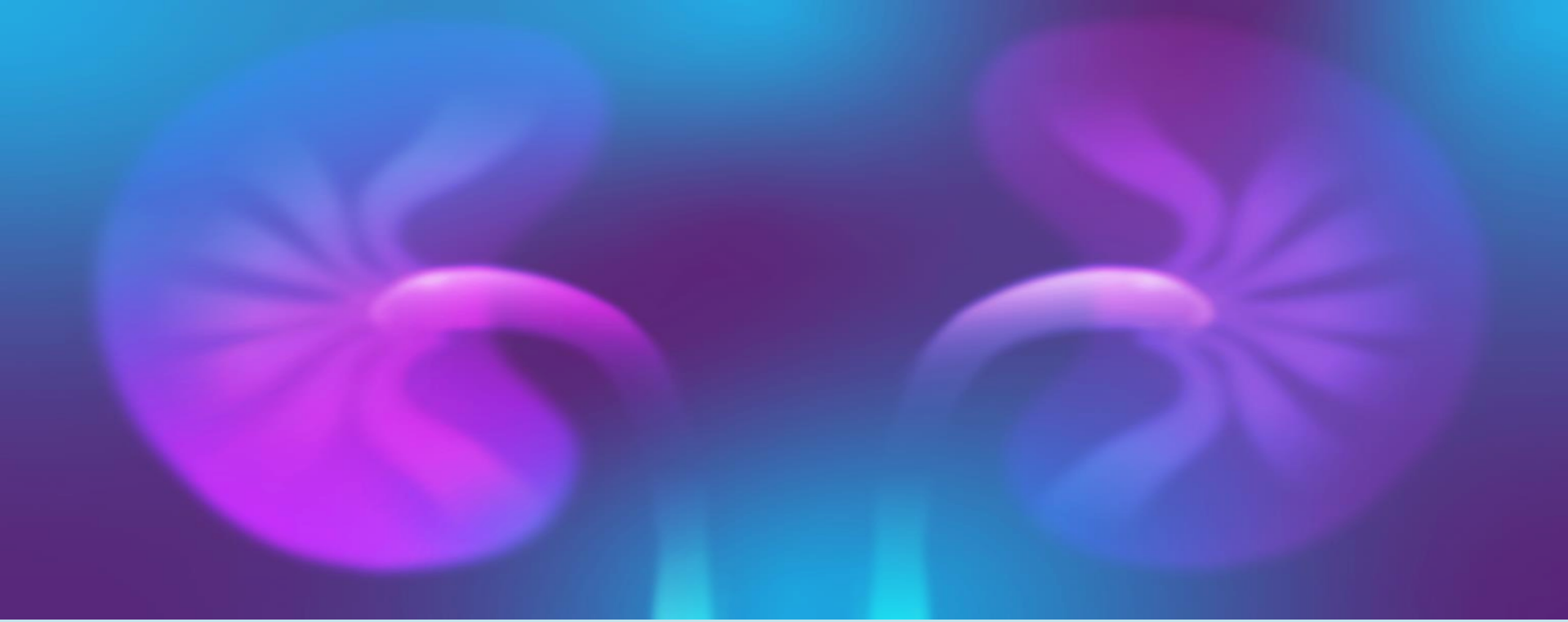


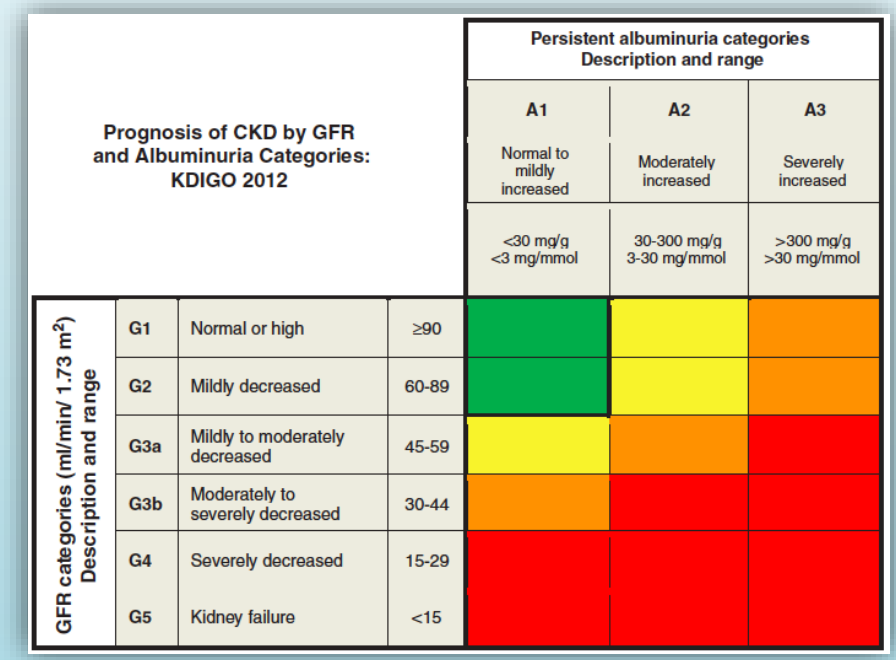
A Practical Approach to Managing Cardiovascular-Kidney-Metabolic Syndrome

Dr. Joseph Vassalotti, MD
12/03/2024

Practical Approach to Managing Cardiovascular-Kidney-Metabolic (CKM) Syndrome: Matching the Risk to the Interventions

Tuesday 3 December 12:00 – 1:00pm

Joseph A. Vassalotti, MD
Chief Medical Officer
National Kidney Foundation
Clinical Professor of Medicine,
Icahn School of Medicine at Mount Sinai
@Joe_Vassalotti
joseph.vassalotti@mountsinai.org



Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30-300 mg/g 3-30 mg/mmol	A3 Severely increased >300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m²) Description and range	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			

National Kidney Foundation™

Icahn School of Medicine at Mount Sinai

Disclosure of Financial Relationships

Joseph A. Vassalotti, MD

Support for this program is provided by Abbott.

This speaker is presenting at the request of Abbott.

This speaker disclosed relationships with an entity producing, marketing, reselling, or distributing health care goods or services consumed by, or used on, patients.

Consultantship

Novo Nordisk, Inc (US Nephrology Advisory Board)

Renalytix, plc (CKD biomarkers)

Sanofi, Inc (influenza in CKD)

Honoraria

As above

Research Grants/Contracts

No commercial grants

Speaker's Bureau

No speaking roles in any consultantship

Objectives

- Detect and risk stratify CKD with both estimated GFR (eGFR) and urine albumin-creatinine ratio (uACR).
- Assess kidney and cardiovascular risk using heat maps and prediction equations.”
- Use risk stratification to inform kidney and cardioprotective interventions.
- Integrate Cardiovascular-Kidney-Metabolic (CKM) focused screening and management into routine practice.

Case Presentation

- 65-year-old man
- Type-2 diabetes since 2005, dyslipidemia and hypertension complicated by Heart Failure with preserved Ejection Fraction (HFpEF).
- Diabetic retinopathy
- Medications:
  - ✓ lisinopril 20 mg daily,
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- BP 136/84 P72 BMI 32 kg/m^2

? You are doing the initial evaluation.

What CKD tests do you order?

What CKD Tests do you order?

- Creatinine – which panel?
- Cystatin C – no available panel
- Urinalysis
- Urine albumin-creatinine ratio
- Urine protein-creatinine ratio

What is the recommended test of kidney function for outpatients in routine practice?

A. Cockcroft Gault creatinine clearance

B. eGFR using the MDRD Study equation

C. eGFR using the 2009 CKD-EPI equation using creatinine with and without a race coefficient

D. eGFR using the 2009 CKD-EPI equation using creatinine without a race coefficient

E. eGFR using the 2021 CKD-EPI equation using creatinine refit without a race coefficient.

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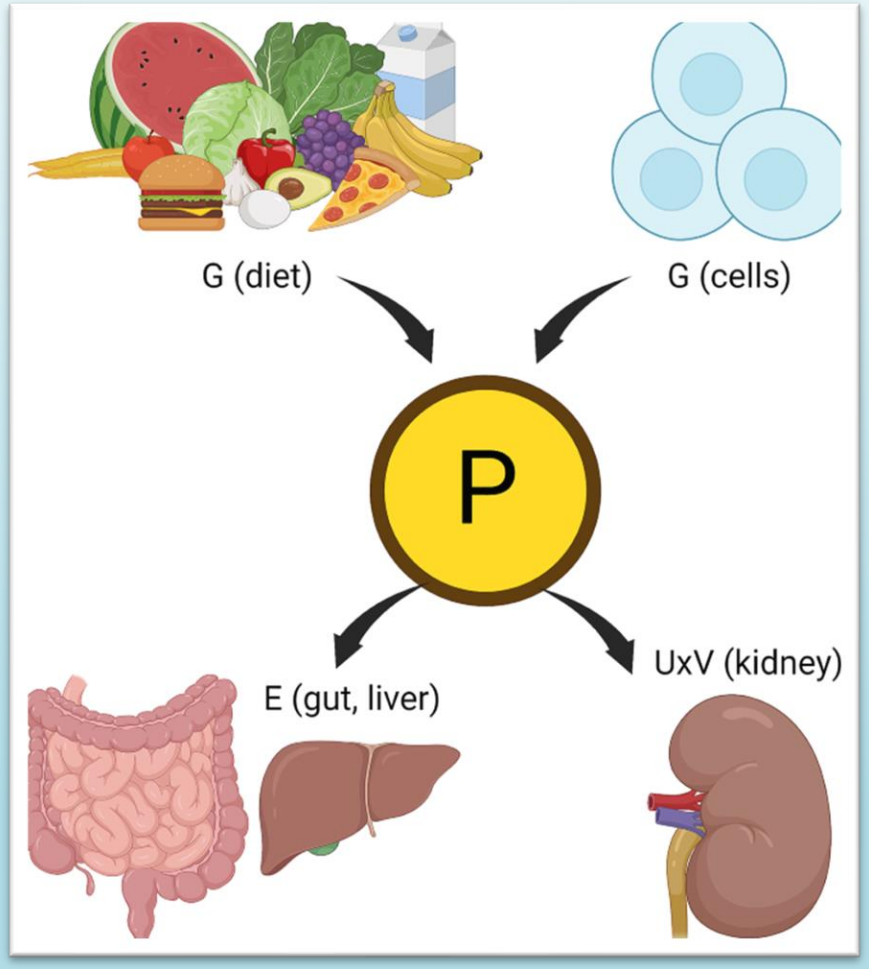
General Concept
GFR and non-GFR determinants for a plasma biomarker (P)

GFR determinants include:
Urine concentration of P (U) and
Urine volume (V).

Non-GFR determinants include:
Generation (G)
Non-renal elimination (E)
Tubular secretion and
Tubular reabsorption (not labeled)



Farrell DR, Vassalotti, JA. Screening, identifying, and treating chronic kidney disease: why, who, when, how, and what? *BMC Nephrology* 2024; 25(1):34

Race-Free eGFR Equations

2020 National Kidney Foundation (NKF) and American Society of Nephrology (ASN) Task Force was formed to develop future recommendations.

2021 **New Equations Developed and Published**[1]
2021 CKD-EPI Creatinine
2021 CKD-EPI Creatinine-Cystatin C

2021 NKF/ASN Task Force Final Recommendations Published[2]

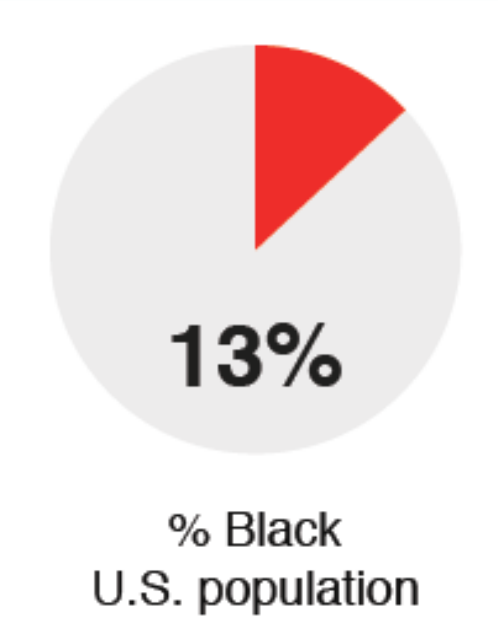
1) Implement 2021 CKD-EPI creatinine equation in all laboratories
2) Facilitate use of cystatin C in individuals at increased risk of CKD
3) Further research on eGFR with new markers to eliminate race and ethnic disparities

1. Inker LA, Eneanya ND, Coresh J et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med.* 2021; 385:1737-1749

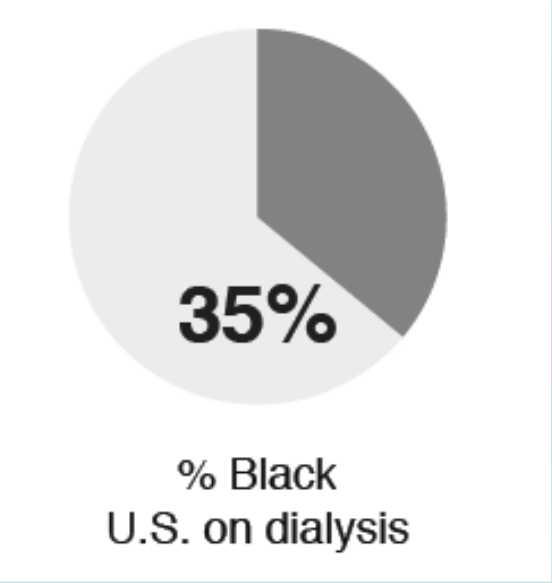
2. Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease. Am J Kidney Dis. 2021;78(1):103-115.

Kidney Health Inequity

- **Kidney health inequity** includes disproportionate prevalence of diabetes, hypertension, CKD and dialysis treatment for Blacks or African Americans and other races.



- **Kidney health inequity** includes lower access to nephrology care, home dialysis and kidney transplant for Blacks or African Americans and other races.



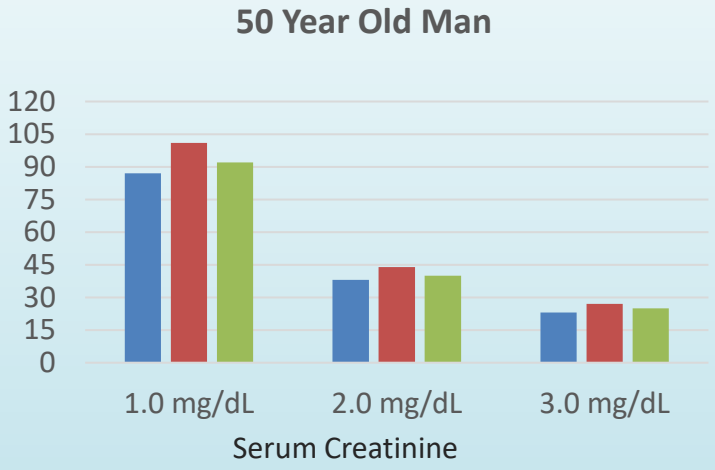
United States Renal Data System www.usrds.org
CDC CKD Surveillance System https://nccd.cdc.gov/CKD

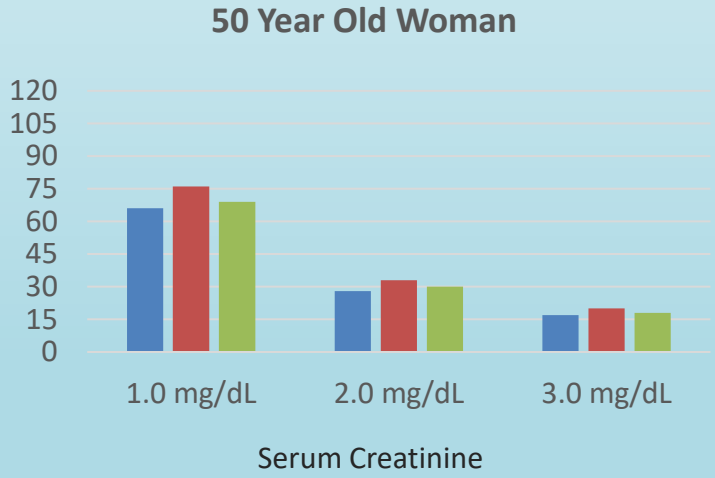
"Race is not dichotomous, and models that attempt to distill its complexity and heterogeneity as such introduce more bias and imprecision than 3.7 mL/min/1.73 m^2 of estimated GFR. Moreover, dermal pigmentation does not modify or mediate kidney disease risk. Socioeconomic status does, racism does, and genetic ancestry may."

JACC: Cardiovascular Interventions 2023; 16: 2309-2320.

Comparison of CKD-EPI eGFRcr Equations 2009 vs 2021

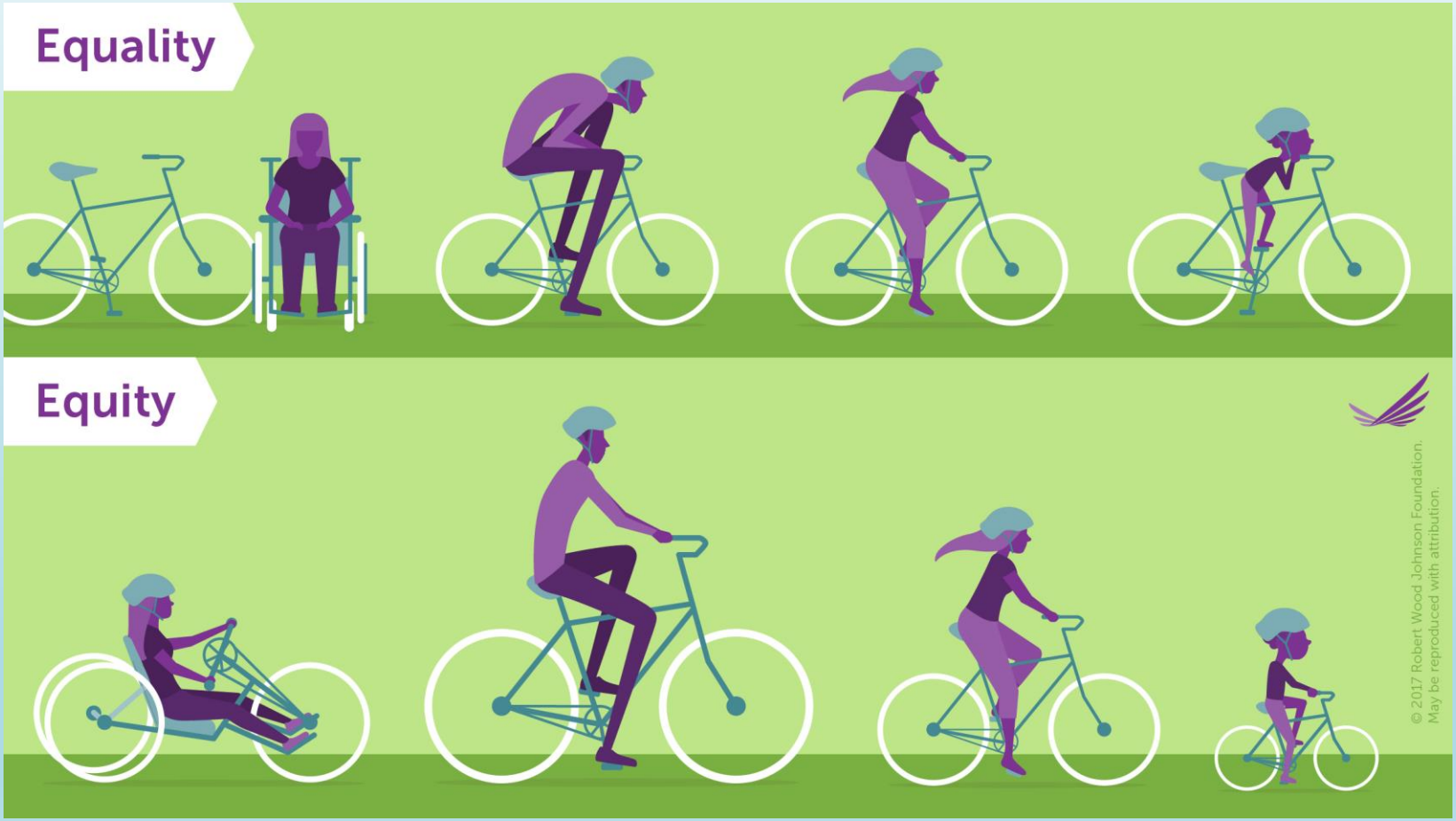
- Blacks or African Americans will have slightly lower eGFR.
- All others will have slightly higher eGFR.
- The “e” in eGFR stands for estimate.



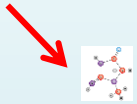


Inker LA, Eneanya ND, Coresh J et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med.* 2021; 385:1737-1749

Health Equality versus Health Equity Concepts: Bike Graphic



Serum Creatinine and Cystatin C

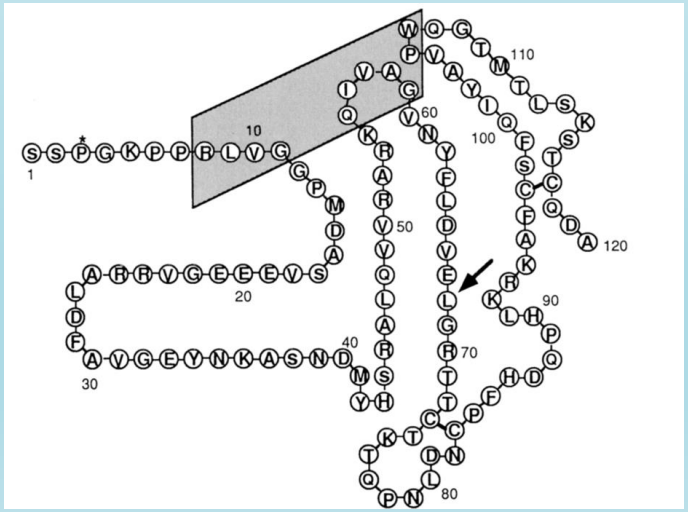


Creatinine

- Size ~ 1 aa
- Kidney function biomarker
- Skeletal Muscle source
- Dietary source
- Tubular secretion elimination

Cystatin C

- 120 aa, 13 kDa protein
- Kidney function biomarker
- Inflammatory marker
- All tissues - minimal muscle and diet influence



Grubb, AO. Cystatin C properties and use as a biomarker. *Adv Clin Chem*. 2000;35:63-99

Creatinine and Cystatin C
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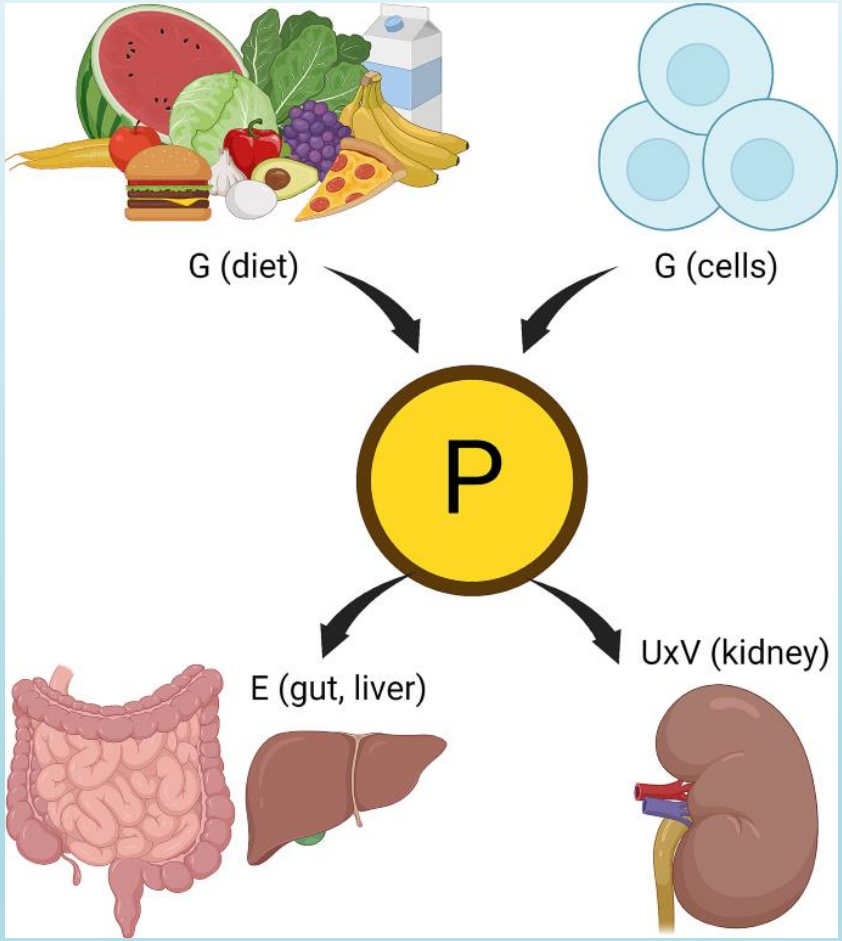


Farrell DR, Vassalotti, JA. Screening, identifying, and treating chronic kidney disease: why, who, when, how, and what? *BMC Nephrology* 2024; 25(1):34

Clinical contexts in which Cystatin C may yield more accurate estimates of GFR

Serum Creatinine GENERATION IS LOW

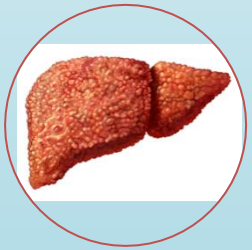
ELDERLY

INACTIVITY
AMPUTATION

MALIGNANCY

VEGGIE DIET

HIV



CIRRHOSIS

Serum Creatinine GENERATION IS HIGH

WEIGHT-
LIFTING

MEAT DIET

PROTEIN
SUPPLEMENTS

Drugs that inhibit tubular creatinine secretion

TRIMETHOPRIM
FENOFIBRATE
CIMETIDINE
DOLUTEGRAVIR/RALTEGRAVIR
COBICISTAT
RITONAVIR
RILPIVIRINE
TYROSINE KINASE INHIBITORS

Advantages, limitations, and clinical considerations in using cystatin C to estimate GFR
Kidney360 2022;3(10):807-814.

Suggestions for Indications for Cystatin C Testing

- $eGFR_{cr}$ 45-60 ml/min/1.73 m^2 without markers of kidney damage or CKD stage G3aA1
- Conditions associated with non-GFR determinants of creatinine
- Near clinical cut points in decision making
- Clinicians could consider eGFR 60-74 without markers of kidney damage to confirm absence of CKD
- Area for clinical investigation

Frequently Asked Questions about GFR Estimates
https://www.kidney.org/sites/default/files/441-8491_2202_faqs_aboutgfr_v5.pdf

What is the recommended test of kidney damage for outpatients in routine practice?

A. 24-hour urine protein

B. 24-hour urine creatinine clearance

C. Urine dipstick for protein

D. Urine protein-creatinine ratio

E. Urine albumin-creatinine ratio

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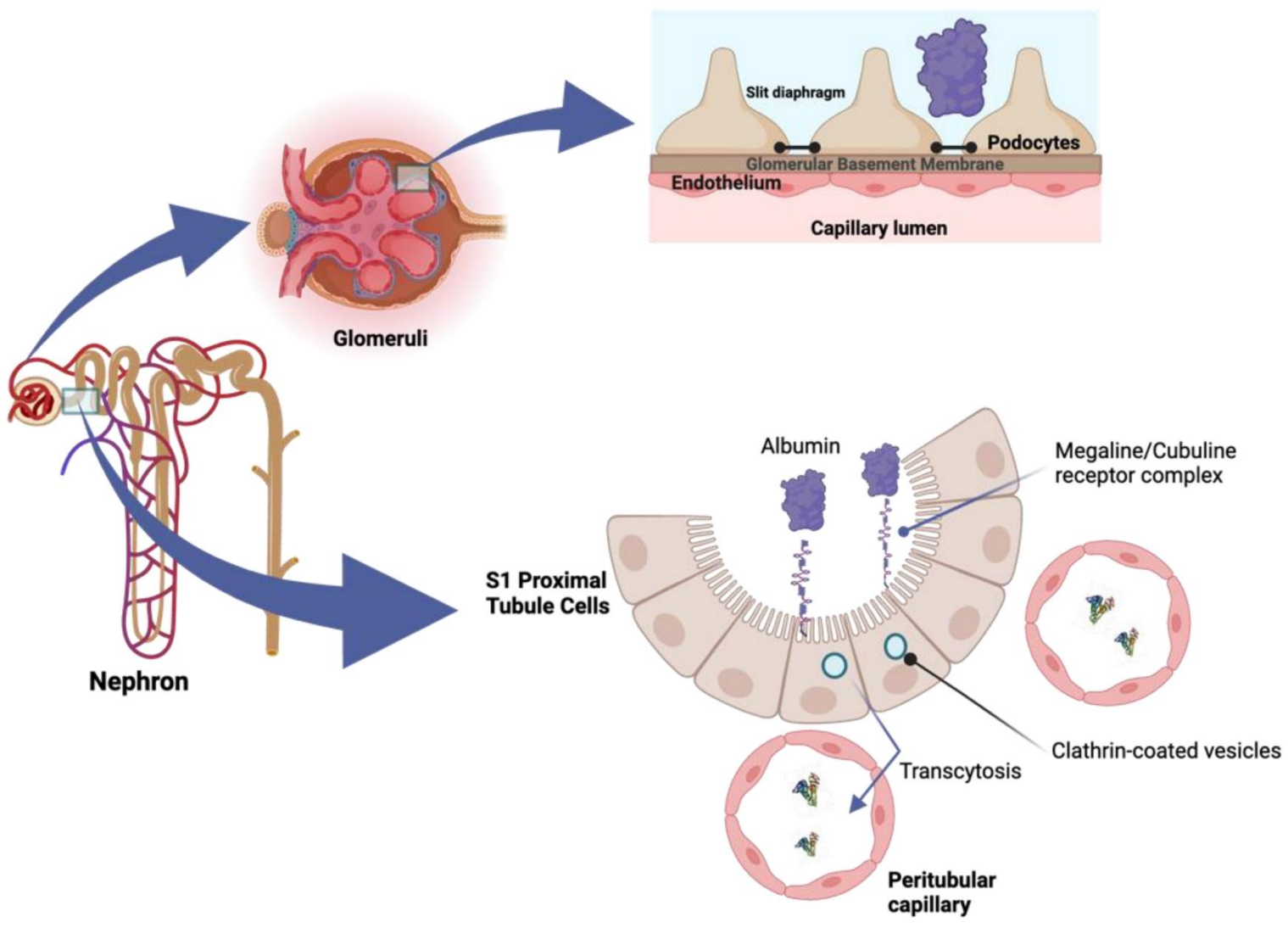
Albuminuria Mechanism



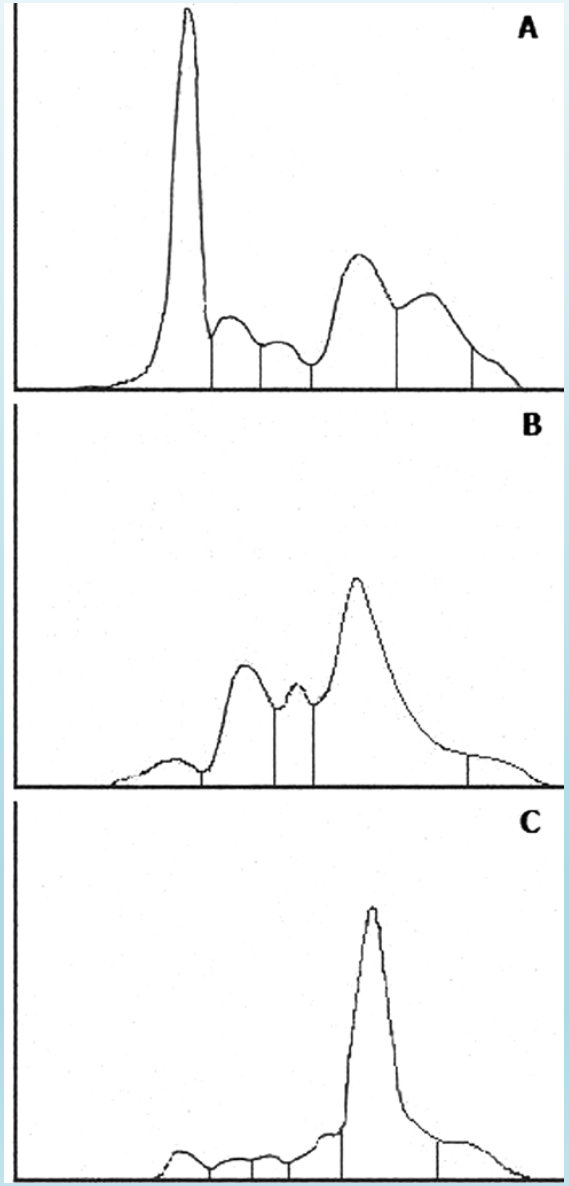
J. Clin. Med. 2024:13(3):777.

Proteinuria subtypes

Glomerular
60 to 80% albumin

Tubular

Overflow



Nephrology at Point of Care 2016;2(1)e8-e16

Albuminuria is the preferred kidney damage test

Albuminuria Or Proteinuria Description+	Albuminuria Or Proteinuria Category	Albumin mg/24-hour urine+	uACR+ mg/g	uPCR* mg/g	Dipstick Proteinuria
Normal to mildly increased	A1	< 30	< 30	< 150*	Negative to trace
Moderately increased	A2	30 to 300	30 to 300	150 to 650*	Trace to +1
Severely Increased	A3	> 300	> 300	> 650*	+2 or greater
Nephrotic Range	A3 Nephrotic Range	>2,000*	>2,000*	>3,500+ (by definition)	+2 or greater

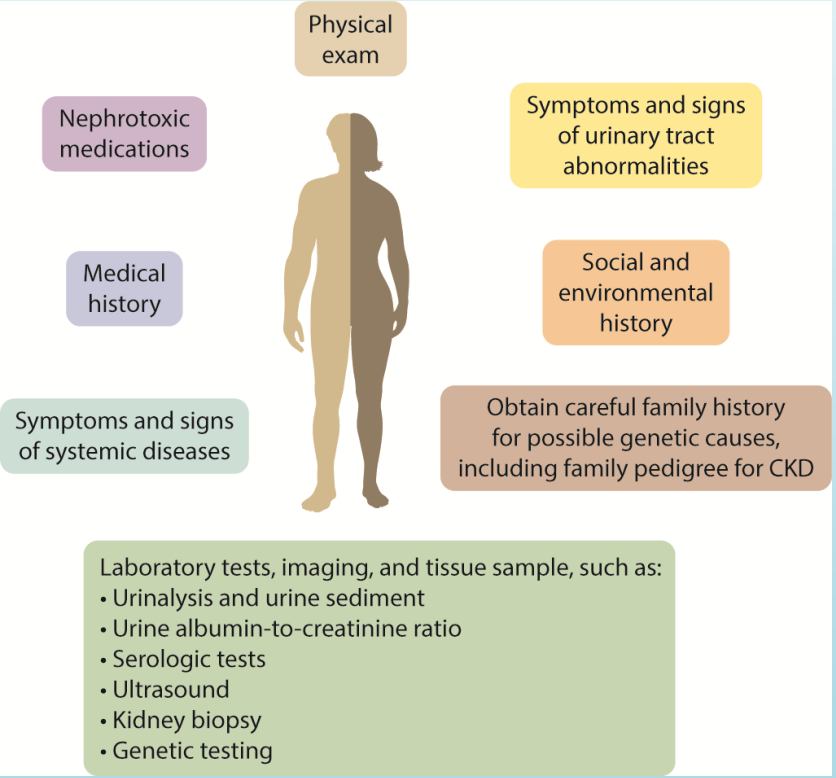
+These categories are adapted from KDIGO; Kidney Disease Improving Global Outcomes.

*These categories are from a meta-analysis of uPCR to uACR approximate conversion. Ann Intern Med 2020;173(6):426-435

J Appl Lab Med. 2023;8(4):789–816.

Evaluation – CKD Definition

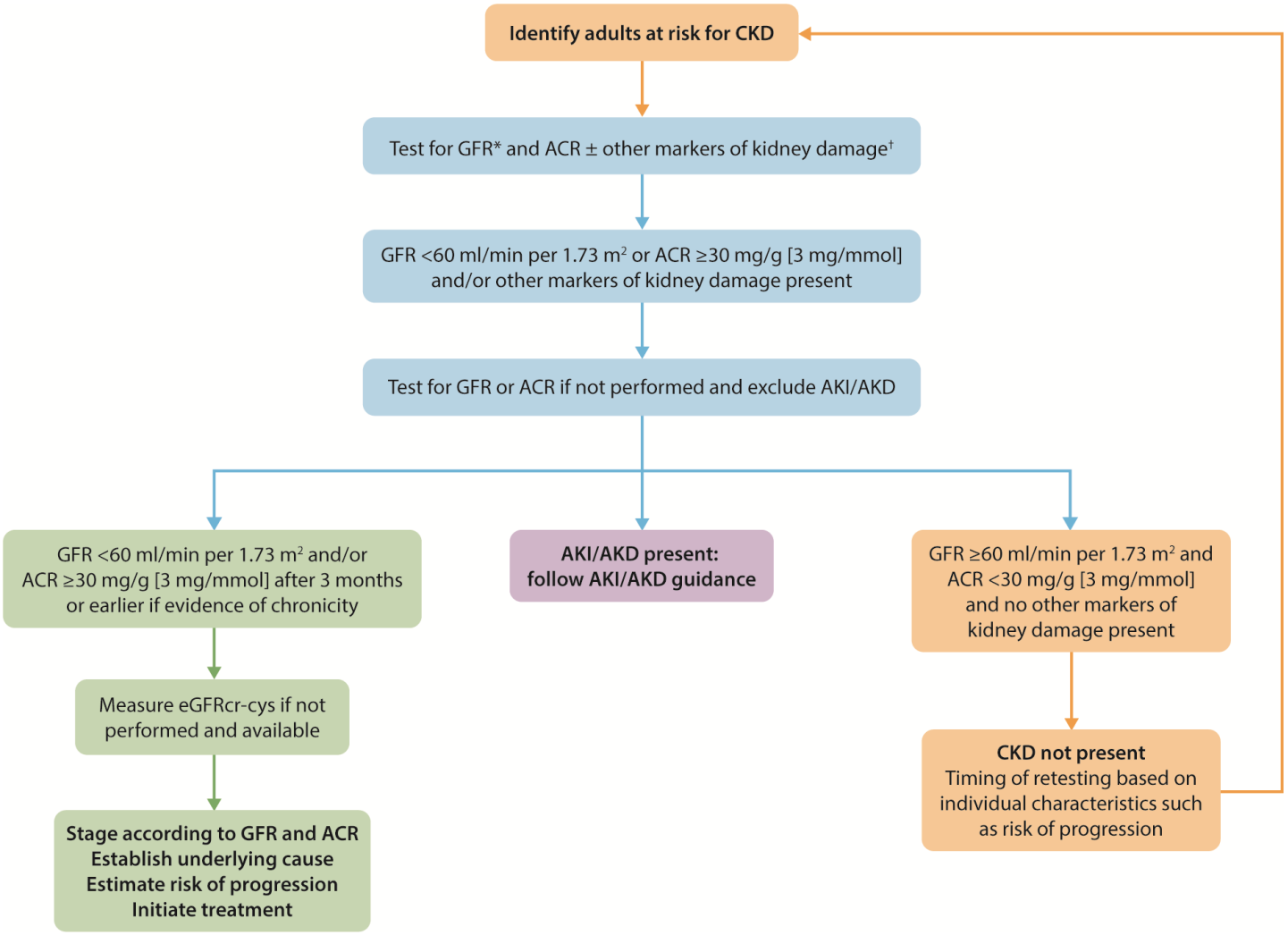
CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. The definition includes many different markers of kidney damage, not just decreased GFR and ACR and the cause of CKD should be actively sought (Figure). CKD is classified according to **C**ause, **G**FR, and **A**CR to establish severity and guide the type and timing of interventions.



Kidney Int. 2024;105(4):S117-S314.

Evaluation – Distinguish Between AKD and CKD

It is important to distinguish between AKD and CKD and to establish chronicity.



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Case Presentation

- 65-year-old man
- Type-2 diabetes since 2005, dyslipidemia and hypertension complicated by Heart Failure with preserved Ejection Fraction (HFpEF).
- Diabetic retinopathy
- Medications:
  - ✓ lisinopril 20 mg daily,
  - ✓ metoprolol succinate 100 mg daily,
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  - ✓ aspirin 81 mg daily,
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- BP 136/84 P72 BMI 32 kg/m^2

? You are doing the initial evaluation.

What CKD tests do you order?

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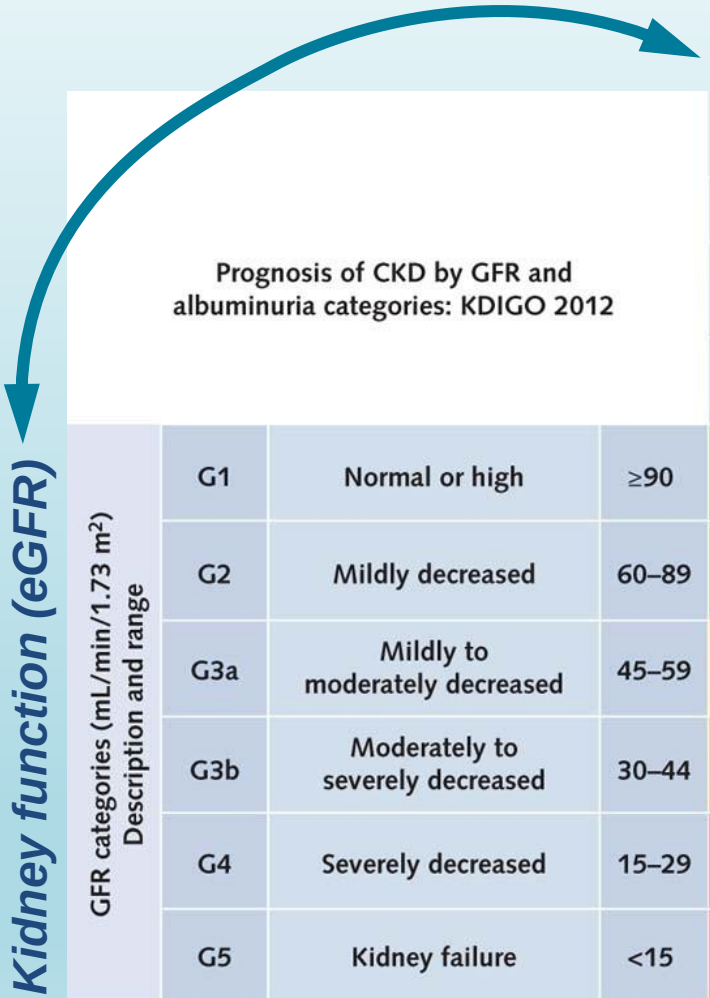
- **Creatinine 1.40 + eGFR 46 = CKD G3a**
- **uACR 2200 mg/g = CKD A3 or CKD G3aA3**
- **uPCR 3600 mg/g**

The CKD tests: eGFR and uACR



Kidney damage (uACR)

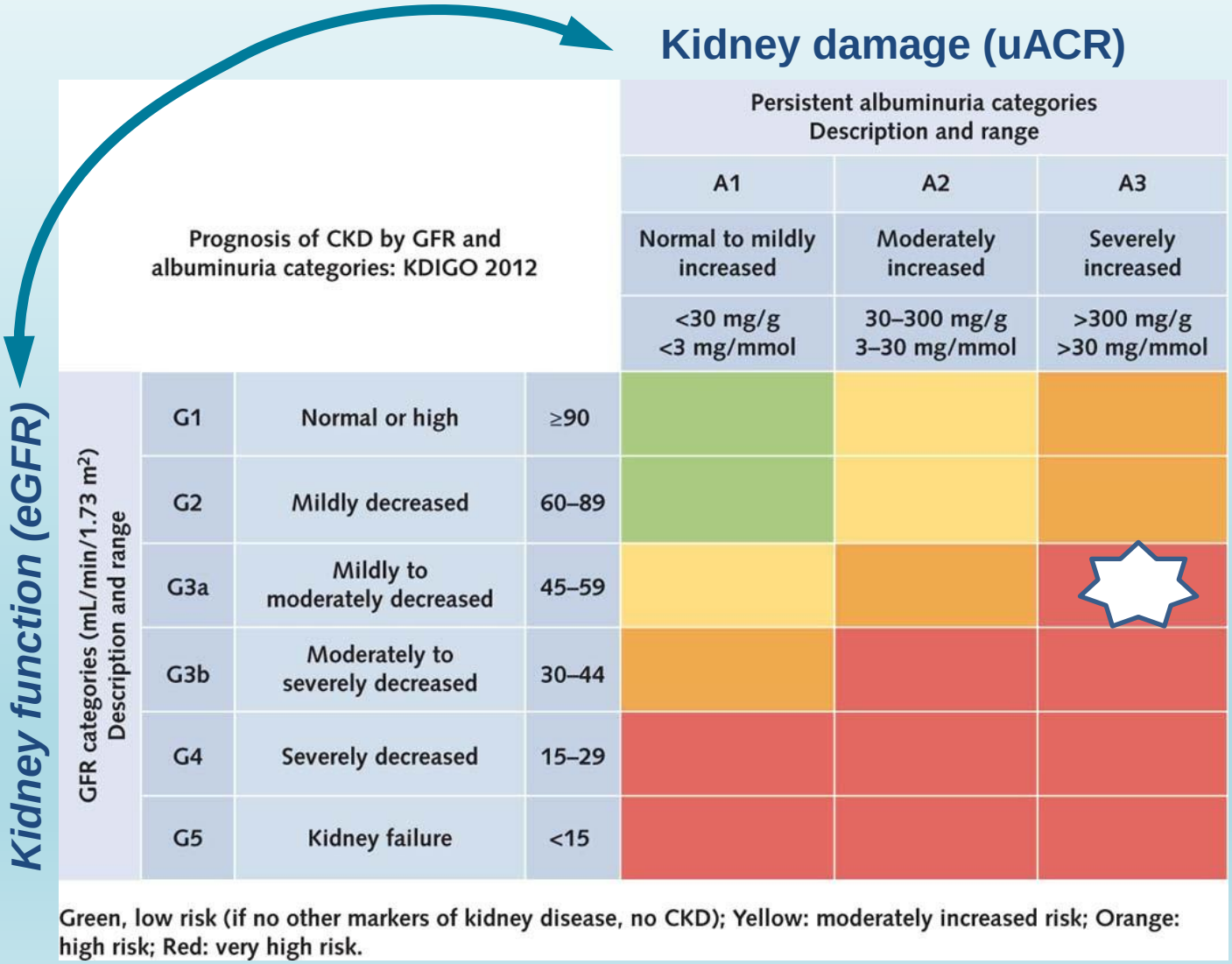
Kidney function (eGFR)

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				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
GFR categories (mL/min/1.73 m²) Description and range	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.

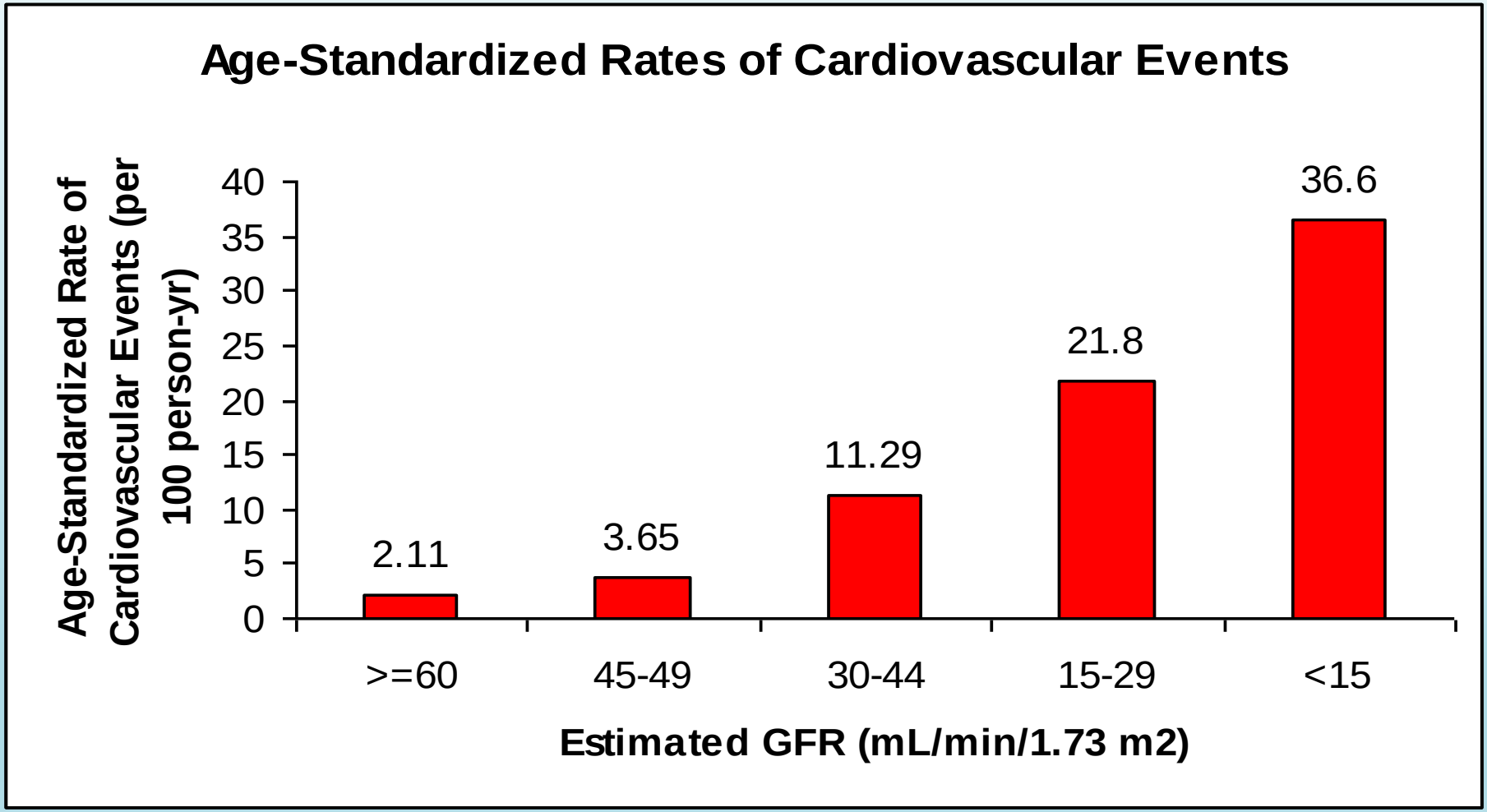
Kidney Int. 2024;105(4):S117-S314.

The CKD tests: eGFR and uACR



Kidney Int. 2024;105(4):S117-S314.

CKD Severity Predicts CVD Risk: Cardiovascular events by eGFR

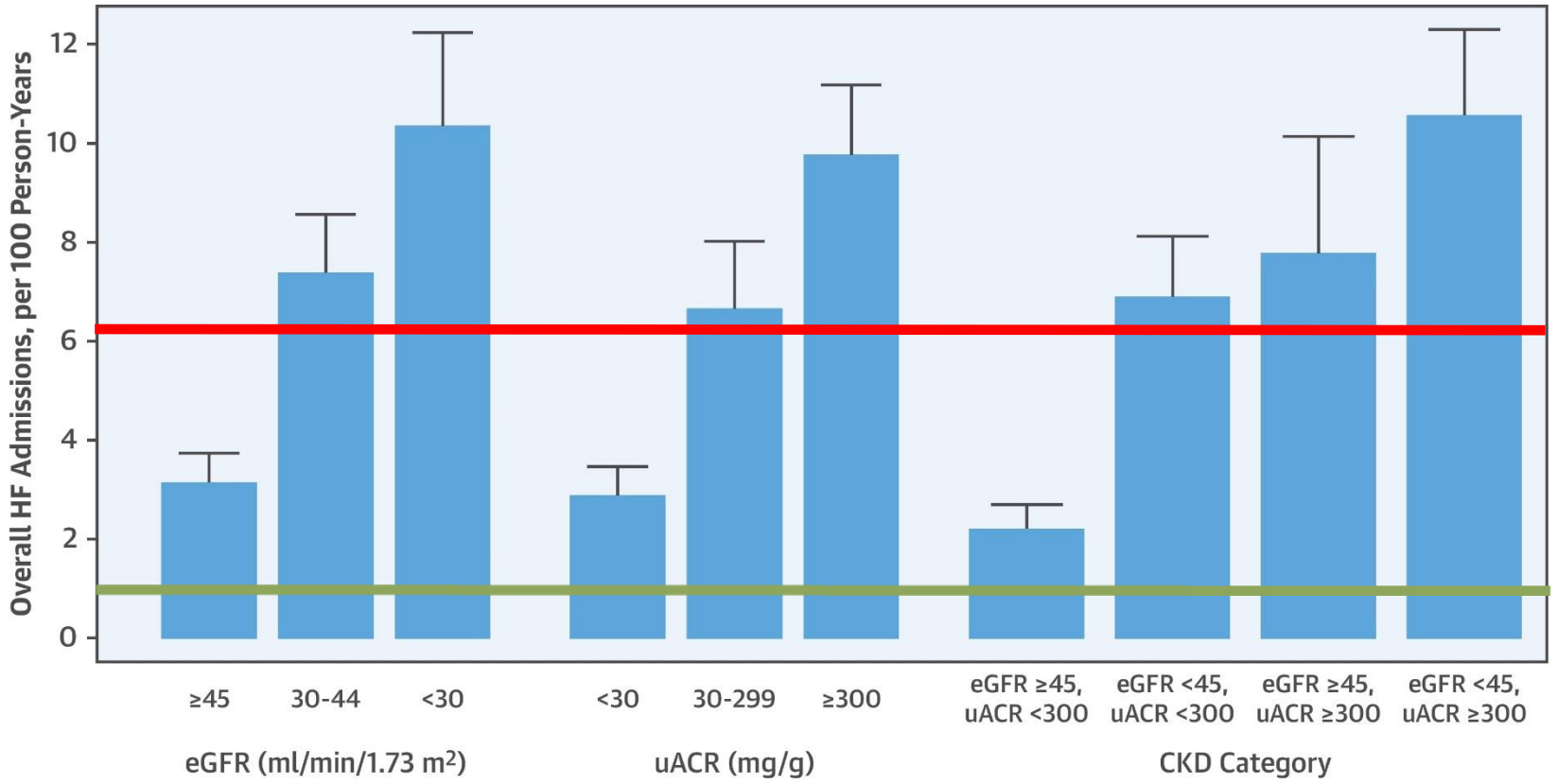


Kaiser outpatients with at least one sCr
n = 1,120,295

Go AS, et al: NEJM. 2004: 351;1296-1305

Heart Failure Hospitalizationby eGFR and uACR

CENTRAL ILLUSTRATION: Heart Failure in Chronic Kidney Disease



Bansal, N. et al. J Am Coll Cardiol. 2019;73(21):2691-700.

CRIC cohort n = 3,791, unadjusted rates shown, & Figure adapted with
Crude CKD cohort rate 5.8
Crude population rate 0.5

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➢ **Creatinine 1.40 + eGFR 46 = CKD G3a**

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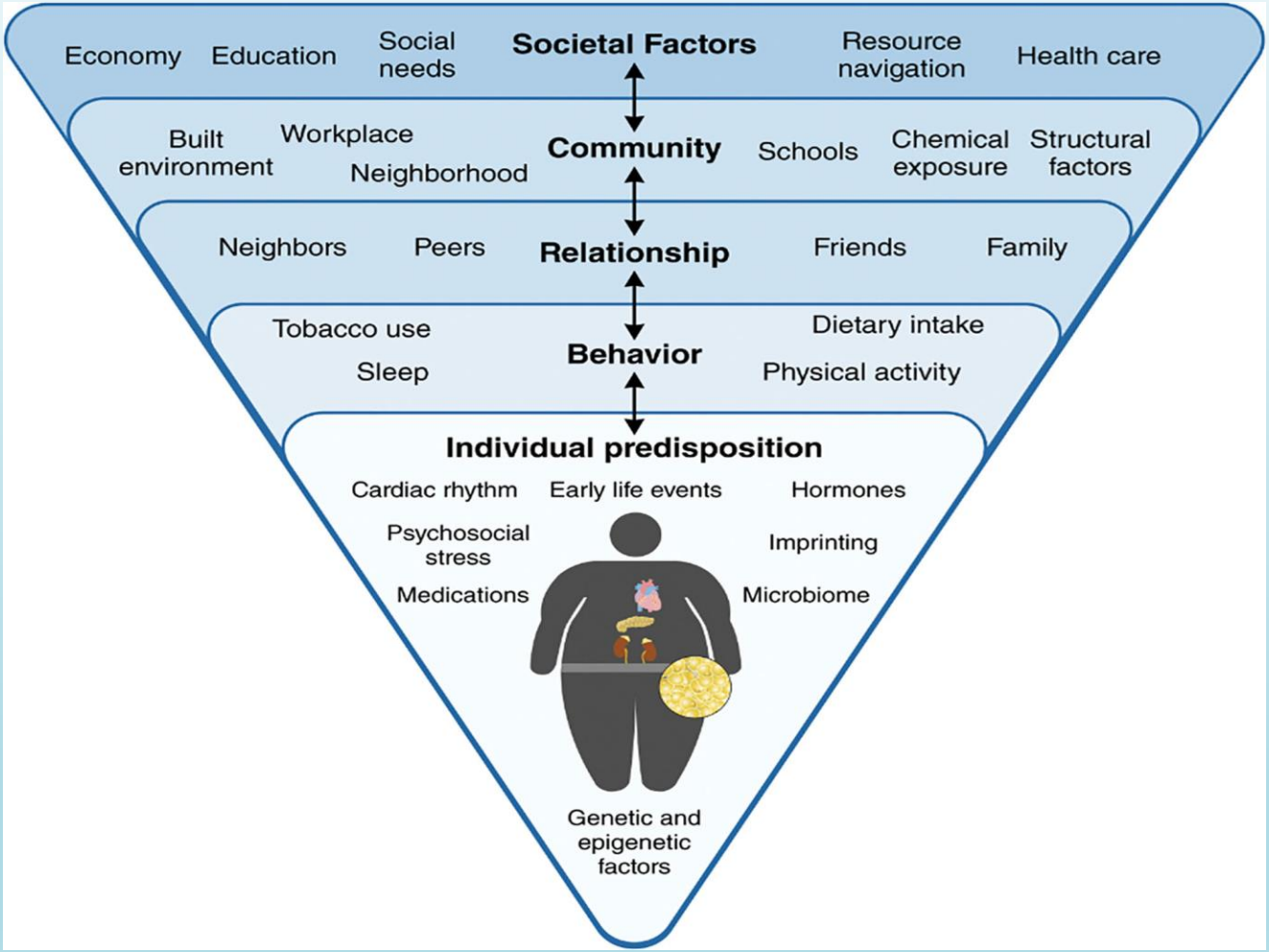
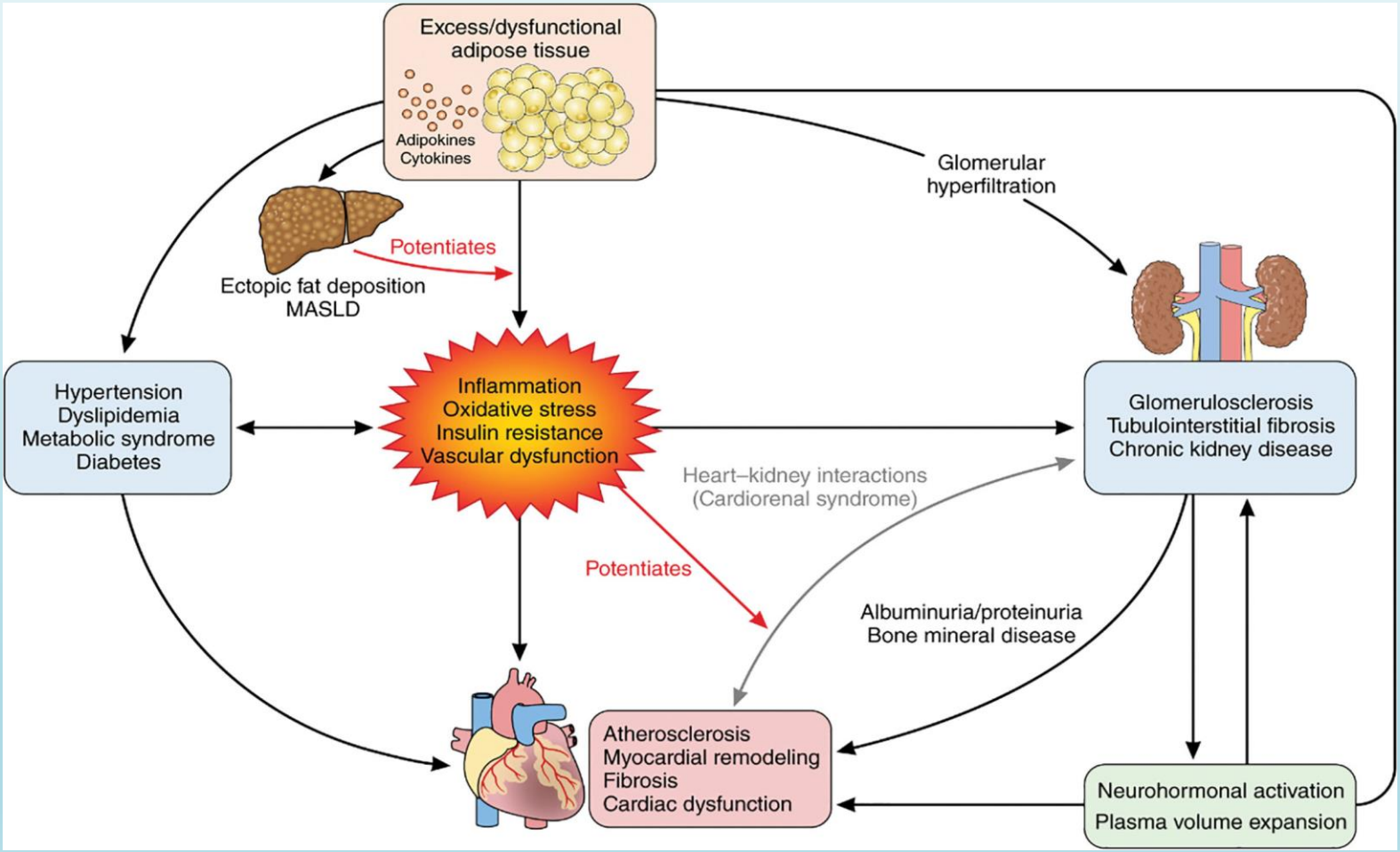
- BMI 32 kg/m^2

Obesity Initiation



Circulation. 2023;148(20):1636-1664.

Conceptual Diagram of the Cardiovascular-Kidney-Metabolic (CKM) Syndrome



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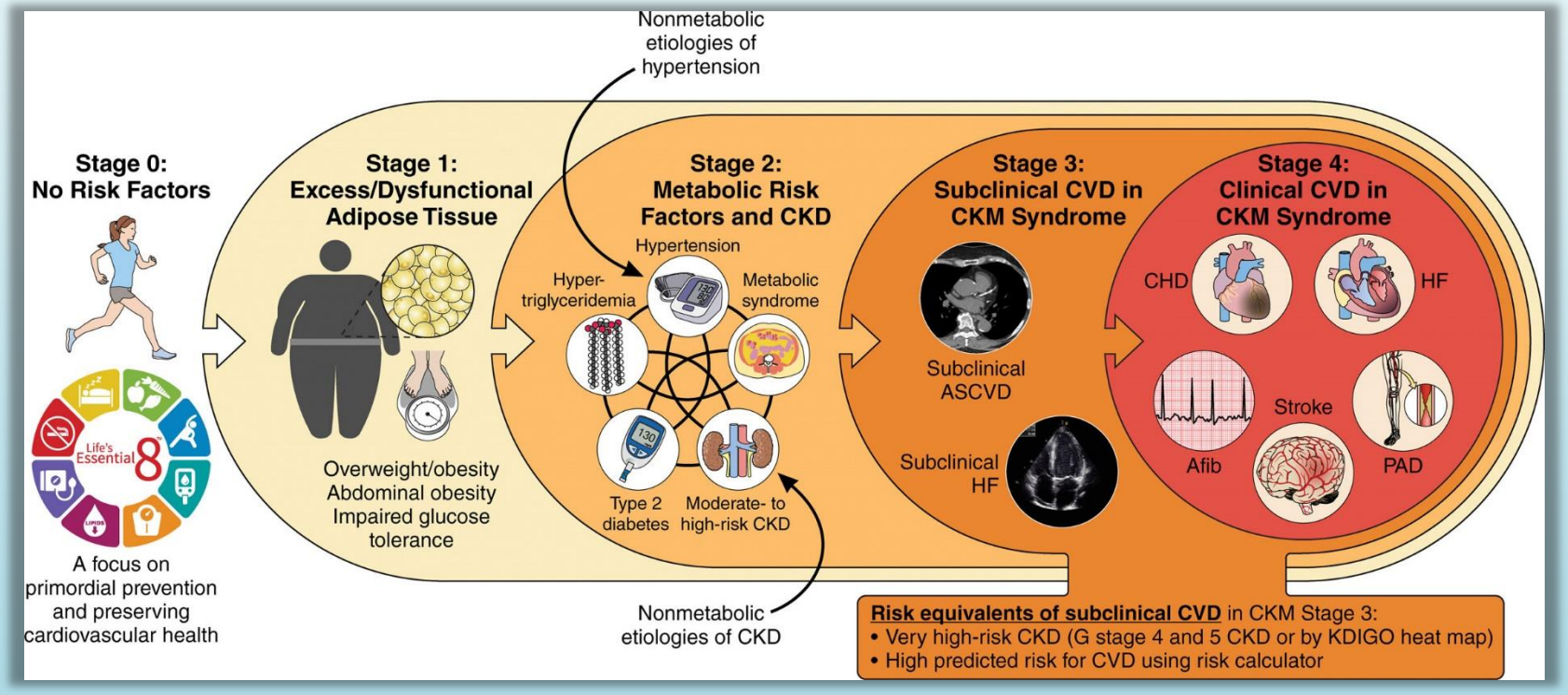
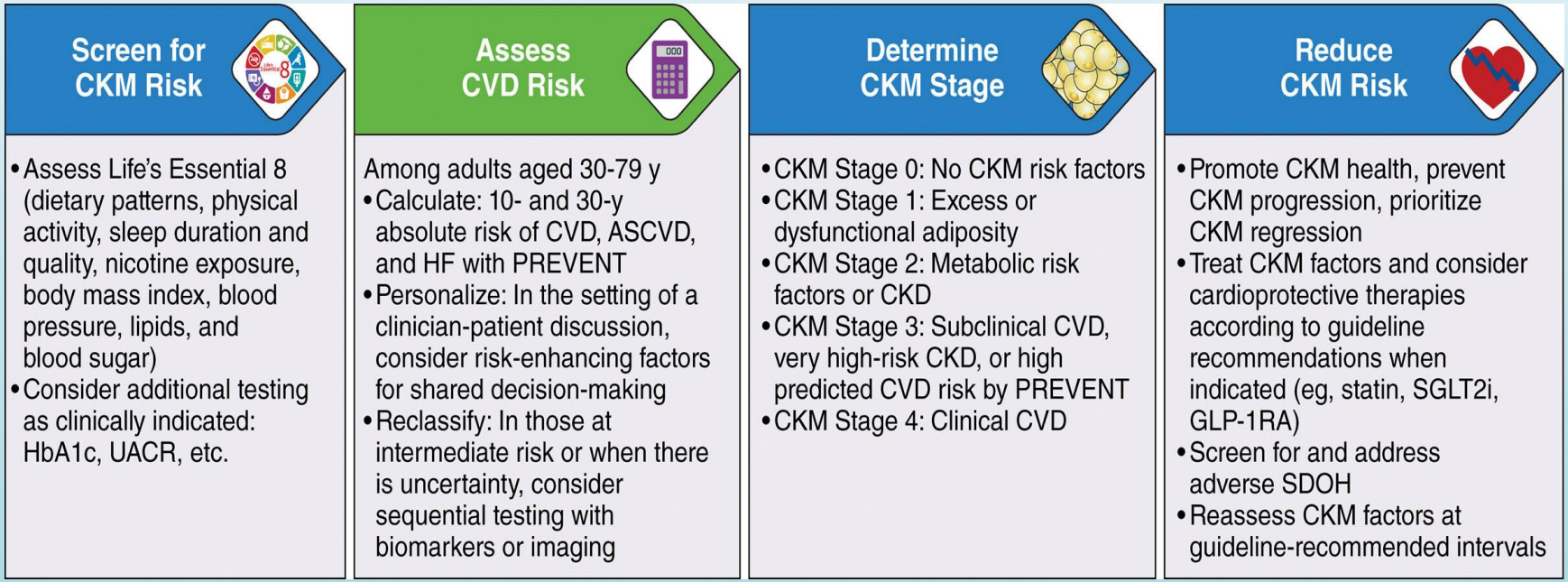
Cardiovascular-Kidney-Metabolic (CKM) Syndrome



Ndumele CE, et al. Circulation. 2023;148:1606-1635.

Conceptual Framework for the Cardiovascular Kidney Metabolic Syndrome



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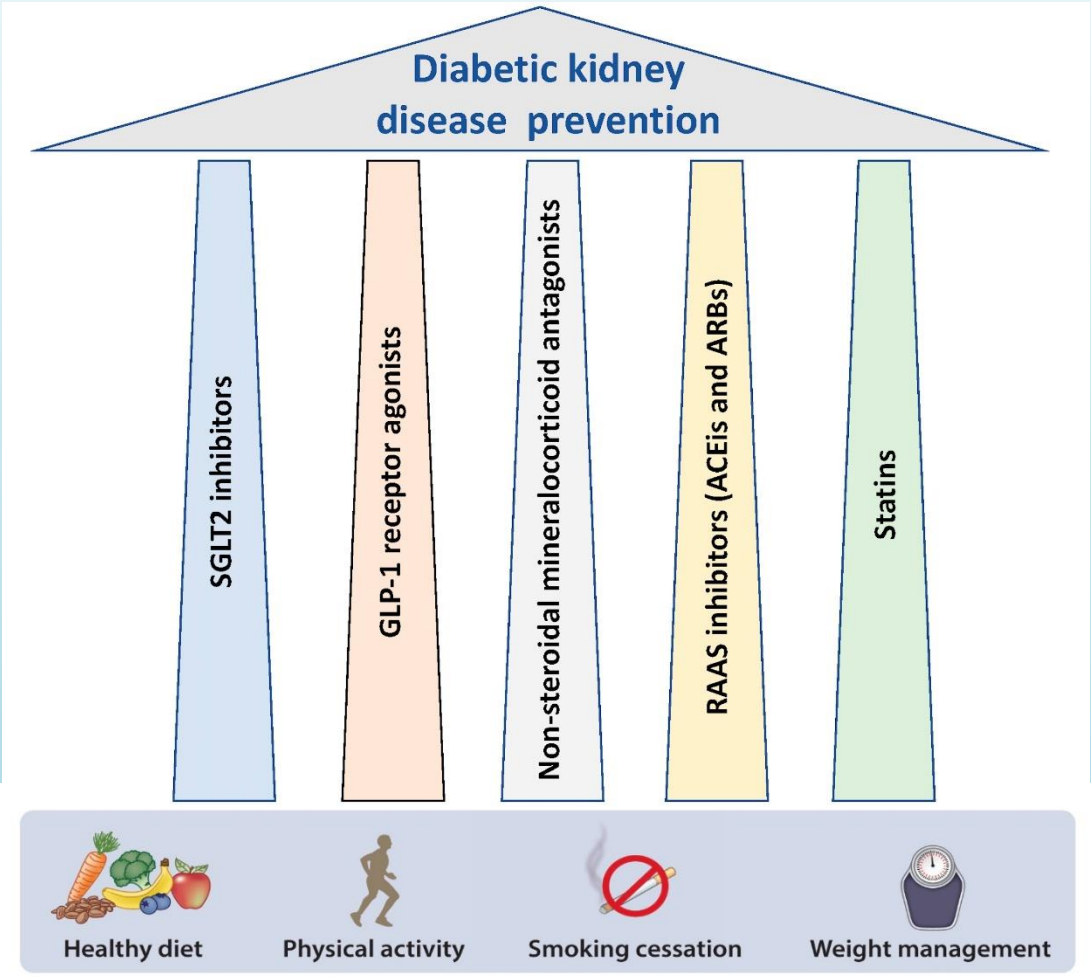
Lifestyle Foundation

Circulation. 2022 Aug 2;146(5):e18-e43

Kidney and Cardiovascular Protection



Pharmaceutics 2023;15:1343
Diabetes Care 2022;45:3075

Nova classification of food processing

THE 4 NOVA GROUPS

1 Unprocessed or minimally processed foods
Fruits, vegetables, beans, nuts, seeds, eggs, juice, meat, poultry, seafood, grains (whole or refined), pasta, yogurt, milk, tea, coffee, etc.

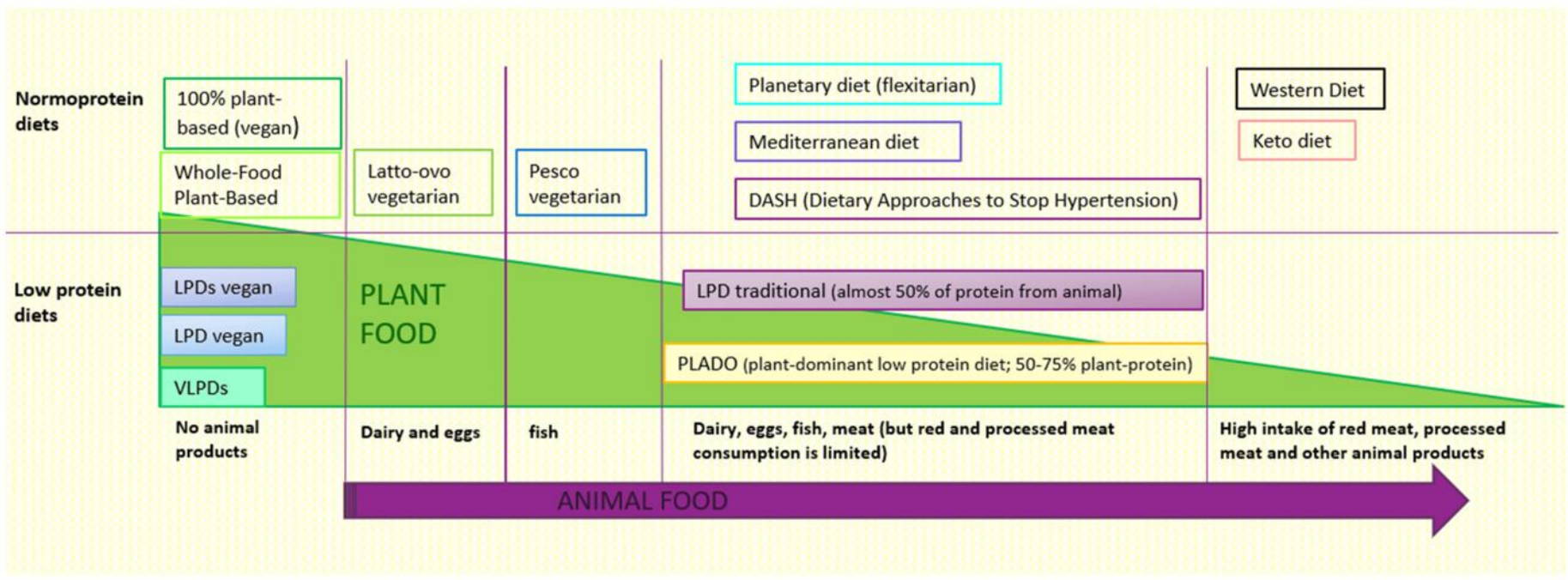
2 Processed culinary ingredients
Sugar, honey, maple syrup, butter, lard, vegetable oils, salt, etc.

3 Processed foods
Salted nuts; cured meats or fish; canned or bottled fish, vegetables, beans, or fruit; unpackaged cheeses or breads (from a bakery), etc.

4 Ultra-processed foods
Packaged breads, most breakfast cereals, bars, flavored yogurts, ice cream, chocolate, candies, cookies, pastries, cakes, margarine, frozen pizza, sausages, hot dogs, chicken nuggets, most sugary drinks, instant soups, sauces, noodles, etc.

Center for Science and Public Interest
https://www.cspinet.org/article/6-things-know-about-ultra-processed-foods

Dietary patterns



Abbreviations: DASH – Dietary Approaches to Stop Hypertension; LPD – low protein diet; PLADO – plant-dominant low protein diet; VLPD – very low protein diet.

J Clin Med. 2023;12(19):6137.

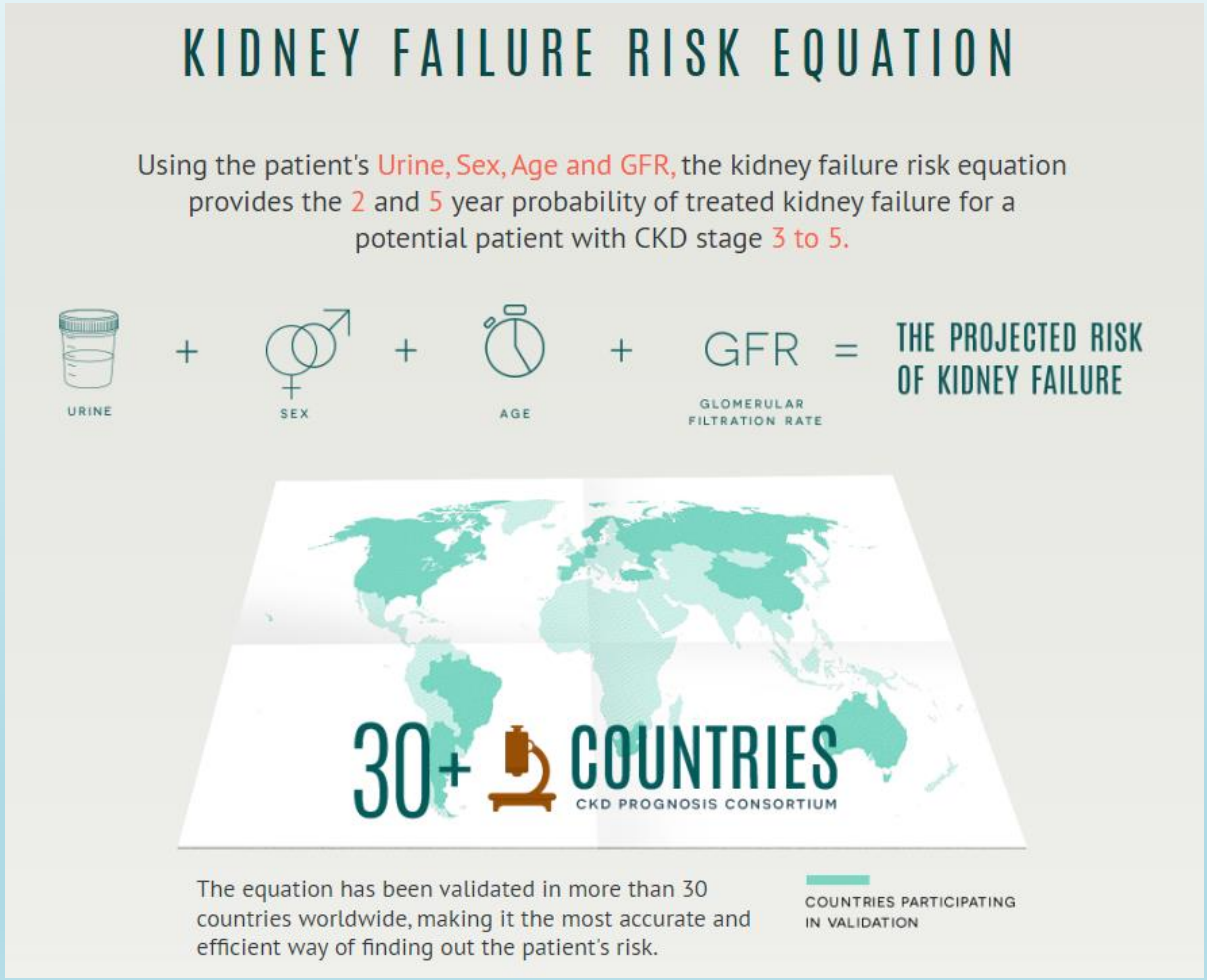
Case Presentation

- 65-year-old man
- Type-2 diabetes since 2005, dyslipidemia and hypertension complicated by Heart Failure with preserved Ejection Fraction (HFpEF).
- Diabetic retinopathy
- Creatinine 1.40 + eGFR 46 = CKD G3a
- uACR 2200 mg/g = CKD A3 or CKD G3aA3
- uPCR 3600 mg/g

- Medications:
  - ✓ lisinopril 20 mg daily,
  - ✓ metoprolol succinate 100 mg daily,
  - ✓ clopidogrel 30 mg daily,
  - ✓ aspirin 81 mg daily,
  - ✓ atorvastatin 40 mg daily,
  - ✓ insulin lispro and glargine.
- BP 136/84 P72 BMI 32 kg/m^2

Kidney Failure Risk Equation use is another reason to check albuminuria

KidneyFailureRisk.com



What is individual risk of progression to kidney failure requiring dialysis or transplant?

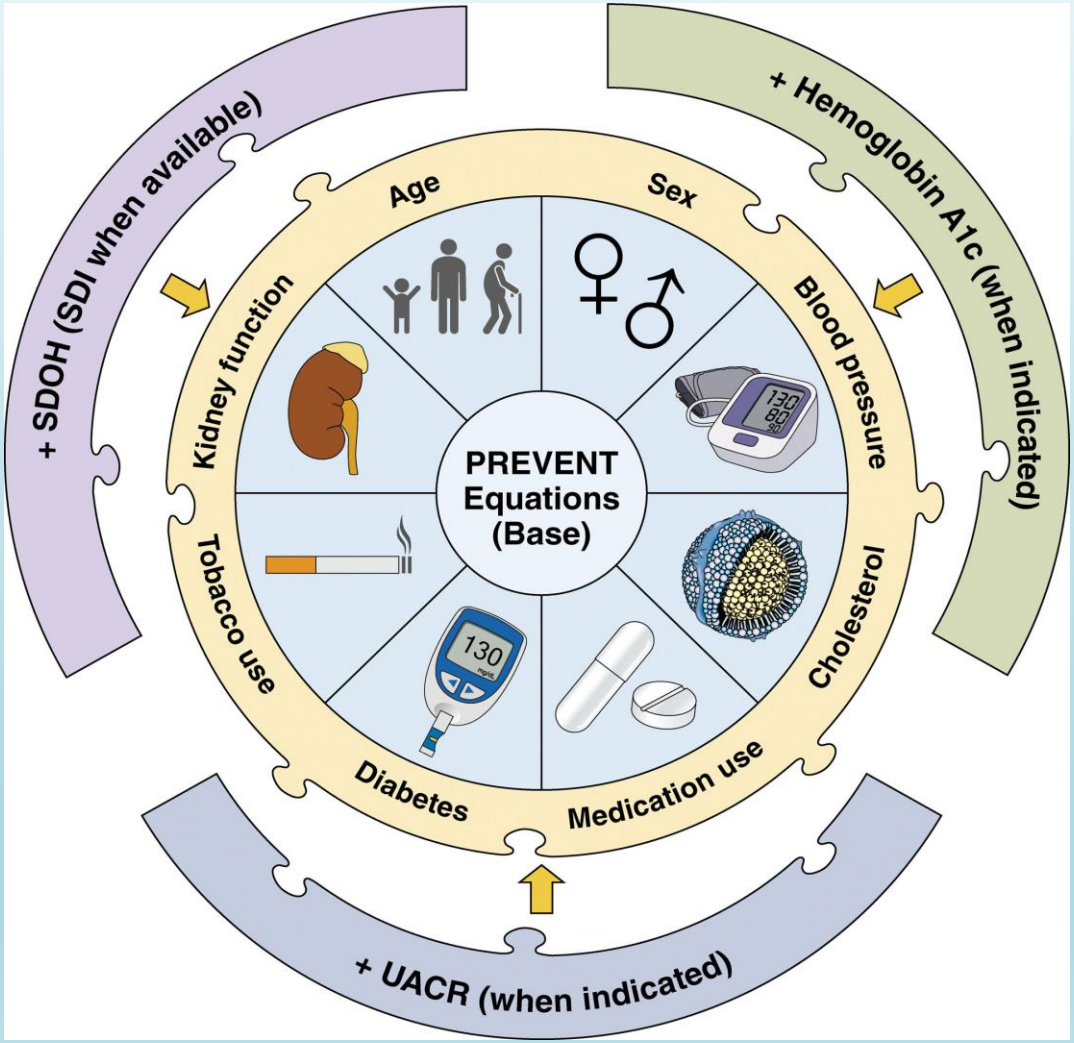
AT 2 YEARS	AT 5 YEARS
~3%	~10%

Risk thresholds used in health systems include:

- 3-5% at 5 years for referral to nephrologist
- 10% at 2 years for team-based care (Nurse, Dietitian, Pharmacist)
- 20-40% at 2 years for planning a transplant or dialysis

JAMA. 2016;315(2):1-11
https://kidneyfailurerisk.com/

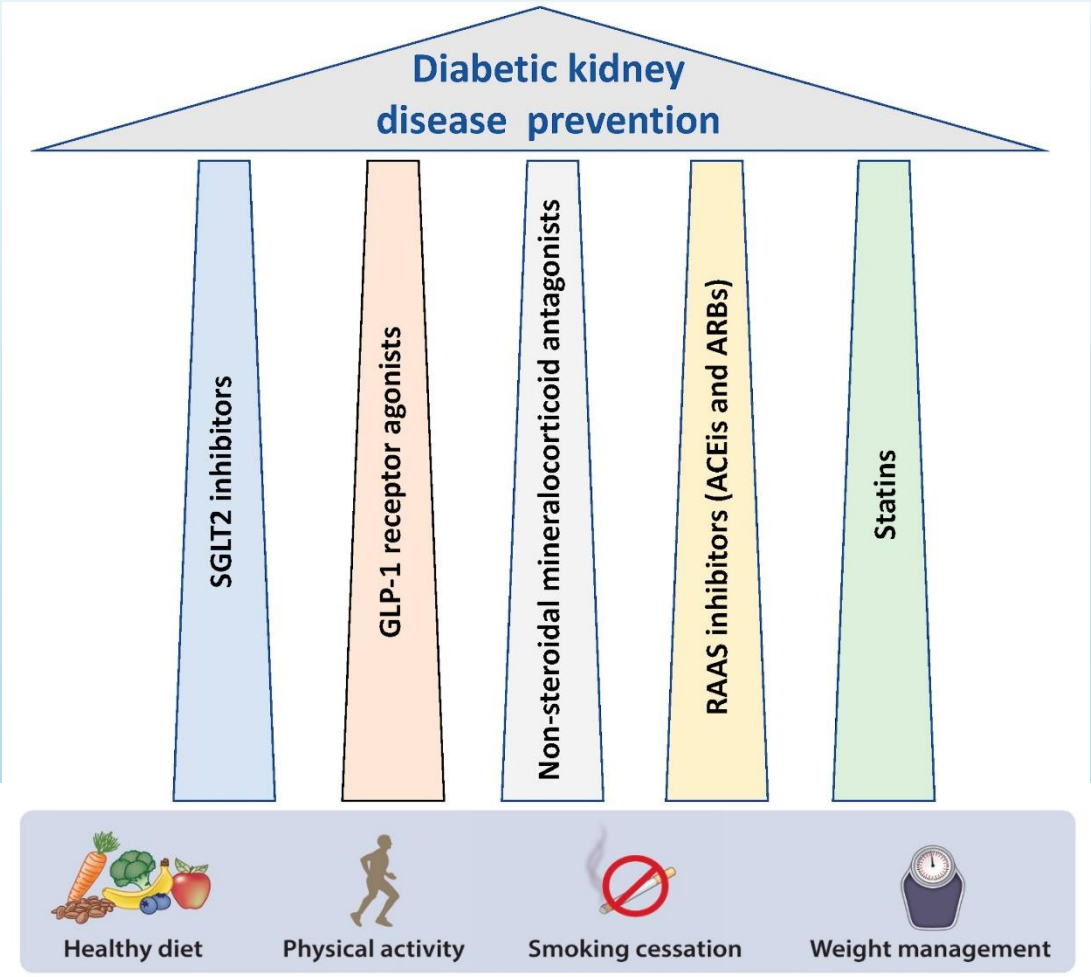
PREVENT Equation
Predicting Cardiovascular Risk



10-year risk
1) Cardiovascular Disease (CVD) overall:
2) Atherosclerotic CVD
3) Heart Failure CVD

https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

Kidney and Cardiovascular Protection



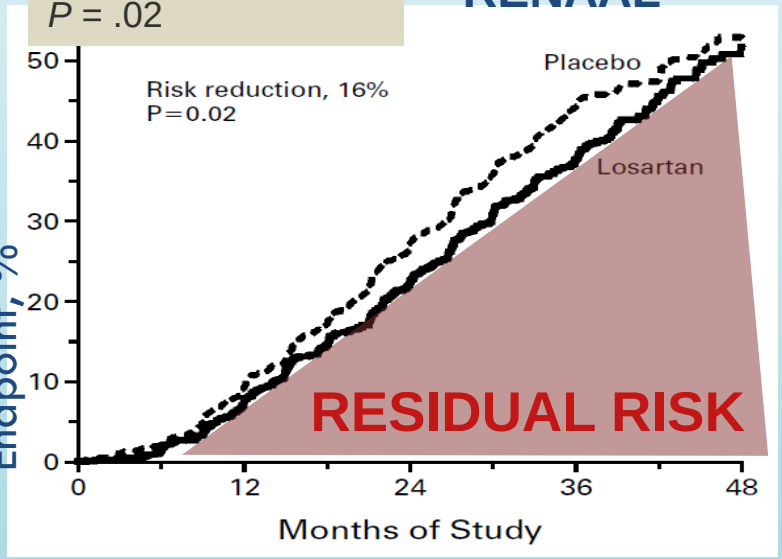
Pharmaceutics 2023;15:1343
Diabetes Care 2022;45:3075

Kidney Protection With ARBs in Type 2 Diabetes With Hypertension and Albuminuria

Doubling of serum creatinine, ESKD, or death

Risk reduction, 16%
P = .02

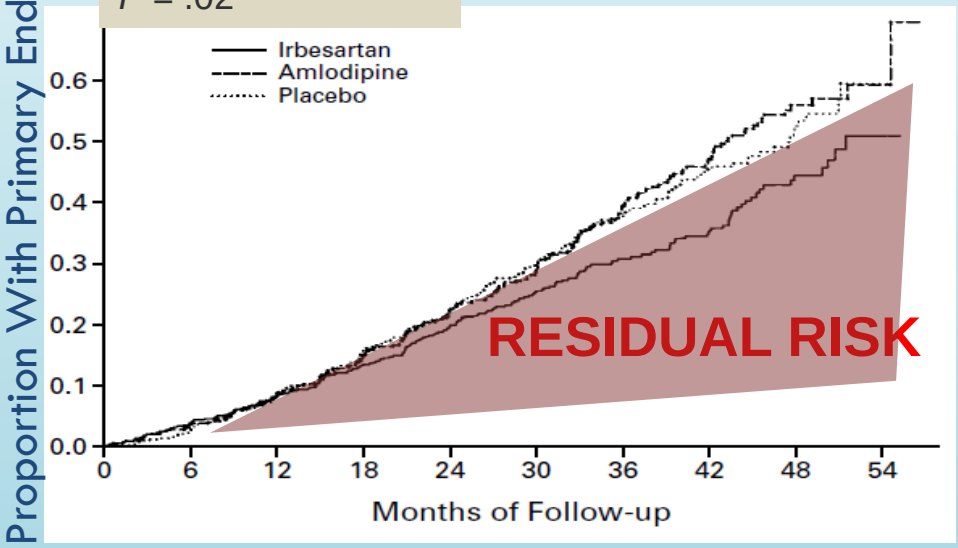
RENAAL



RENAAL – Reduction of Endpoints With the Angiotensin Receptor II Antagonist Losartan
**No increase in the incidence of adverse events with losartan*
Brenner B, et al. *N Engl J Med*. 2001;345:861-9.

Risk reduction, 20%
P = .02

IDNT



IDNT – Irbesartan Diabetic Nephropathy Trial
SAEs: greater number of patients developing hyperkalemia in irbesartan group (P=.01); 23.7% of patients stopped study medication before end of study discontinuations were evenly distributed between treatment groups; most common reason for discontinuation was clinical cardiovascular event.
Lewis EJ, et al. *N Engl J Med*. 2001;345:851-60.

Slowing CKD Progression: ACEi *or* ARB

- Check labs within two weeks after initiation (opinion).
  - Potassium
  - If less than 30% serum creatinine (Scr) increase, continue and monitor.
  - If more than 30% Scr increase, stop drug and evaluate for renal artery stenosis (RAS) and volume contraction.

- **Avoid ACEi *and* ARB in combination[1-3]**
  - Risk of adverse events (hemodynamic AKI, hyperkalemia)

- ACEi vs ARB have similar outcomes data, but tolerability is better for ARB.

1) Kunz R, et al. *Ann Intern Med*. 2008;148:30-48
2) Mann J, et al. ONTARGET study. *Lancet*. 2008;372:547-553
3) Fried LF, et al. VA Nephron D Study. *N Engl J Med.* 2013;369:1892-1903

Predictors of Hyperkalemia before Starting Therapy Derived from Trials

- eGFR <45 mL/min/1.73m^2
- Serum potassium >4.5 mEq/L
- eGFR <45 mL/min/1.73m^2 + serum K >4.5 mEq/L

(*Strongest Predictor*)

Lazich I, et al. *Semin Nephrol* 2014; 22(2):123-32
Khosla N, et al. *Am J Nephrol* 2009; 30(5):418-424

Predictors of Hyperkalemia before Starting Therapy Derived from Trials

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(*Strongest Predictor*)

- **eGFR <30** mL/min/1.73m^2 obviously high risk

Lazich I, et al. *Semin Nephrol* 2014; 22(2):123-32
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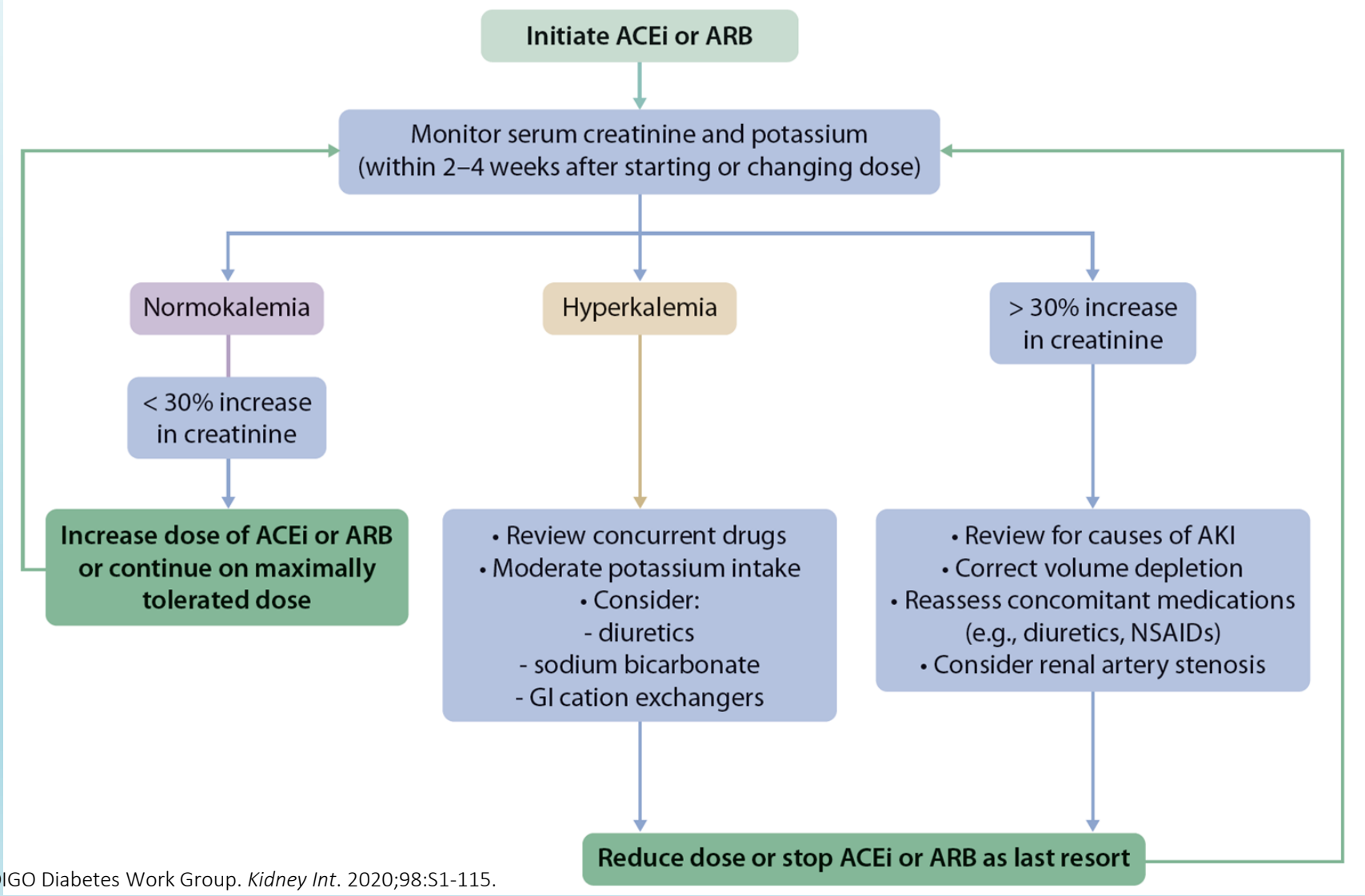
Predictors of Hyperkalemia before Starting Therapy Derived from Trials

- eGFR <45 mL/min/1.73m^2
- Serum potassium >4.5 mEq/L
- eGFR <45 mL/min/1.73m^2 + serum K >4.5 mEq/L (***Strongest Predictor***)
- **eGFR <30** mL/min/1.73m^2 obviously high risk
- In general continue ACEi or ARB for eGFR <30 mL/min/1.73m^2, discontinuing only for intractable hyperkalemia or concerns about low eGFR.

Lazich I, et al. *Semin Nephrol* 2014; 22(2):123-32
Khosla N, et al. *Am J Nephrol* 2009; 30(5):418-424

ACEI or ARB: Dose Titration and Side Effect Monitoring

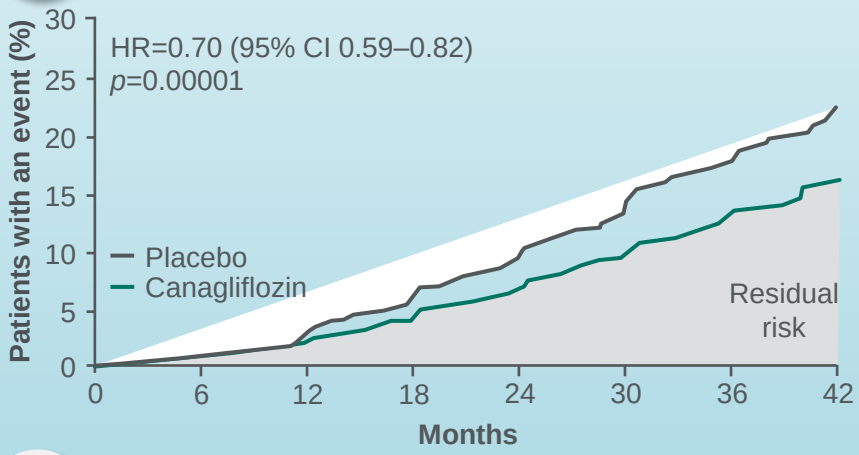


KDIGO Diabetes Work Group. *Kidney Int*. 2020;98:S1-115.

Despite RAS blockade and SGLT-2 inhibition, patients with T2DM and advanced CKD are at risk of CKD progression

CREDENCE: Canagliflozin (+ ACEi/ARB) vs placebo[1]

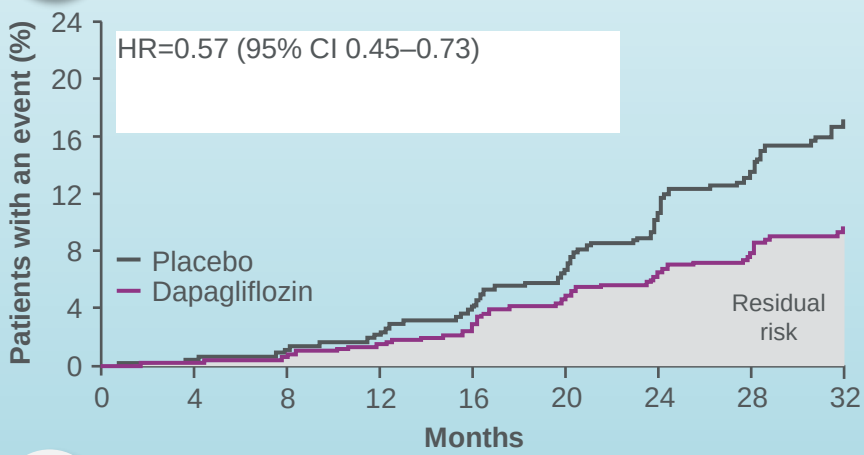
Primary composite outcome:
Kidney failure, doubling of SCr or death from kidney/CV causes



Patients with severely increased albuminuria: 88%
Median uACR: 927 mg/g

DAPA-CKD: Dapagliflozin (+ACEi/ARB) vs placebo (T2D subgroup)[2]

Secondary composite renal outcome:
Sustained ≥50% eGFR decline, ESKD or renal death

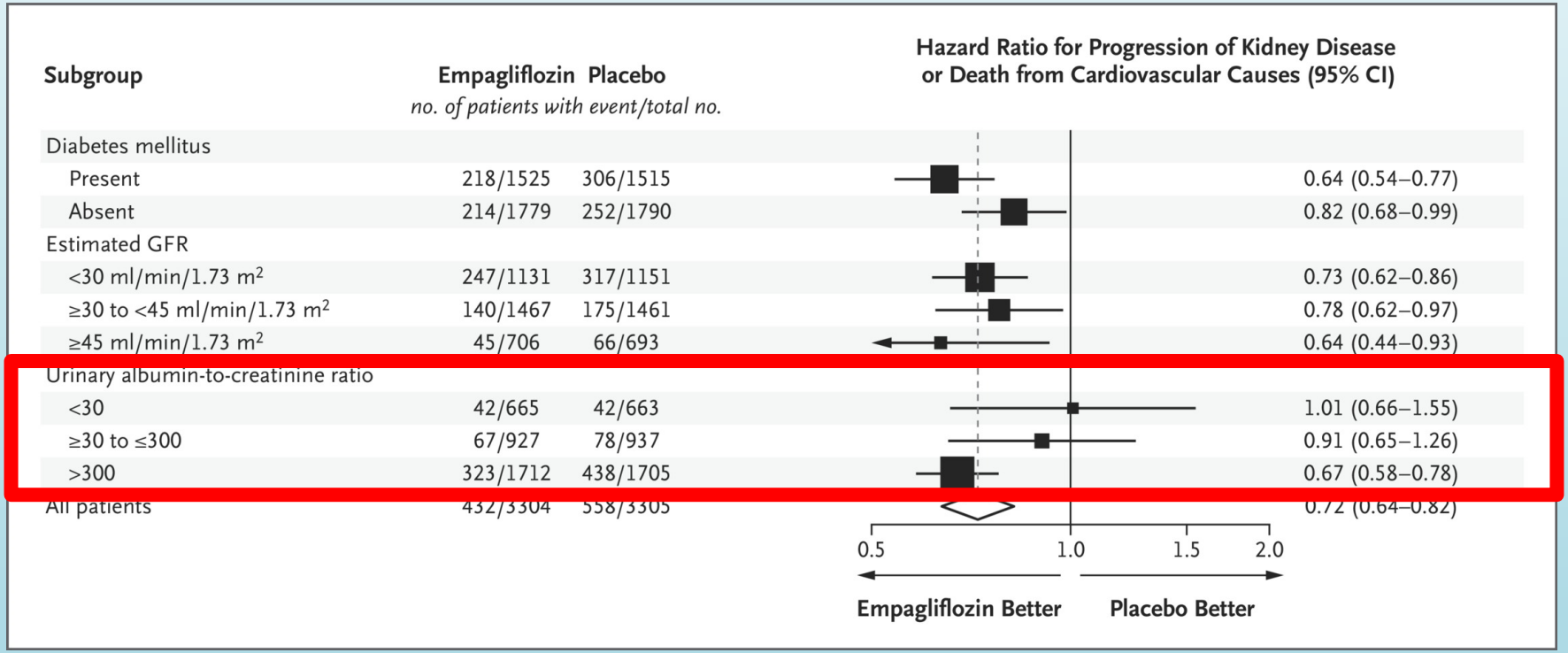


Patients with severely increased albuminuria: 89.7%
Median uACR: 949 mg/g

ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CI, confidence interval; ESKD, end-stage kidney disease; HR, hazard ratio; NNT, number needed to treat; SGLT-2, sodium-glucose co-transporter-2

1. Perkovic V, *et al*. *N Engl J Med* 2019;380:2295–2306.
2. Wheeler DC, *et al*. *Lancet Diabetes Endocrinol* 2021;9:22–31

EMPA-KIDNEY Primary Outcome
Empagliflozin vs Placebo
Impact of Albuminuria

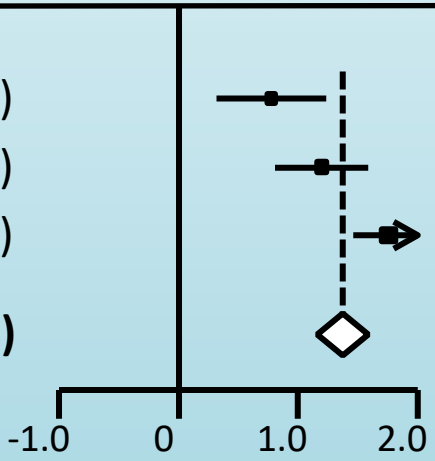


Primary Outcome = CKD progression or cardiovascular mortality

N Engl J Med 2023;388:117-127.

EMPA-KIDNEY eGFR Slopes by Albuminuria: Benefit across albuminuria levels

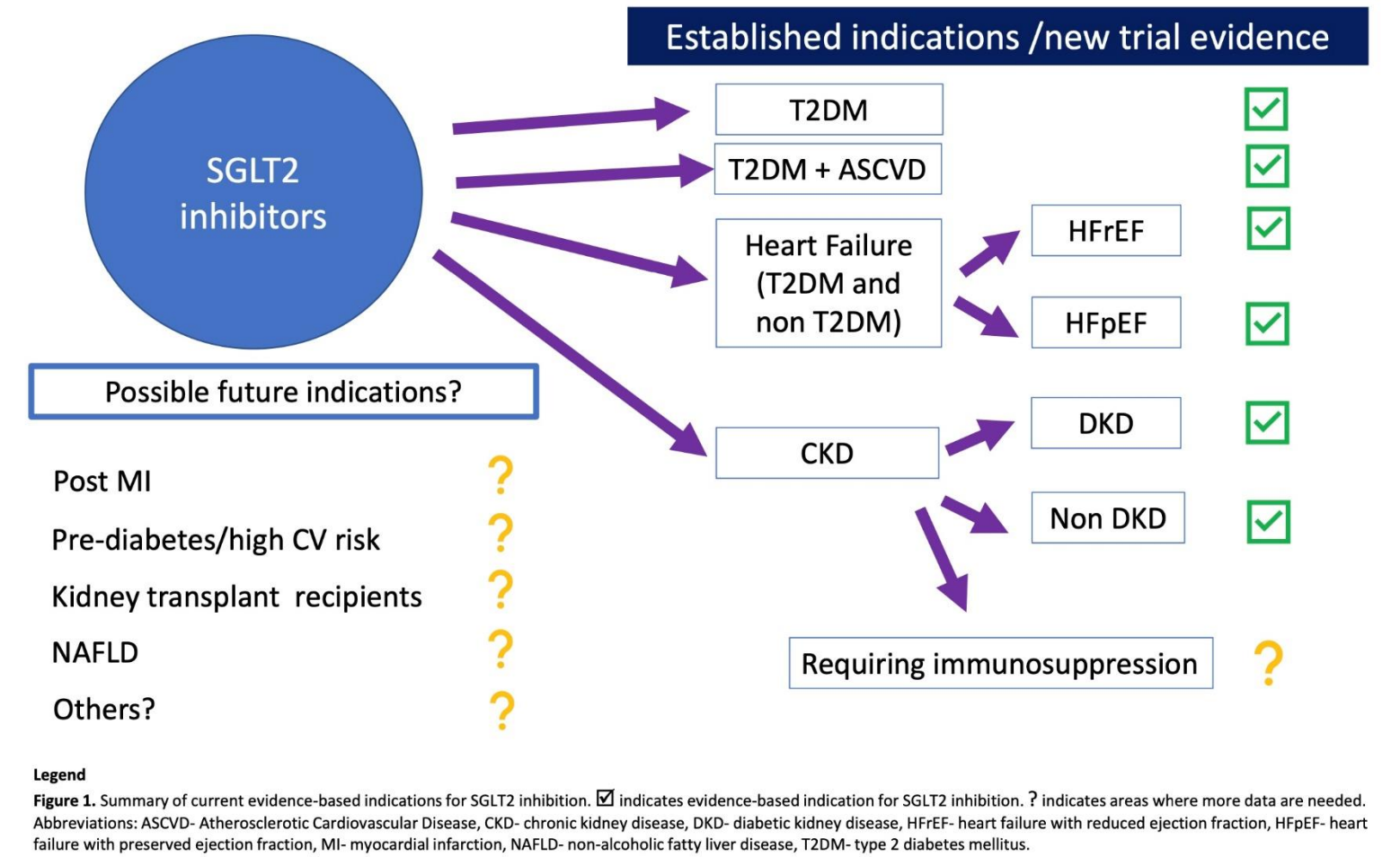
uACR (mg/g)	Mean slope (SE) mL/min/1.73m²/year Empagliflozin	Placebo	Difference between mean slopes (95% CI)
<30	-0.11 (0.17)	-0.89 (0.16)	0.78 (0.32, 1.23)
≥30 <300	-0.49 (0.14)	-1.69 (0.14)	1.20 (0.81, 1.59)
≥300	-2.35 (0.11)	-4.11 (0.11)	1.76 (1.46, 2.05)
All	**-1.37 (0.08)**	**-2.75 (0.08)**	**1.37 (1.16, 1.59)**



Difference of at least **0.5** is considered effective

N Engl J Med 2023;388:117-127.

Summary of Evidence-based SGLT-2 Inhibitor Use



Legend

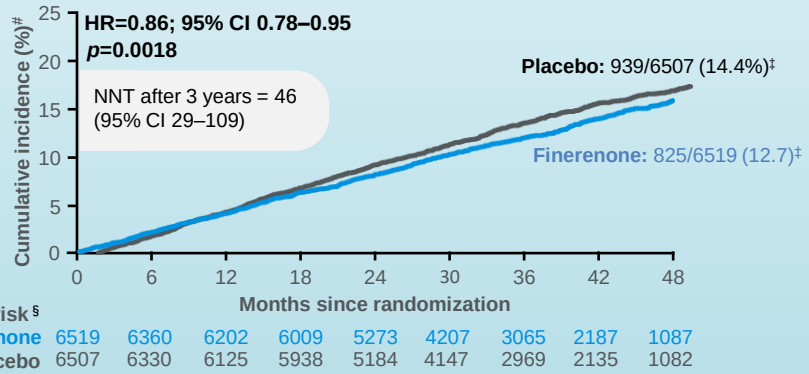
Figure 1. Summary of current evidence-based indications for SGLT2 inhibition. ☑ indicates evidence-based indication for SGLT2 inhibition. ? indicates areas where more data are needed. Abbreviations: ASCVD- Atherosclerotic Cardiovascular Disease, CKD- chronic kidney disease, DKD- diabetic kidney disease, HFrEF- heart failure with reduced ejection fraction, HFpEF- heart failure with preserved ejection fraction, MI- myocardial infarction, NAFLD- non-alcoholic fatty liver disease, T2DM- type 2 diabetes mellitus.

Lancet 2022;400(10365):1745-1747.

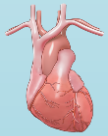
The FIDELITY primary analysis showed significant risk reductions in CV and kidney outcomes

CV composite

Time to CV death, nonfatal MI, nonfatal stroke, or HHF



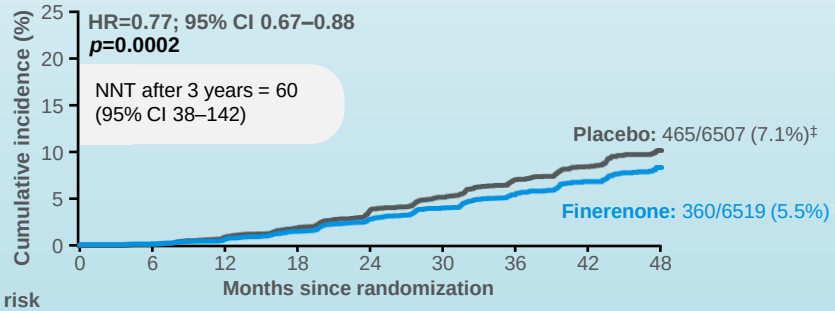
No. at risk §									
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082



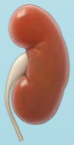
reduced **risk of CV morbidity and mortality** vs placebo (HR=0.86; 95% CI 0.78–0.95)[1]

Kidney composite

Time to kidney failure*, sustained ≥57% decrease in eGFR from baseline, or kidney-related death



No. at risk									
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962



reduced **risk of CKD progression*** vs placebo (HR=0.77; 95% CI 0.67–0.88)[1]

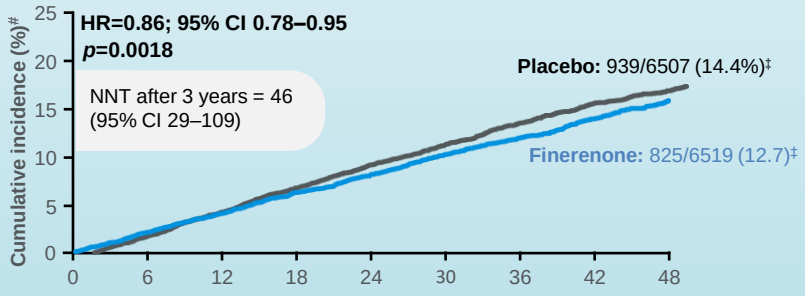
*ESKD or an eGFR <15 mL/min/1.73 m^2; events were classified as renal death if: (1) the patient died; (2) KRT had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; #Cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; ‡number of patients with an event over a median of 3.0 years of follow-up; § at-risk subjects were calculated at start of time point; CI, confidence interval; ESKD, end-stage kidney disease; HR hazard ratio; KRT, kidney replacement therapy; NNT, number needed to treat.

Agarwal R, *et al. Eur Heart J* 2021; 42(2):152-161.

The FIDELITY primary analysis showed significant risk reductions in CV and kidney outcomes

CV composite

Time to CV death, nonfatal MI, nonfatal stroke, or HHF



No. at risk §									
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082

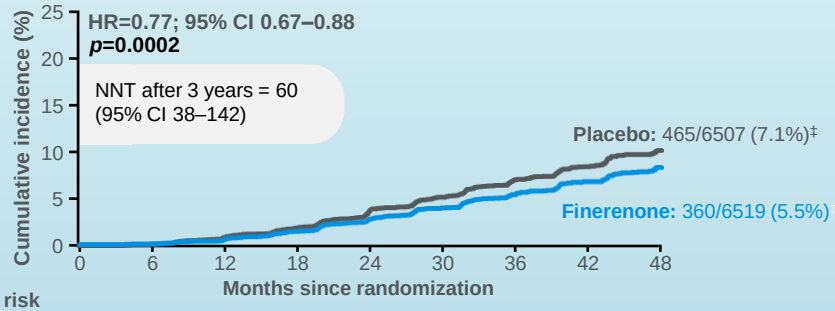
14% reduced **risk of CV morbidity and mortality** vs placebo

NNT 46

(HR=0.86; 95% CI 0.78–0.95)[1]

Kidney composite

Time to kidney failure*, sustained ≥57% decrease in eGFR from baseline, or kidney-related death



No. at risk									
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962

23% reduced **risk of CKD progression*** vs placebo

NNT 60

(HR=0.77; 95% CI 0.67–0.88)[1]

*ESKD or an eGFR <15 mL/min/1.73 m^2; events were classified as renal death if: (1) the patient died; (2) KRT had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; #Cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; ‡number of patients with an event over a median of 3.0 years of follow-up; § at-risk subjects were calculated at start of time point; CI, confidence interval; ESKD, end-stage kidney disease; HR hazard ratio; KRT, kidney replacement therapy; NNT, number needed to treat.

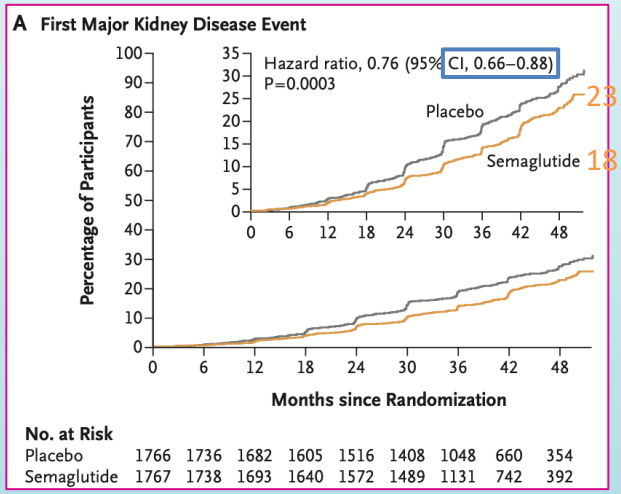
Agarwal R, *et al. Eur Heart J* 2021; 42(2):152-161.

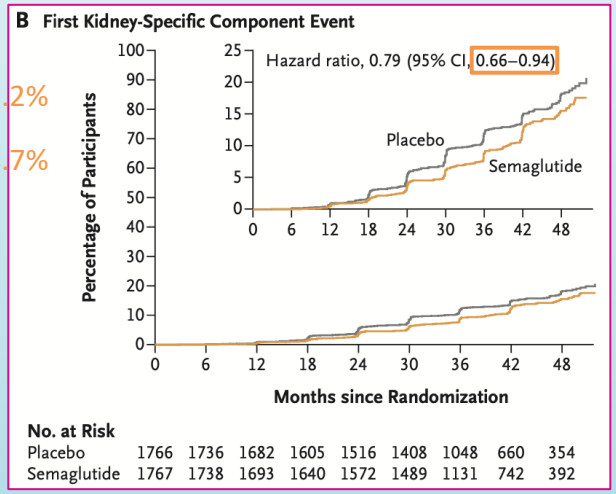
Five facts of Finerenone for use in CKD in T2DM

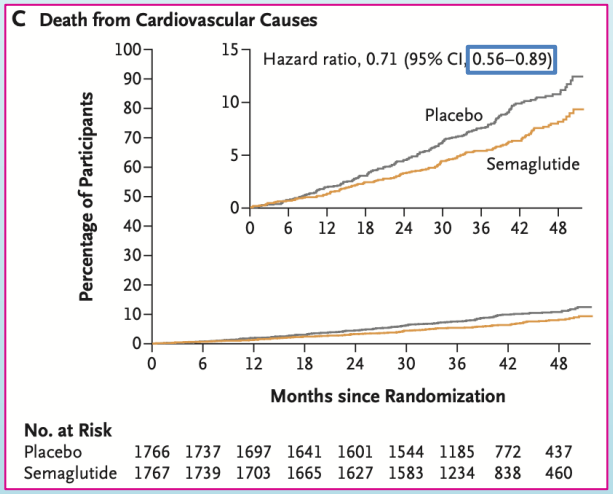
- start if K < 5
- keep going till K at most 5.5.
- use if eGFR > 25 (5 x 5).
- expect a 5th reduction in dialysis
- and more than a 5th reduction in Heart Failure Hospitalization.

Adapted from Rajiv Agarwal

GLP1RA significantly improves kidney outcomes and decreases risk of death from CV causes in T2DM







RRR: 24%
NNT: 20 per 3 years

N Engl J Med. 2024:391(2):109-121.

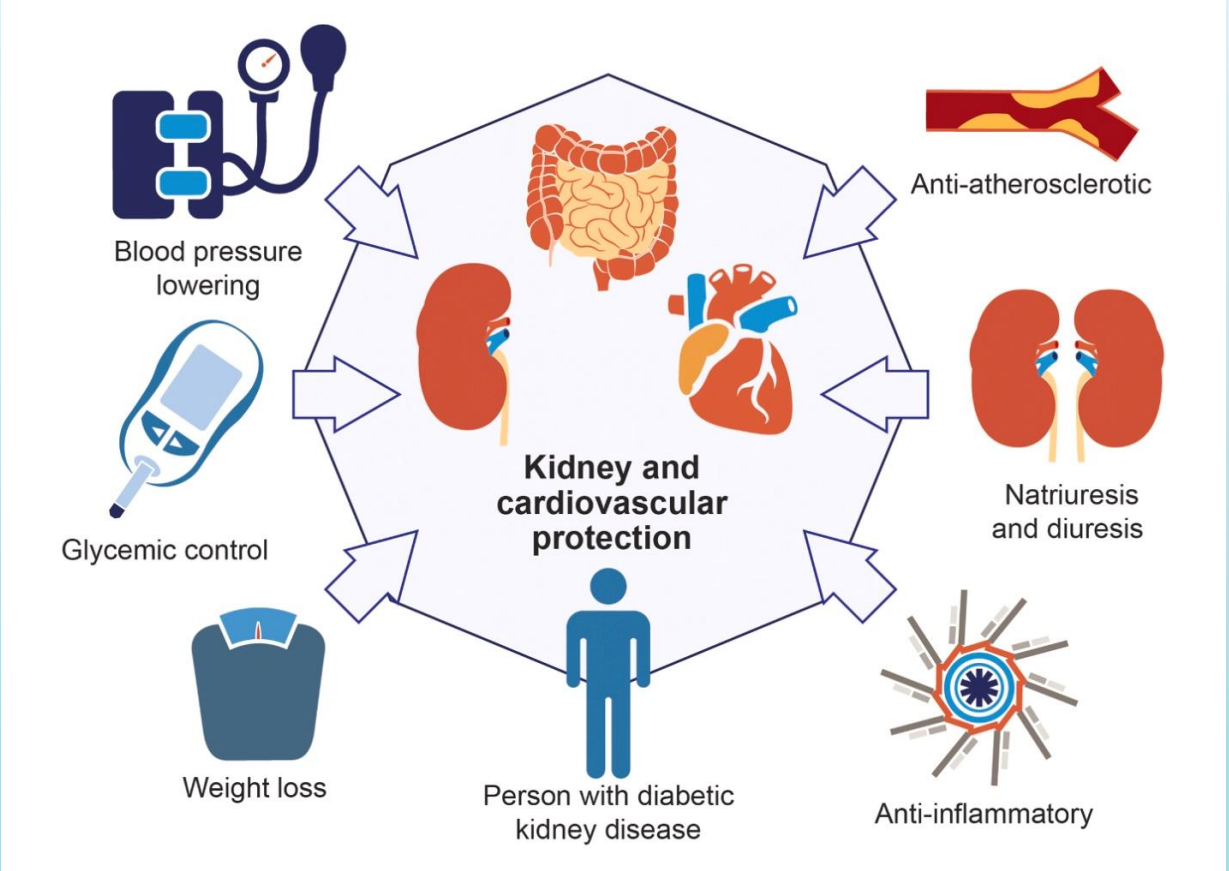
GLP1RA Potential Mechanisms of Kidney and Cardiovascular Protection

FLOW
Semaglutide vs placebo
Trial week 104

The mean SBP reduction
2.23 mm Hg
(95% CI, 1.13 to 3.33)

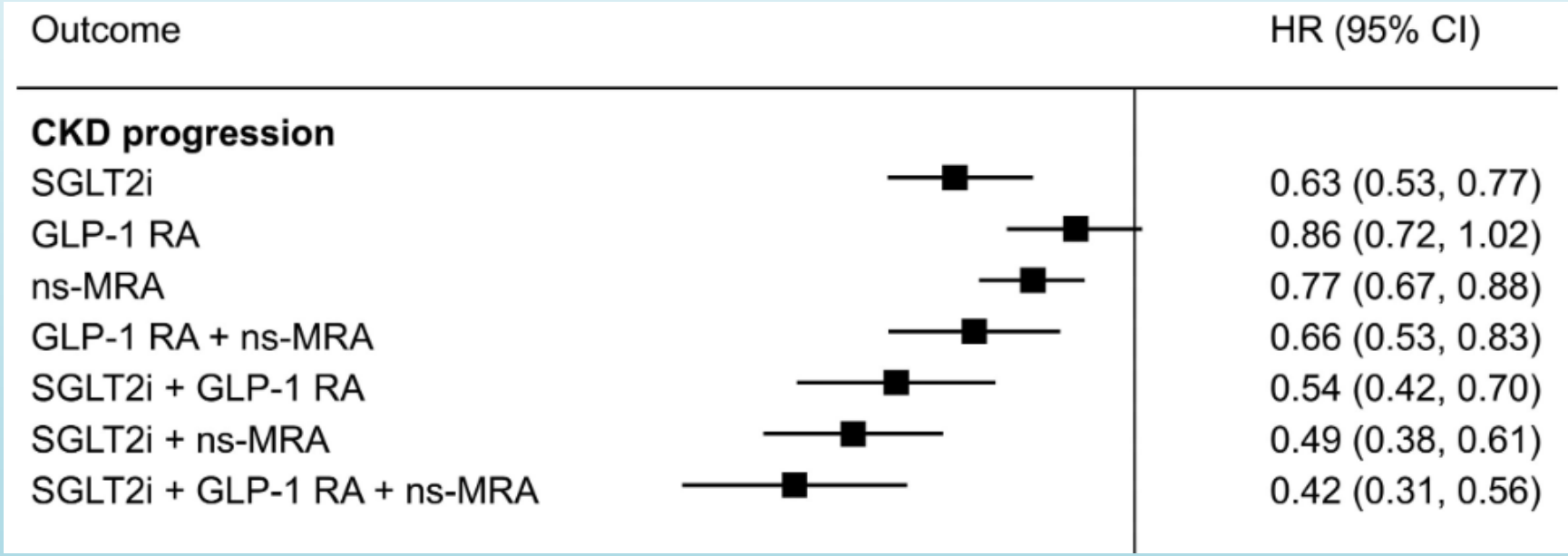
The mean A1c reduction
0.81%
(95% CI, 0.72 to 0.90)

Weight loss 4.10 kg
(95% CI, 3.65 to 4.56)



Am J Prev Cardiol. 2023;24:14:100502.

Estimated treatment effects on CKD progression with SGLT2i, GLP-1RA, and ns-MRA, alone and in combination, when added to ACEi or ARB in patients with T2DM and uACR at least 30 mg/g



Data from RCTs: SGLT2i (2), ns-MRA (2) and 8 GLP1RA (8) other than FLOW

Circulation. 2024; 6;149(6):450-462.

Nephrology Referral Indications - opinion

KDIGO Heat Map

Guide to Frequency of Monitoring (number of times per year) + Referral decision making by GFR and Albuminuria Category				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
GFR categories (ml/min/ 1.73 m^2), Description and range	**G1**	Normal or high	≥90	1 if CKD	1 Monitor	2 Refer*
	G2	Mildly decreased	60-89	1 if CKD	1 Monitor	2 Refer*
	G3a	Mildly to moderately decreased	45-59	1 Monitor	2 Monitor	3 Refer
	G3b	Moderately to severely decreased	30-44	2 Monitor	3 Monitor	3 Refer
	G4	Severely decreased	15-29	3 Refer*	3 Refer*	4+ Refer
	G5	Kidney failure	<15	4+ Refer	4+ Refer	4+ Refer

GFR and albuminuria grid to reflect the risk of progression by intensity of coloring (green, yellow, orange, red, deep red). The numbers in the boxes are a guide to the frequency of monitoring (number of times per year). The words in the boxes are a guide for referral decision making (monitor or referral to specialist kidney care services). *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring.

KDOQI US Commentary on the 2012 KDIGO Evaluation and Management of CKD.

Nephrology Referral Indications - opinion

GFR < 30 ml/min/1.73 m^2 (GFR categories G4-G5)
A 25% or greater drop in eGFR
CKD Progression with a sustained decline in eGFR > 5 ml/min/1.73 m^2 per year
A consistent finding of significant albuminuria (category A3)
Persistent unexplained hematuria
Secondary hyperparathyroidism, persistent anion gap acidosis, non deficiency anemia
CKD and hypertension refractory to treatment with 4 or more antihypertensive agents
Persistent abnormalities of serum potassium
Recurrent or extensive nephrolithiasis
Hereditary kidney disease or unknown cause of CKD

KDOQI US Commentary on the 2012 KDIGO Evaluation and Management of CKD.

Why Refer to Nephrology

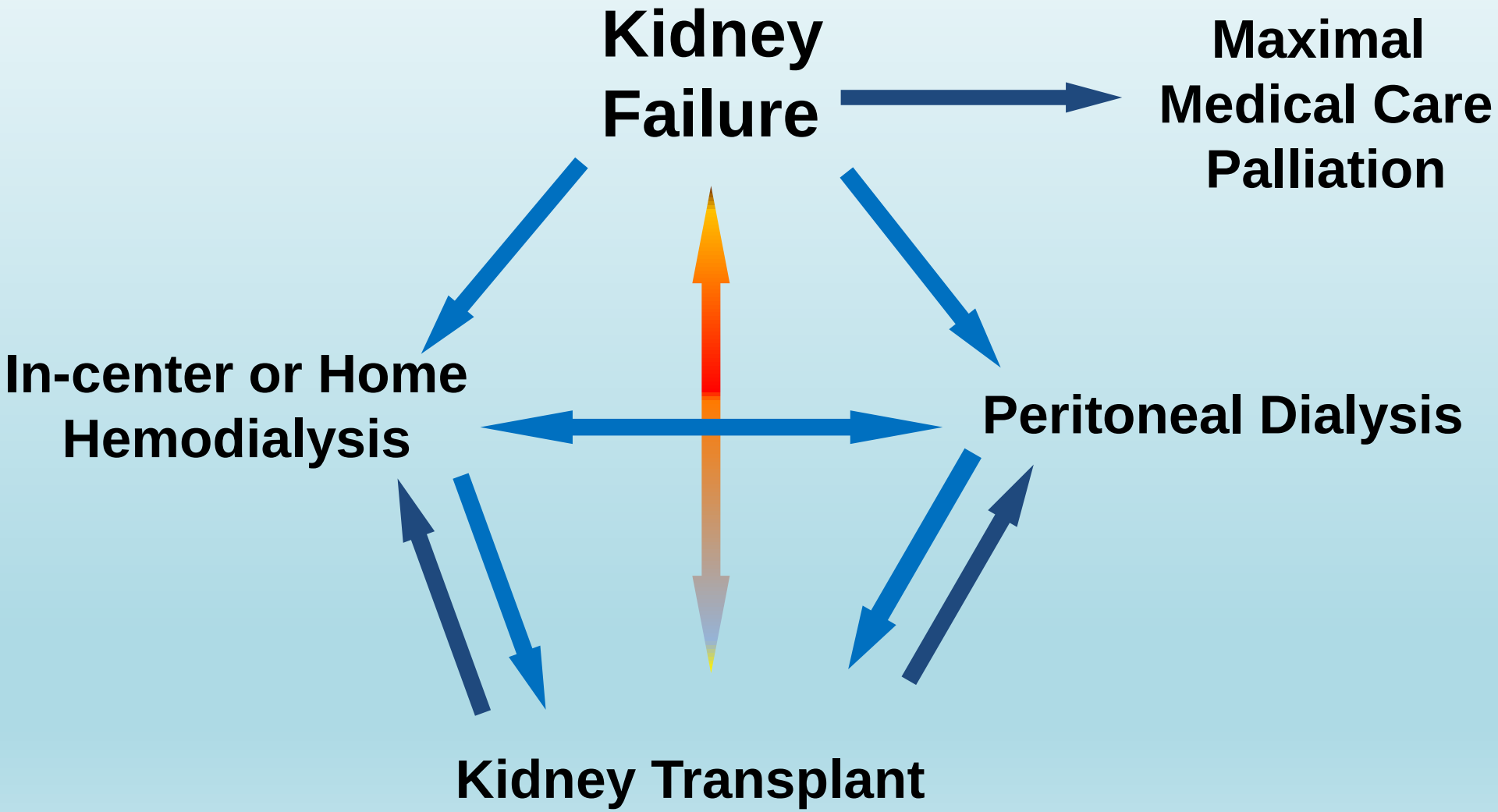
- Identify Cause – Kidney biopsy in selected cases
- Slow Progression of CKD
- CKD Complications management
  - CKD Anemia
  - CKD Hyperkalemia
  - CKD Mineral and Bone Disease
  - CKD Metabolic Acidosis
  - CKD Malnutrition
- Medication management
- Kidney Failure Replacement Therapy (KFRT) decision making and planning

Observational Studies of Early versus Late Nephrology Consultation

Variable	Early referral Mean (SD)	Late referral mean (SD)	P value
Overal mortality %	11 (3)	23 (4)	<0.0001
1-year motality %	13 (4)	29 (5)	0.028
Hospital stay, days	13.5 (2.2)	25.3 (3.8)	0.0007
KRT serum albumin (mg/dL)	3.62 (0.05)	3.40 (0.03)	0.001
KRT hematocrit %	30.54 (0.18)	29.71 (0.10)	0.013

Chan M, et al. *Am J Med*. 2007;120:1063-1070.
KDIGO CKD Work Group. *Kidney Int Suppls*. 2013;3:1-150.

Kidney Failure Replacement Therapy

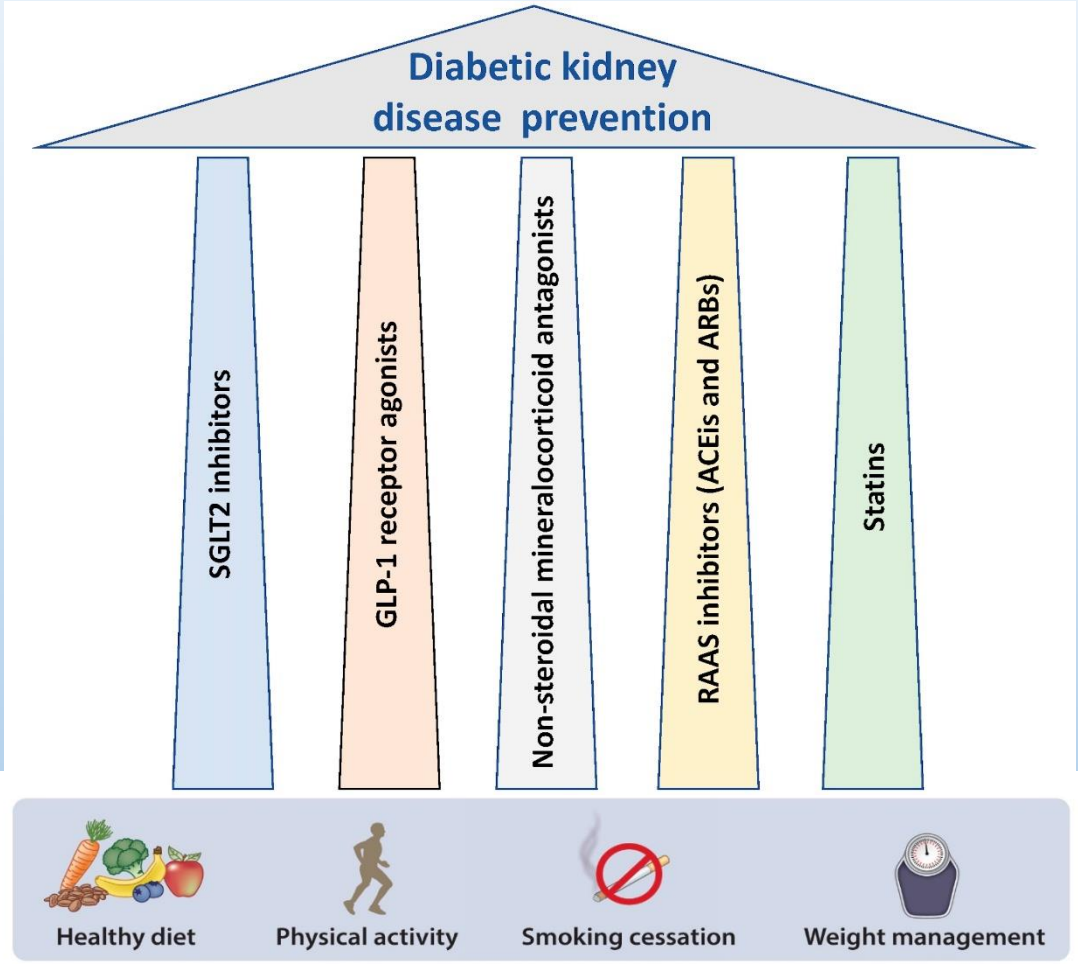


Nephrology Consultant Selection: Suggestions based on opinion and data

- Uses the same electronic health record[1]
- Communicates effectively[1]
- Offers e-consultations[2]
- Is your peer or your co-trainee?[3]
- Offers the full spectrum of kidney failure replacement therapies

1. J Gen Intern Med 2019;34:1228-1235
2. Am J Kidney Dis 2017;70:122-131
3. JAMA Intern Med 2023;183(2):124-132

Kidney and Cardiovascular Protection



Pharmaceutics 2023;15:1343
Diabetes Care 2022;45:3075

THANK YOU