Slow Your Roll:

Pharmacotherapy to Delay Progression of CKD

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January 7, 2026

Disclosures

The planner(s) and speaker(s) have indicated that there are no relevant financial relationships with any ineligible companies to disclose.

Learning Objectives

At the end of this session, learners should be able to:

- Recall what CKD is as a disease state and associated comorbidities
- Recognize the KDIGO guidelines on diagnosis and appropriate pharmacologic therapy
- Outline literature to support the use of pharmacologic measures in managing CKD
- Apply available evidence regarding CKD to recommend appropriate drug therapy in a patient case.

Abbreviation Key

- AER – albumin excretion rate
- AHA/ACC – American Heart Association/American College of Cardiology
- ACE-I – angiotensin converting enzyme inhibitor
- ACR – albumin-to-creatinine ratio
- ADE – adverse drug effect
- AKI – acute kidney injury
- ARB – angiotensin II receptor blocker
- BP – blood pressure
- BUN – blood urea nitrogen
- CI – confidence interval
- CKD – chronic kidney disease
- CV - cardiovascular
- CVD – cardiovascular disease
- DALY – disability adjusted life years
- eGFR – estimated glomerular filtration rate

Abbreviation Key

- GFR – glomerular filtration rate
- GLP-1 – glucagon-like peptide-1
- HF – heart failure
- HFrEF – heart failure reduced ejection fraction
- HR – hazard ratio
- HTN – hypertension
- KDIGO – Kidney Disease Improving Global Outcomes
- MI – myocardial infarction
- MRA – mineralocorticoid receptor antagonist
- OR – odds ratio
- RCT – randomized controlled trials
- RR – risk ratio
- SCr – serum creatinine
- SGLT-2 – sodium glucose transporter-2 inhibitor
- T2DM – type 2 diabetes mellitus
- UACR – urine albumin creatinine ratio

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Chronic Kidney Disease: Overview

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Epidemiology

Globally

- Prevalence: ~790 million (14.2%)
  - 35.5 million (14%) in the United States
- Mortality: 1.48 million deaths in 2023
  - #9 leading cause of death
- DALY: #12 leading cause

DALY: disability adjusted life years

CDC. Centers for Disease Control and Prevention. May 15, 2024.
GBD 2023 Chronic Kidney Disease Collaborators. *Lancet*. Published online November 7, 2025.

Chronic Kidney Disease: KDIGO Definition & Diagnosis

General Definition

- Kidney disease: abnormality in kidney structure and/or function
- Chronic: occurring for greater than or equal to three months

CKD Diagnosis Criteria

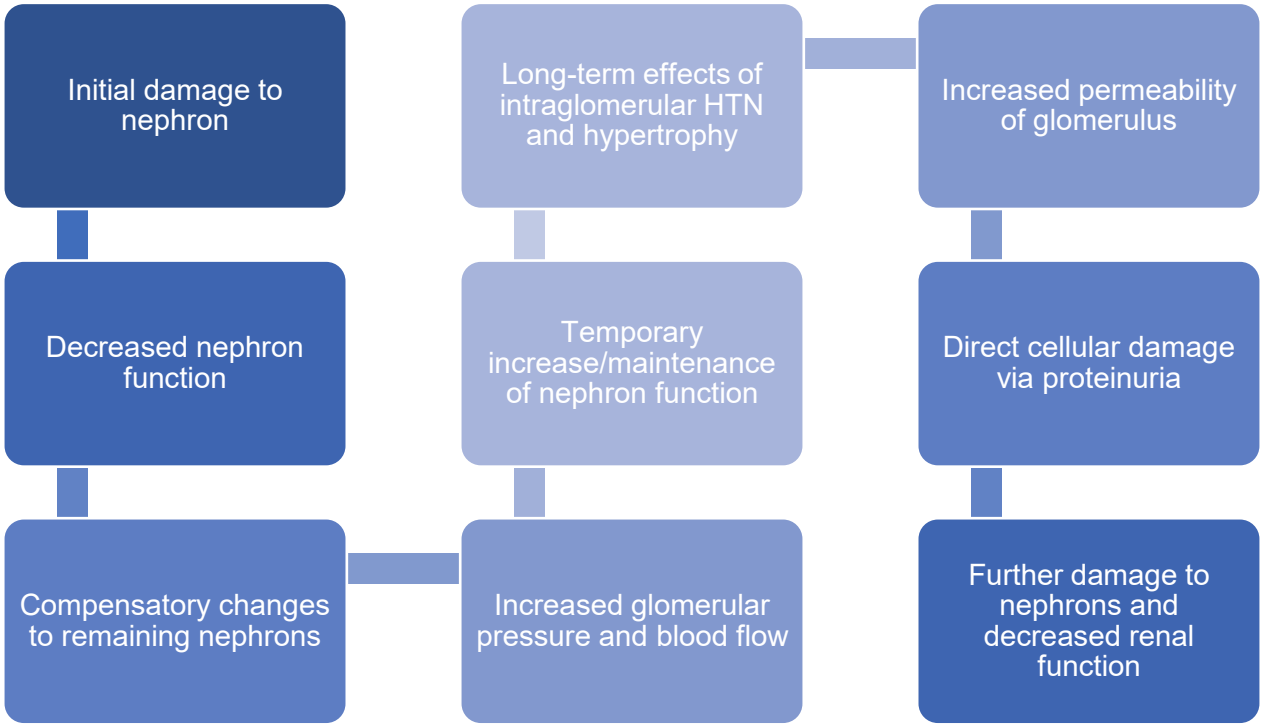
- One or more markers of kidney damage

and/or

- Decreased GFR (<60mL/min/1.73m^2)

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

CKD Pathophysiology



Bargman JM, et al. *Harrison's Principles of Internal Medicine, 22nd Edition*. McGraw Hill; 2026
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

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KDIGO Criteria: Markers of Kidney Damage

Markers of Kidney Damage
• Albuminuria
• Imaging showing structural abnormalities
• Electrolyte abnormalities
• Persistent hematuria
• History of kidney transplantation

Albuminuria Categories				
Category	AER (mg/day)	ACR (mg/mmol)	ACR (mg/g)	Meaning
A1	<30	<3	<30	Normal-mildly increased
A2	30-300	3-30	30-300	Moderately increased
A3	>300	>30	>300	Severely increased

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

KDIGO Criteria: Glomerular Filtration Rate Categories

GFR Categories	GFR (mL/min/1.73m^2)	Meaning
G1	≥90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

KDIGO Criteria: Glomerular Filtration Rate Categories

Calculating eGFR

- Chronic Kidney Disease Epidemiology Collaboration
- European Kidney Function Consortium
- Modification of Diet in Renal Disease

Markers

- Endogenous:
  - Serum creatinine
  - Cystatin-C
- Exogenous:
  - Inulin
  - Iohexol
  - Iothalamate

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

KDIGO CKD Classification: GFR & Albuminuria

GFR Categories	Albuminuria Categories: A1	A2	A3
G1	Screen (1)	Treat (1)	Treat & refer (3)
G2	Screen (1)	Treat (1)	Treat & refer (3)
G3a	Treat (1)	Treat (2)	Treat & refer (3)
G3b	Treat (2)	Treat & refer (3)	Treat & refer (3)
G4	Treat & refer (3)	Treat & refer (3)	Treat & refer (4+)
G5	Treat & refer (4+)	Treat & refer (4+)	Treat & refer (4+)

de Boer IH, et al. *Diabetes Care*. 2022
Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

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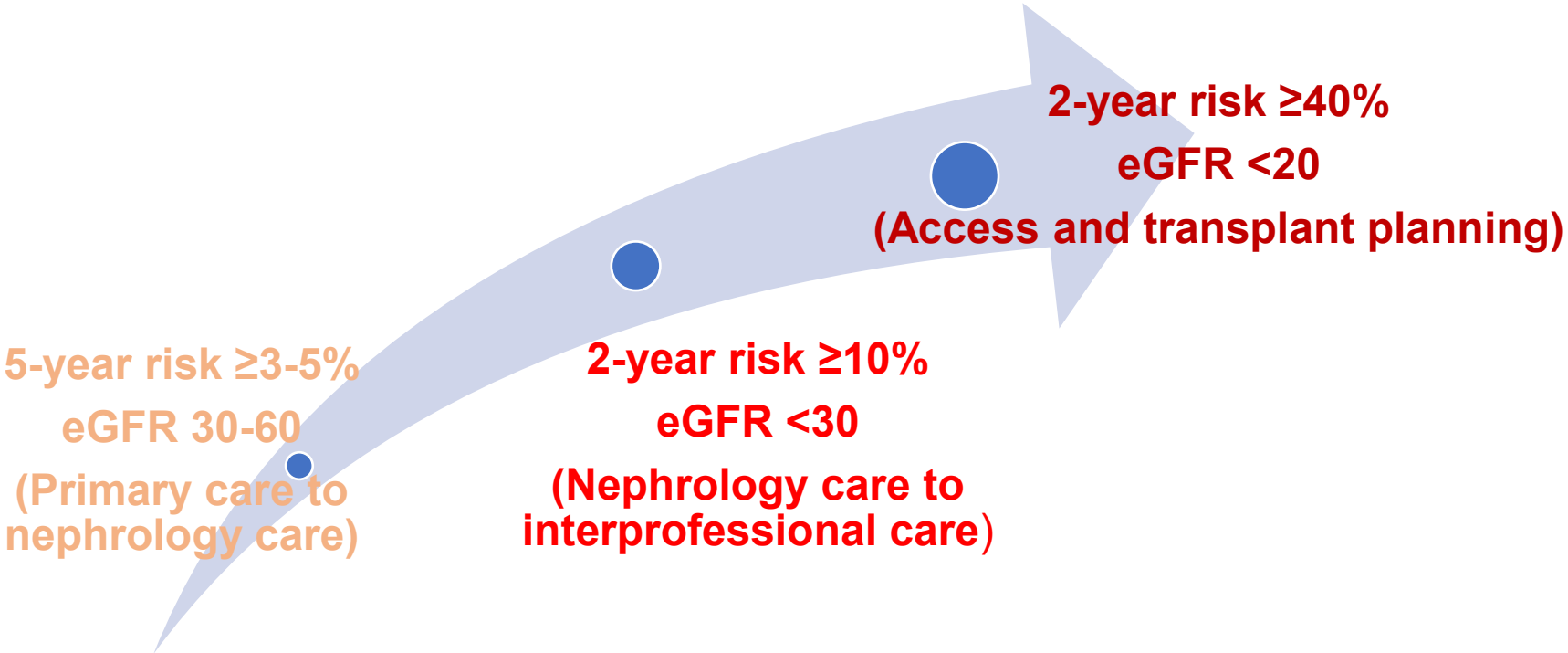
KDIGO CKD Risk Assessment: Kidney Failure



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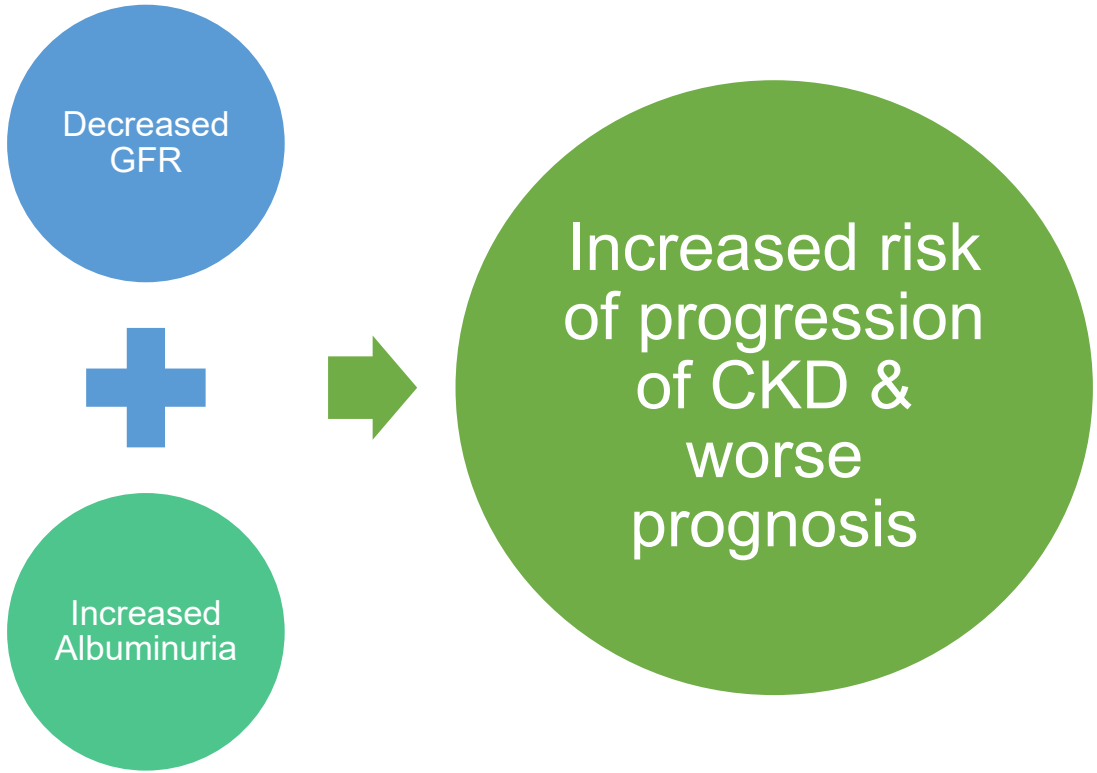
Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024

KDIGO CKD Risk Assessment: Summary



Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

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Assessment Question #1

If the patient had an eGFR of 45 mL/min/1.73 m^2 and/or urine ACR >300mg/g for ≥3 months, what categories of GFR and albuminuria would she fall into per KDIGO classification?

A. G2/A3
B. G3a/A3
C. G3b/A2
D. G4/A3

GFR Categories	GFR (mL/min/1.73m^2)
G1	≥90
G2	60-89
G3a	45-59
G3b	30-44
G4	15-29
G5	<15

Albuminuria Categories			
Category	AER (mg/day)	ACR (mg/mmol)	ACR (mg/g)
A1	<30	<3	<30
A2	30-300	3-30	30-300
A3	>300	>30	>300

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Risk Factors for Development of CKD

- Diabetes
- Hypertension
- Autoimmune Diseases
- Systemic Infections
- Nephrotoxins
- Neoplasia

Demographic Risks
Older age
Males
Family history
Minorities
Lower income/education

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

Risk Factors for Progression of CKD

Uncontrolled Diabetes

- 2022 KDIGO Diabetes in CKD: A1c <6.5% - <8%
- 2025 American Diabetes Association Standards of Care: A1c <7%

Uncontrolled Hypertension

- 2021 KDIGO Blood Pressure in CKD: Systolic BP <120 mmHg
- 2025 AHA/ACC Hypertension: Systolic BP <130 mmHg

Albuminuria

- KDIGO pharmacotherapy measures to prevent progression of CKD also focuses on decreasing albuminuria

American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2025
Bargman JM, et al. *Harrison's Principles of Internal Medicine, 22nd Edition*. McGraw Hill; 2026
Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. *Kidney Int*. 2021
Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. *Kidney Int*. 2022
Wanzman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026

Clinical Signs and Symptoms of CKD

Signs	• Edema • Foaming of urine
Symptoms	• Asymptomatic until later stages • Fatigue, altered mental status, nausea, itching, cold intolerance
Labs	• Elevated: Scr, BUN, potassium, phosphorus, ACR • Decreased: eGFR, vitamin D, calcium, hemoglobin, iron
Secondary Complications	• Anemia, uremia, metabolic acidosis • Electrolyte disturbances, mineral bone disorder, HTN

Bargman JM, et al. *Harrison's Principles of Internal Medicine, 22nd Edition*. McGraw Hill; 2026
Bello AK, et al. *Kidney Int Suppl (2011)*. 2017
Hudson JQ, et al. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

Patient Case

SH is a 50-year-old African-American female who presents to her primary care provider for a regular check-up.

PMH: seizures, gout, HTN, T2DM

Allergies: chronic cough with prior use of ACE inhibitors

Current medications (all oral): valsartan 80mg daily, levetiracetam 1000mg twice a day, allopurinol 300mg daily, metformin 1000mg twice a day

No adverse side effects

Relevant vitals and labs: Wt 45kg, BP 135/80 mmHg, A1c 7.5%, eGFR 45 mL/min/1.73 m^2, UACR >300 mg/g, potassium 5.2 mmol/L

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Assessment Question #2

Per 2024 KDIGO guidelines, what contributory comorbidity/comorbidities does the patient have that may have contributed to the further decline of CKD?

A. Gout
B. HTN
C. T2DM
D. Seizures
E. A & C
F. B & C

Assessment Question #3

If SH experiences a further decline in renal function at or near G5 (GFR <15) what secondary complications may she present with that would require additional treatment?

A. Anemia
B. Uremia
C. Electrolyte disturbances
D. Mineral and bone disorders
E. All of the above

Chronic Kidney Disease: Pharmacotherapy

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KDIGO: Goals of Pharmacotherapy

Delay and prevent further progression of CKD

Treat underlying comorbidities causing or contributing to progression of CKD

Treat secondary complications of CKD

KDIGO Recommended Pharmacotherapy: Delaying Progression of CKD

- ACE inhibitors & ARBs
- SGLT-2 inhibitors
- Non-steroidal Mineralocorticoid receptor antagonists
- GLP-1 receptor agonists

ACE-Inhibitors & ARBs

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ACE-Inhibitors & ARBs: Recommendations

KDIGO Recommendations

- CKD and severely increased albuminuria without diabetes (G1-G4, A3)
- CKD and moderately-severely increased albuminuria with diabetes (G1-G4, A2 & A3)
- CKD and moderately increased albuminuria without diabetes (G1-G4, A2)

Mechanism of Action

- Decreases intraglomerular pressure and proteinuria
- General antihypertensive effects

Considerations/Monitoring

- Any drug in the class to maximum tolerated dose
- Consider use in CKD with normal or low albuminuria in those with comorbidities (HTN, HFrEF)
- Continue use even when eGFR reaches <30 mL/min/1.73 m^2
- Monitor every 2-4 weeks after initiation and change in dosing for progression of CKD and hyperkalemia

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

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ACE-Inhibitors & ARBs:
Literature Background and Methods

Renin-Angiotensin System Inhibitors and Kidney and Cardiovascular outcomes in Patients with CKD: A Bayesian Network Meta-analysis of Randomized Clinical Trials Xie X, et al. 2016	
Purpose	Evaluate available evidence on ACE-I and ARBs to determine renal and cardiovascular outcomes in CKD
Design	Systematic review and meta-analysis
Selection	Inclusion: RCTs, >20 participants with CKD, treated with ACE-I or ARBs for ≥6 months Exclusion: Studies that compared non-ACE-I/ARBs to each other or to placebo

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Xie X, et al. *Am J Kidney Dis*. 2016

ACE-Inhibitors & ARBs:
Outcomes and Demographics

Xie X, et al. 2016	
Outcomes	Renal outcomes: Kidney failure CV outcomes: Major CV events Others: All-cause death, drug related ADEs
Relevant Patient Demographics	Sample size: 64,768 patients with CKD Mean age: 62.9 years Mean follow-up: 3.6 years Diabetic nephropathy: n=30,054 Non-diabetic nephropathy: n=5786 On dialysis: n=2247

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Xie X, et al. *Am J Kidney Dis*. 2016

ACE-Inhibitors & ARBs:
Results and Conclusion

Xie X, et al. 2016	
Results (95% CI)	Renal outcomes: • **ACE-I/ARBs reduced odds of kidney failure** vs placebo by 39% and 35% (OR 0.61, 0.47-0.79; OR 0.65, 0.51-0.8) • No statistical difference between ACE-I and ARBs vs placebo CV outcomes: • **ACE-I/ARBs reduced odds of CV events** vs placebo by 18% and 24% (OR 0.82, 0.71-0.92; OR 0.76, 0.62-0.89) • No statistical benefit for CV protection vs active controls or between ACE-I vs ARBs All cause mortality: • **Only ACE-I had statistically significant odds reduction** vs active controls by 28 (OR 0.72, 0.53-0.92) Adverse drug events: • **ACE-I and ARBs increased odds of hyperkalemia** vs placebo (OR 2.16, 1.24-3.68; OR 6.39, 2.31-15.49)
Conclusion	• ACE-I likely to have most benefit in kidney failure, CV death, and all-cause deaths in those with CKD • ARBs show kidney protective effects but superiority with ACE-I in other outcomes based on analysis

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Xie X, et al. *Am J Kidney Dis*. 2016

ACE-Inhibitors & ARBs: Summary

- ACE-inhibitors and ARBs are shown to reduce odds of:
  - Renal failure
  - CV outcomes

- In general, KDIGO guidelines recommend ACE-inhibitors and ARBs for patients with or without diabetes who also have albuminuria

SGLT-2 Inhibitors

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SGLT-2 Inhibitors: Recommendations

KDIGO Recommendations

- CKD with T2DM and eGFR ≥20
- CKD with eGFR ≥20 with ACR ≥200 or eGFR ≥20 with HF
- CKD with eGFR 20-45 with ACR <200

Mechanism of Action

- Reduces glomerular HTN and hyperfiltration, eventually decreasing albuminuria
- General antidiabetic and slight antihypertensive effects

Agents Used

- Proven renal benefits: Canagliflozin 100mg, Empagliflozin 10mg, Dapagliflozin 10mg

Considerations/Monitoring

- Continue SGLT2 even after eGFR <20 unless not tolerated or renal replacement started
- Monitor for ADEs: euglycemic diabetic ketoacidosis, dehydration, mycotic genital infections

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

SGLT-2 Inhibitors:
Literature Background and Methods

Impact of Diabetes on the Effects of Sodium Glucose Co-transporter-2 Inhibitors on Kidney Outcomes: Collaborative Meta-analysis of Large Placebo-Controlled Trials The Nuffield Department of Population Health Renal Studies Group, et al. 2022	
Purpose	Compile randomized control trial evidence of SGLT-2 inhibitors on renal outcomes for people with CKD
Design	Systematic Review and meta-analysis
Selection	Inclusion: Assessed SGLT-2 inhibitors, double-blinded, placebo-controlled, participants ≥18 years old, ≥500 participants in each arm, ≥6-month duration, reported pre-specified efficacy or safety outcomes

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Nuffield Department of Population Health Renal Studies Group, et al. *Lancet*. 2022

SGLT-2 Inhibitors:
Outcomes and Demographics

The Nuffield Department of Population Health Renal Studies Group, et al. 2022	
Outcomes	Renal outcomes: CKD progression, AKI CV outcomes: Composite of CV death or hospitalization for HF Other outcomes: CV and non-CV death, all-cause mortality, safety
Relevant Patient Demographics	Sample size: 90413 participants Mean age: 61.9-71.8 years Follow-up: 0.8 to 4.2 years across all studies T2DM and high-risk atherosclerotic CVD: n=42568 (in four studies) Heart failure: n=21947 (in four studies) CKD: n=25898 (in four studies)

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Nuffield Department of Population Health Renal Studies Group, et al. *Lancet*. 2022

SGLT-2 Inhibitors:
Results and Conclusion

The Nuffield Department of Population Health Renal Studies Group, et al. 2022	
Results (CI 95%)	Renal outcomes: • **SGLT-2 reduced risk of kidney disease progression** vs placebo by 37% (RR 0.63, 0.58-0.69) • **SGLT-2 reduced risk of AKI** vs placebo by 23% (RR 0.77, 0.7-0.84) • No statistically significant difference between those with diabetes and without or with different mean baseline eGFR CV outcomes: • **SGLT-2 reduced risk of composite of CV death or hospitalization for HF** vs placebo by 23% (RR 0.77, 0.74-0.81) • **SGLT-2 reduced risk of CV death** vs placebo by 14% (RR 0.86, 0.81-0.92) • No statistically significant difference between those with diabetes and without or with different mean baseline eGFR • No statistically significant difference in risk reduction for non-CV death with SGLT-2
Conclusion	• SGLT-2 inhibitors reduce the risk of kidney disease progression in those with or without diabetes • SGLT-2 inhibitor effects are not isolated to specific baseline eGFR and safe to use for lower eGFRs

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Nuffield Department of Population Health Renal Studies Group, et al. *Lancet*. 2022

SGLT-2 Inhibitors: Summary

- SGLT-2 inhibitors are shown to reduce risk of:
  - CKD progression
  - CV outcomes and mortality
- SGLT-2 inhibitors are safe for use with lower eGFR and continuation for eGFR <25
- In general, KDIGO guidelines recommend SGLT-2 inhibitors for those with CKD and concurrent comorbidities (T2DM, HF) and those with CKD and albuminuria

Non-Steroidal MRAs

Non-steroidal MRAs

KDIGO Recommendations

- CKD with T2DM, eGFR >25, normal serum potassium, and albuminuria despite maximum tolerated ACE-I/ARB
- Steroidal MRA suggested for HF, hyperaldosteronism, refractory HTN

Mechanism of Action

- Reduces inflammation and fibrosis of the kidneys and decreases albuminuria
- Manages “aldosterone escape”
- General antihypertensive effects of steroidal MRAs
  - Non-steroidal MRAs have limited BP lowering effects but less gynecomastia

Agents Used

- Finerenone

Considerations/Monitoring

- Monitor for hyperkalemia which may require potassium-binders

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int*. 2024
Weltman MR. *DiPiro’s Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

Non-steroidal MRAs:
Literature Background and Methods

FIDELIO-DKD: Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes Bakris GL, et al. 2020	
Purpose	Determine if finerenone slows CKD progression and decreases CV morbidity and mortality in those with CKD and T2DM
Design	Phase 3, double-blinded, placebo-controlled, multicenter, RCT

Methods	Eligibility:
	• ≥18 years old, T2DM, and CKD treated with maximum tolerated ACE-I/ARB dose without ADEs
	• Must have serum potassium ≤4.8 mmol/L
	Interventions:
	• Participants randomized 1:1 into oral finerenone or placebo
	  • If eGFR 25 to <60 → finerenone 10mg daily
	  • If eGFR ≥60 → finerenone 20mg daily
	• Titration to finerenone 20mg encouraged at 1 month if eGFR stable and potassium ≤4.8
	• Decrease to finerenone 10mg possible at any point
	• Finerenone and placebo held if potassium >5.5; restarted once ≤5

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Bakris GL, et al. *N Engl J Med*. 2020

Non-steroidal MRAs:
Outcomes

Bakris GL, et al. 2020	
Outcomes	<u>Primary: Composite Renal Outcome</u> • Kidney failure, sustained decrease ≥40% in eGFR from baseline maintained over ≥4 weeks, death from renal causes <u>Secondary Outcomes:</u> • CV composite: CV death, nonfatal MI, nonfatal stroke, hospitalization for HF • All-cause mortality • All-cause hospitalization • Change in UACR from baseline to month 4 • Additional renal composite

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Bakris GL, et al. *N Engl J Med*. 2020

Non-steroidal MRAs:
Demographics

Bakris GL, et al. 2020	
Relevant Patient Demographics	Sample size: 5734 Mean age: 65.6 years Median follow-up: 2.6 years Mean eGFR: 44.3 mL/min/1.73 m^2 Median UACR: 852 mg/g Mean HbA1c: 7.7% Mean potassium: 4.37 mmol/L Baseline medications: 34.2% on ACE-I; 65.7% on ARBs

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Bakris GL, et al. *N Engl J Med*. 2020

Non-steroidal MRAs:
Results and Conclusion

Bakris GL, et al. 2020	
Results	<u>Renal Outcome:</u> • **Finerenone had decreased risk of the composite renal outcome** vs placebo by 18% (HR 0.82; 95% CI, 0.73-0.93; P=0.001) <u>Secondary Outcomes:</u> • **Finerenone had decreased risk of the composite CV outcome** vs placebo by 14% (HR 0.86; 95% CI, 0.75-0.99; P=0.03) • Finerenone had decreased risk of secondary composite renal outcomes events vs placebo by 24% (HR 0.76; 95% CI, 0.65-0.9) • **Finerenone had a greater decrease in UACR** vs placebo by 31% • No statistically significant difference in all-cause mortality • **Finerenone had significant increased risk for hyperkalemia** vs placebo
Conclusions	Based on results, finerenone is possibly an effective treatment for renal and CV protection in those with CKD, T2DM, and on maximum tolerated dose of ACE-I/ARBs

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Bakris GL, et al. *N Engl J Med*. 2020

Non-steroidal MRAs: Summary

- Non-steroidal MRAs are shown to reduce risk of:
  - Kidney outcomes
  - Select cardiovascular outcomes
- Caution with serum potassium levels
- In general, KDIGO guidelines suggest non-steroidal MRAs for those with CKD with T2DM and albuminuria despite maximum tolerated ACE-I/ARB
  - Steroidal MRAs are suggested for those with CKD and concurrent comorbidities (HF, resistant HTN)

GLP-1 Receptor Antagonists

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GLP-1 Receptor Agonists: Recommendations

KDIGO Recommendations

- CKD and T2DM unable to reach glycemic target using metformin and SGLT2 inhibitor
- CKD and T2DM unable to use metformin or SGLT2 inhibitor

Mechanism of Action

- Renal protective effects possibly due to direct reduction in inflammation, oxidative stress, and fibrosis
  - Reduces new-onset severely increased albuminuria, onset of renal failure, and eGFR decline
- Current KDIGO guideline recommendation primarily for the cardiovascular benefits

Agents Used

- Long-acting GLP-1 receptor agonists: Semaglutide, Liraglutide, Dulaglutide

Considerations/Monitoring

- Monitor for gastrointestinal ADEs
- Second line behind concomitant SGLT2 inhibitor, if possible, for uncontrolled T2DM patients with CKD

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Weltman MR. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026.

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GLP-1 Receptor Agonists:
Literature Background and Methods

FLOW (Evaluate Renal Function with Semaglutide Once Weekly Trial): Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes Perkovic V, et al. 2024	
Purpose	Determine efficacy and safety of once weekly semaglutide in slowing progression of kidney function, to kidney failure, and preventing death from kidney-related or CV causes in patients with T2DM and CKD
Design	Double-blinded, placebo-controlled, international multicenter, RCT

Methods	Eligibility:
	• ≥18 years old, T2DM with A1c ≤10%, and CKD treated with maximum tolerated ACE-I/ARB
	
	Interventions:
	• Participants randomized 1:1 into semaglutide or placebo
	  • 0.25mg/week x 4 weeks → 0.5mg/week x 4 weeks → 1mg/week
	  • Could extend intervals, hold treatment, or keep lower maintenance dose if ADEs occur

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Perkovic V, et al. *N Engl J Med*. 2024

GLP-1 Receptor Agonists:
Outcomes

Perkovic V, et al. 2024	
Outcomes	<u>Primary Composite Renal Outcome:</u> • Major kidney events: onset of kidney failure, sustained 50% reduction in eGFR from baseline, death from kidney-related or CV causes <u>Secondary Outcomes:</u> • Total eGFR slope • Major CV events: composite of nonfatal MI, nonfatal stroke, death from CV causes • All-cause mortality • Safety outcomes

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Perkovic V, et al. *N Engl J Med*. 2024

GLP-1 Receptor Agonists:
Demographics

Perkovic V, et al. 2024	
Relevant Patient Demographics	Sample size: 3533 Mean age: 66.6 years Median follow-up: 3.4 years Mean eGFR: 47 mL/min/1.73 m^2 Median UACR: 567.6 mg/g Macroalbuminuria: 68.5% Mean HbA1c: 7.8% Mean BMI: 32 Prior MI/Stroke: 22.9% Baseline medications: 35.1% on ACE-I; 60.2% on ARBs

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Perkovic V, et al. *N Engl J Med*. 2024

GLP-1 Receptor Agonists

Perkovic V, et al. 2024	
Results	<u>Primary Composite Renal Outcome:</u> • **Semaglutide group had decreased risk of major kidney events** vs placebo by 24% (HR 0.76; 95% CI, 0.66-0.88; P=0.0003) <u>Secondary Outcomes:</u> • **Semaglutide group had less steep mean annual slope of eGFR decline** vs placebo (between-group difference 1.16; 95% CI, 0.86-1.47; P<0.001) • **Semaglutide group had greater reduction of UACR and decreased loss of kidney function** • **Semaglutide group had decreased risk of major CV events** vs placebo by 18% (HR 0.82; 95% CI, 0.68-0.98; P=0.029) • **Semaglutide group had decreased risk of all-cause mortality** vs placebo by 20% (HR 0.8; 95% CI, 0.67-0.95, P-0.01)
Conclusions	Based on results, once weekly semaglutide shows clinical benefits in renal, CV, and survival outcomes in those with T2DM and CKD

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Perkovic V, et al. *N Engl J Med*. 2024

GLP-1 Receptor Agonists: Summary

- Long-acting GLP-1 receptor agonists are shown to reduce risk of:
  - Major kidney outcomes
  - Major CV outcomes
  - Mortality
- Long-acting GLP-1 receptor agonists also decrease rate of eGFR decline
- In general, the current KDIGO guidelines recommend long-acting GLP-1 receptor agonists for those with CKD and T2DM who require additional A1c lowering or cannot tolerate other options (SGLT-2, metformin)
  - Newer evidence supports use for the renal protective effects but not in the 2024 KDIGO guidelines

Patient Case

SH is a 50-year-old African-American female who presents to her primary care provider for a regular check-up.

PMH: seizures, gout, HTN, T2DM

Allergies: chronic cough with prior use of ACE inhibitors

Current medications (all oral): valsartan 80mg daily, levetiracetam 1000mg twice a day, allopurinol 300mg daily, metformin 1000mg twice a day

No adverse side effects

Relevant vitals and labs: Wt 45kg, BP 135/80 mmHg, A1c 7.5%, eGFR 45 mL/min/1.73 m^2, UACR >300 mg/g, potassium 5.2 mmol/L

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Assessment Question #4

What pharmacotherapy option for CKD per *current* 2024 KDIGO guidelines can be recommended for this patient based on her presentation to help delay CKD progression?

A. ACE inhibitor
B. SGLT-2 inhibitor
C. MRA
D. GLP-1 receptor agonist

Assessment Question #5

SH's elevated potassium was the result of her continuing to take a discontinued potassium chloride 20mEq daily prescription. At her next nephrology visit, her nephrologist wants to start another agent due to persistent ACR >300mg/g and on the maximum Valsartan dose that she can tolerate. What additional pharmacotherapy option(s) could be recommended to the provider based on *established and/or new evidence* to help delay CKD progression for SH?

A. Lisinopril 10mg daily
B. Dapagliflozin 10mg daily
C. Finerenone 10mg daily
D. Semaglutide 0.25mg SQ weekly
E. A & C
F. C & D
G. All of the above

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Summary of Key Points

- CKD is a progressive renal disease with goals of therapy revolving around preventing and delaying further loss of renal function
- Management in slowing progression focuses on decreasing albuminuria with pharmacotherapy and treating comorbidities
- Current CKD GDMT utilizes ACE-I/ARBs, SGLT-2 inhibitors, MRAs, and GLP-1 receptor agonists to slow progression of CKD, individualized to patients based on presentation and comorbidities
- Later stages of CKD and patients with higher risk of progression to ESRD requires a multidisciplinary approach to address treatment and outcomes
- Pharmacists not only have a role in adjusting drugs based on renal function, but also recognizing when treatment of CKD is warranted in those that are not being effectively treated for this underlying disease state

References

American Diabetes Association Professional Practice Committee. 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1 Suppl 1):S239-S251. doi:10.2337/dc25-S011

Bakris GL, Agarwal R, Anker SD, et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. *N Engl J Med*. 2020;383(23):2219-2229. doi:10.1056/NEJMoa2025845

Bargman JM, Skorecki KL. Chronic Kidney Disease. In: Longo D, Fauci A, Kasper D, Hauser S, Jameson J, Loscalzo J, Holland S, Langford C. eds. *Harrison's Principles of Internal Medicine, 22nd Edition*. McGraw Hill; 2026. Accessed November 11, 2025. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3541&sectionid=296166630

Bello AK, Alrukhaimi M, Ashuntantang GE, et al. Complications of chronic kidney disease: current state, knowledge gaps, and strategy for action. *Kidney Int Suppl (2011)*. 2017;7(2):122-129. doi:10.1016/j.kisu.2017.07.007

CDC. Chronic kidney disease in the United States, 2023. Centers for Disease Control and Prevention. May 15, 2024. Accessed November 20, 2025. https://www.cdc.gov/kidney-disease/php/data-research/index.html.

de Boer IH, Khunti K, Sadusky T, et al. 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. doi:10.2337/dci22-0027

GBD 2023 Chronic Kidney Disease Collaborators. Global, regional, and national burden of chronic kidney disease in adults, 1990-2023, and its attributable risk factors: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet*. Published online November 7, 2025. doi:10.1016/S0140-6736(25)01853-7

Hudson JQ. Chronic Kidney Disease: Management of Secondary Complications. In: Haines ST, Nolin TD, Ellingrod VL, Posey L, Cocohoba J, Holle L. eds. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026. Accessed November 11, 2025. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3386&sectionid=301508427

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References

Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int*. 2021;99(3S):S1-S87. doi:10.1016/j.kint.2020.11.003

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117-S314. doi:10.1016/j.kint.2023.10.018

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. doi:10.1016/j.kint.2022.06.008

Nuffield Department of Population Health Renal Studies Group; SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium. Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials. *Lancet*. 2022;400(10365):1788-1801. doi:10.1016/S0140-6736(22)02074-8

Perkovic V, Tuttle KR, Rossing P, et al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. *N Engl J Med*. 2024;391(2):109-121. doi:10.1056/NEJMoa2403347

Weltman MR. Chronic Kidney Disease. In: Haines ST, Nolin TD, Ellingrod VL, Posey L, Cocohoba J, Holle L. eds. *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*. McGraw Hill; 2026. Accessed November 11, 2025. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3386&sectionid=301508325

Writing Committee Members*, Jones DW, Ferdinand KC, et al. 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Hypertension*. 2025;82(10):e212-e316. doi:10.1161/HYP.0000000000000249

Xie X, Liu Y, Perkovic V, et al. Renin-Angiotensin System Inhibitors and Kidney and Cardiovascular Outcomes in Patients With CKD: A Bayesian Network Meta-analysis of Randomized Clinical Trials. *Am J Kidney Dis*. 2016;67(5):728-741. doi:10.1053/j.ajkd.2015.10.011

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Questions?

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