Housekeeping Items

- Welcome to L.A. Care Provider Continuing Education (PCE) Program's Live Webinar!
- The Live Webinar is being recorded.
- Webinar participants are muted upon entry and exit of webinar.
- ***Webinar attendance will be noted via log in and call in with assigned unique Attendee ID #. Please log in through a computer (instead of cell phone) to Join Webinar / Join Event and choose the Call In option to call in by telephone with the event call in number, event access code and assigned unique attendee ID number. If your name does not appear on our WebEx Final Attendance and Activity Report (only as Caller User #) and no submission of online survey, no CME or CE certificate will be provided.***
- Questions will be managed through the Chat feature and will be answered at the end of the presentation. ***Please keep questions brief and send to All Panelists. One of our Learning and Development Team members and/or webinar host***, will read the questions via Chat when it's time for Q & A session (last 30 minutes of live webinar).
- Please send a message to the Host via Chat if you cannot hear the presenter or see the presentation slides.

L.A. Care PCE Program Friendly Reminders

- ***Partial credits are not allowed at L.A. Care's CME/CE activities for those who log in late (more than 15 minutes late) and/or log off early.***

- PowerPoint Presentation is allotted 60 minutes and last 30 minutes for Q&A session, total of 90-minute webinar, 1.50 CME credits for L.A. Care Providers and other Physicians, 1.50 CE credits for NPs, RNs, LCSWs, LMFTs, LPCCs, LEPs, and other healthcare professionals. Certificate of Attendance will be provided to webinar attendees without credentials.

- **Friendly Reminder,** a survey will pop up on your web browser after the webinar ends. Please do not close your web browser and wait a few seconds, and please complete the survey. ***Please note:*** ***the online survey may appear in another window or tab after the webinar ends.***

- Within two (2) weeks after webinar and upon completion of the online survey, you will receive the PDF CME or CE certificate based on your credential and after verification of your name and attendance duration time of at least 75 minutes for this 90-minute webinar.

- The PDF webinar presentation will be available within 6 weeks after webinar date on lacare.org website located at https://www.lacare.org/providers/provider-central/provider-programs/classes-seminars

- Any questions about L.A. Care Health Plan's Provider Continuing Education (PCE) Program and our CME/CE activities, please email Leilanie Mercurio at lmercurio@lacare.org

Presenter’s Bio

- **Introducing Rahul Dhawan, DO:** A distinguished physician specializing in Internal Medicine and Nephrology/Hypertension, Dr. Dhawan boasts dual board certifications and a UNOS certification in Abdominal Transplant.

- Currently, Dr. Rahul Dhawan is a primary care doctor in East Los Angeles and also a transplant nephrologist who works with groups with MedPOINT Management including Healthcare LA, Global and Bella Vista Medical Group IPA as a Medical Director.

- Dr. Dhawan has made significant contributions through his roles in primary care, nephrology subspecialty, and leadership as the former CMO of St. Francis Medical Center. Holding key positions such as National Medical Director of Medicaid at Anthem, Inc., and Medical Director for Kidney Disease at United Health Group/Optum, he has demonstrated an unwavering commitment to advancing healthcare accessibility and quality.
- Dr. Dhawan's impact extends beyond practice, as evidenced by his numerous publications in areas like CKD, ESRD, and Population Health. A visionary in his field, he combines his clinical acumen with AI and Machine Learning to usher in a new era of healthcare, focusing on improved outcomes for patients with chronic conditions. Dr. Dhawan's unique blend of clinical expertise, AI proficiency, and gerontology background positions him at the forefront of healthcare transformation.

Chronic Kidney Disease (CKD) in Primary Care

Rahul Dhawan, DO, MMM

Medical Director, MedPOINT Management

April 18, 2024 Live Webinar via Cisco WebEx

12:00 pm – 1:30 pm PST, 1.50 CME/CE Credits

Directly Provided CME/CE Activity by L.A. Care Health Plan

Disclosures

The following CME planners and faculty do not have any financial relationships with ineligible companies in the past 24 months:

- Leilanie Mercurio, L.A. Care PCE Program Manager, CME Planner
- Rahul Dhawan, DO, Medical Director, MedPOINT Management; CME Planner and CME Faculty

An ineligible company is any entity whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Commercial support was not received for this CME activity.

About Me

- Board Certified:
  - Internal Medicine
  - Nephrology
- UNOS Certified Abdominal Transplant
- Experience:
  - Primary Care in East Los Angeles
  - Nephrology Sub-specialist: Outpatient/In-Patient
  - Previous CMO of St Francis Medical Center
  - Plan Experience:
    - Anthem, Inc.: National Medical Director of Medicaid

Learning Objectives

1. Identify at least two (2) risk factors and two (2) early signs of chronic kidney disease (CKD) to enable early detection and intervention.

2. Apply the diagnostic criteria and stages of CKD for accurate assessment and risk stratification of patients.

3. List at least two (2) recommended monitoring and laboratory tests to assess kidney function and disease progression in CKD patients.

4. Develop comprehensive management plans for patients with CKD, including lifestyle modifications and appropriate pharmacological interventions.

Problem Statement

Chronic Kidney Disease (CKD) is a growing health concern globally, with a high burden of morbidity and mortality. Despite its seriousness, the disease often goes undetected and undertreated, leading to a late referral to nephrologists. This delay in specialized care not only escalates the risk of patients starting dialysis in an emergency setting but also significantly impacts their overall prognosis and quality of life.

Important Statistics:

According to the National Kidney Foundation, as of 2021, an estimated 37 million American adults have CKD, but approximately 90% of those with the disease don't even know they have it.

- The Global Burden of Disease Study reported in 2017 that CKD was the 12th most common cause of death, accounting for 1.23 million deaths worldwide.
- According to a study published in the American Journal of Kidney Diseases, approximately 25-40% of patients in the U.S. see a nephrologist less than 90 days before initiating dialysis. This late referral to specialized care can have profound impacts on patient outcomes.
- CKD patients who do not see a nephrologist before starting dialysis have a 1-year mortality rate almost double compared to those who had nephrology care for more than a year before dialysis initiation, according to a study published in the Journal of the American Society of Nephrology.

What can Primary Care Do? A LOT!

•Risk Factor Identification
- Identify patients at high risk of CKD such as those with diabetes, hypertension, family history of kidney disease, or those over 60 years old.

- Regular Screening
  - Regularly screen high-risk patients for CKD. This includes blood tests for creatinine to calculate estimated Glomerular Filtration Rate (eGFR), and urine tests for albuminuria (protein in the urine).

- Optimal Management of Comorbidities
  - Manage comorbidities like diabetes and hypertension optimally to slow down CKD progression. This includes recommending lifestyle modifications and medications to control blood sugar and blood pressure.

- Lifestyle Modifications
  - Encourage patients to adopt a healthy lifestyle which includes regular exercise, maintaining a healthy weight, smoking cessation, and a diet low in sodium and protein.

- Medication Review
  - Review patient's medications regularly to avoid nephrotoxic drugs and adjust doses of medications cleared by the kidneys.

- Timely Referral
  - Refer patients to a nephrologist and a kidney disease management program timely when there is a rapid decline in kidney function, complications, or when approaching advanced stages of CKD (eGFR < 30 mL/min/1.73 m^2).

- Patient Education
  - Educate patients about the importance of regular follow-ups, medication adherence, potential symptoms, and complications of CKD.

Case Presentation

- 65-year-old man
- Type-2 diabetes since 2005, dyslipidemia and hypertension complicated by HFpEF and CAD s/p MI and LAD ICS.
- Diabetic retinopathy
- Medications: lisinopril 20 mg daily, metoprolol succinate 100 mg daily, clopidogrel 75 mg daily, aspirin 81 mg daily, atorvastatin 40 mg daily, & insulin lispro and glargine.
- BP 142/78 P 72

- How would you test for CKD and evaluate risk?

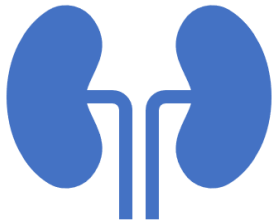
When to Refer to Nephrology?

- Nephrology specialists can be of particular assistance to primary care providers in treating patients who are at different stages of CKD
- Indications for referral vary across guidelines but there is one commonality:
  - Patients with a severely decreased estimated glomerular filtration rate (eGFR) of < between 45-30 mL/min per 1.73 m^2 require prompt referral to a nephrologist for comanaged care.
  - Research shows that late referral to nephrology is associated with significantly higher rates of mortality within the first 90 days of dialysis

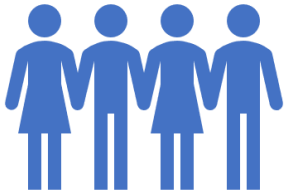
Other Key Criteria for Referral

- Urine albumin-to-creatinine ratio > 300 mg/g (34 mg/mmoL), including nephrotic syndrome
- Hematuria that is not secondary to urologic conditions
- Inability to identify a presumed cause of CKD
- eGFR decline of > 30% in less than 4 months without an obvious explanation
- Difficult-to-manage complications, such as anemia requiring erythropoietin therapy or abnormalities of bone and mineral metabolism requiring phosphorus binders or vitamin D preparations
- Serum potassium > 5.5 mEq/L
- Difficult-to-manage drug complications
- Age < 18 y
- Resistant hypertension
- Recurrent or extensive nephrolithiasis
- Confirmed or presumed hereditary kidney disease (eg, polycystic kidney disease, Alport syndrome, or autosomal dominant interstitial kidney disease)

Epidemiology



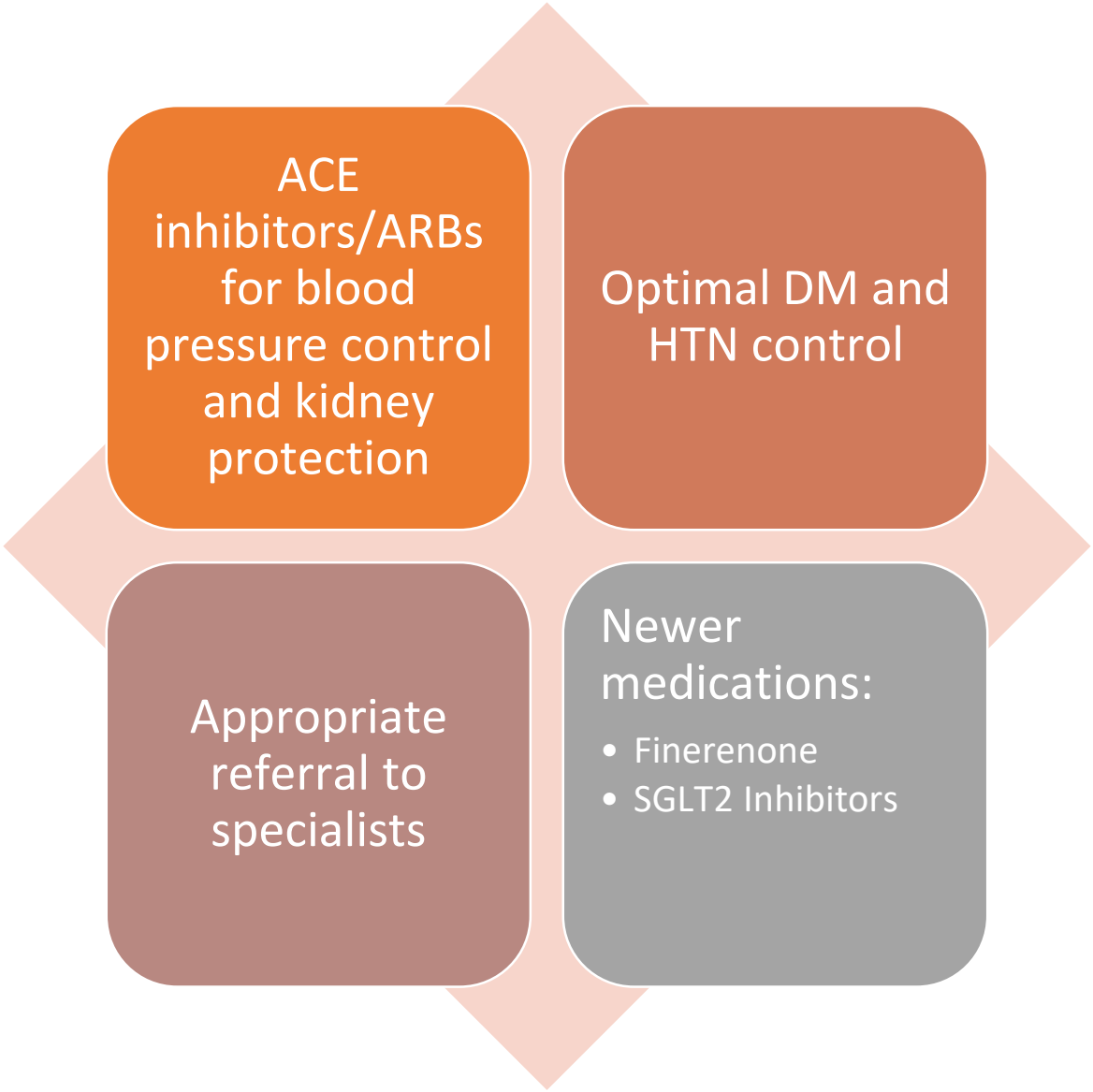
Chronic Kidney Disease (CKD): A progressive loss of kidney function over time



Prevalence in the USA:

Stage 3 CKD: ~9.1% of adults
Stage 4 CKD: ~0.5% of adults
Stage 5 CKD: ~0.1% of adults

Primary Care Management of CKD



Early Diagnosis and Screening Benefits

Timely intervention can slow disease progression

Improved management of comorbid conditions

Reduced complications and hospitalizations

Top Causes of CKD

- Diabetes mellitus (DM): Accounts for ~45% of CKD cases
- Hypertension (HTN): Accounts for ~28% of CKD cases
- Autoimmune diseases (e.g., lupus): Less common but significant cause

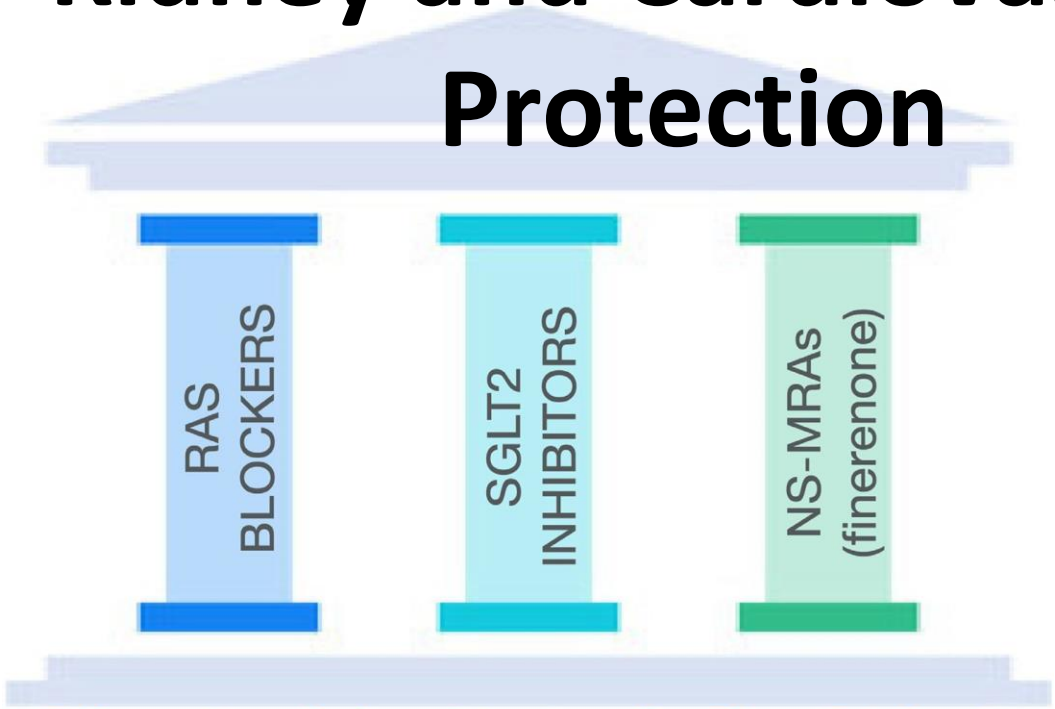
Screening for CKD

- Estimated glomerular filtration rate (eGFR): Indicator of kidney function
- Urine protein-to-creatinine ratio: Assesses proteinuria
- Urine microalbumin: Detects early kidney damage

Types of Renal Disease

- Prerenal: Issues affecting blood flow to the kidneys, such as dehydration, infection, cirrhosis and some medications such as ACE and NSAIDS
- Intrinsic: Damage to the kidneys themselves, including glomerular disease
- Postrenal: Obstruction of urine flow, such as with prostate cancer or uterine cancer or radiation related fibrosis

Kidney and Cardiovascular Protection



Pillars Needed to Maximally Slow Diabetic Kidney Disease Progression and Reduce Heart Failure Risk

Lifestyle

Regular risk factor reassessment (every 3–6 months)

Foundation of Delaying CKD Progression

- Cessation of tobacco smoking
- Glycemic control, the level of which is individualized.
- Treated blood pressure to a target range of systolic 110 – 130 mm Hg
- Management of dyslipidemia centered on statin-based therapy
- Healthy diet with a low glycemic index and restricted in sodium
- Maintenance of a healthy weight
- Optimizing physical activity

Nephrology Dialysis Transplantation 2023;38:253-257

Assessment of both albuminuria and eGFR is required for early CKD diagnosis[1–4]

CKD is defined as abnormalities in kidney structure or function, present for >3 months, which have implications for health[1]

Early detection of kidney dysfunction or impairment facilitates the appropriate diagnosis and treatment of CKD[2]

The clinical diagnosis of CKD in a person with diabetes is based on:[1–4]

The presence of albuminuria*
uACR >30 mg/g (>3 mg/mmol)

and/or

Reduced kidney function
(eGFR <60 ml/min/1.73 m^2)

in the absence of signs or symptoms of other primary causes of kidney damage

*Elevated UACR should be confirmed in the absence of urinary tract infection with two additional early-morning urine samples collected over the next 2 months

1. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int Suppl* 2013;3:1–163; 2. Levey AS, *et al. JAMA* 2015;313:837–846;
3. National Kidney Foundation. *Am J Kidney Dis* 2007;49(Suppl 2):S1–S180; 4. American Diabetes Association. *Diabetes Care* 2022;45(Suppl 1):S175–S184

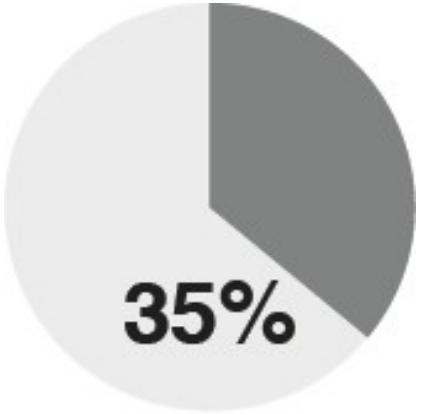
Socio-economic Status and Diversity in CKD Being Addressed

Use of race in clinical algorithms is problematic.

- Race is a social, not a biological construct ≠ genetic ancestry.
- Genetic ancestry variation within racial groups is substantial and genetic admixture across groups is common.
- Increasing biracial and multiracial individuals in the U.S. make racial categorization impractical.
- When assigning race in clinical algorithms, we risk accepting health inequities as immutable facts rather than injustices

N Engl J Med 2021; 384:474-480.
N Engl J Med 2020; 383:874-882

% Black
U.S. population



% Black
U.S. on dialysis

Kidney Disease in the U.S. Today

- **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

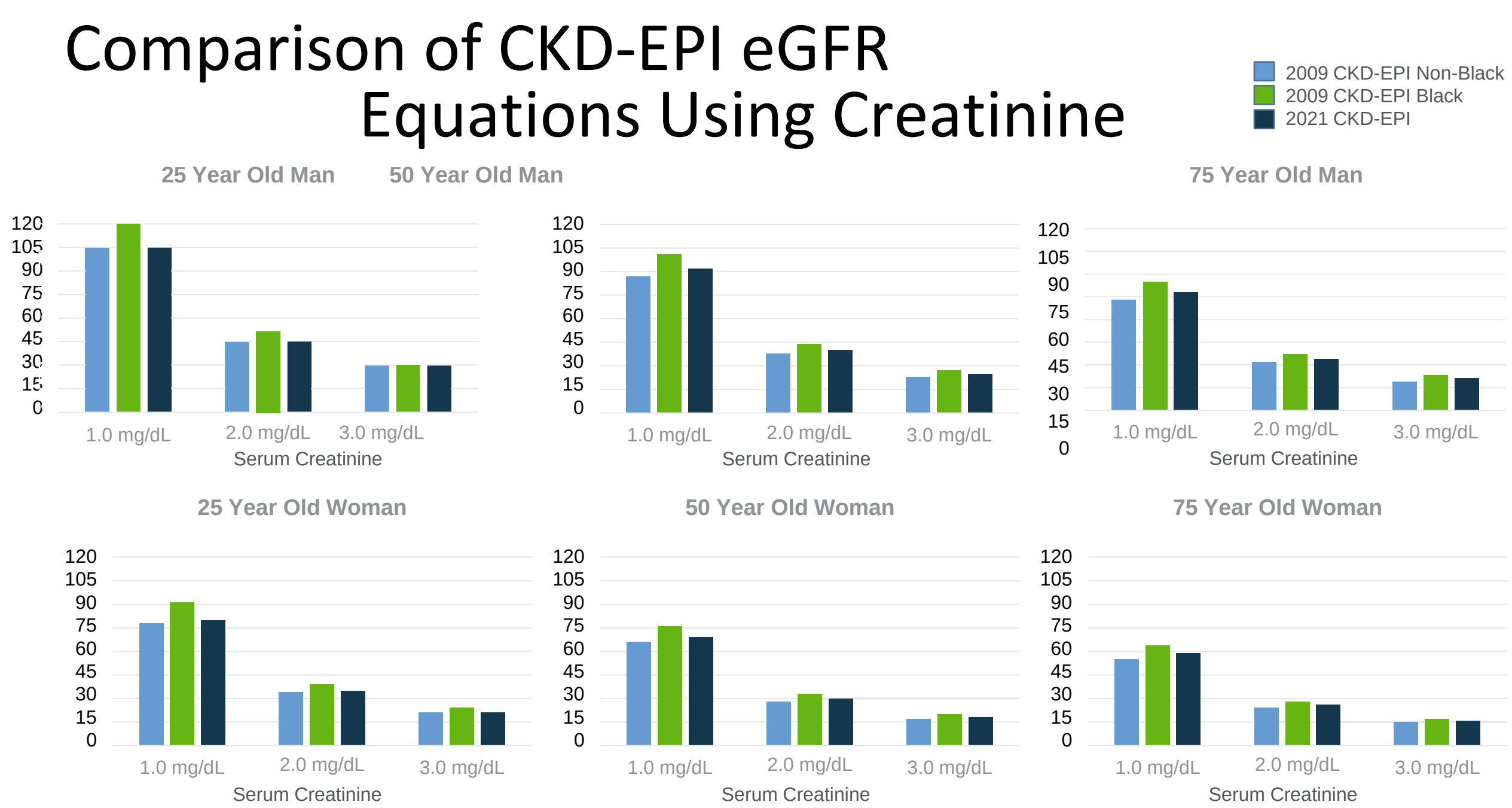
CDC CKD Surveillance System
https://nccd.cdc.gov/CKD

National Kidney Foundation-American Society of Nephrology Task Force Recommendations

1. Immediate implementation of 2021 CKD-EPI eGFRcr equation refit without race
2. National efforts to facilitate increased, routine, and timely use of cystatin C
3. Research on GFR estimation with new endogenous filtration markers and on interventions to eliminate race and ethnic disparities should be encouraged and funded

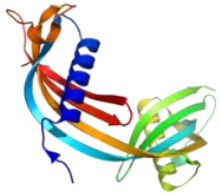
Am J Kidney Dis 2021; 78(1):103-115.

Comparison of CKD-EPI eGFR Equations Using Creatinine



Serum Creatinine versus Serum 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
- All tissues source
- Minimal muscle and diet influence
- Inflammatory marker

Adapted from W. Greg Miller, PhD

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

Serum Creatinine generation is LOW

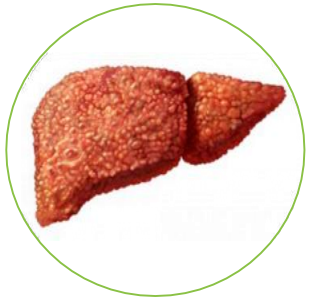
ELDERLY
FRAILTY

INACTIVITY
AMPUTATION

MALIGNANCY

VEGITARIAN 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

Chen DC, et al. Kidney 360 2022; 3:1807-1814 (adapted)

What is new with Albuminuria?

Who and when to screen?

T1D Yearly starting 5 years after diagnosis

T2D Yearly starting at diagnosis

How to screen?

Spot urine ACR

and

eGFR

What to do with a positive result?

Repeat and confirm:
- Evaluate possible temporary or spurious causes
- Consider using cystatin C and creatinine to more precisely estimate GFR
- Only persistent abnormalities define CKD

Initiate evidence-based treatments

What defines CKD diagnosis?

Persistent urine ACR ≥30 mg/g

and/or

Persistent eGFR <60 mL/min/1.73 m^2

and/or

Other evidence of kidney damage

Diabetes Management in Chronic Kidney Disease: A Consensus Report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). Diabetes Care 2022;45(12):3075-3090.

Albuminuria and Proteinuria Tests Approximate Equivalents

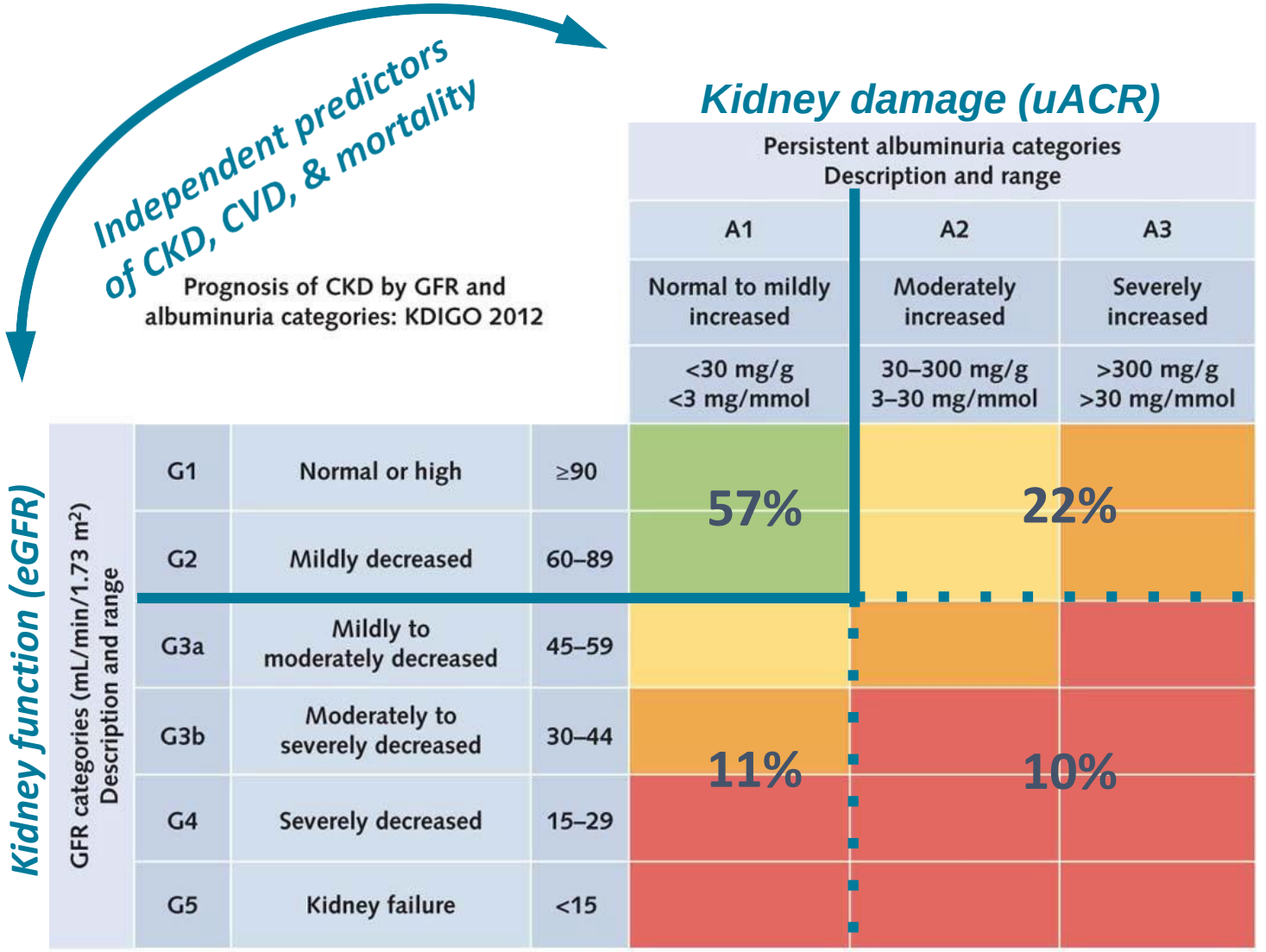
Albuminuria Or Proteinuria Description+	Albuminuria Or Proteinuria Category	Albumin mg/24-hour urine+	uACR+ mg/g	uPCR* mg/g	Dipstick Proteinuria
Normal to mildly increased	A1	< 30	< 30	< 150*	Negative to trace
Moderately increased	A2	30 to 300	30 to 300	150 to 650*	Trace to +1
Severely Increased	A3	> 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 This Table is in press in Clinical Chemistry 2023

Missing Albuminuria is a Missed Opportunity

- Both tests must be used
  - to identify new or undiagnosed CKD
  - to risk-stratify patients with CKD
- CKD diagnosis: decreased kidney function or increased damage for ≥ 3 months
  - eGFR < 60 ml/min/1.73m^2 **or**
  - uACR ≥ 30 mg/g
- **Half** of patients with T2D & CKD had elevated uACR *without* decreased eGFR (22% of 43%)
  - These patients would not be identified by eGFR alone.



Green, low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk.

BMC Res Notes. 2014 Jul 2;7:415. doi: 10.1186/1756-0500-7-415.

Kidney Health Evaluation for Patients with Diabetes HEDIS+ Measure

Measure =

Patients who received a kidney profile defined by an estimated Glomerular Filtration Rate (eGFR) AND urine Albumin-Creatinine Ratio (uACR) within a 12-month period

---

Patients aged 18-85 years with a diagnosis of diabetes with at least one in person or telehealth visit within a 12-month period

Denominator exclusions: Diagnosis of CKD stage G5 or ESRD, palliative care services and hospice enrollment

+Healthcare Effectiveness Data and Information Set beginning measurement year 2020

https://www.ncqa.org/hedis/measures/kidney-health-evaluation-for-patients-with-diabetes/

Kidney Health Evaluation for Patients with Diabetes Low Measure Satisfaction

Year	Commercial HMO	Commercial PPO	Medicaid HMO	Medicare HMO
2021 (%)	43.9	39.6	33.5	44.2

Missing albuminuria is a missed opportunity.

https://www.ncqa.org/hedis/measures/kidney-health- evaluation-for-patients-with-diabetes/

Nephrotoxic Medications Summary

- Every drug a patient puts into their body is at least partly excreted through the kidneys.
- If the drug or vitamin is not taken following a healthcare provider's instructions, or if it is an illegal substance, it can cause injury to the kidneys.
- There are certain medications that have higher incidence of acute kidney injury which we should be aware of

Classes of Medications to Monitor

- Antibiotics
- Pain medicine
- Alcohol
- Supplements
- Prescription laxatives
- Contrast dye
- Illegal drugs

National Kidney Foundation Recommendations:

- **What should you advise your patients?**
- Do not take any medicine, drug or substance unless you are under a healthcare provider's supervision.
- Do not take pills or substances given to you by a stranger or even a friend.
- If you do take a medication or other substance and feel ill, contact your healthcare provider immediately.
- If you need to have an imaging test or colonoscopy, let your healthcare provider know if you have kidney disease or are at risk for getting it.

Over the counter vs Prescription

- Over the counter medications can cause harm and are readily available and patients should be educated
- **Cholesterol medications.** The dosing of certain cholesterol medications, known as "statins", may need to be adjusted if you have chronic kidney disease.
- **Pain medications.** If you have decreased kidney function some over-the-counter and prescription pain medications, including nonsteroidal anti-inflammatory drugs (NSAIDs), are not recommended because they can reduce blood flow to the kidneys. Certain narcotic pain medications can build up in the body and cause serious problems for patients with chronic kidney disease.
- **Anti-microbial meds.** Many anti-fungal, antibiotic and antiviral medications are cleared by the kidneys. It's important that you and your clinician are aware of your level of kidney function so that a kidney-safe medication can be prescribed for your treatment.
- **Diabetes medications.** Insulin and certain medications used by people with diabetes are cleared by the kidneys. Because diabetes is a leading cause of kidney disease, it's important that those with diabetes control their blood sugar levels. Blood sugar control typically involves a combination of diet, physical activity, and medication. If you have diabetes and chronic kidney disease, check with your physician to see if any dosing changes need to be made based on your level of kidney function.
- **Upset stomach/antacid medications.** This group of over-the-counter medications can disrupt the body's electrolyte balance if you have chronic kidney disease. Check with your doctor to see if these are safe for you to use.

Diabetes Medications and CKD/ESRD

- High risk of hypoglycemia if not dose adjusted
- Educate patients regarding importance of monitoring blood sugar
- Educate re: signs and symptoms of hypoglycemia and treatment plan (keeping sugar candies, life alert, etc)

Risk Factors for AKI/CKD due to Medications

- Some patient-related risk factors for drug-induced nephrotoxicity are:
- age older than 60 years,
- underlying renal insufficiency (e.g., glomerular filtration rate of less than 60 mL per minute per 1.73 m^2),
- volume depletion
- Diabetes
- heart failure
- sepsis

How to prevent kidney disease due to medications

- General preventive measures include:
  - using alternative non-nephrotoxic drugs whenever possible
  - correcting risk factors, if possible
  - assessing baseline renal function before initiation of therapy, followed by adjusting the dosage
  - monitoring renal function and vital signs during therapy
  - Of course: avoiding nephrotoxic drug combinations.

Statistics

- Drugs cause approximately 20 percent of community-and hospital-acquired episodes of acute renal failure
- Among older adults, the incidence of drug-induced nephrotoxicity may be as high as 66 percent.
- Compared with 30 years ago, patients today are:
  - older
  - have a higher incidence of diabetes and cardiovascular disease
  - take multiple medications
  - are exposed to more diagnostic and therapeutic procedures with the potential to harm kidney function.

Pathogenic Mechanisms

- altered intraglomerular hemodynamics
- tubular cell toxicity
- inflammation
- crystal nephropathy
- Rhabdomyolysis
- thrombotic microangiopathy

Analgesics

- Acetaminophen, aspirin: Chronic interstitial nephritis
- Nonsteroidal anti-inflammatory drugs: Acute interstitial nephritis, altered intraglomerular hemodynamics, chronic interstitial nephritis, glomerulonephritis

Anti Depressants

- Amitriptyline (Elavil*), doxepin (Zonalon), fluoxetine (Prozac):
  - Rhabdomyolysis
  - Lithium: Chronic interstitial nephritis, glomerulonephritis, rhabdomyolysis

Rare but Interesting

- Antihistamines including Diphenhydramine (Benadryl), doxylamine (Unisom) can cause Rhabdomyolysis!
- Other medications that can cause renal failure more commonly include chemotherapy agents and herbs including herbals with aristocholic acid: Chronic interstitial nephritis

Other ways to prevent kidney injury

- General preventive measures include using equally effective but non-nephrotoxic drugs whenever possible
- correcting risk factors for nephrotoxicity
- assessing baseline renal function before initiating therapy
- adjusting the dose of medications for renal function
- avoiding nephrotoxic drug combinations

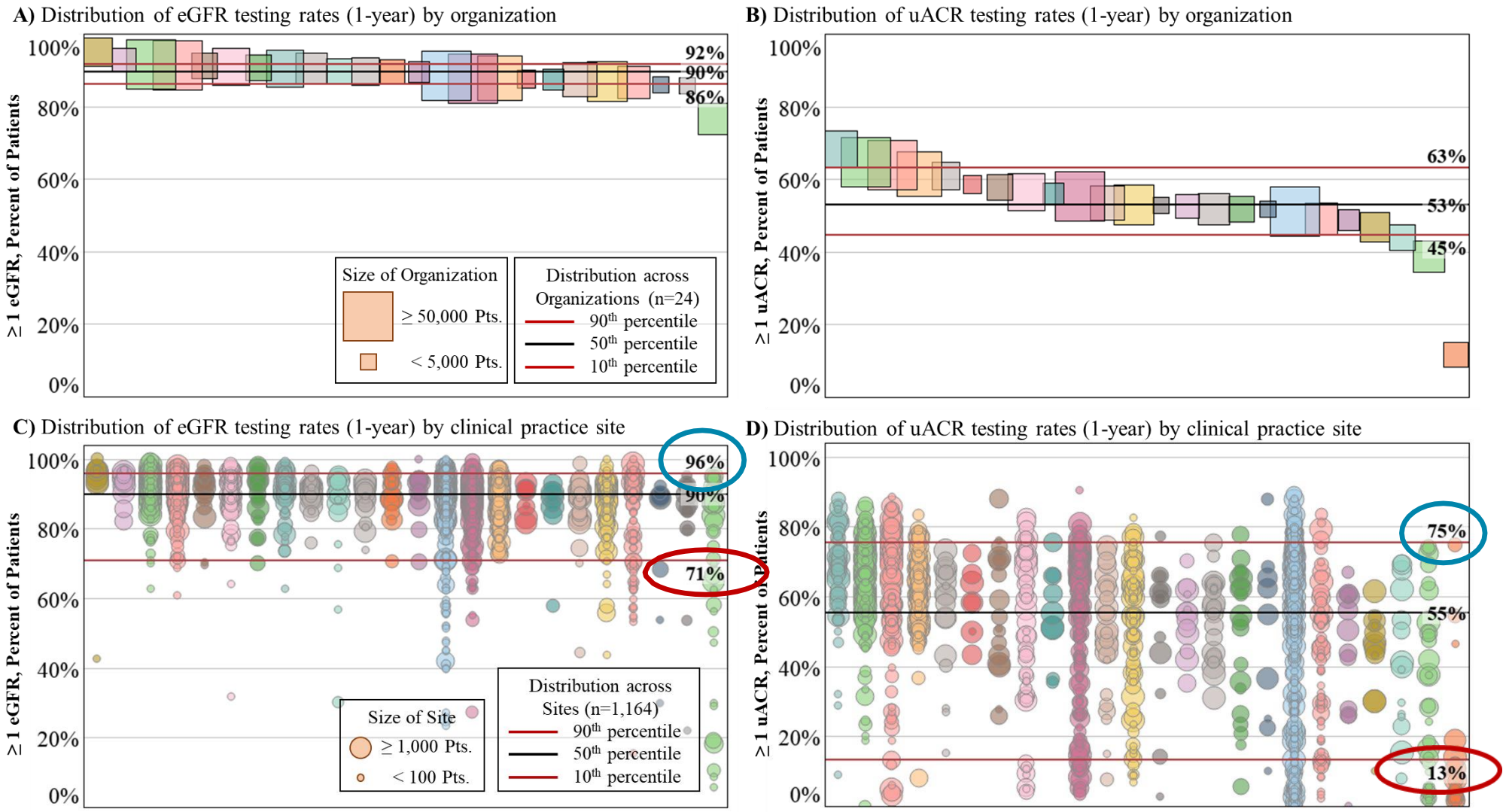
CKD Testing Among T2DM in US Healthcare Organizations

Albuminuria is most often Missing.

Many organizations have at least 1 site among the **Lowest-** & **highest-** performing sites across all organizations.

Even high testing organizations have improvement opportunities.

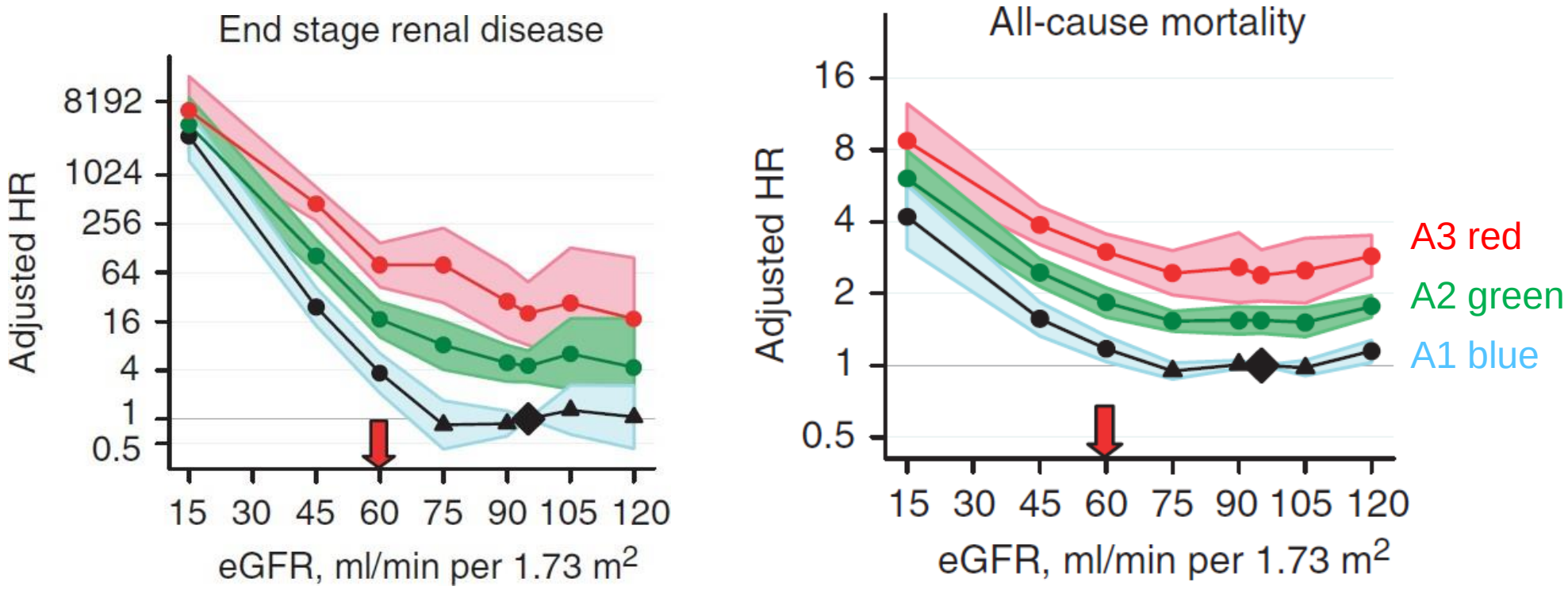
Figure 1: eGFR (panels: A, C) and uACR (panels: B, D) 1 year measurement rates by HCO (panels: A, B) and sites of care within HCOs (panels: C, D)



Each square reflects a different healthcare organization (HCO) which are ranked (horizontally) in descending order based on measurement rates. Each set of colored circles reflects the sites of care within the respective HCO with the same color above.

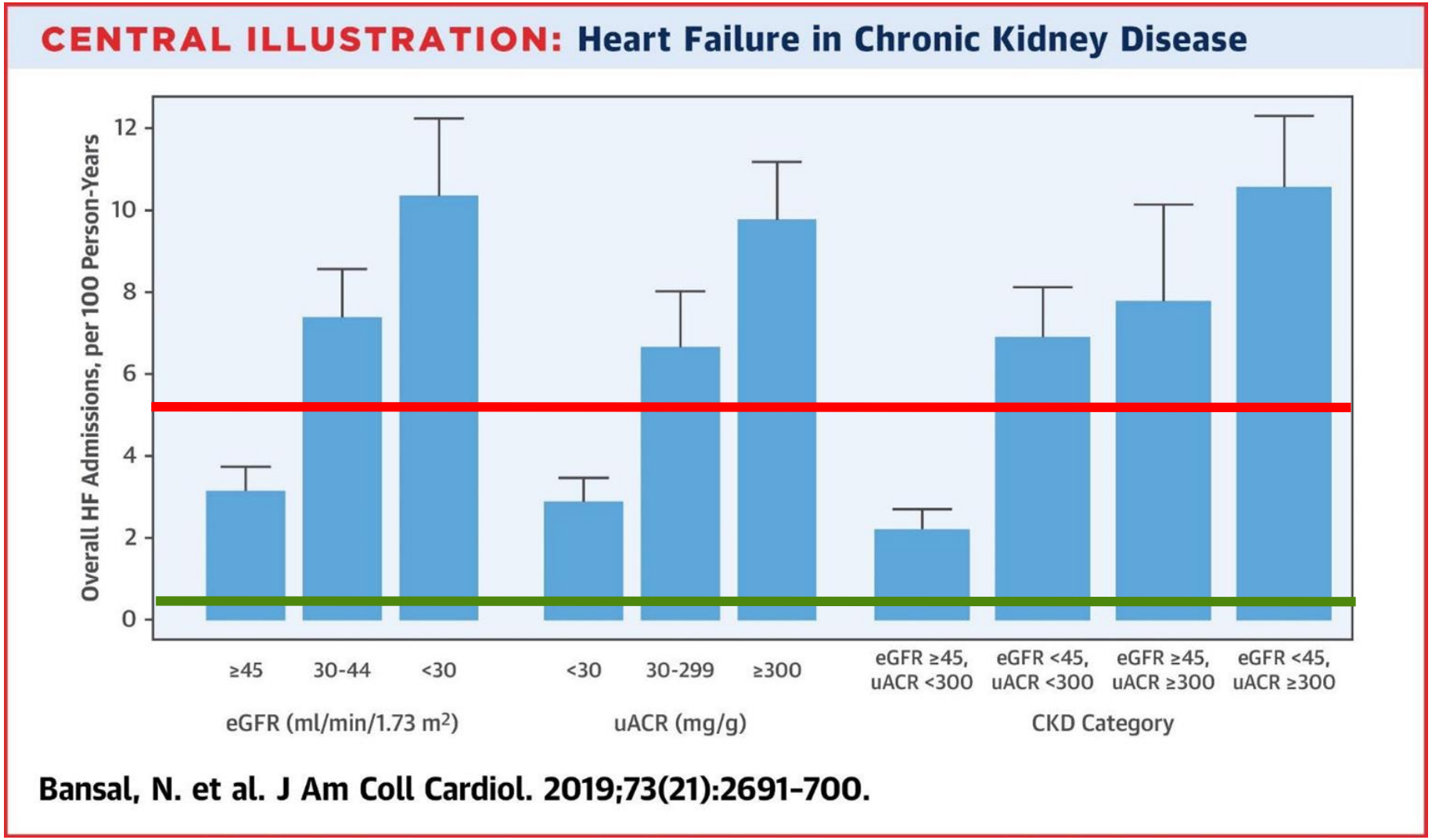
Diabetes Care 2021; 44:2000–2009

Low eGFR and Albuminuria Predict Kidney Failure and Mortality



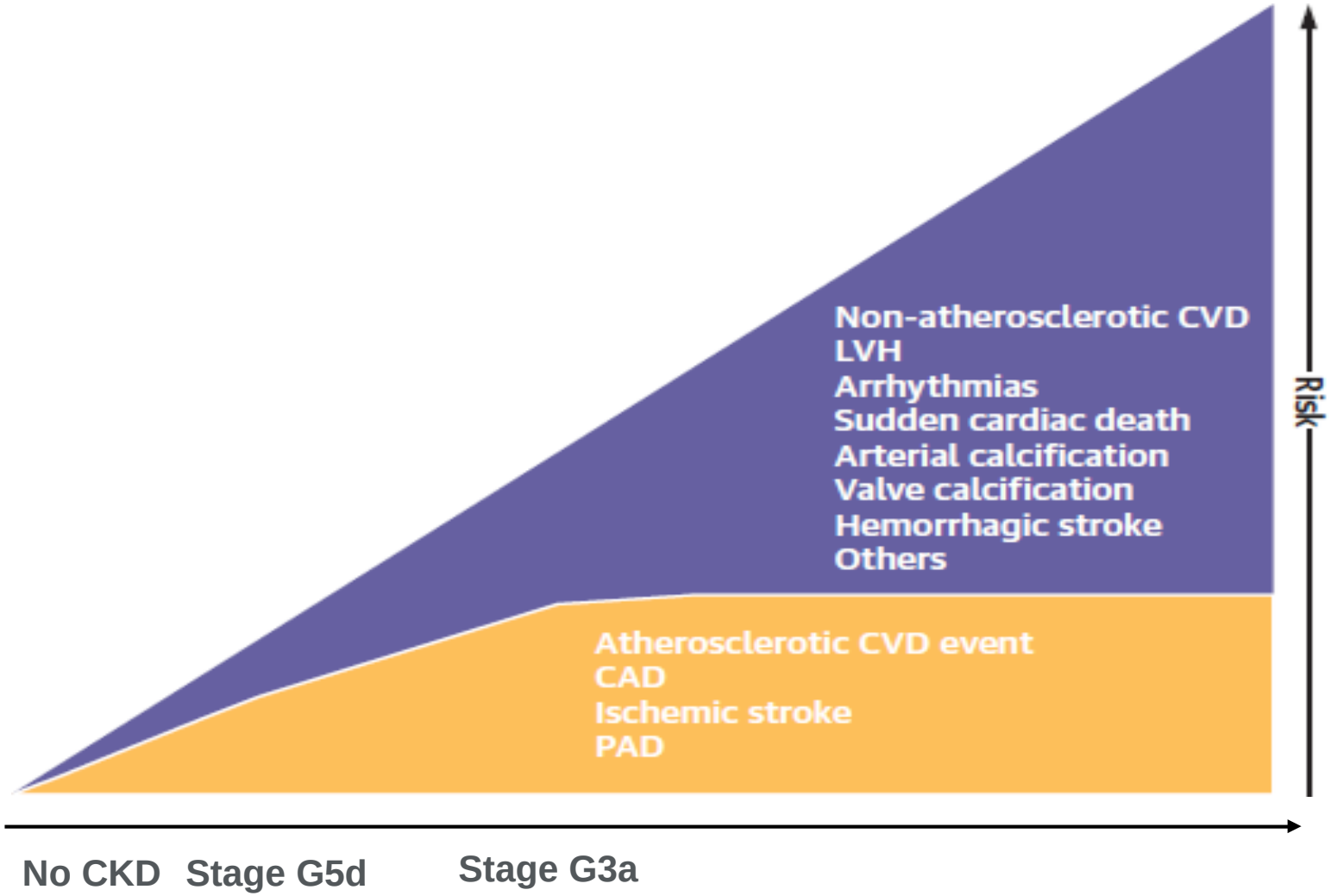
Kidney Int Suppl. 2013; 3: 1-150.

Heart Failure Hospitalization by eGFR and Albuminuria (uACR)



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

In CKD, the natural history of CVD is different from the General Population with more non-atherosclerotic disease



CAD, coronary artery disease; CKD, chronic kidney disease; CVD, cardiovascular disease; LVH, left ventricular hypertrophy; PAD, peripheral artery disease

Wanner C, et al. Lancet 2016;388:276-284

Classification of CKD

- Cause (C)
- GFR (G)
- Albuminuria (A)

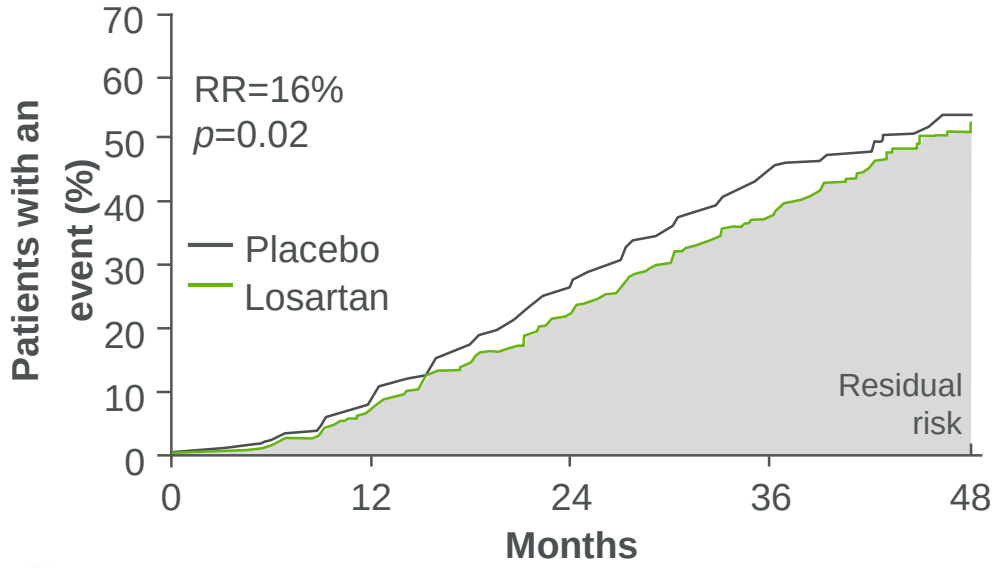
KDIGO 2012

				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, Description and Range (mL/min/ 1.73 m^2)	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			

Despite RAS blockade, patients with T2DM and advanced CKD are at risk of CKD progression

RENAAL: Losartan vs placebo[1]

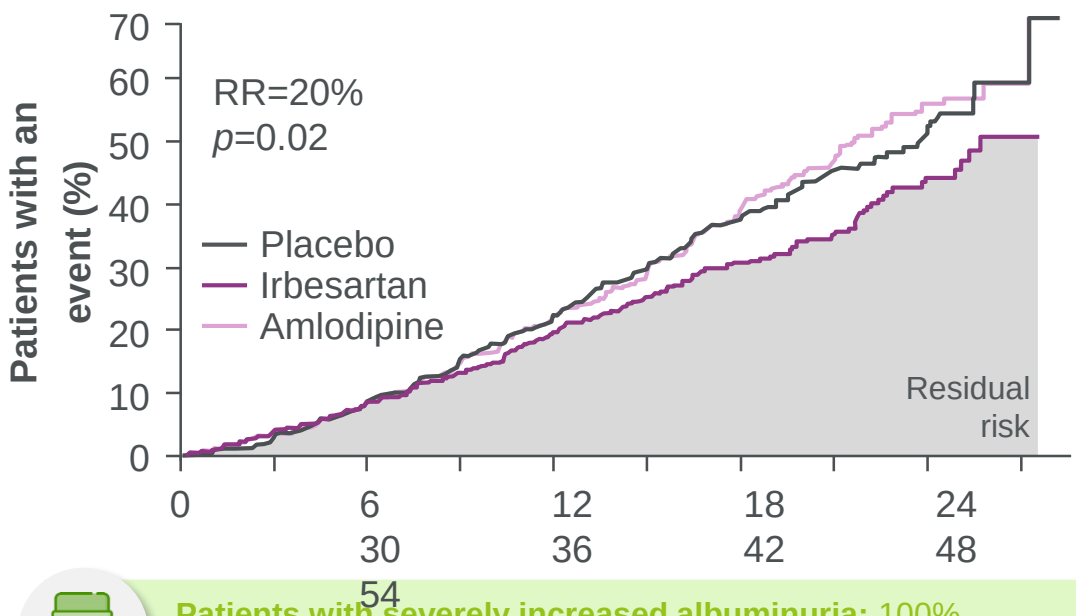
Primary composite endpoint:
Doubling of SCr, kidney failure or death



Patients with severely increased albuminuria: 100%
Median uACR: 1249 mg/g

IDNT: Irbesartan vs amlodipine vs placebo[2]

Primary composite endpoint:
Doubling of SCr, kidney failure or death



Patients with severely increased albuminuria: 100%
Median uACR: 1900 mg/g

RAS, renin–angiotensin system; RR, risk reduction; SCr, serum creatinine; SOC, standard of care

1. Brenner BM, *et al. N Engl J Med* 2001;345:861–869; 2. Lewis EJ, *et al. N Engl J Med* 2001;345:851–860

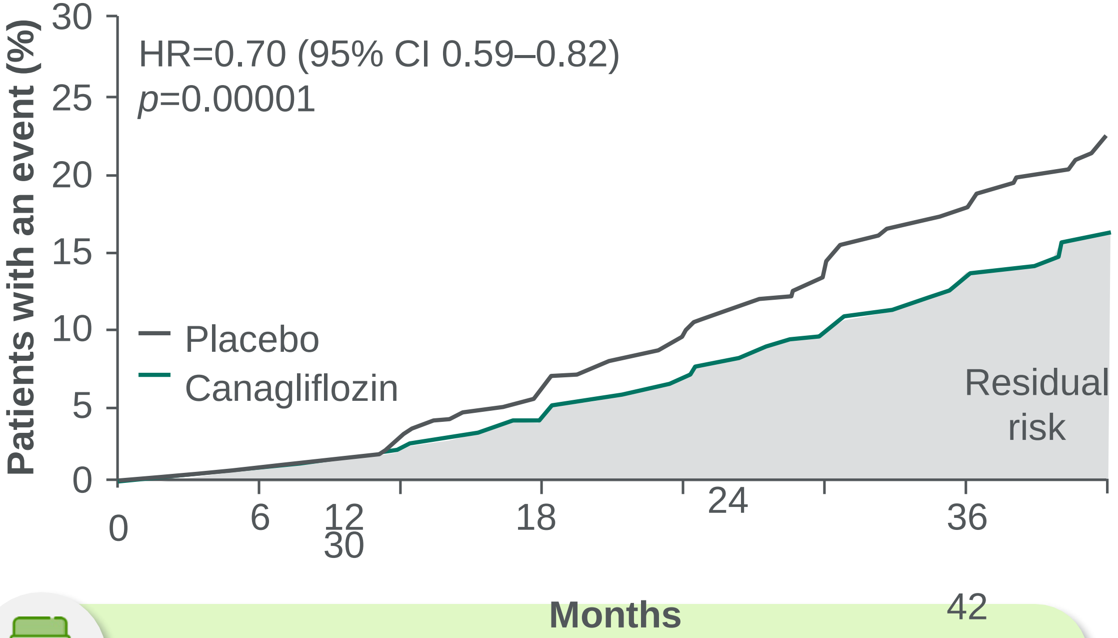
Newer Medications to Treat CKD

- Finerenone
- SGLT2 Inhibitors

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]

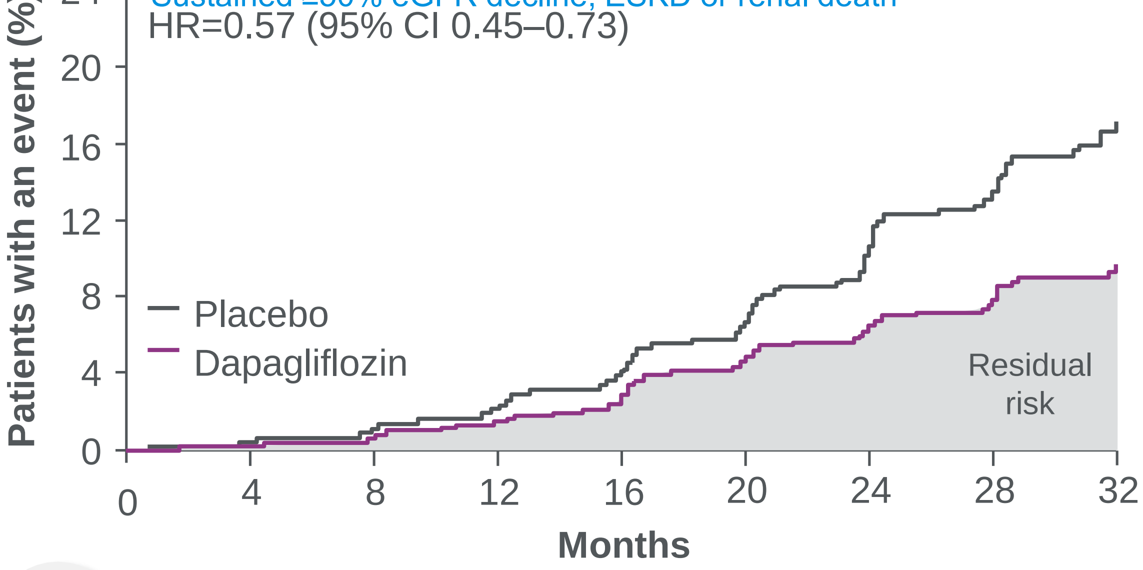
Primary composite outcome:
Kidney failure, doubling of SCr or death from kidney/CV causes



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

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

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



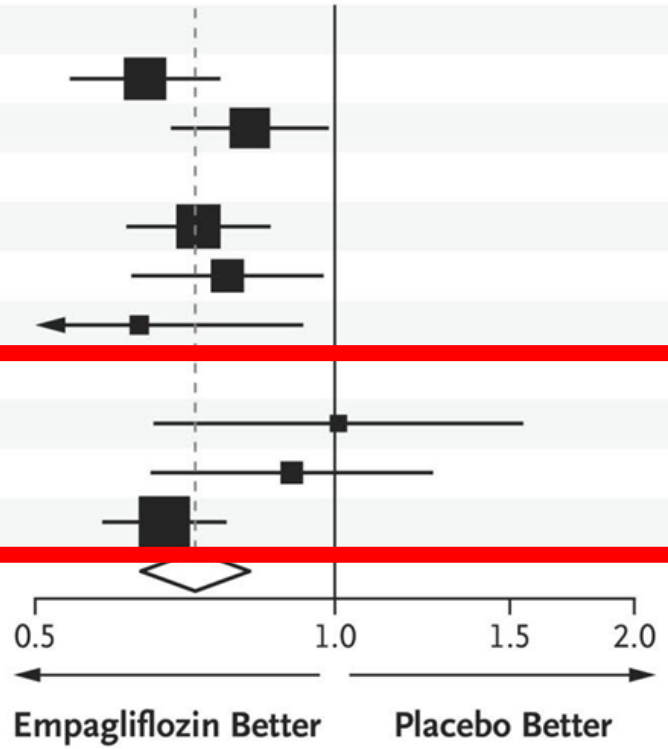
Patients with severely increased albuminuria: 89.7%
Median uACR: 949 mg/g

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

Subgroup	Empagliflozin (no. of patients with event/total no.)	Placebo (no. of patients with event/total no.)	Hazard Ratio for Progression of Kidney Disease or Death from Cardiovascular Causes (95% CI)
Diabetes mellitus			
Present	218/1525	306/1515	0.64 (0.54–0.77)
Absent	214/1779	252/1790	0.82 (0.68–0.99)
Estimated GFR			
<30 ml/min/1.73 m^2	247/1131	317/1151	0.73 (0.62–0.86)
≥30 to <45 ml/min/1.73 m^2	140/1467	175/1461	0.78 (0.62–0.97)
≥45 ml/min/1.73 m^2	45/706	66/693	0.64 (0.44–0.93)
Urinary albumin-to-creatinine ratio			
<30	42/665	42/663	1.01 (0.66–1.55)
≥30 to ≤300	67/927	78/937	0.91 (0.65–1.26)
>300	323/1712	438/1705	0.67 (0.58–0.78)
All patients	432/3304	558/3305	0.72 (0.64–0.82)

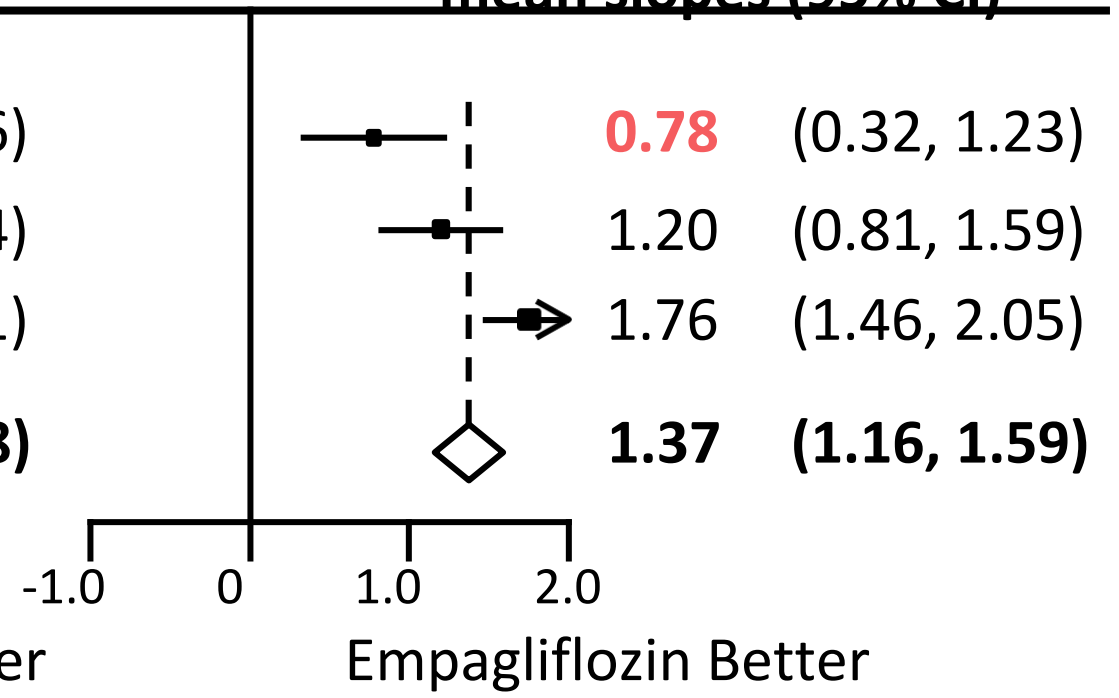


Primary Outcome = CKD progression or cardiovascular mortality

N Engl J Med 2023;388:117-127

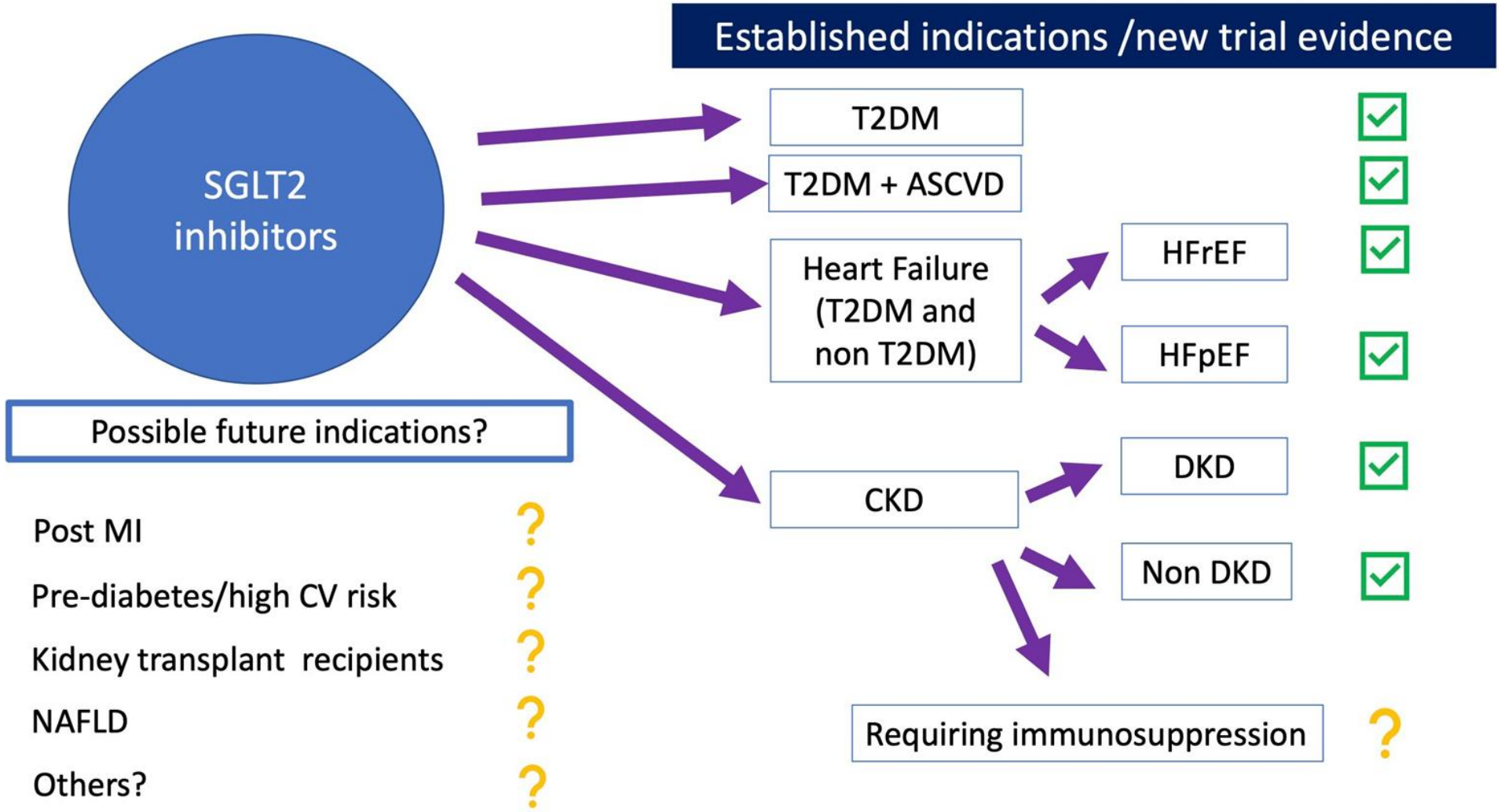
EMPA-KIDNEY eGFR Slopes by Albuminuria: Benefit across albuminuria levels

uACR (mg/g)	Mean slope (SE) mL/min/1.73m²/yea		Difference between mean slopes (95% CI)	
	Empagliflozin	Placebo		
<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



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.

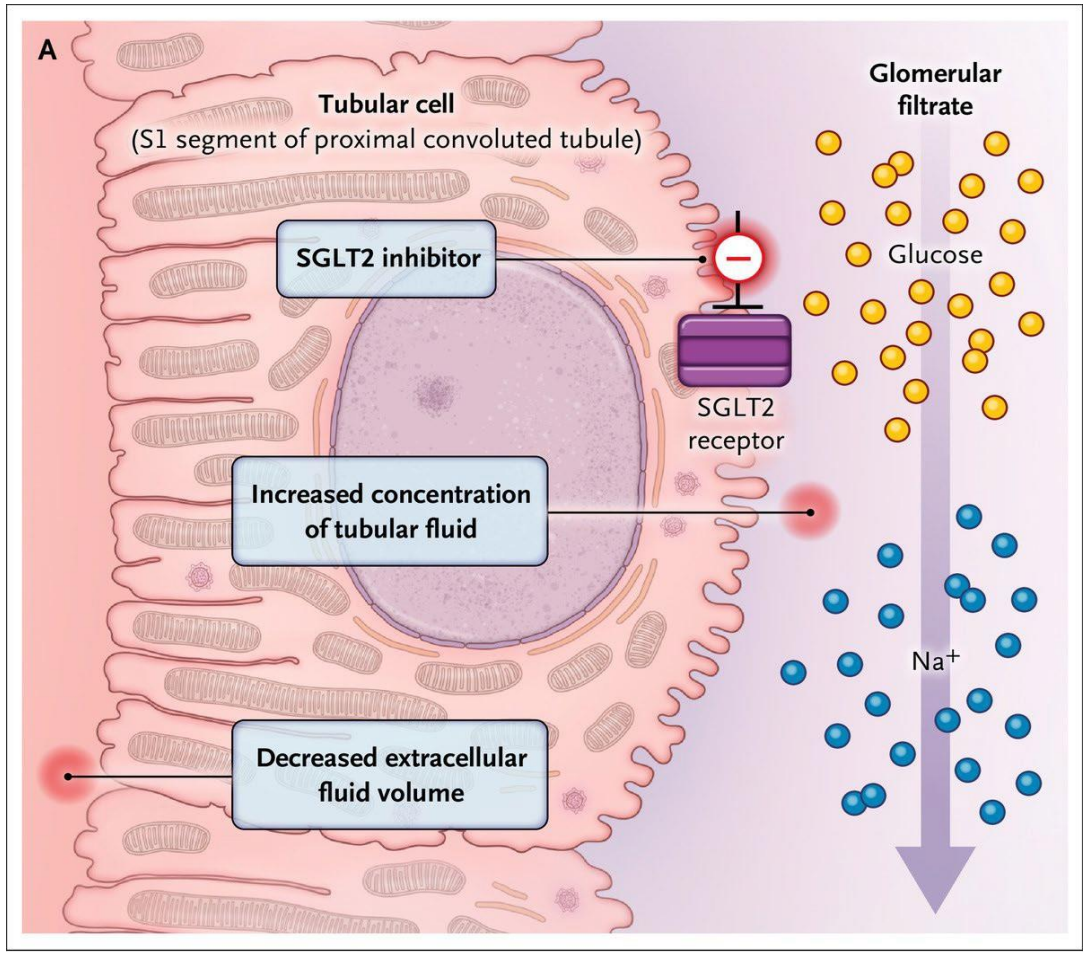
Lancet 2022:400(10365): 1745-1747

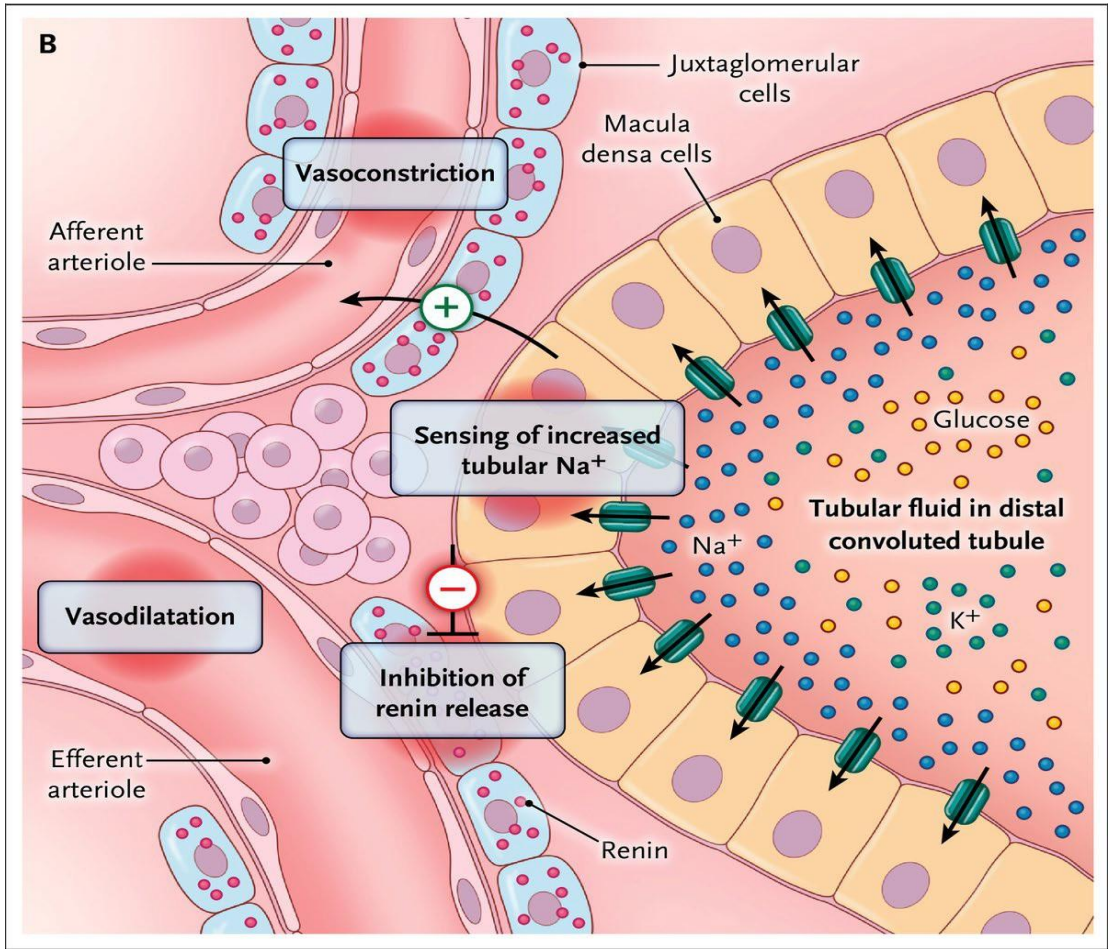
What do the clinical practice guidelines say about SGLT-2 inhibitors in CKD?

In summary, most current guidelines agree with the recommendation to use SGLT2i in CKD (grade 1A where reported) with minor differences in eGFR thresholds, but with substantial variation regarding albuminuria levels (if any). Most guidelines also mention that SGLT2i can be continued up to the initiation of renal replacement therapy or kidney transplantation. From a glycemic therapy, SGLT2i have evolved into organ-protective therapy with several indications and a solid evidence base.

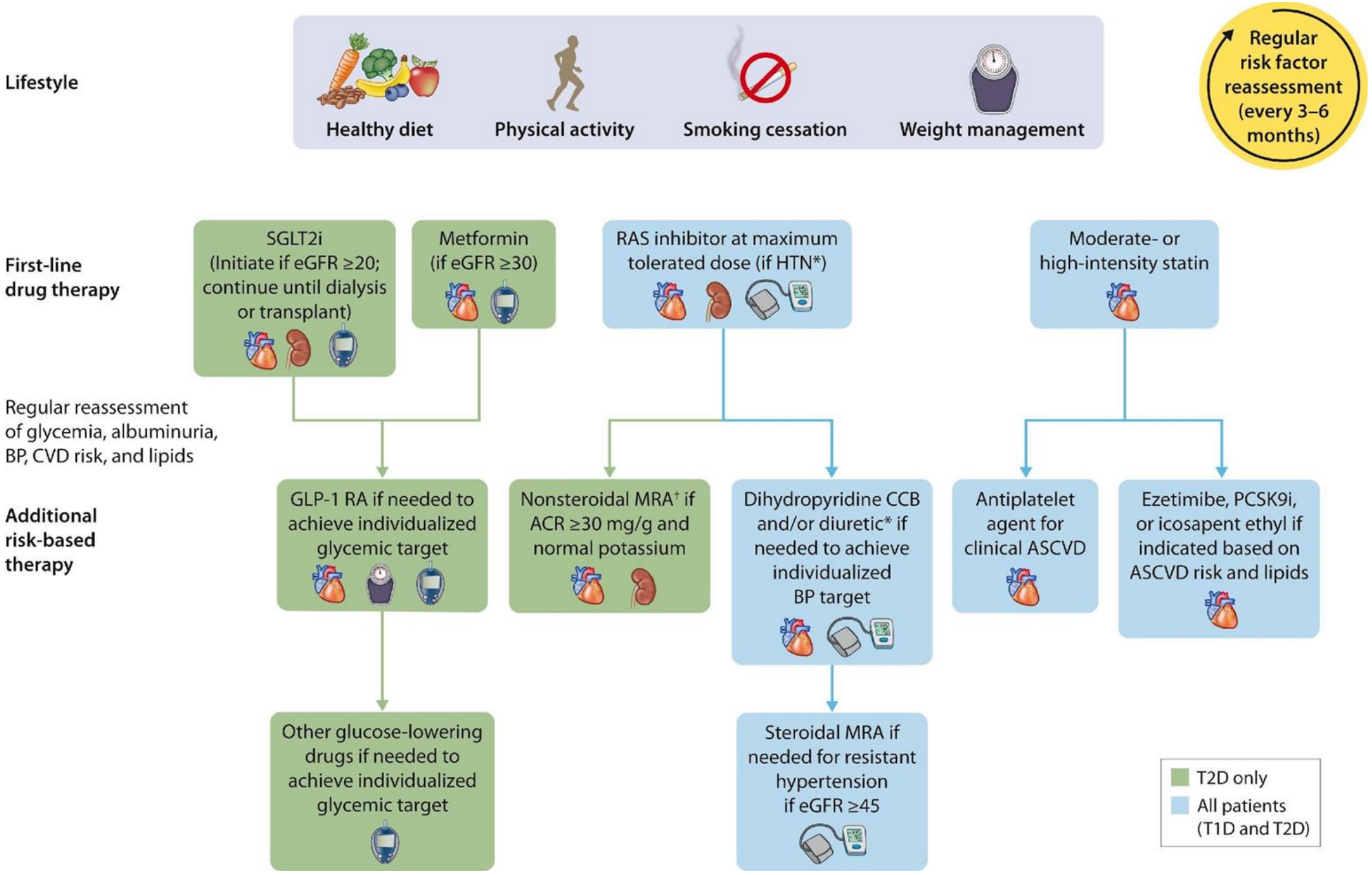
Zhang, RM, Persson, F, McGill, JB, Rossing P. NDT 2023; 38:542-550.

Effects of SGLT-2 Inhibition





Brunwald E. N Engl J Med 2022; 386: 2024-2034

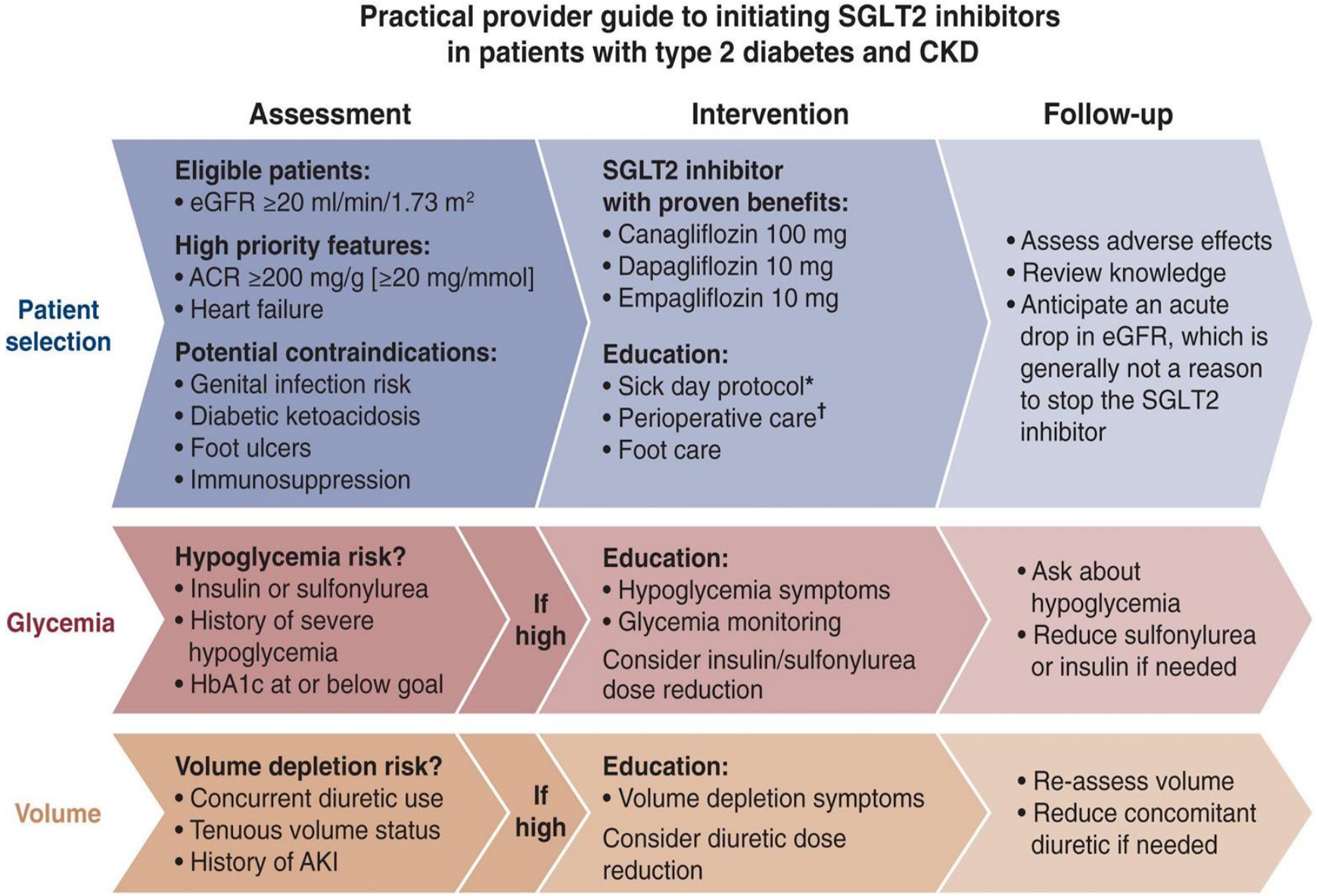


KDIGO Diabetes in CKD
Kidney Int 2022;102
(Suppl S5):S1-S127

Patient Selection, Intervention and Follow-up for SGLT-2 inhibitor Use in CKD with T2D

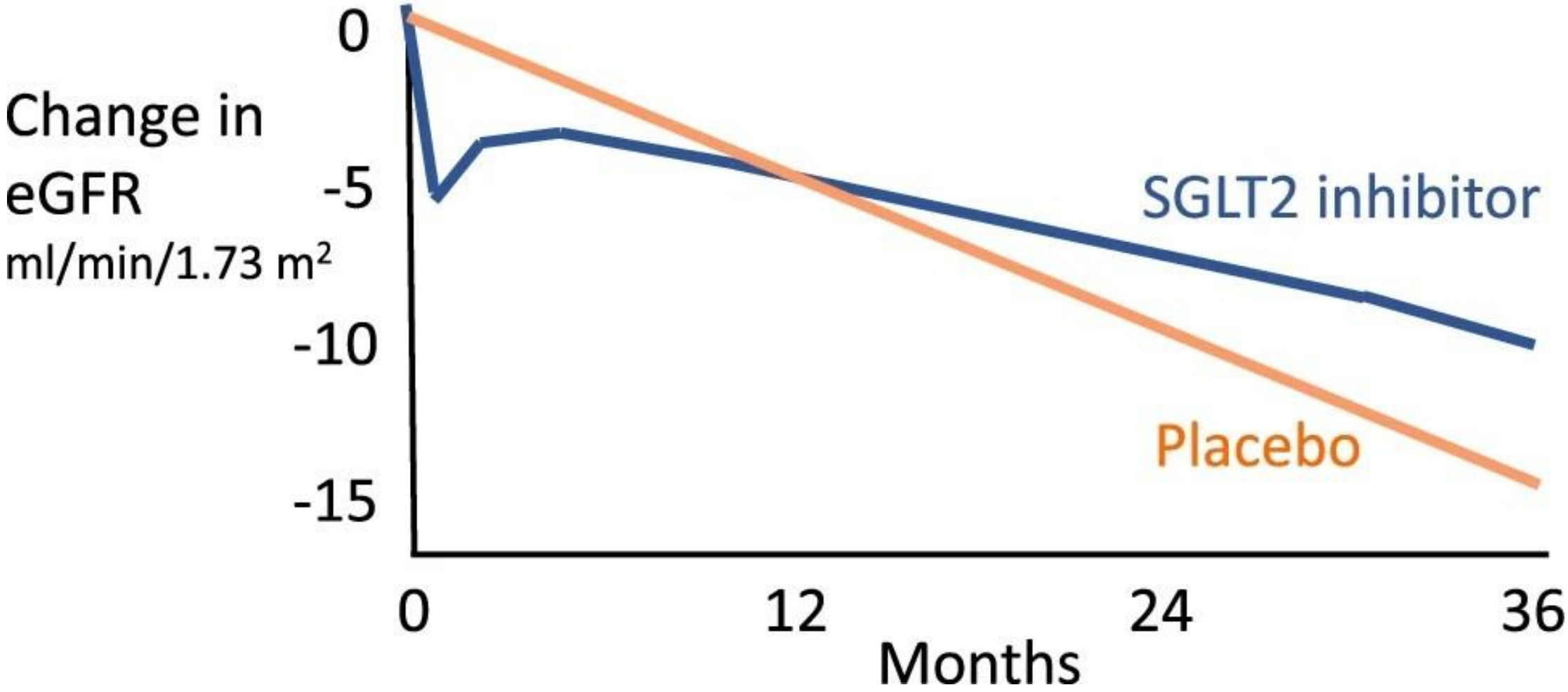
Recommendation

1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i *(1A)*.



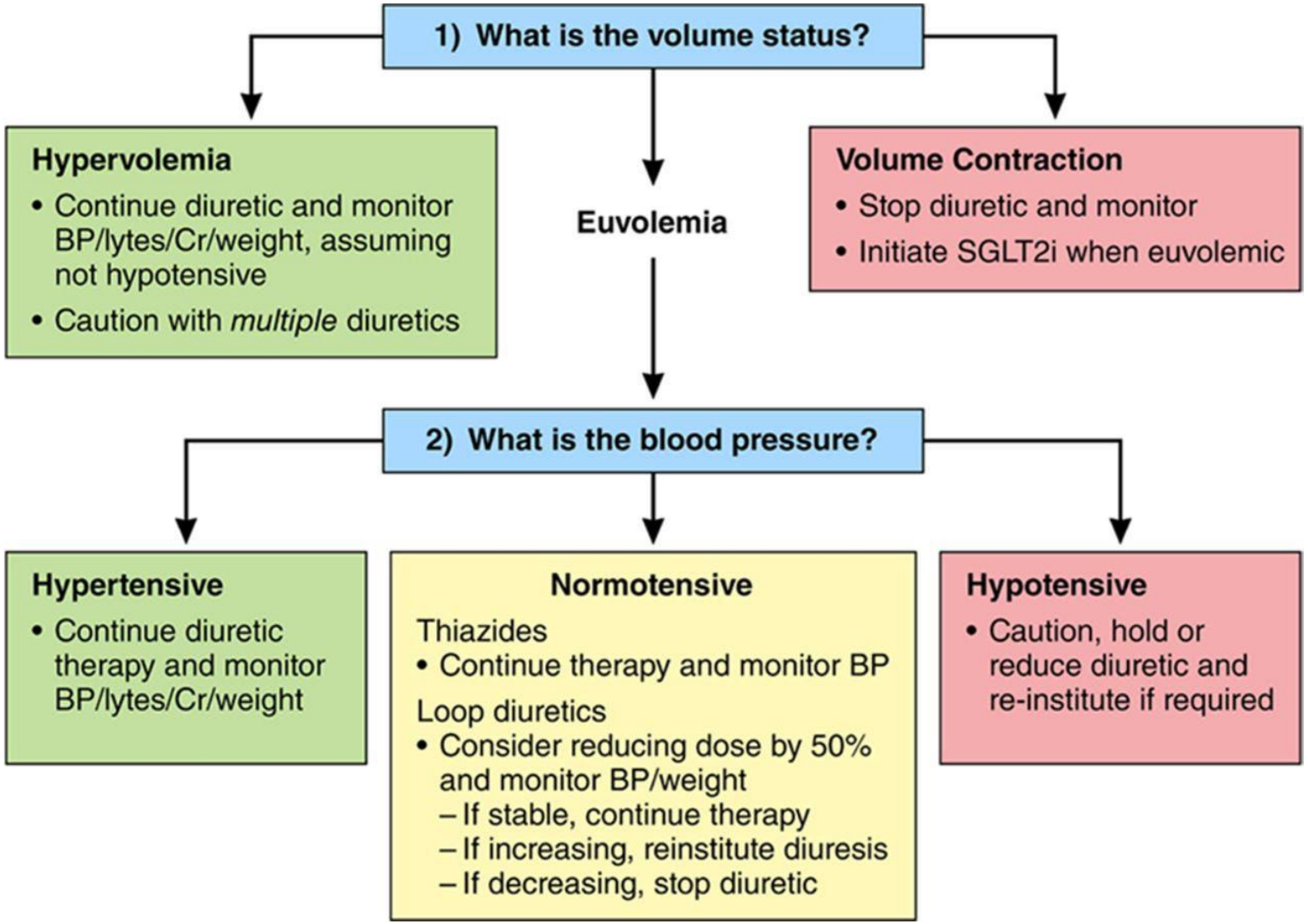
Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int 2022;102(5S):S1–S127.

Expect Hemodynamic Loss of eGFR in the First 4 Weeks After Starting an SGLT-2 Inhibitor



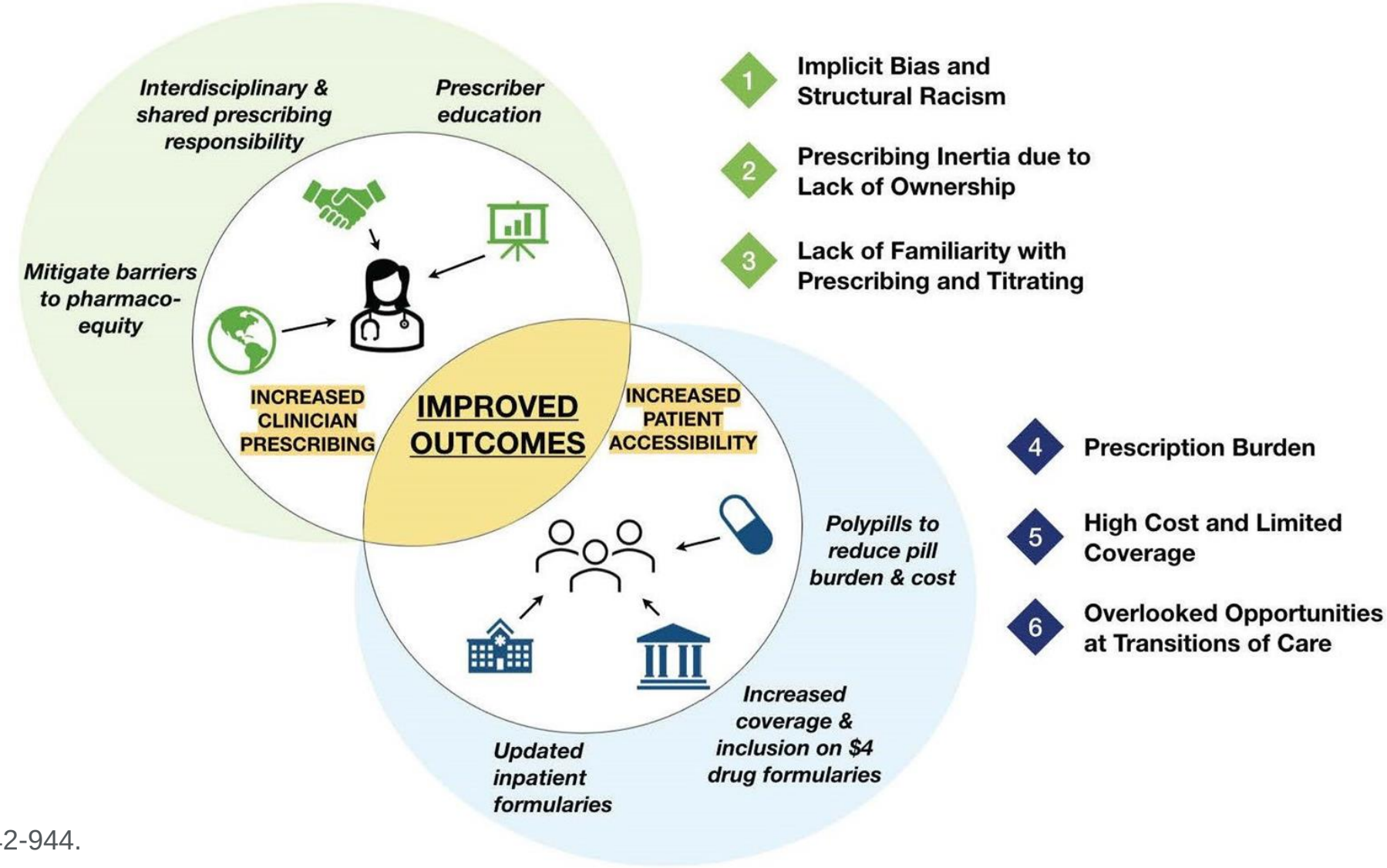
Curr Diab Rep 2022;22(1):39-52. Concept slide loosely based on EMPA-REG, CREDENCE and DAPA-CKD trials

An Approach to Diuretic Use With SGLT-2 inhibitors



Circulation 2016; 134(24):915-1917

Achieving Equitable Access to SGLT-2 inhibitors and Finerenone

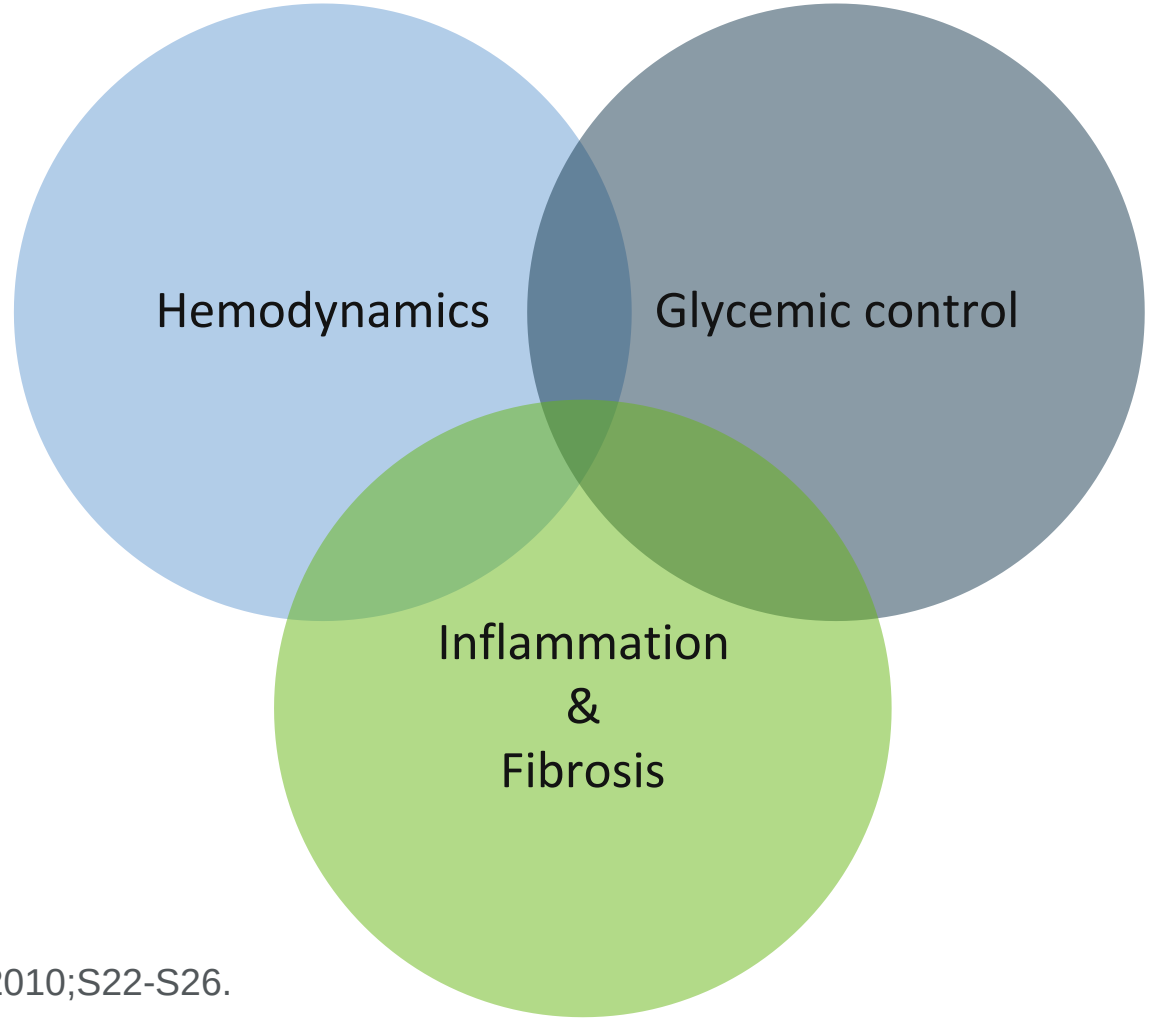


Kidney360. 2022;3(5)942-944.

Annals Int Med 2023;176(3):417-418.

Strategies to Slow Progression of Chronic Kidney Disease

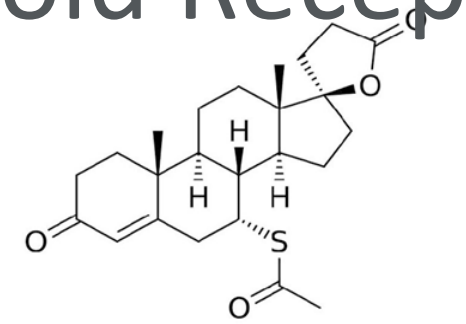
ACE inhibitors
ARBs
SGLT-2 inhibitors

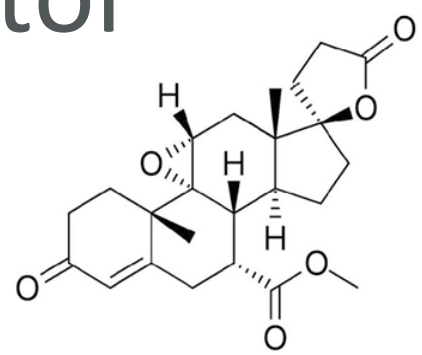


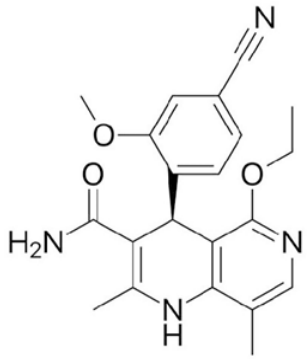
Metformin,
SGLT-2 inhibitors
(several mechanisms may be independent of glucose–lowering)

Lee SB, et al. *Kidney Int Suppl*. 2010;S22-S26.

Mineralocorticoid Receptor Antagonists



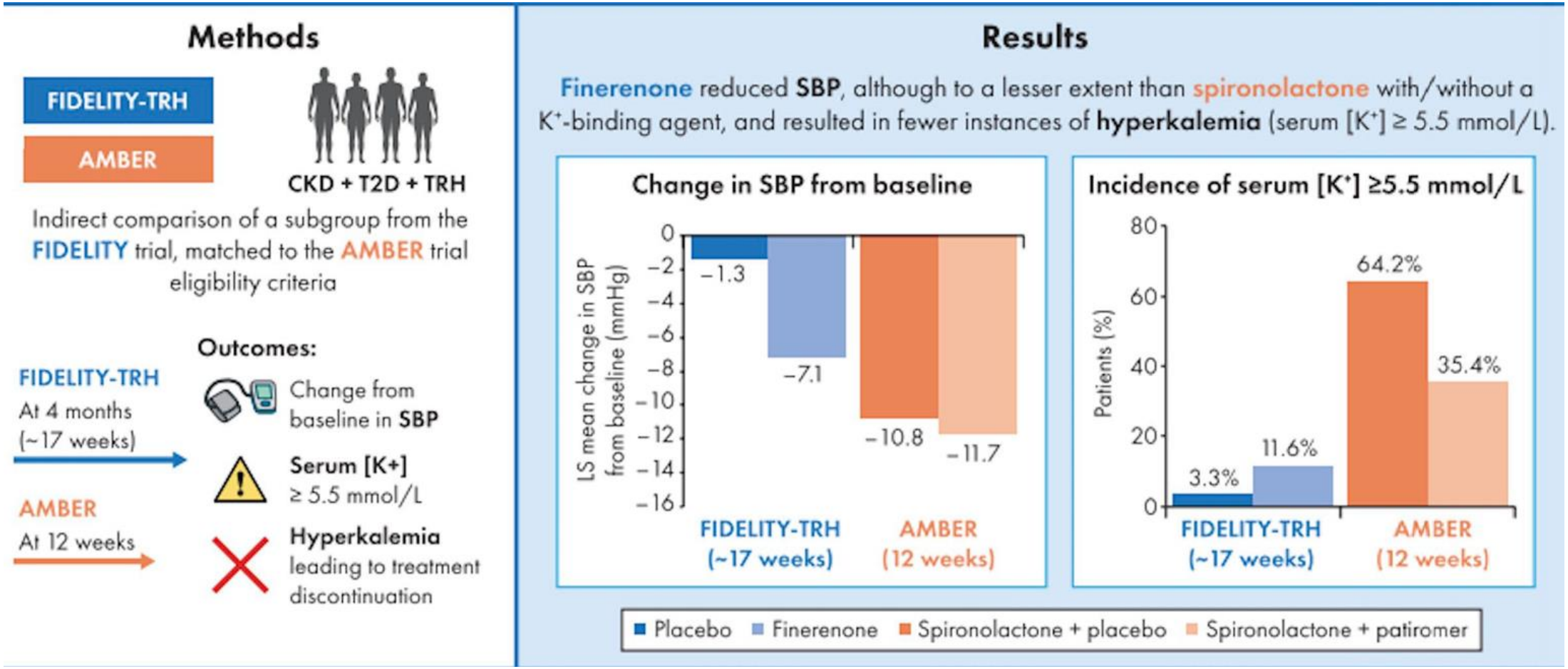




	Spironolactone	Eplerenone	Finerenone
Structure	Flat (steroidal)	Flat (steroidal)	Bulky (non-steroidal)
Potency to MR	+++	+	+++
Selectivity to MR	+	++	+++
Tissue distribution	Kidney > heart	Kidney > heart	Balanced kidney-heart
Active metabolites	+++	-	-
Half-life	Long*	4-6 hours	2-3 hours
Sexual side-effects	++	+	-

Am J Hypertens. *2023:* 36(3):135-143.https://doi.org/10.1093/ajh/hpac124

Spironolactone versus Finerenone: Comparative Post Hoc Analysis



Clin Kidney J 2022;16(2):293-302.

Phase III Clinical Trials of Finerenone in T2DM with CKD

FIDELIO-DKD

A randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven phase III study to investigate the safety and efficacy of finerenone, in addition to standard of care, on the progression of kidney disease in subjects the clinical diagnosis of chronic kidney disease in T2D.[1]

FIGARO-DKD

A randomized, double-blind, placebo-controlled, parallel-group, multicenter, event-driven phase III study to investigate the safety and efficacy of finerenone, in addition to standard of care, on the reduction of cardiovascular morbidity and mortality in subjects with the clinical diagnosis of chronic kidney disease in T2D.[2]

1. Bakris GL, et al. *Am J Nephrol*. 2019;50:333-344; 2. Ruilope LM, et al. *Am J Nephrol*. 2019;50:345-356.

Key question posed by the phase 3 finerenone program: FIDELITY analysis

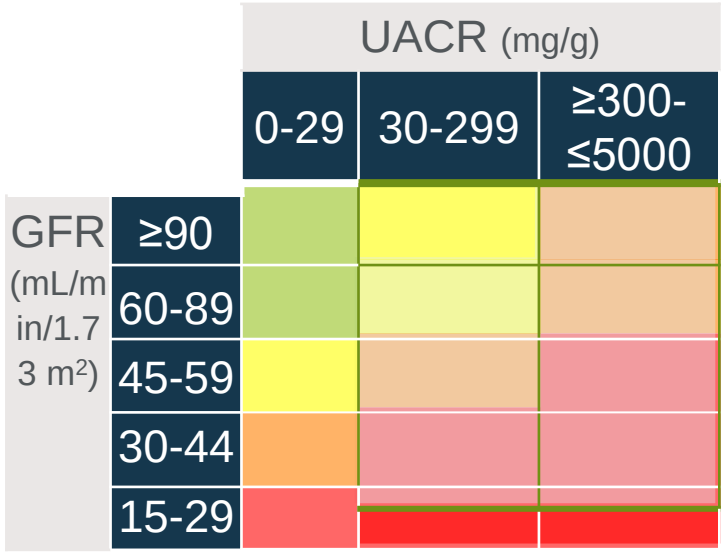
- Does finerenone, a non-steroidal mineralocorticoid receptor antagonist, added to maximized RAS inhibition reduce cardiovascular disease and kidney disease progression over a broad range of chronic kidney disease in people with type 2 diabetes?

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

FIDELITY ANALYSIS: Inclusion & Exclusion criteria

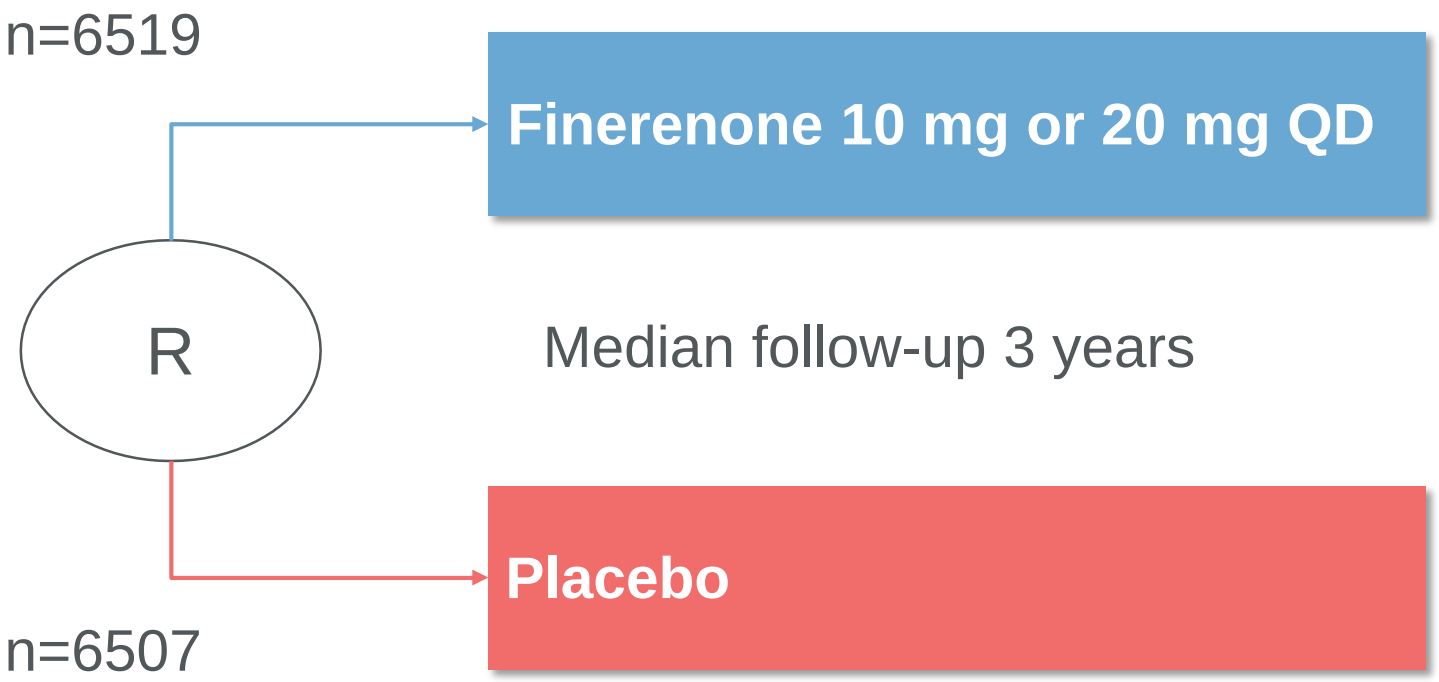
✓ T2D + CKD
eGFR ≥25 mL/min/1.73 m^2
UACR 30-5000 mg/g
Serum [K^+] ≤ 4.8 mmol/L
Maximum tolerated labeled dose of RAS

✗ Symptomatic HFrEF



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

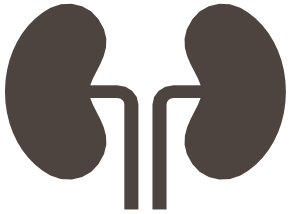
FIDELITY Protocol



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

FIDELITY Outcomes

CV composite:
Time to CV death, non-fatal MI, non-fatal stroke, or HHF



≥57% kidney composite: Time to kidney failure, sustained ≥57% decrease in eGFR, or renal death

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

At baseline, patients had well-controlled blood pressure and HbA1c, and CV medications were used by most patients

Characteristic	Total (n=13,026)
Age, years	65
Male, %	70
Duration of T2D, years	15.4
HbA1c, %	7.7
SBP/DBP, mmHg	**137/76**
History of CV disease, n (%)	**5935 (46)**
History of HF, %	**1007 (7.7)**
Serum [K^+], mmol/l	4.4

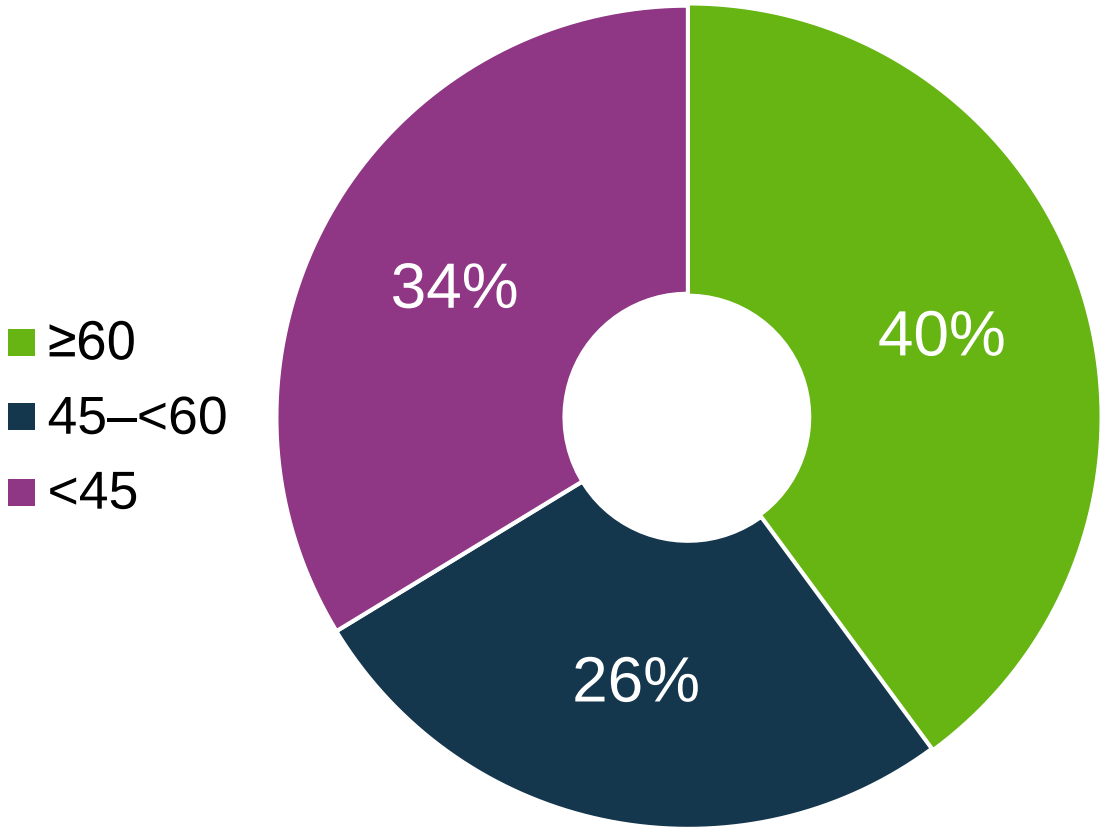
Medications, n (%)	Total (n=13,026)
CV medications	
RASi	**13,003 (100)**
Statins	**9399 (72)**
Beta-blocker	6504 (50)
Calcium antagonist	7358 (57)
Diuretic	**6710 (52)**
Glucose-lowering therapy	12,720 (98)
Metformin	7557 (58)
Insulin	7630 (59)
GLP-1RA	944 (7.2)
SGLT-2i	877 (6.7)

CV, cardiovascular; DBP, diastolic blood pressure; GLP-1RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated haemoglobin; HF, heart failure; RASi, renin–angiotensin system inhibitor; SBP, systolic blood pressure; SGLT-2, sodium-glucose co-transporter-2 inhibitors; T2D, type 2 diabetes

1. Agarwal R, *et al. Eur Heart J* 2021; doi: 10.1093/eurheartj/ehab777

In FIDELITY, 40% patients had CKD with an eGFR ≥60 ml/min/1.73 m²

Baseline eGFR (ml/min/1.73 m²)*



A high proportion of patients had albuminuric CKD with preserved kidney function (eGFR ≥60 ml/min/1.73 m²)

- This highlights the importance of uACR assessment to detect patients at risk

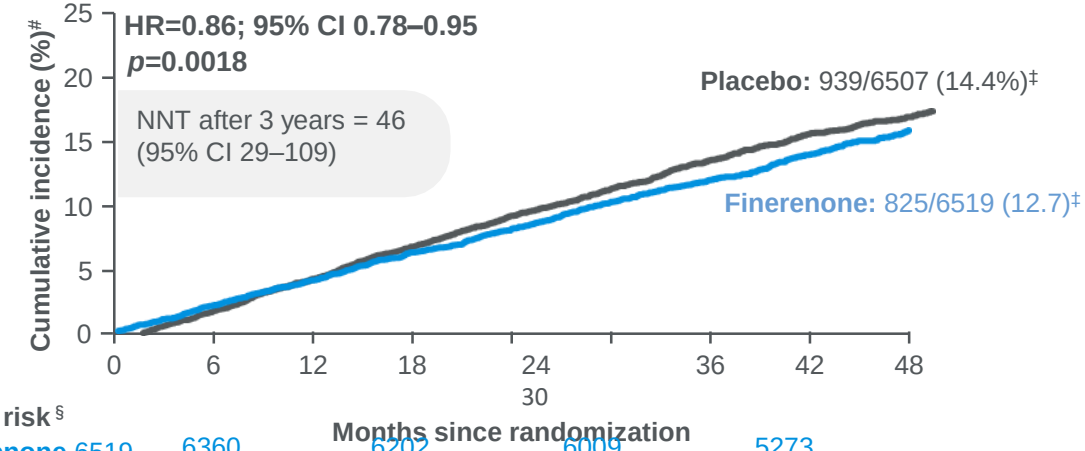
*Data were missing for 3 patients

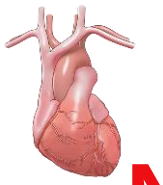
Filippatos G, *et al*. *ESC* 2021; oral presentation

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



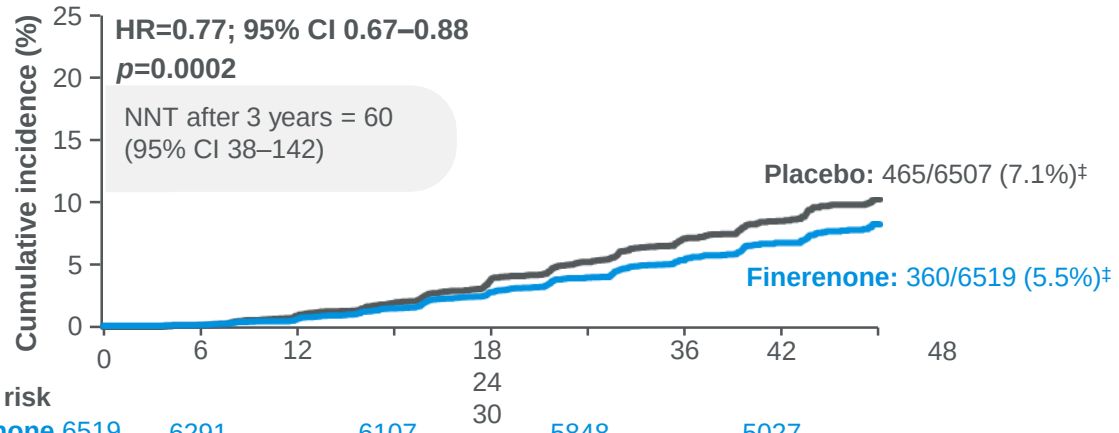


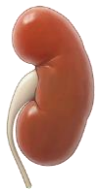
14% reduced **risk of CV morbidity and mortality** vs placebo (HR=0.86; 95% CI 0.78–0.95)[1]

NNT 46

Kidney composite

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





23% reduced **risk of CKD progression*** vs placebo (HR=0.77; 95% CI 0.67–0.88)[1]

NNT 60

*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

1. Agarwal R, *et al. Eur Heart J* 2021; doi: 10.1093/eurheartj/ehab777

Finerenone significantly reduced the risk of all non-fatal components of the ≥57% eGFR kidney composite

Component of ≥57% eGFR kidney composite	Finerenone (n=6519) n (n/100 PY)	Placebo (n=6507) n (n/100 PY)	HR (95% CI)	*p*-value
Kidney failure	254 (1.38)	297 (1.62)	0.84 (0.71–0.99)	0.039
ESKD*	151 (0.76)	188 (0.96)	0.80 (0.64–0.99)	0.040#
eGFR <15 ml/min/1.73 m²‡	195 (1.06)	237 (1.29)	0.81 (0.67–0.98)	0.026#
≥57% decrease in eGFR‡¶	257 (1.40)	361 (1.98)	0.70 (0.60–0.83)	<0.0001
Renal death	2 (0.01)		0.53 (0.10–2.91)	–

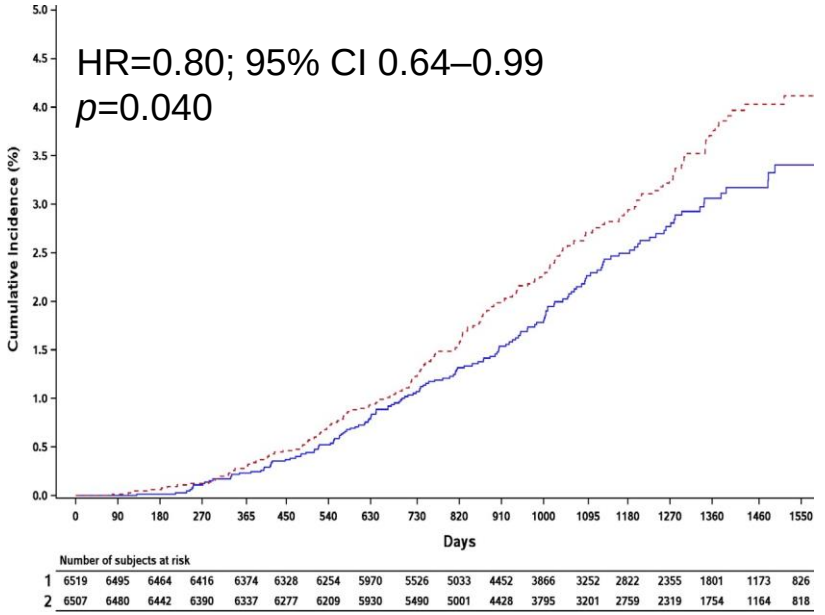
0.5 2.0

Favors finerenone

Favors placebo

Finerenone reduced the risk of ESKD* by 20% vs placebo

HR=0.80; 95% CI 0.64–0.99
p=0.040



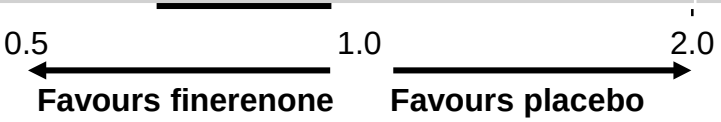
easurements ≥4 weeks apart; ¶from baseline

PY, patient-years

1. Agarwal R, *et al. Eur Heart J* 2021; doi: 10.1093/eurheartj/ehab777

The CV benefits of finerenone were primarily driven by reduction in HHF, and also CV death

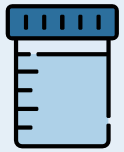
Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	HR (95% CI)	*p*-value
Composite CV outcome	825 (12.7)	939 (14.4)	0.86 (0.78–0.95)	0.0018
HHF	256 (3.9)	325 (5.0)	0.78 (0.66–0.92)	0.0030
CV death	322 (4.9)	364 (5.6)	0.88 (0.76–1.02)	0.092
Non-fatal MI	173 (2.7)	189 (2.8)	0.91 (0.74–1.12)	0.36
Non-fatal stroke	198 (3.0)	198 (3.0)	0.99 (0.82–1.21)	0.95



CV, cardiovascular; HHF, hospitalization for heart failure; HR, hazard ratio; MI, myocardial infarction

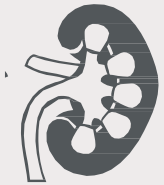
1. Agarwal R, *et al. Eur Heart J* 2021; doi: 10.1093/eurheartj/ehab777

Practical considerations for finerenone use



Measure uACR

To identify patients at highest risk of CKD progression and CV events[1] and who stand to benefit from finerenone treatment[2,3]



Measure eGFR[2,3]

Starting dose of finerenone depends on a patient's eGFR*

Measure serum [K+] regularly to minimize risk of hyperkalemia[2–4]

During treatment, the dose of finerenone depends on a patient's serum [K+]#

Temporarily withhold finerenone if serum [K+] >5.5 mmol/l‡

Continue standard of care therapy, including RASi and blood glucose lowering drugs[5]

*10 mg od for patients with an eGFR <60 ml/min/1.73 m^2, 20 mg od for patients with an eGFR ≥ 60 ml/min/1.73 m^2; #serum [K+] ≤4.8 mmol/l, 20 mg od; serum [K+] >4.8–≤5.0 mmol/l, maintain dose (10 mg od or 20 mg od); ‡restart treatment at 10 mg od when serum [K+] <5.0 mmol/l

1. Kidney Disease Improving Global Outcomes. *Kidney Int* 2013;3:1–150; 2. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 3. Pitt B, *et al*. *N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956;
4. Agarwal R. *WCN* 2021; abstract WCN21-0607; 5. American Diabetes Association. *Diabetes Care* 2021;44:S151–S167

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

What do the guidelines say about GLP1RAs in CKD?

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) have benefits in improving CV outcomes in RCTs. The KDIGO 2020 guidelines recommend a long-acting GLP-1 RA for patients with T2D and CKD unable to reach glycemic targets with or unable to tolerate metformin and a SGLT2i [17]. In the ADA 2022 guidelines, patients with T2D and at risk for or with atherosclerotic cardiovascular disease (ASCVD), heart failure or CKD should receive a GLP-1 RA or SGLT2i with CV benefit for glycemic control and CV risk reduction regardless of HbA_{1c} [31]. For nonalbuminuric CKD, a GLP-1 RA with proven CV benefit can be used to reduce CV risk. Further, for CKD subjects with albuminuria $\geq$200 mg/g, the ADA guidelines recommend GLP-1 RA if SGLT2i is unable to be used [31]. Finally, the ESC 2019 guidelines recommends the use of liraglutide and semaglutide for T2D when eGFR >30 mL/min/1.73 m^2 due to the association with a "lower risk of renal endpoints" [21]. In summary, GLP-1 RA are an important adjunctive therapy for patients with T2D and CKD in all guidelines, though dedicated renal outcome trials have not been completed.

Zhang, RM, Persson, F, McGill, JB, Rossing P. NDT 38: 542-550, 2023

Interdisciplinary Kidney Health Care

- Internist
- Pharmacist
- Dietitian or
  Diabetes Educator
- Endocrinologist
- Cardiologist
- Nephrologist

Outcomes of CKD

- Hospitalization rates: ~3 times higher for CKD patients compared to the general population
- Readmission rates: 30% higher for CKD patients within 30 days of discharge
- Comorbid conditions:
  - Cardiovascular disease: 2-3 times higher risk in CKD patients
  - Mental health: Increased prevalence of depression and anxiety in CKD patients

Resources

- Focus on early diagnosis, access to primary care
- Screening for disease, following NKF and HEDIS measures
- Behavioral health, endocrine, and nephrology resources
- Multidisciplinary care can help delay disease progression

Conclusion

- Central Role of Primary Care
  - Primary care physicians play a vital role in the early detection, management, and prevention of CKD due to their long-term and comprehensive care for patients.

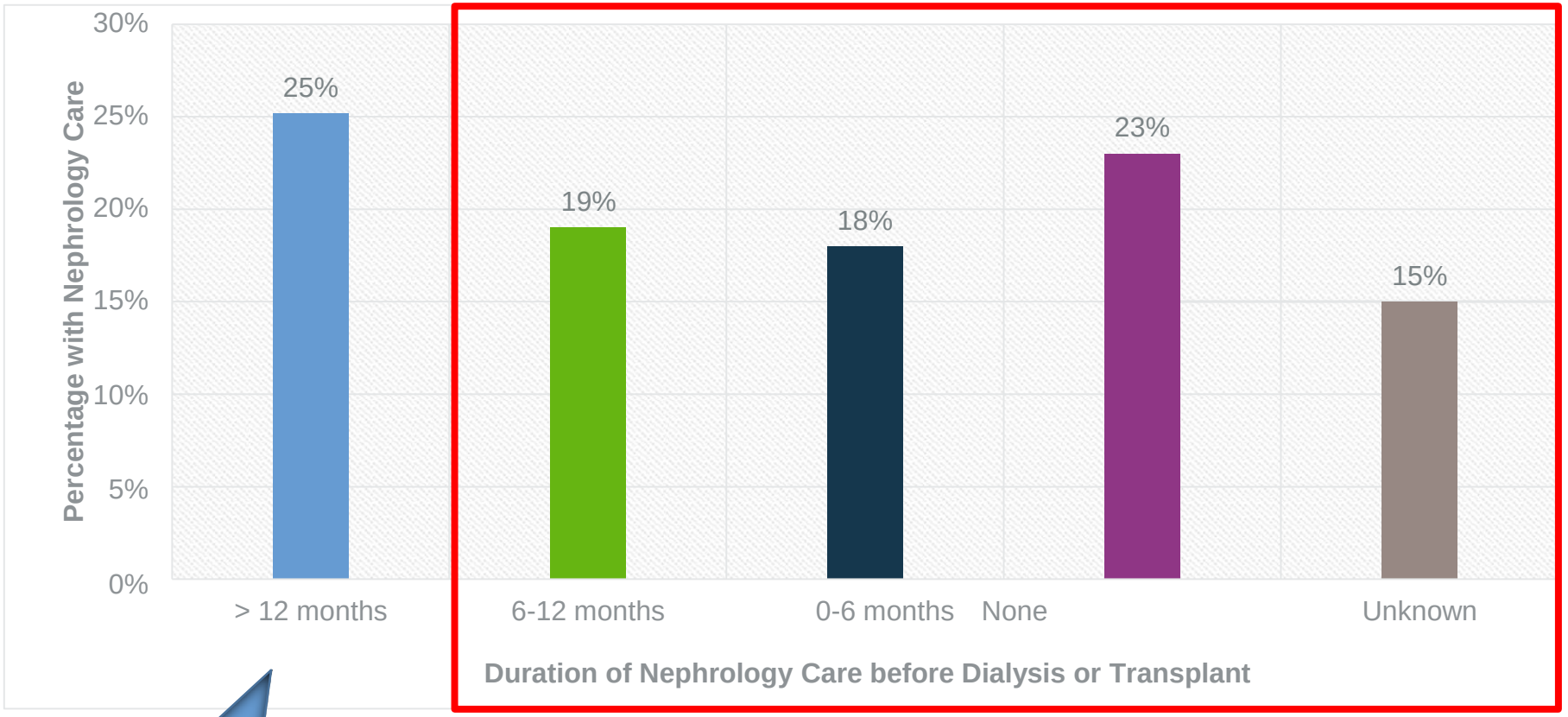
- High-Risk Group Focus
  - Focused attention on high-risk groups like those with diabetes, hypertension, and a family history of kidney disease is essential for early detection and treatment.

  Lifestyle and Medication Management
  - Primary care interventions such as promoting a healthy lifestyle, optimal management of comorbidities, regular medication review, and patient education can significantly slow down the progression of CKD.

- Timely Referral
  - Timely referral to nephrologists can improve patient outcomes and quality of life by providing advanced care when needed.

- Ongoing Research and Training
  - The importance of ongoing research and training for primary care providers in CKD management cannot be overstated to ensure the application of the latest evidence-based practices.

Late Nephrology Referral is Common



Only 1/4th have more than 1 year of Nephrology Care

United States Renal Data System. 2022 *USRDS Annual Data Report: Epidemiology of kidney disease in the United States.* National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2022.

References

- Vaselotti, National Kidney Foundation Pillars of CKD and CHF
- National Kidney Foundation
- American Society of Nephrology
- References included in each slide

Thank you!

Leilanie Mercurio | PCE Program Manager III
Provider Continuing Education (PCE) Program
Provider Support Services Department

Frequently Asked Questions (FAQs)

1. What are the common risk factors for developing chronic kidney disease?

Risk factors for CKD include diabetes, hypertension, obesity, family history of kidney disease, older age, smoking, and cardiovascular disease.

2. How is chronic kidney disease diagnosed, and what are the stages?

CKD is diagnosed based on blood and urine tests to measure kidney function and the presence of protein or other abnormalities. The stages of CKD are categorized from Stage 1 (mild) to Stage 5 (end-stage renal disease).

Frequently Asked Questions (FAQs)

3. What lifestyle changes can help slow the progression of CKD?

Lifestyle modifications, such as a balanced diet with limited salt and protein, regular exercise, maintaining a healthy weight, and avoiding smoking and excessive alcohol consumption, can help slow the progression of CKD.

4. What treatment options are available for managing chronic kidney disease?

Treatment options for CKD may include blood pressure control with ACE inhibitors or ARBs, glucose management in diabetes patients, cholesterol-lowering medications, and dietary modifications. In later stages, dialysis or kidney transplantation may be necessary.

Q & A Session

L.A. Care PCE Program Friendly Reminders

Friendly Reminder, a survey will pop up on your web browser after the webinar ends. Please do not close your web browser and wait a few seconds, and please complete the online survey.

Please note: ***the online survey may appear in another window or tab after the webinar ends.***

Upon completion of the online survey, you will receive the PDF CME or CE certificate based on your credential, verification of name and attendance duration time of at least 75 minutes, ***within two (2) weeks after today's webinar.***

Webinar participants will only have up to two weeks after webinar date to email Leilanie Mercurio at lmercurio@lacare.org to request the evaluation form if the online survey is not completed yet. No name, no survey or completed evaluation and less than 75 minutes attendance duration time via log in means No CME or CE credit, No CME or CE certificate.

Thank you!