Updates in Chronic Kidney Disease Care

What Every Primary Care Physician Needs to Know

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Learning Objectives

01

Screening & Staging

Apply updated CKD screening and staging using the race-free CKD-EPI 2021 equation and cystatin C confirmation.

02

Risk Stratification

Use the Kidney Failure Risk Equation (KFRE) to guide nephrology referral decisions with precision.

03

Four-Pillar Pharmacotherapy

Implement RAS inhibitors, SGLT2 inhibitors, GLP-1 RAs, and finerenone across eligible patients.

04

Care Coordination

Recognize when to refer and how to coordinate care effectively with nephrology.

Why CKD Matters in Primary Care

~15% of US Adults

Affects an estimated 37 million Americans — the majority unaware.

Managed in Primary Care

Most patients with CKD never see a nephrologist. The primary care clinician is the quarterback.

CV Death — Not Kidney Failure

Cardiovascular disease remains the leading cause of death in CKD patients at every stage.

New Therapies

Four evidence-based pillars now exist to meaningfully slow CKD progression and reduce mortality.

The Screening Gap

Who Should Be Screened?

- Type 2 diabetes (annually)
- Type 1 diabetes (5 years after diagnosis)
- Hypertension or established CVD
- Age ≥ 60, family history of kidney disease
- Prior AKI or history of preeclampsia

⚠ **Less than 50% of patients with type 2 diabetes are screened annually.** Always screen with BOTH eGFR AND urine albumin-to-creatinine ratio (UACR) — using either alone misses significant disease.

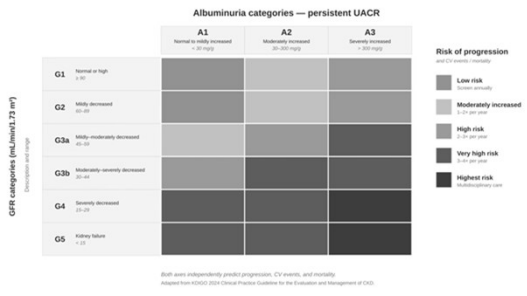
Updated eGFR Estimation

CKD-EPI 2021 Creatinine
The new standard — validated without a race coefficient. Use for all initial eGFR estimation.

Add Cystatin C
Use eGFRcr-cys when creatinine may be unreliable: extremes of muscle mass, plant-based diets, or certain medications (e.g., creatine supplements, trimethoprim).

Confirm Before Diagnosing
Repeat abnormal eGFR and UACR at **3 months** before labeling a patient with CKD. Transient abnormalities are common.

CKD Staging: The KDIGO Heat Map



Both axes — GFR category and albuminuria category — independently predict CKD progression, cardiovascular events, and mortality. Risk classification drives monitoring frequency and referral decisions.

Kidney Failure Risk Equation (KFRE)

About the KFRE

Uses **4 variables**: age, sex, eGFR, and UACR to predict 2- and 5-year risk of kidney failure. Validated in over 2 million patients across 60+ cohorts worldwide. Free calculator: **kidneyfailurerisk.com**

5-year KFRE > 3–5%
Consider nephrology referral

2-year KFRE > 10%
Multidisciplinary CKD clinic; begin kidney replacement therapy (KRT) planning

Low KFRE
Reassurance appropriate for mild CKD (e.g., G3a A1)

When to Refer to Nephrology

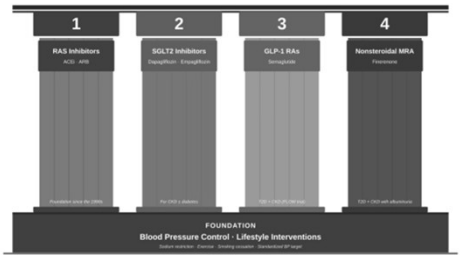
→ **Advanced or Worsening CKD**
eGFR < 30 (G4–G5) or UACR > 300 mg/g (A3), especially if rising. Rapid decline > 5 mL/min/year or ≥ 25% drop from baseline.

→ **Unexplained Findings**
Unexplained hematuria, nephrotic-range proteinuria, or suspected glomerular disease.

→ **Refractory Complications**
Hypertension requiring ≥ 4 agents, recurrent hyperkalemia, or hereditary kidney disease (ADPKD, Alport).

→ **KFRE-Based Referral**
5-year KFRE > 3–5%. Apply a lower threshold in younger patients (< 50 years).

The Four Pillars of CKD Pharmacotherapy



Build on a foundation of blood pressure control and lifestyle change — then layer evidence-based pharmacotherapy for maximum kidney and cardiovascular protection.

Pillar 1: RAS Inhibitors — The Foundation

Indications & Dosing

- First-line for CKD with albuminuria (UACR ≥ 30 mg/g), with or without diabetes
- Titrate to **maximum tolerated dose** — full-dose benefit demonstrated in trials
- Check creatinine and potassium within **2–4 weeks** of initiation or dose change

Key Cautions

- Continue unless creatinine rises > 30% within 4 weeks
- **Do not** combine ACE inhibitor + ARB — more harm, no added benefit
- Hyperkalemia is usually manageable without stopping the drug

Blood Pressure Targets in CKD

KDIGO 2021
SBP < 120 mmHg using **standardized office measurement**. Do not apply this target to non-standardized BP readings.

ADA 2026
< 130/80 mmHg; SBP < 120 if tolerated in patients with diabetes.

ACC/AHA 2025
SBP < 130 mmHg — balances cardiovascular benefit against adverse events.

Trial Evidence
SPRINT CKD subgroup: intensive SBP < 120 reduced CV events. BPROAD trial: intensive control yielded a **21% reduction** in CV composite in diabetes.

Pillar 2: SGLT2 Inhibitors — A Paradigm Shift

Who Gets It?

Recommended for CKD **regardless of diabetes status**. Initiate if eGFR ≥ 20; continue until dialysis.

Mechanism Beyond Glucose

Benefits are independent of glucose-lowering effects — driven by hemodynamic, anti-inflammatory, and cardioprotective mechanisms.

FDA-Approved Agents

Dapagliflozin (Farxiga) and empagliflozin (Jardiance) are approved specifically for CKD indication.

SGLT2 Inhibitors: The Evidence

39%

DAPA-CKD

Reduction in kidney composite endpoint; 31% reduction in all-cause mortality

28%

EMPA-KIDNEY

Reduction in CKD progression (HR 0.72)

37%

Meta-Analysis

13 trials, 90,409 patients — reduction in kidney progression

23%

CV Benefit

Reduction in CV death or heart failure hospitalization across trials

Benefits are **consistent in patients with AND without diabetes**, and extend down to an eGFR of 20 mL/min/1.73 m².

SGLT2 Inhibitors: Practical Pearls

Expect the eGFR Dip

An initial drop of ~3–5 mL/min is hemodynamic and **protective**. Reflects reduced hyperfiltration — do not stop the drug.

Sick Day Rules

Hold during acute illness, dehydration, or perioperatively. Resume once patient is stable and euvolemic.

Patient Counseling

Counsel on genital mycotic infections. No glucose monitoring needed in non-diabetic patients.

Initiate in Primary Care

No nephrology referral required to start. Primary care clinicians should initiate without delay.

Pillar 3: GLP-1 RAs — The FLOW Trial

FLOW — NEJM 2024

First dedicated kidney outcomes trial for a GLP-1 RA. 3,533 patients with T2D and CKD; semaglutide 1 mg weekly vs. placebo. **Stopped early for efficacy.**

Kidney Composite	eGFR Slope	CV Death	All-Cause Mortality
24% reduction (HR 0.76)	1.16 mL/min/year slower decline	29% reduction (HR 0.71)	20% reduction (HR 0.80)

GLP-1 RAs: Where Do They Fit?

Approved Indication
Semaglutide (Ozempic) — FDA-approved for T2D + CKD. ADA 2026 recommends a GLP-1 RA with proven kidney benefit for this population.

Additive to SGLT2i
FLOW subgroup analysis suggests complementary benefits when combined with SGLT2 inhibitors — use both when indicated.

eGFR Caution
Avoid lixisenatide and exenatide if eGFR < 30. Semaglutide requires no eGFR-based dose adjustment.

Non-Diabetic CKD
Not yet proven for CKD without diabetes — dedicated trials are ongoing. Weight, CV, and MACE benefits are established.

Pillar 4: Finerenone — Nonsteroidal MRA

Mechanism & Indication

Selective nonsteroidal mineralocorticoid receptor antagonist with **anti-inflammatory and anti-fibrotic** effects. Indicated for T2D + CKD with UACR ≥ 30 mg/g and eGFR ≥ 25. Add to maximally tolerated RAS inhibitor.

FIDELIO-DKD
18% reduction in kidney composite (HR 0.82)

FIGARO-DKD
13% reduction in CV composite (HR 0.87)

FIDELITY Pooled
23% lower kidney failure; 14% lower CV composite

Finerenone: Practical Considerations

Pre-Initiation Potassium
Requires serum potassium ≤ **4.8 mmol/L** before starting. Check at 1 month, then periodically.

Dosing by eGFR
10 mg daily if eGFR 25–60; **20 mg daily** if eGFR ≥ 60.

Hyperkalemia Risk
Discontinuation for hyperkalemia: ~2.3% vs. 0.9% with placebo. Co-administered SGLT2 inhibitor may mitigate this risk.

Advantages Over Spironolactone
More receptor-selective — less hyperkalemia, no gynecomastia, and no progesterone cross-reactivity.

Putting It All Together: A Stepwise Approach

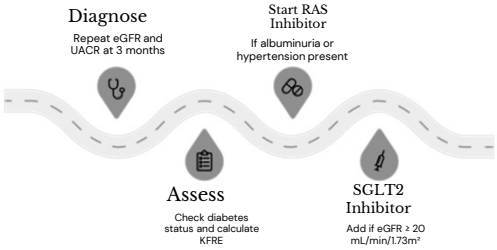
Step 1 — Lifestyle Foundation
Sodium restriction, regular exercise, smoking cessation, dietary protein 0.6–0.8 g/kg/day.

Step 2 — RAS Inhibitor
Titrate ACE inhibitor or ARB to maximum tolerated dose in all CKD with albuminuria.

Step 3 — SGLT2 Inhibitor
Add for all CKD at risk of progression with eGFR ≥ 20, regardless of diabetes status.

Steps 4–5 — T2D + CKD Add-Ons
Add semaglutide for kidney/CV protection. Add finerenone if UACR ≥ 30 and K ≤ 4.8. Statin for age ≥ 50 or younger with CV risk factors.

CKD Management Algorithm



This stepwise framework ensures that every eligible patient receives guideline-directed therapy in a logical, evidence-based sequence — without waiting for specialist input to begin.

SGLT2i vs. GLP-1 RA: Head-to-Head Data

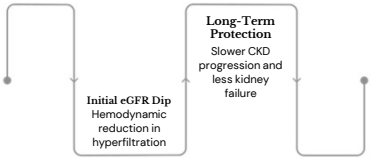
Key Findings — JAMA Internal Medicine 2026

No head-to-head RCTs exist. In this comparative effectiveness study:

- SGLT2i: lower CKD risk and fewer AKI events vs. GLP-1 RA initiators
- SGLT2i: greater benefit for eGFR decline and kidney failure prevention
- GLP-1 RA: may be more effective for albuminuria reduction and mortality

Mechanisms are **complementary** — combination therapy is supported for eligible patients.

The Initial eGFR Dip: Don't Panic



Acceptable Thresholds

- **RAS inhibitors:** up to 30% dip is acceptable and expected
- **SGLT2 inhibitors:** typically a 3–5 mL/min dip

When to Investigate

Only if eGFR drops > 30% — evaluate for volume depletion or renal artery stenosis. Otherwise, continue therapy.

Hyperkalemia: Don't Stop the Drug

Hyperkalemia is the most common reason RAS inhibitors and MRAs are prematurely discontinued. A stepwise approach should be exhausted before stopping.

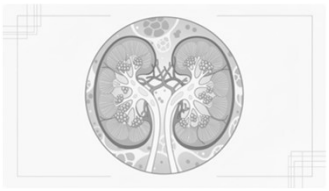
01
Dietary Counseling
Reduce dietary potassium intake — avoid high-potassium foods (bananas, oranges, potatoes).

02
Correct Acidosis
Treat metabolic acidosis with sodium bicarbonate — acidosis drives potassium out of cells.

03
Diuretic Adjustment
Adjust or add a loop or thiazide diuretic to promote renal potassium excretion.

04
Potassium Binders
Patiromer or sodium zirconium cyclosilicate (SZC). Reduce dose before discontinuing. SGLT2 inhibitor co-administration may mitigate risk with finerenone.

Beyond DKD: IgA Nephropathy Updates



Background

IgA nephropathy is the most common primary glomerular disease worldwide. Two novel agents have recently received approval:

Both agents are **additive to RAS inhibitors and SGLT2 inhibitors**.

Sparsentan (Filspari)
Dual endothelin/angiotensin receptor antagonist for proteinuric IgAN

Atrasentan (Vanrafia)
Selective endothelin A antagonist for UPCR ≥ 1.5 g/g. ALIGN (NEJM 2025): 36-point proteinuria reduction at 36 weeks

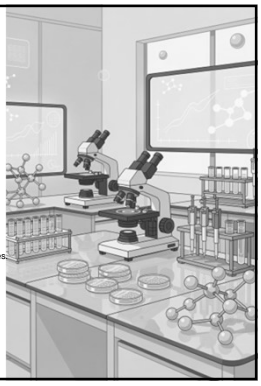
Emerging Therapies on the Horizon

Aldosterone Synthase Inhibitors
Trials ongoing for CKD without diabetes — may extend MRA benefits to a broader population.

Tirzepatide (Dual GIP/GLP-1)
Post hoc data demonstrate reduced albuminuria — dedicated kidney outcomes trial anticipated.

Endothelin Receptor Antagonists
Expanding beyond IgA nephropathy to other proteinuric glomerular diseases.

Anti-Senescence Therapies
Under investigation for endothelial protection and attenuation of fibrosis in CKD.



Lifestyle Interventions: Still the Foundation

Dietary Sodium
Target 2,000–2,300 mg per day to support blood pressure control and reduce proteinuria.

Physical Activity
Moderate intensity, ≥ 150 minutes per week. Improves BP, weight, and metabolic profile.

Smoking Cessation
Smoking accelerates CKD progression and amplifies cardiovascular risk — cessation is mandatory.

Diet & Nephrotoxin Avoidance
Protein 0.6–0.8 g/kg/day in stages 3–4. Plant-based diets reduce inflammation. Avoid NSAIDs; adjust all medications for eGFR.

Monitoring CKD: How Often?

Each Visit: Core Labs

- Blood pressure, eGFR, UACR, potassium

Stage 3+ Annual Add-Ons

- Hemoglobin, calcium, phosphate, PTH
- Vitamin D, bicarbonate

Medication Review

- Reassess and adjust all medication doses as eGFR changes — particularly metformin, finerenone, and analgesics.

Medication Adjustments by eGFR

Medication	Initiate	Dose Adjustment	Stop / Monitor
Metformin	eGFR ≥ 45	Reduce at eGFR < 45	Stop at eGFR < 30
SGLT2 inhibitor	eGFR ≥ 20	No adjustment needed	Continue to dialysis
GLP-1 RA (semaglutide)	Any eGFR	No adjustment needed	—
Finerenone	eGFR ≥ 25	10 mg (eGFR 25–60); 20 mg (eGFR ≥ 60)	Monitor K closely
ACE inhibitor / ARB	Any eGFR	Titrate to max tolerated	K uncontrolled or Cr rise > 30%

Contrast-Associated AKI: Updated Perspective

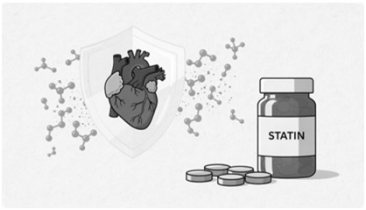
Risk Stratification

- Significant risk primarily in eGFR < 30 (G4–G5)
- Pre- and post-procedural IV hydration for at-risk patients
- Hold **metformin** at time of contrast if eGFR 30–60; recheck creatinine at 48 hours
- Hold **SGLT2 inhibitors** on day of contrast per institutional protocol

Clinical Bottom Line

Contrast-associated AKI risk is **frequently overestimated** in clinical practice. Do not withhold necessary imaging — the diagnostic benefit almost always outweighs the risk in patients with eGFR > 30.

Statin Therapy in CKD



Who Should Receive a Statin?

- All CKD patients aged ≥ **50**
- Ages 18–49 with additional CV risk factors (diabetes, CVD, hypertension)

Key Points

- CKD itself is a **cardiovascular risk equivalent**
- No dose adjustment needed for most statins in CKD
- Statins reduce CV events and mortality — they do **not** slow CKD progression

Anemia and CKD-MBD: Brief Overview

Anemia Management

Check hemoglobin annually beginning at CKD stage 3+. Obtain iron studies before initiating erythropoiesis-stimulating agents (ESAs) — iron deficiency is the most common correctable cause.

CKD-MBD Monitoring

Check calcium, phosphate, PTH, and vitamin D starting at stage 3a. Supplement vitamin D for confirmed deficiency.

Phosphate Management

Begin with dietary counseling; phosphate binders are reserved for advanced CKD. Typically co-managed with nephrology in stages 4–5.

2025 VA/DoD CKD Guideline: Highlights

Team-Based Care
Emphasizes primary care–led, team-based management as the standard model

Four Pillars Endorsed
All four pharmacotherapy pillars endorsed using GRADE methodology across 23 recommendations

KFRE-Guided Referral
Supports KFRE for referral decisions; discourages unnecessary nephrology referrals for low-risk CKD

Shared Decision-Making
Prioritizes patient-centered planning for kidney replacement therapy discussions

Common Pitfalls in Primary Care CKD

Missing Albuminuria
Not checking UACR — eGFR alone misses early CKD and underestimates risk in a large proportion of patients.

Stopping Protective Drugs
Discontinuing RAS inhibitors for mild creatinine rise or mild hyperkalemia — often unnecessary and harmful long-term.

Underutilizing SGLT2i
Not starting SGLT2 inhibitors in non-diabetic CKD, or waiting for nephrology before initiating guideline-directed therapy.

Missed Opportunities
Overestimating contrast nephropathy risk; not using KFRE to guide referral; failing to address sodium intake, exercise, and smoking.

Case 1: 62-Year-Old with T2D and CKD

Patient Profile

PMH: Type 2 diabetes (A1c 7.8%), hypertension, BMI 34
Labs: eGFR 38, UACR 650 mg/g, K 4.3 mmol/L
Current meds: Metformin 1000 mg BID, lisinopril 20 mg, atorvastatin 40 mg

Recommended Actions

- Titrate lisinopril to maximum dose (40 mg)
- Add dapagliflozin or empagliflozin 10 mg (eGFR ≥ 20)
- Reduce metformin dose (eGFR < 45)
- Add semaglutide — kidney/CV protection plus glycemic and weight benefit
- Consider finerenone (UACR > 30, K ≤ 4.8, eGFR ≥ 25)
- Calculate KFRE — likely warrants nephrology referral

Case 2: 55-Year-Old, Nondiabetic CKD

Patient Profile

PMH: Hypertension, obesity (BMI 31)
Labs: eGFR 42, UACR 280 mg/g, K 4.5 mmol/L
Current meds: Amlodipine 10 mg only

Recommended Actions

- Start an ACE inhibitor or ARB (A2 albuminuria + hypertension)
- Add an SGLT2 inhibitor (eGFR ≥ 20, albuminuria present)
- Target SBP 120–130 mmHg
- Lifestyle: sodium restriction, exercise, weight loss
- Finerenone and GLP-1 RA: **not indicated** (no diabetes)
- Calculate KFRE; monitor eGFR and UACR every 3–6 months

Key Takeaways

- **Screen Completely**
  Always check BOTH eGFR AND UACR — albuminuria testing remains critically underutilized.
- **Use the KFRE**
  The Kidney Failure Risk Equation guides referral timing and reassures low-risk patients.
- **Foundation for Nearly All CKD**
  RAS inhibitor + SGLT2 inhibitor is the core therapeutic pair — initiate in primary care without delay.
- **T2D + CKD: Go Further**
  Add semaglutide and finerenone when indicated — four-pillar therapy is the new standard.
- **Don't Stop, Don't Wait**
  Expected eGFR dips are protective. Primary care can and should initiate all four pillars.

Resources for Your Practice

- **KFRE Calculator**
  kidneyfailurerisk.com — 4-variable risk prediction for 2- and 5-year kidney failure
- **CKD-EPI eGFR Calculator**
  kidney.org/eGFR — race-free CKD-EPI 2021 creatinine and cystatin C equations
- **KDIGO 2024 CKD Guideline**
  kdigo.org — comprehensive evaluation and management guidelines with heat map staging
- **ADA & VA/DoD Guidelines**
  ADA 2026 Section 11: diabetesjournals.org · 2025 VA/DoD CKD Guideline: healthquality.va.gov