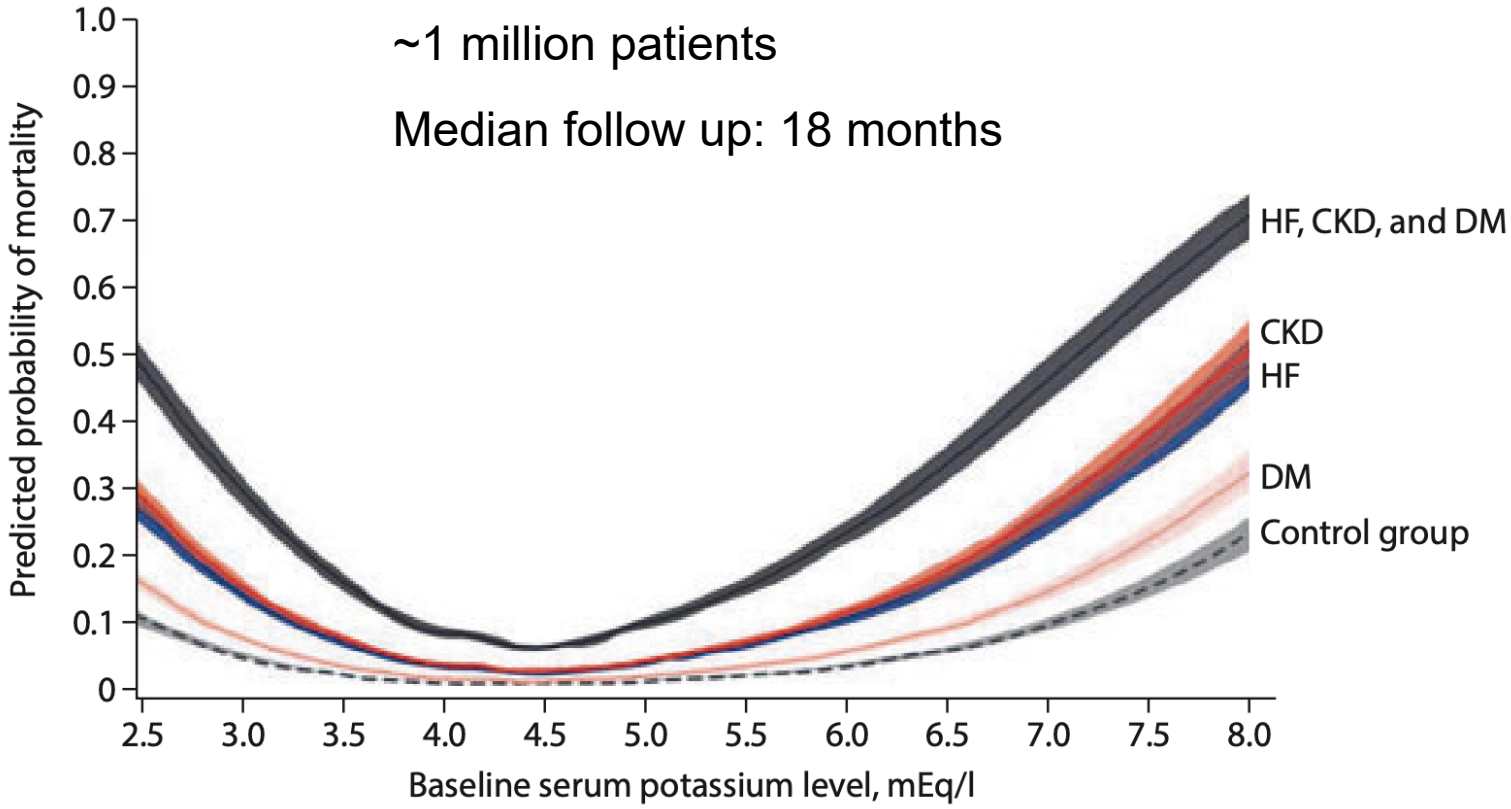
*Spironolactone (if tolerated) is an excellent BP medication

Hyperkalemia



Kovesdy, EHJ, 2018

K and mortality risk



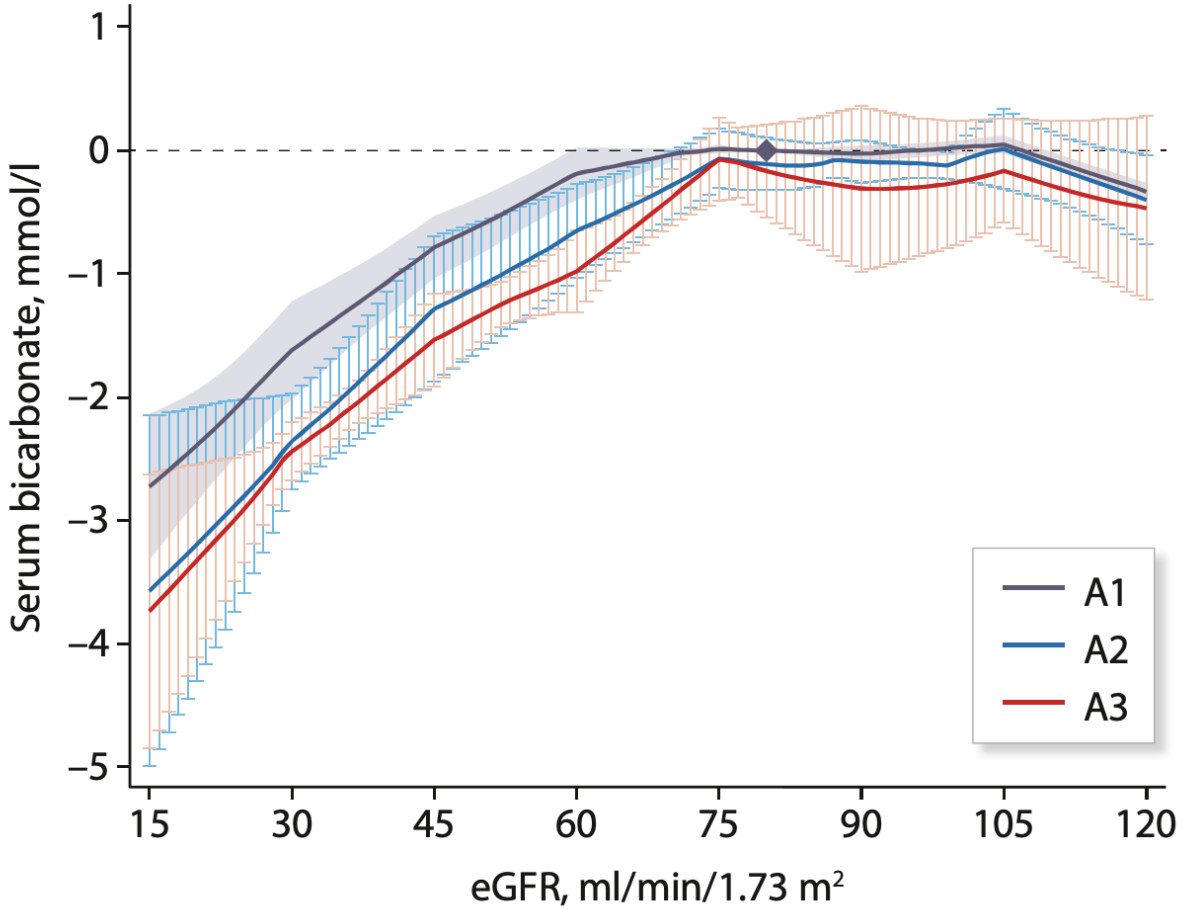
Collins, AJN, 2017

Binders

Feature	Patiromer	Sodium Zirconium Cyclosilicate (SZC)
Mechanism of Action	Calcium-potassium exchange polymer	Crystalline compound that traps K^+ in exchange for hydrogen and sodium cations
Counterion Content	1600 mg of calcium per 8.4 g of patiromer	Approximately 400 mg of sodium per 5 g of SZC
Cations Bound	Potassium, magnesium, and phosphate	Potassium
Initial Dosage	8.4 g orally once per day	10 g orally 3 times per day for up to 48 hours
Onset of Effect	4–7 hours	Starts within 1 hour; normokalemia typically at 24–48 hours
Administration Pearls	Separate from oral medications by at least 3 hours	No separation required generally; separate by 2 hours for pH-dependent medications
Adverse Effects	GI events, electrolyte disturbances (hypokalemia, hypercalcemia, hypomagnesemia)	Hypokalemia, edema, and milder GI events

Acidemia

Maintain HCO3 ≧ 18



Inker, AJKD, 2018

Reminder of Take Home Points

Definition of CKD (eGFR + UACR).

Therapies in diabetic and non-diabetic CKD.

Diet, Acid, Potassium…

The incidence of ESRD has been falling…

References

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 Apr;105(4S):S117-S314.

Ndumele, C, Rodriguez, F, Dixon, D. et al. 2026 AHA/ACC/ADA/ASN Guideline for the Prevention, Detection, Evaluation, and Management of Cardiovascular-Kidney-Metabolic Syndrome: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *JACC.* 2026 Jun, 87 (22_Supplement) e1889–e2007.