

# Diabetic Kidney Disease

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# Disclosure Statement

I do not have a relevant financial relationship with a commercial interest whose products or services relate to the content of the educational presentation.



# Learning Objectives:

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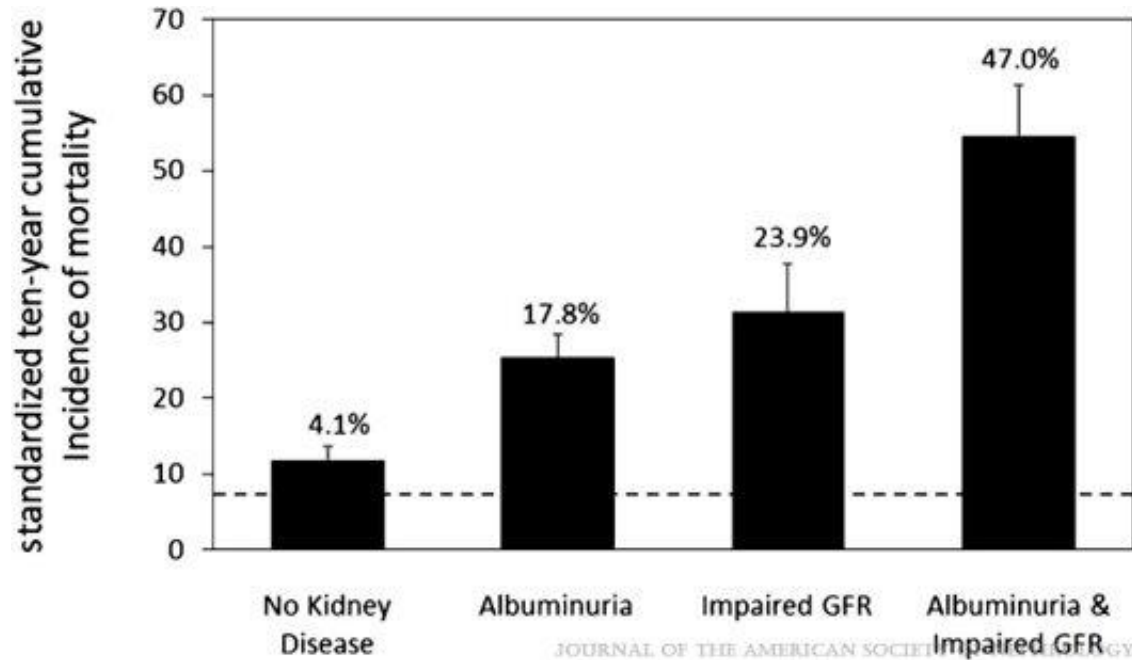
- Epidemiology and Progression of Diabetic Kidney Disease (DKD)
- Screening test for DKD
- Risk Factors for DKD
- Treatment Guidelines for DKD

# Diabetic Kidney Disease (DKD)

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- ❑ Diabetes Mellitus is the leading cause of CKD and ESRD worldwide.
- ❑ CKD is common in patients with DM
- ❑ Type 1 DM ~30% and Type 2 DM ~ 40%
- ❑ 10-15% of the patient will progress to ESRD
- ❑ DKD amplifies the risk of cardiovascular morbidity and mortality

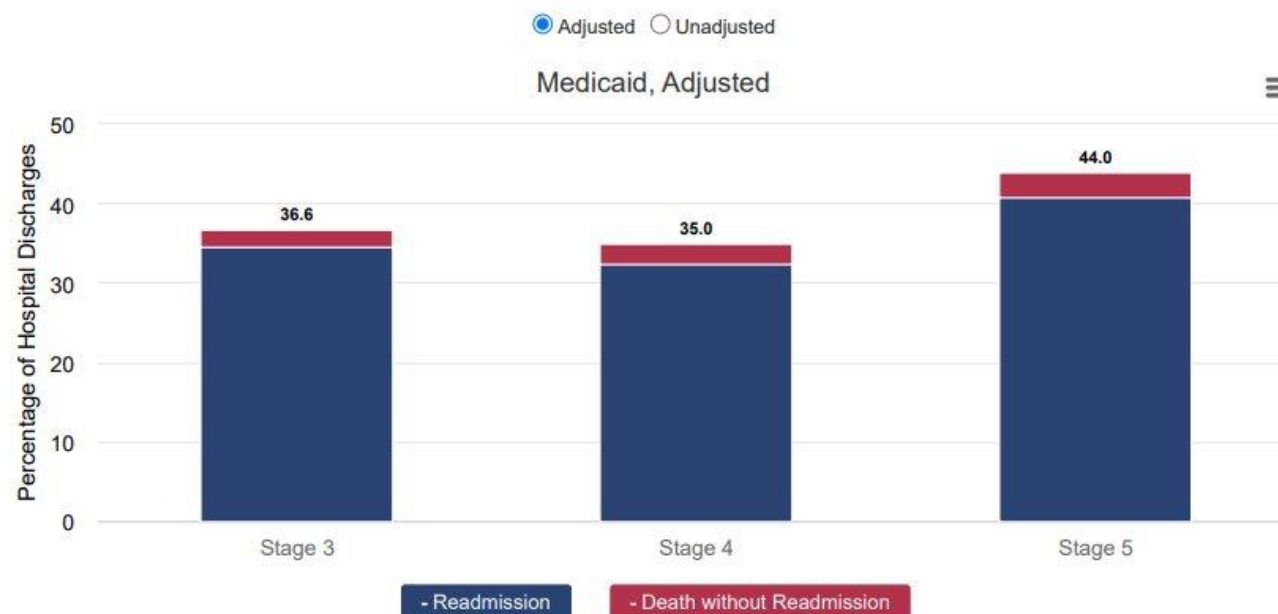
# Kidney Disease in Type 2 Diabetes and Increased Mortality Risk



- Diabetic Kidney Disease is strongly associated with increased risk of all-cause and cardiovascular mortality.
- The association can be seen starting at the stage of albuminuria.

# CKD increases the risk of rehospitalization death post-hospitalization

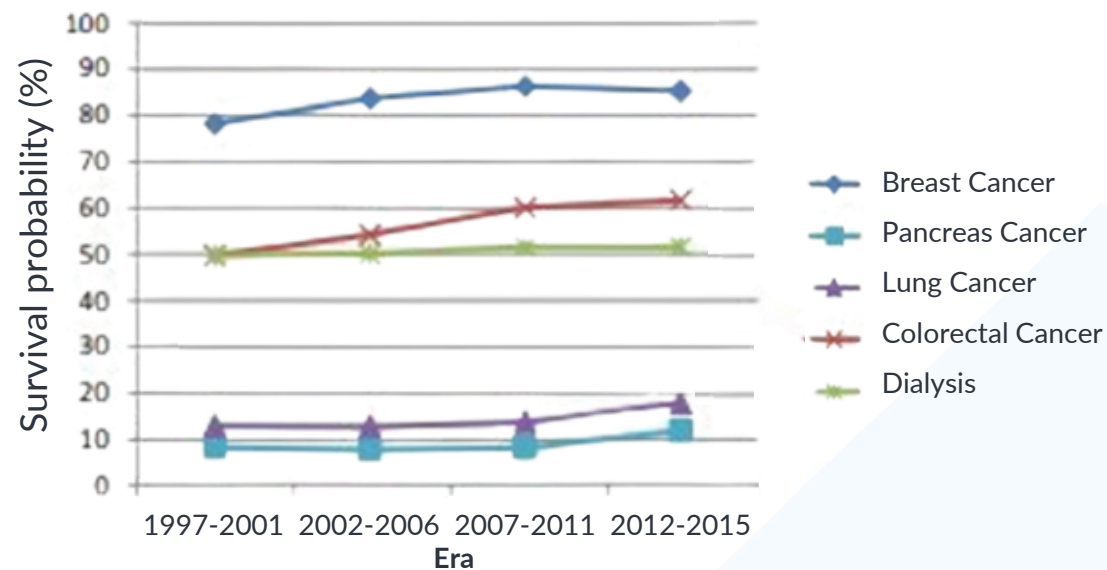
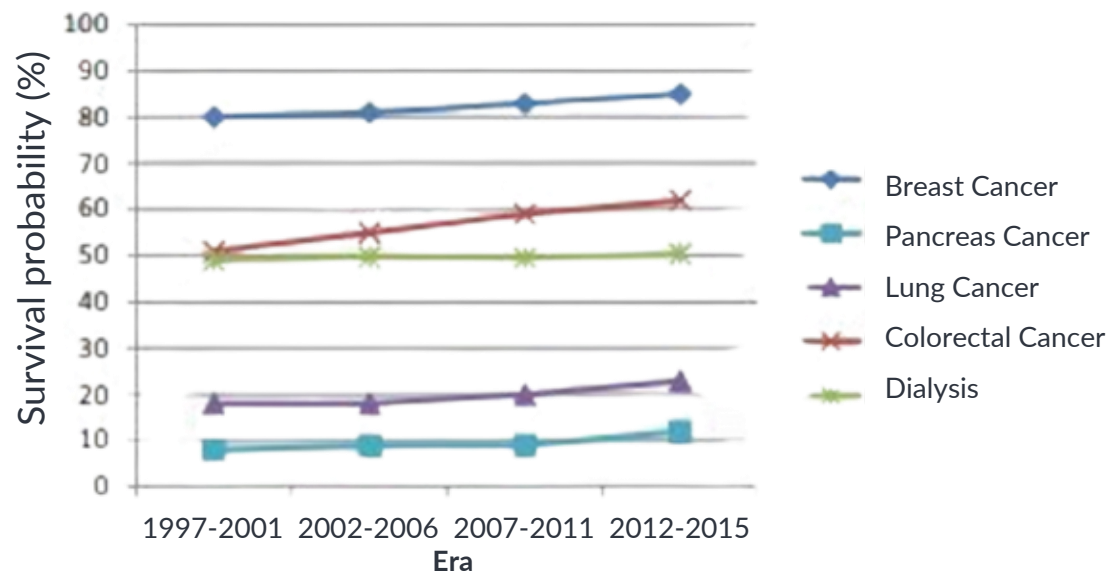
Figure 3.13d Percentage of all-cause hospitalizations resulting in readmission or death within 30 days of discharge in younger adults, Medicaid, 2021



- 36.6% Stage 3 CKD
- 35.0% Stage 4 CKD
- 44.0% Stage 5 CKD

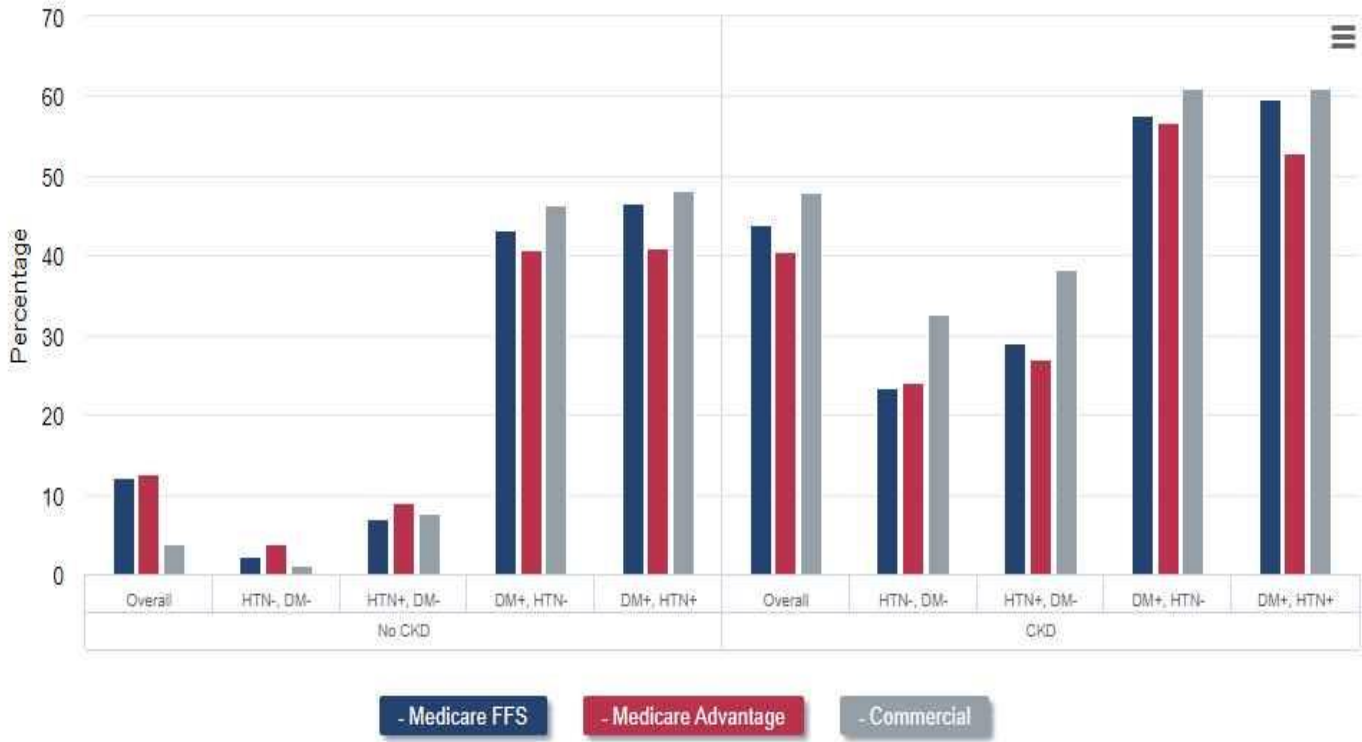
Adjusted % of readmission plus death without readmission in the 30 days following a live discharge among individuals with Medicaid younger adults (those aged 18-64 years)

# Survival in incident dialysis patients is lower than in patients with several different solid-organ cancers



# Screening for Diabetic Kidney Disease

Figure 2.8 Percentage receiving urine protein testing in insured adults, 2020



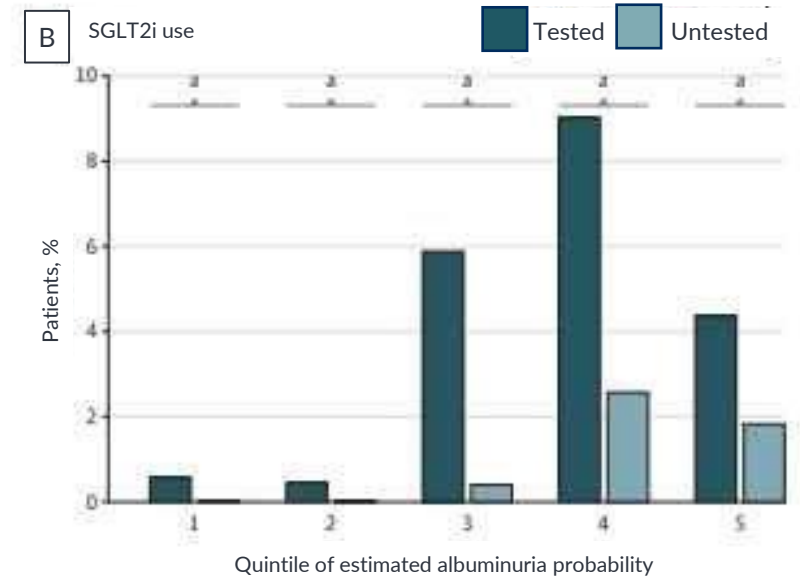
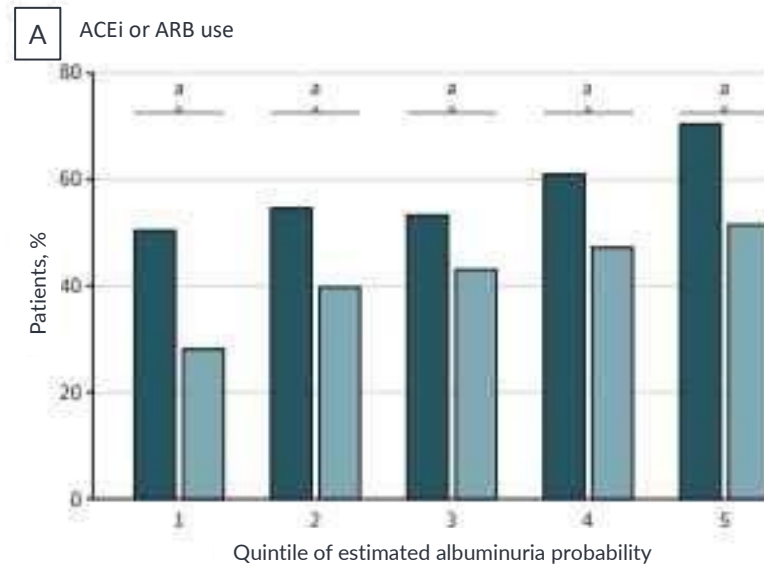
Albuminuria testing is crucial, but it is widely underutilized among persons with or at risk for CKD



## Estimated Prevalence and Testing for Albuminuria in US Adults at Risk for Chronic Kidney Disease

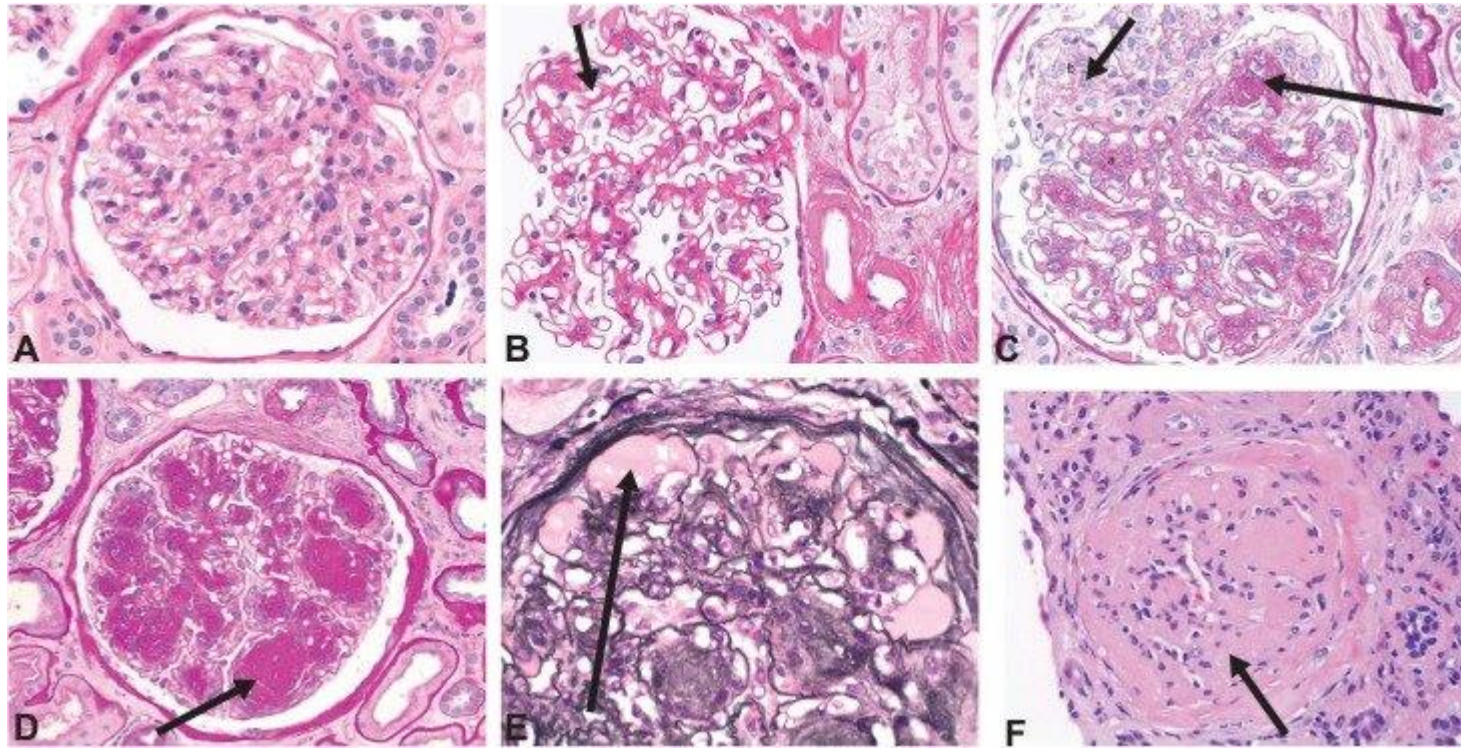
Chi D. Chu, MD, MAS; Fang Xia, PhD; Yuxian Du, PhD; Rakesh Singh, PhD; Delphine S. Tuot, MDCM, MAS; Julio A. Lamprea-Montealegre, MD, PhD; Ralph Gualtieri, MD; Nick Liao, MS; Sheldon X. Kong, PhD; Todd Williamson, PhD; Michael G. Shlipak, MD, MPH; Michelle M. Estrella, MD, MHS

- ❑ In this study, uACR testing was associated with a 2.4-fold odds of receiving ACE/ ARB treatment and 8.2-fold odds of receiving SGLT2i therapy.
- ❑ Improving the detection of CKD with albuminuria testing represents a substantial opportunity to optimize care delivery for reducing CKD progression and cardiovascular complications.



# Diabetic Nephropathy vs Diabetic Kidney Disease

## Changes in Glomerular Histology



- Diabetic nephropathy is defined by the histology of the kidney.
- Diabetic kidney disease is based on clinical history and laboratory evaluation.

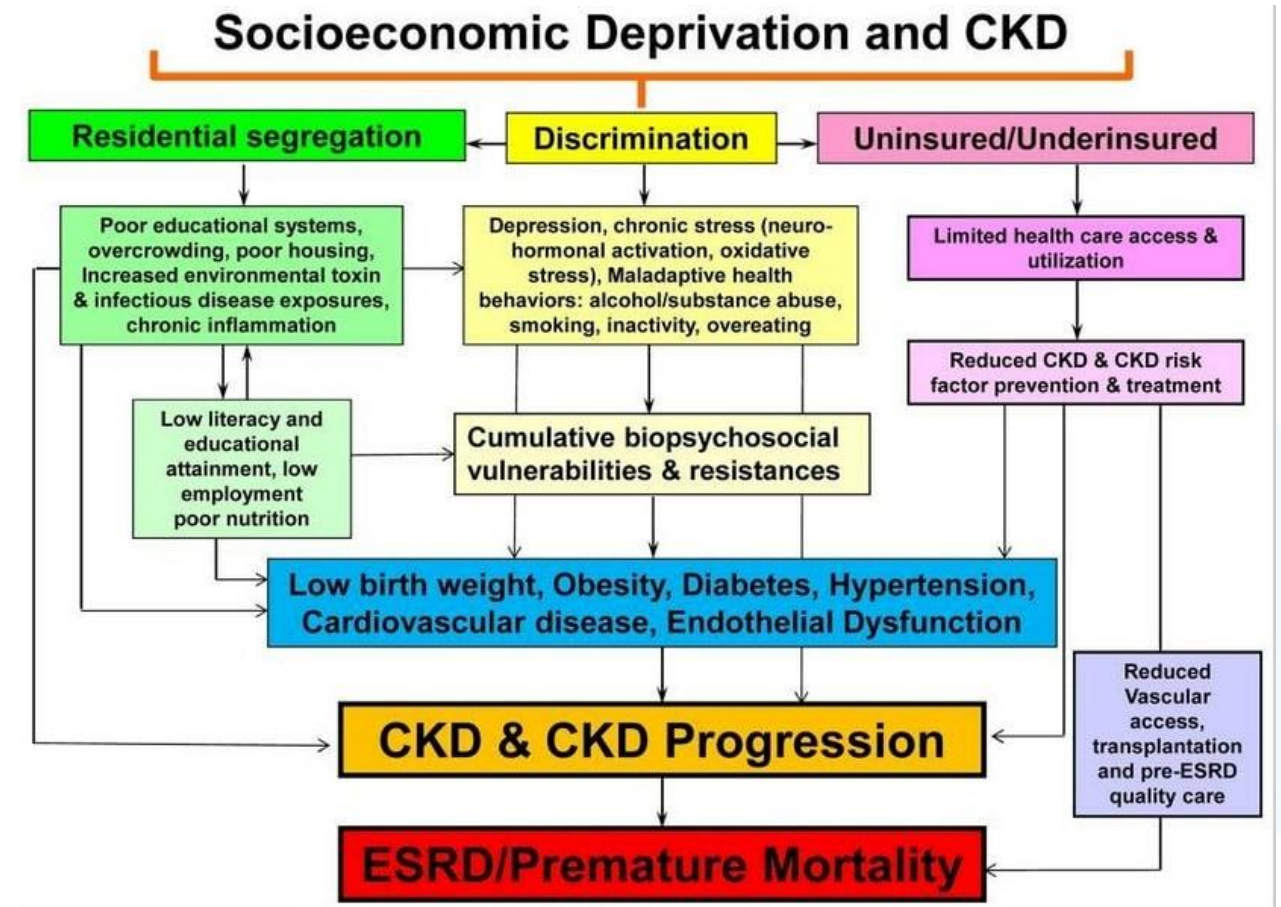
# Risk Factors for Diabetic Kidney Disease

Risk Factor	Susceptibility	Initiation	Progression
<b>Demographic</b>			
Older age	+		
Sex (men)	+		
Race/ethnicity (black, American Indian, Hispanic, Asian/Pacific Islanders)	+		+
<b>Hereditary</b>			
Family history of DKD	+		
Genetic kidney disease		+	
<b>Systemic conditions</b>			
Hyperglycemia	+	+	+
Obesity	+	+	+
Hypertension	+		+
<b>Kidney injuries</b>			
AKI		+	+
Toxins		+	+



# Link between Social Determinants of Health (SDoH) and CKD

- ❑ Many of the determinants of CKD, such as obesity, diabetes, and hypertension, may have their foundation in socioeconomic deprivation
- ❑ These include, but are not limited to:
  - ❑ discrimination and segregation
  - ❑ substandard living conditions
  - ❑ limited quality health care to the uninsured or underinsured
  - ❑ limited health literacy
  - ❑ poor educational systems
  - ❑ chronic stress



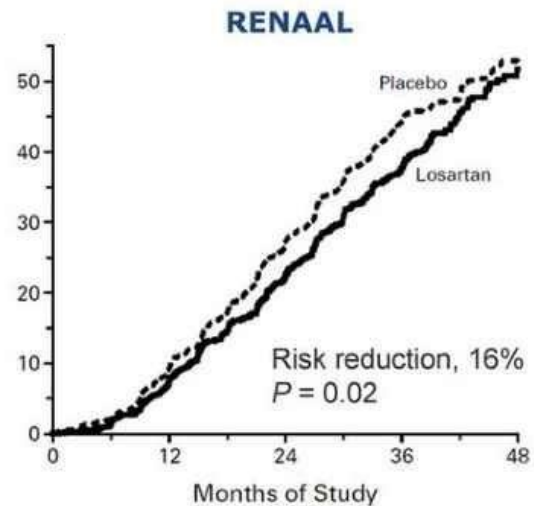
# Treatment Guidelines



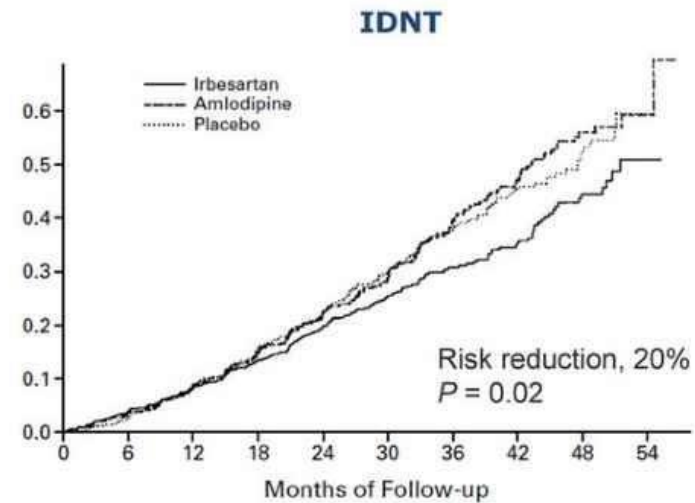
# ACE/ARB use in Type 2 DM and CKD

## The Only Proven Treatment for Renoprotection in T2DM: RENAAL & IDNT

Doubling of serum creatinine, ESKD, or death



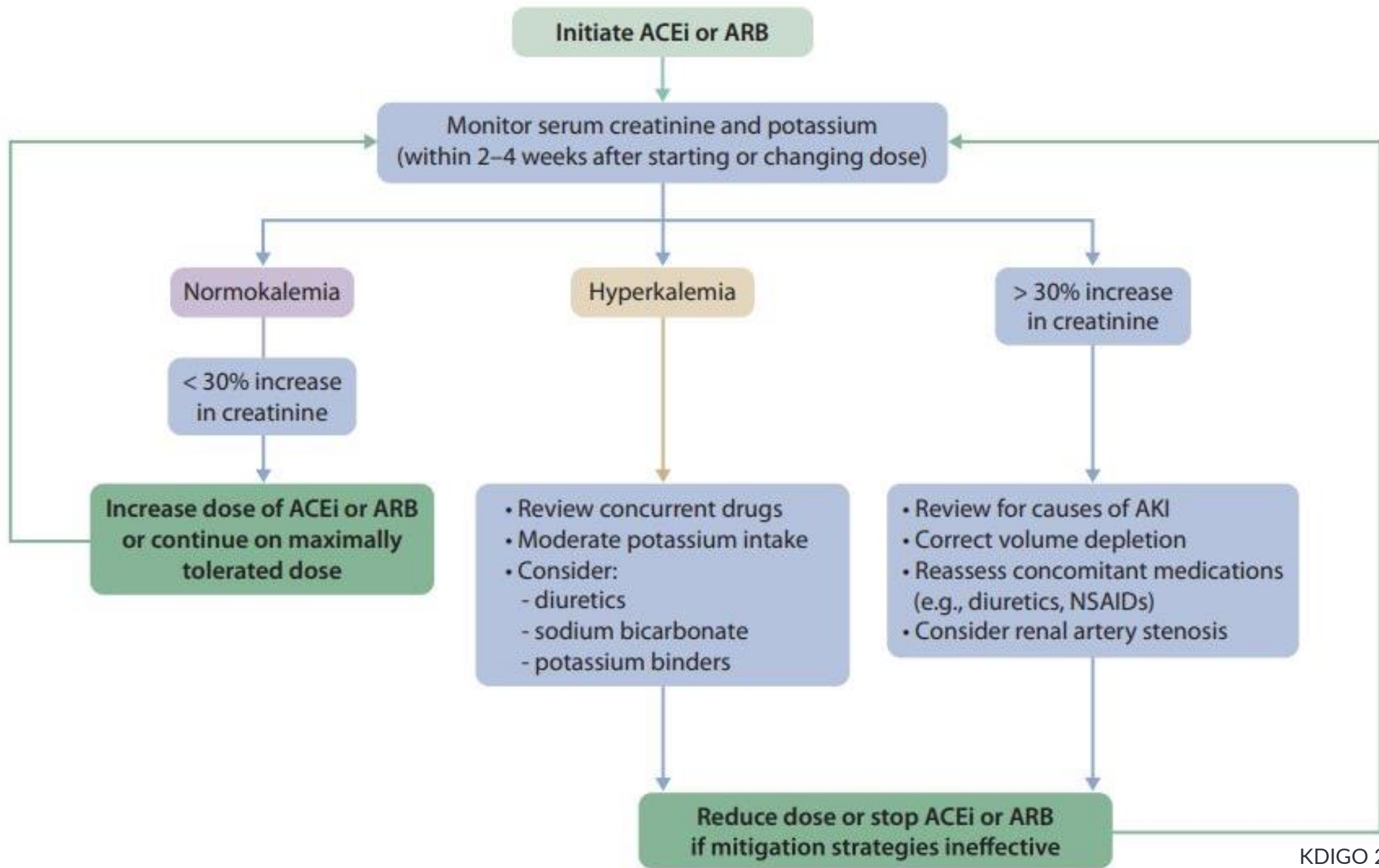
Brenner B, et al. *N Engl J Med.* 2001;345(12):861-869.



Lewis EJ, et al. *N Engl J Med.* 2001;345(12):851-860.

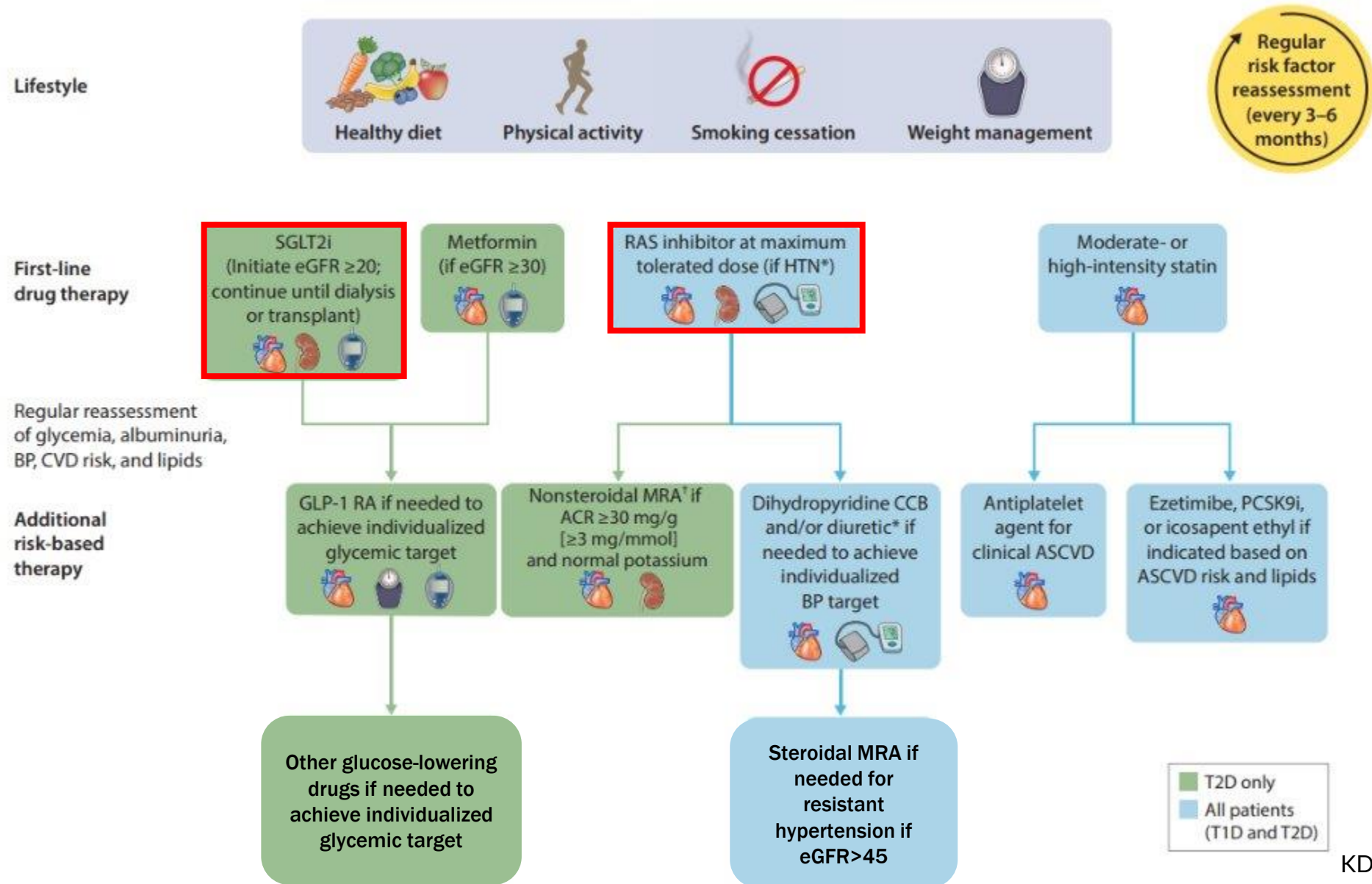


ACE inhibitors and ARB have been the standard treatment for DKD for many years, but their use has not been optimized to its full potential.





# Holistic approach for improving outcomes in patients with diabetes and chronic kidney disease





# SGLT2Inhibitors: Comparison of RCT

## CREDESCENCE

### Canagliflozin VS placebo

Double blind, Placebo-controlled, Multicentric RCT (N=4401)

#### Inclusion:

- Type 2 DM
- eGFR:  $\geq 30-90$ ; and
- UACR  $> 300-\leq 5000$  mg/g

**2019**

Median follow-up: 2.62 yrs

Renal-specific composite of ESKD, 2\* S. Cr or death from renal causes: HR 0.66; (0.53 to 0.81)

CV death, MI, stroke: HR 0.80 (0.67 - 0.95)  
Hospitalization for heart failure: HR 0.61; (0.47 to 0.80)

## DAPA-CKD

### Dapagliflozin VS placebo

Double blind, Placebo-controlled, Multicentric RCT (N=4301)

#### Inclusion:

- eGFR:  $\geq 25-75$ ; and
  - UACR  $\geq 200-\leq 5000$  mg/g
- With or without DM**

**2020**

Median follow-up: 2.4 yrs

Composite of sustained decline in eGFR of at least 50%, ESKD, or death from renal causes: HR 0.56; (0.45 to 0.68)

Composite of death from CV causes or hospitalization for heart failure: HR 0.71; (0.55 to 0.92)

## EMPA - KIDNEY

### Empagliflozin VS placebo

Double blind, Placebo-controlled, Multicentric parallel group RCT (N=6609)

#### Inclusion:

- eGFR:  $\geq 20-45$ ; or
  - eGFR  $\geq 45$  to  $<90$  with UACR  $\geq 200$  mg/g
- With or without DM**

**2022**

Median follow-up: 2.yrs

Progression of kidney disease or death from CV causes: HR 0.72; (0.64 to 0.82)

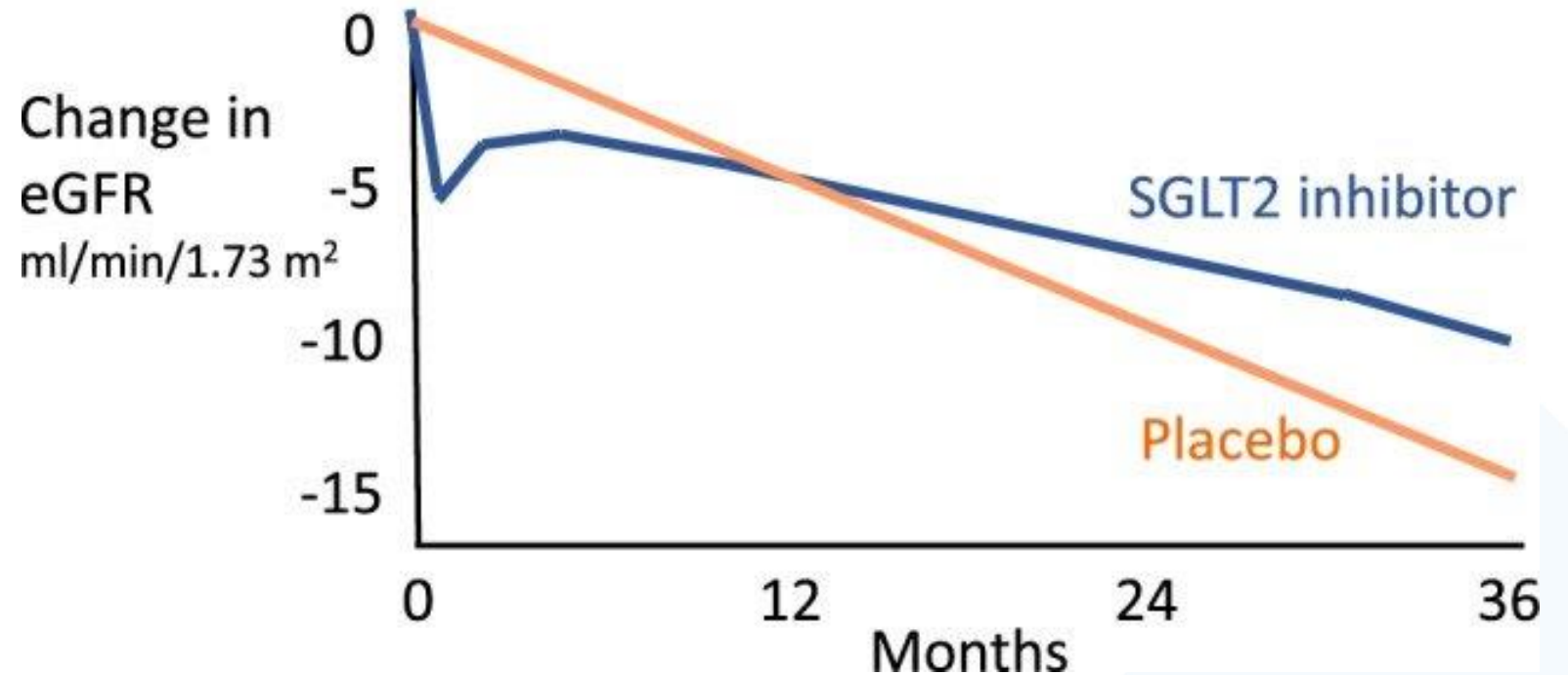
Rate of hospitalization from any cause: HR 0.86; (0.78 to 0.95)



- **All three trials show consistent benefits of reduction in CKD progression.**
- **Most notably, the benefits are in addition to the protective benefits from the use of ACE inhibitors/ARBs.**

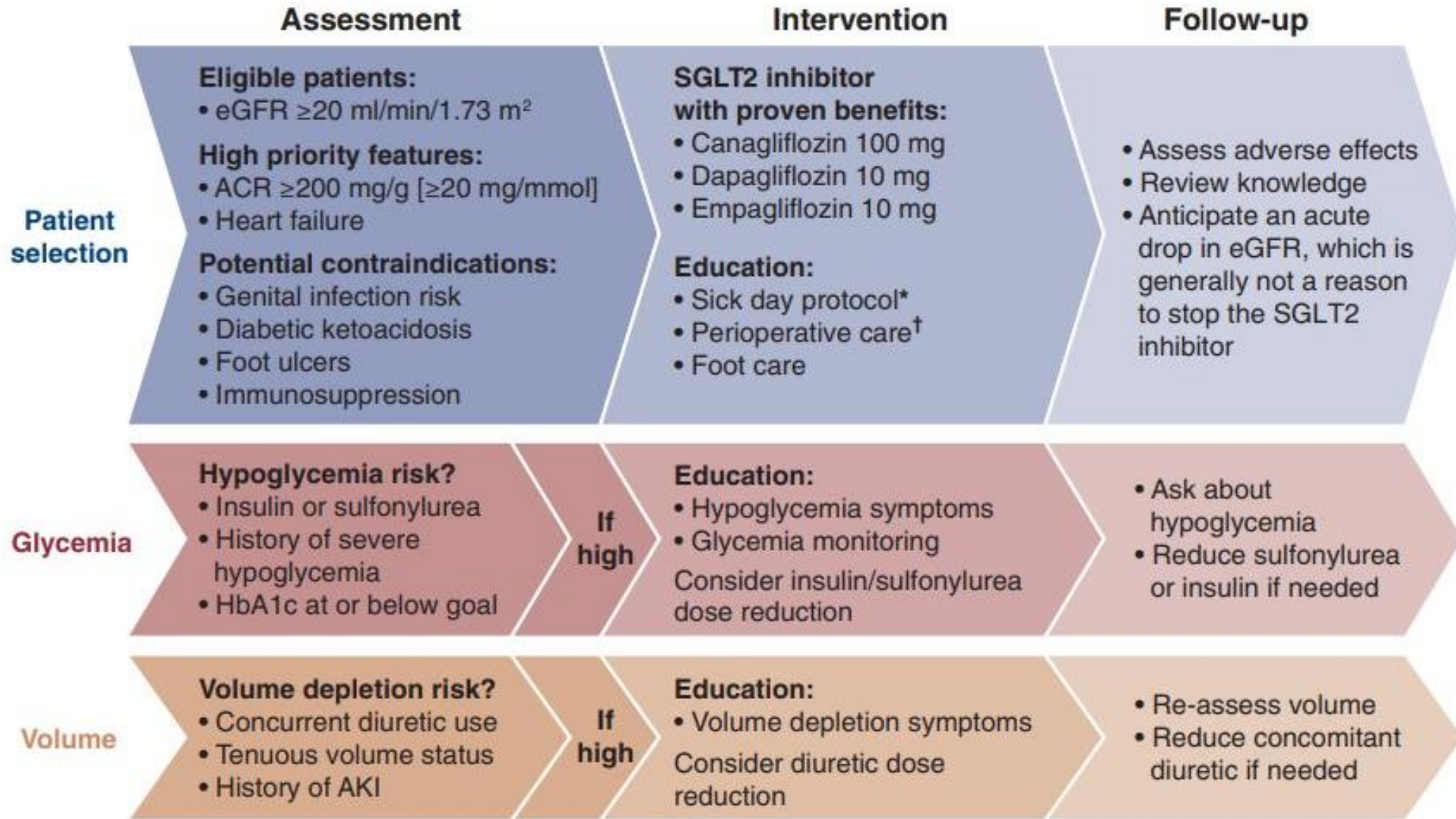
# Renal Protection with SGLT2 Inhibitors

- ❑ The initial dip in eGFR is about 5 ml/min. It reaches a nadir within 1–2 weeks and slowly returns to pretreatment values over the next 3–9 months.
- ❑ Thereafter the rate of decline in eGFR is slower than in individuals who are not treated with an SGLT2 inhibitor.



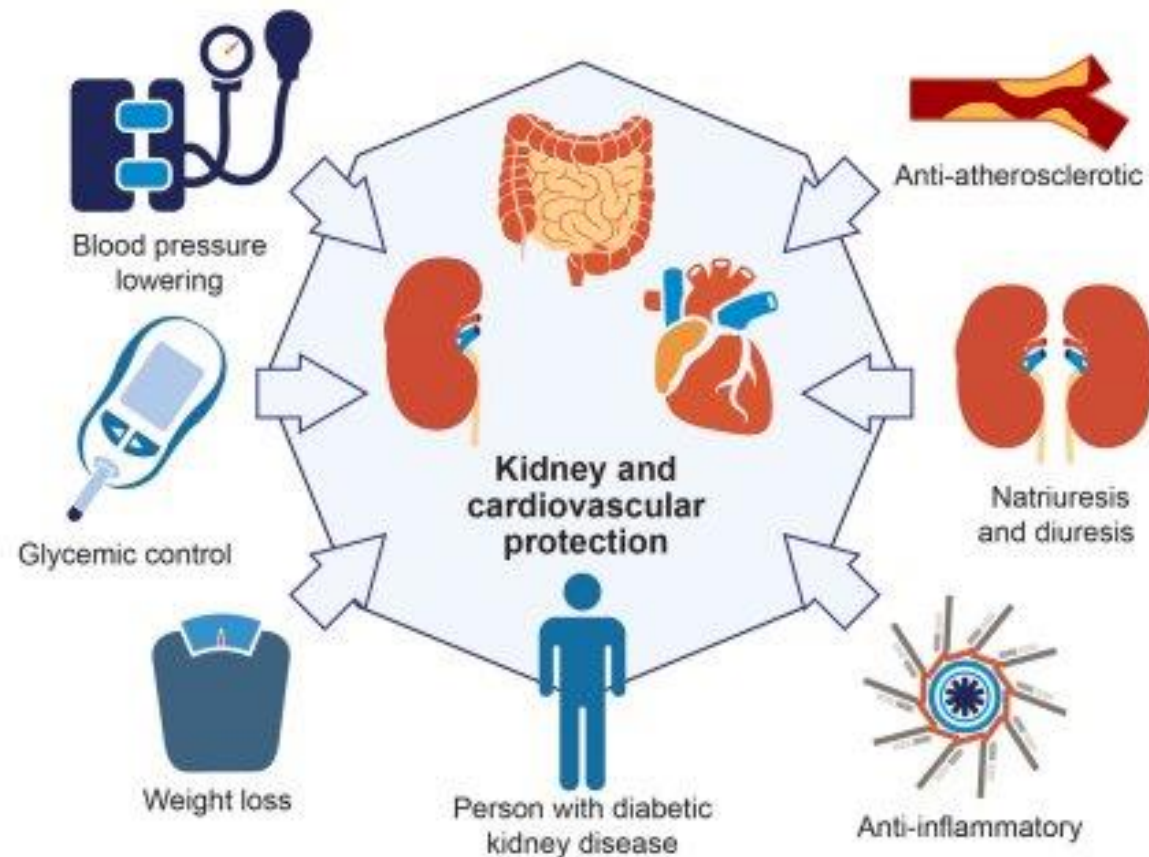
The illustration is loosely based on data from the EMPA-REG, CREDENCE and DAPA-CKD trials

# Practical provider guide to initiating SGLT2 inhibitors in patients with type 2 diabetes and CKD



# Glucagon-like peptide1 receptor agonists (GLP1-RA)

Potential mechanisms by which GLP1-RA confer kidney and cardiovascular protection.





ORIGINAL ARTICLE

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

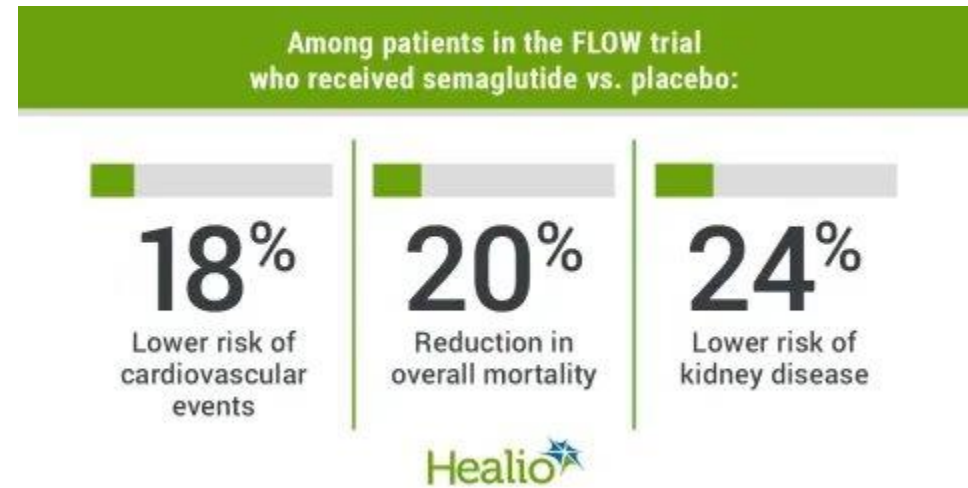
**Inclusion Criteria:**

Patients with T2DM with an eGFR of 50 to 75 ml/min/1.73m<sup>2</sup> and a UACR of greater than 300 mg and less than 5000mg or an eGFR of 25 to less than 50 ml/min/1.73m<sup>2</sup> and a UACR greater than 100mg and less than 5000mg

**Interventions:**

Patients were randomized (1:1) to either receive subcutaneous Semaglutide or placebo

**Results**



*Guideline-directed medical therapy for patients with T2DM and CKD will continue to evolve in the coming year with new pillars of treatment being added.*

# DIABETIC KIDNEY DISEASE

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## Managing DKD involves multiple interventions

- Exercise
- Diet modifications
- Smoking cessation
- Weight Loss and Management of Obesity
- Avoiding NSAIDs
- Psychosocial support
- Blood Pressure Control
- Diabetes Mellitus control
- Management of cholesterol
- Guideline Directed Medical Therapy
- Transplant workup
- Preparing for dialysis

**Reducing CKD progression is a team sport**

# Thank you!

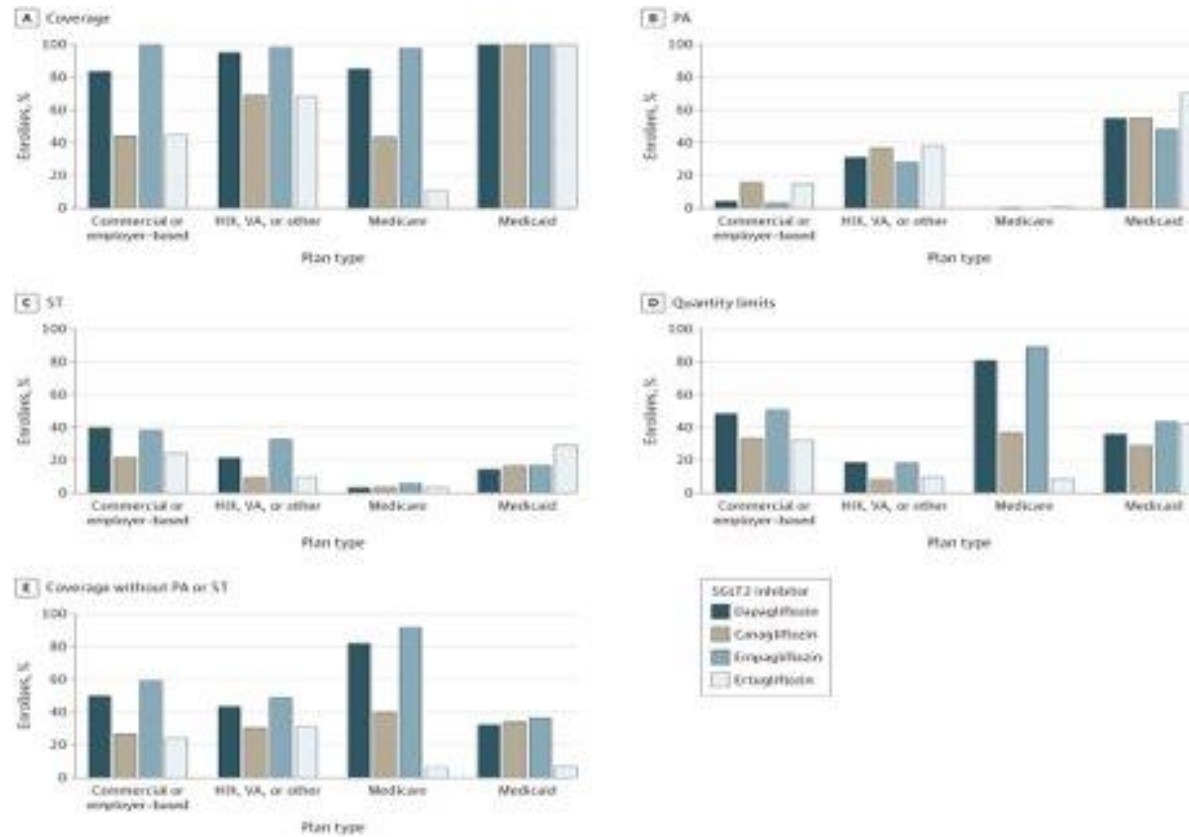
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From: **Coverage, Formulary Restrictions, and Affordability of Sodium-Glucose Cotransporter 2 Inhibitors by US Insurance Plan Types**

JAMA Health Forum. 2021;2(12):e214205. doi:10.1001/jamahealthforum.2021.4205





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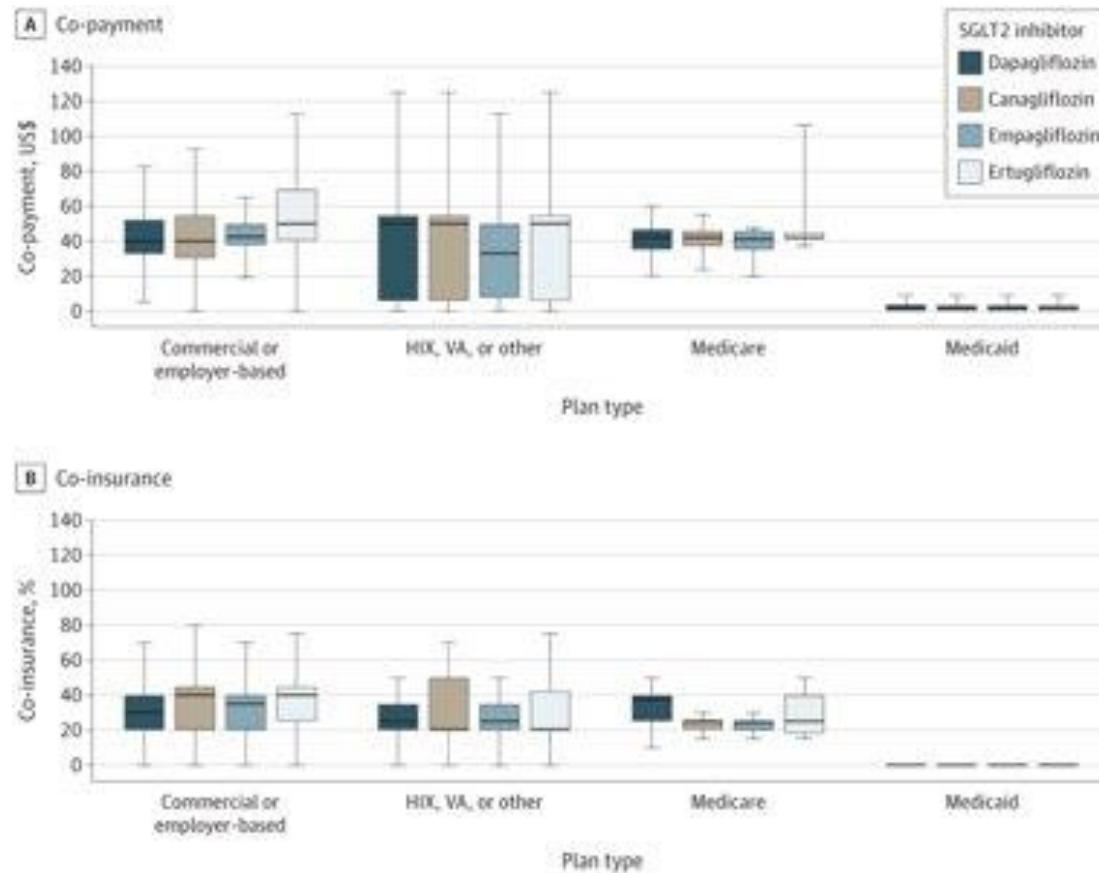


Figure Legend:

From: **Clinical Characteristics of and Risk Factors for Chronic Kidney Disease Among Adults and Children: An Analysis of the CURE-CKD Registry**

JAMA Netw Open. 2019;2(12):e1918169. doi:10.1001/jamanetworkopen.2019.18169

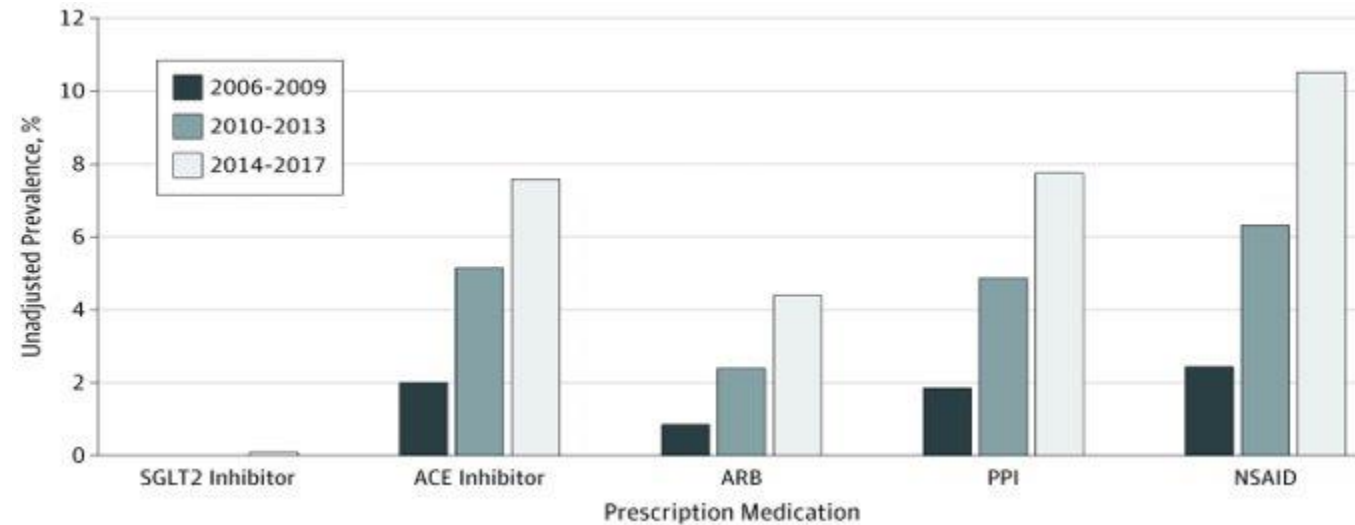


Figure Legend:

Prevalence of Prescription Medication Use in Chronic Kidney Disease Categories 3a to 5 in 2006 to 2009, 2010 to 2013, 2014 to 2017 ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; and SGLT2, sodium-glucose cotransporter 2.

# Nonsteroidal selective mineralocorticoid receptor antagonist: Finerenone

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KDIGO(2A) Recommendation:

*For patients with type 2 diabetes who have measured albuminuria  $\geq 30$  mg/day despite an ACE or ARB inhibitor and an SGLT2 inhibitor, we suggest treatment with a nonsteroidal selective MRA, specifically finerenone, where available, provided the patient has serum potassium  $\leq 5$  mEq/L and eGFR  $\geq 25$  mL/min/1.73 m<sup>2</sup>.*