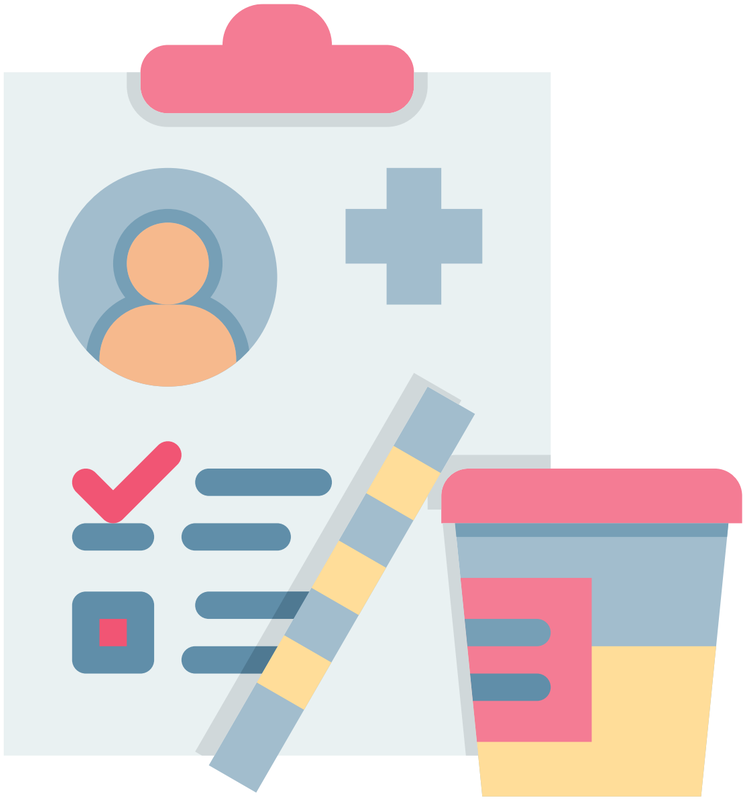
UT Southwestern Medical Center

Beyond the Dipstick: Proteinuria and Kidney Risk in Primary Care

Stephanie Torres Rodríguez, M.D.
Assistant Professor
Division of Nephrology

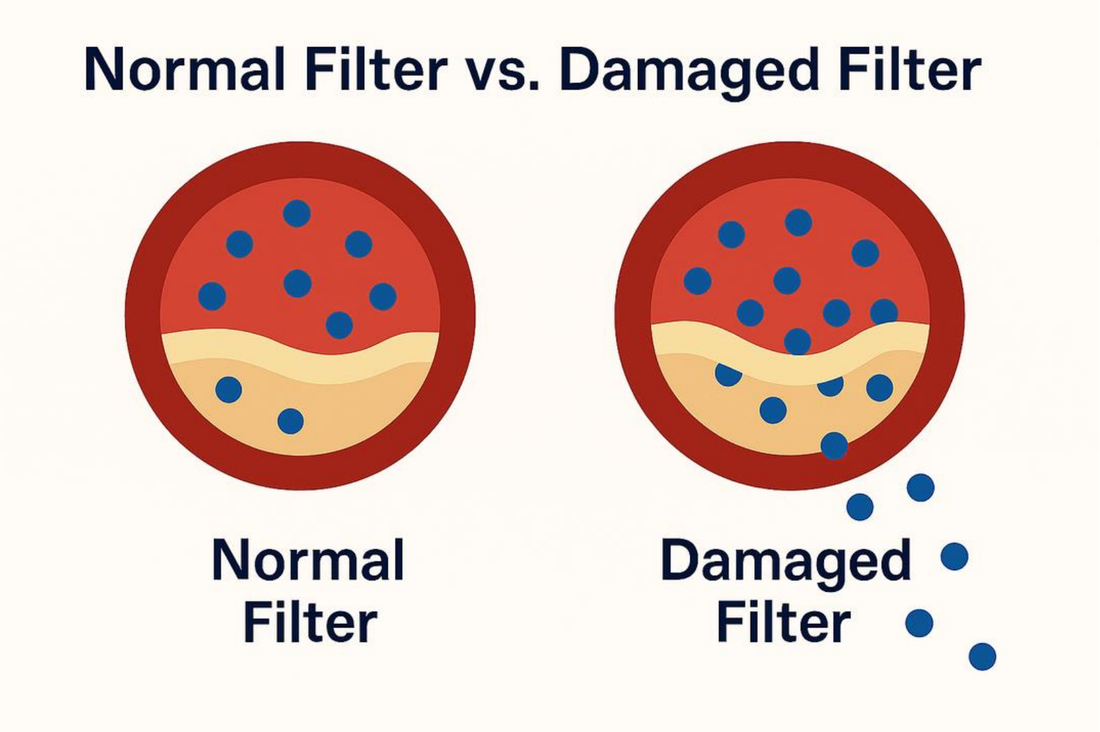


Objectives

- Recognize proteinuria as an early marker of kidney and cardiovascular risk.
- Identify patients who should be screened for proteinuria.
- Interpret levels of proteinuria correctly.
- Identify common causes of proteinuria encountered in primary care.
- Initiate evidence-based therapies to reduce proteinuria and slow CKD progression.
- Monitor proteinuria over time to assess treatment response and disease progression.
- Determine appropriate thresholds for nephrology referral.
- Counsel patients effectively about proteinuria.

What is proteinuria?

- Presence of excess protein in the urine
- It may indicate kidney damage
- Often present before changes in serum creatinine or eGFR

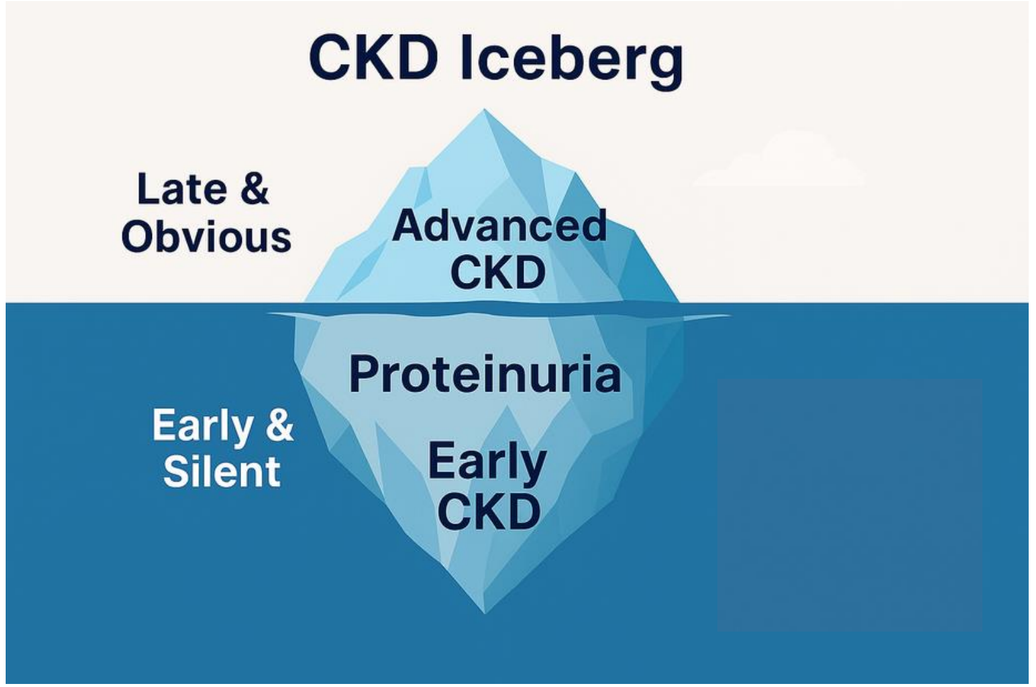


Why proteinuria matters?

- Proteinuria is:
  - Often silent
  - Often missed
  - Often modifiable

- Most CKD care happens in primary care
  - Early identification usually occurs outside nephrology
  - Primary care decisions shape long-term outcomes

- Early detection changes outcomes
  - Slows CKD progression
  - Reduces cardiovascular risk
  - Improves survival



Proteinuria, eGFR, and Cardiovascular Risk

- Risk increases with higher albuminuria at all eGFR levels
- Normal eGFR does not mean low risk
- Albuminuria predicts kidney progression and cardiovascular events

KDIGO: Prognosis of CKD by GFR and albuminuria categories

GFR categories (ml/min/1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

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

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

UTSouthwestern Medical Center

Who Should be Screened for Proteinuria?

Screen annually in patients with:

- Diabetes
  - Type 1 diabetes ≥5 years duration
  - All patients with type 2 diabetes
- Hypertension
- Known CKD or history of AKI
- Cardiovascular disease
- Metabolic risk factors
  - Obesity
  - Metabolic syndrome
- Family history of CKD

Preferred Screening Test:
Spot urine albumin-to-creatinine ratio (ACR)

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Population-Wide Screening?

U.S. Preventive Services Task Force (USPSTF)

- In 2012
  - Insufficient evidence of routine CKD screening using ACR and eGFR in asymptomatic, low-risk adults

Chronic Kidney Disease: Screening

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

This Recommendation is out of date

It has been replaced by the following:

This topic is being updated. Please use the link(s) below to see the latest documents available.

Update in Progress for Chronic Kidney Disease: Screening

The U.S. Preventive Services Task Force (USPSTF) is currently reviewing the evidence and updating its recommendations for this topic. The previous evidence review and recommendation issued in 2012 may contain information that is outdated. The USPSTF encourages primary care clinicians to consult other sources for current evidence while this topic is being updated.

USPSTF. Screening for Chronic Kidney Disease. Ann Intern Med. 2012.

Transient vs Persistent Proteinuria

Feature	**Transient Proteinuria**	**Persistent Proteinuria**
Definition	Temporary protein excretion	Proteinuria present on repeated testing
Duration	Resolves on repeat testing	Present on ≥2 measurements over ≥3 months
Clinical significance	Usually benign	Indicates chronic kidney disease
Common causes	***Fever*** ***Acute illness*** ***Exercise*** ***Dehydration*** ***Orthostatic proteinuria***	Diabetes Hypertension Glomerular disease Obesity-related kidney disease
eGFR relationship	Typically normal	May be normal or decreased
Next step	Repeat urine test after recovery	Risk stratification, treatment, and monitoring

Which Test to Order? Dipstick vs ACR vs UPCR

Dipstick

- Semi-quantitative screening tool
- Detects albumin only
- Affected by urine concentration
- Positive results require confirmation

✅ Use for: quick screen
❌ Do not use alone for CKD diagnosis or risk stratification

False Positives

- Concentrated urine
- Fever or acute illness
- Recent strenuous exercise
- Hematuria or contamination
- Alkaline urine

False Negatives

- Dilute urine
- Non-albumin proteins (e.g., tubular proteinuria, light chains)

Samal L, Linder JA. Clin J Am Soc Nephrol. 2013 — false positives and harms of routine dipstick screening

Which Test to Order? Dipstick vs ACR vs UPCR

- Preferred test in primary care
- Best predictor of:
  - CKD progression
  - Cardiovascular risk

✅ Use for: screening, risk stratification, and monitoring
✅ Detects early albuminuria

- Measures total urine protein
- Includes albumin and other proteins
- Helpful when albumin is not the main concern

✅ Use for:
- Significant proteinuria
- Suspected glomerulonephritis
- Nephrotic-range proteinuria

Which Test to Order? Dipstick vs ACR vs UPCR

- Historically the gold standard
- Rarely needed in primary care
- Consider if:
  - Spot results are inconsistent
  - Precise quantification is required
  - Nephrology specifically requests it

Which Urine Test Should I Order?

Clinical Scenario	Best Test	Why This Test
Asymptomatic patient with diabetes or hypertension	**Urine ACR**	Detects low levels of albumin
Patient with normal eGFR but high CV risk	**Urine ACR**	Albuminuria predicts CV events independent of GFR
Routine annual CKD monitoring	**Urine ACR**	Quantitative and reproducible
Positive dipstick on routine urinalysis	**Urine ACR (confirm)**	Dipstick is semi-quantitative
Febrile illness or recent strenuous exercise	**Repeat later → ACR if persistent**	Likely transient proteinuria
Suspected nephrotic syndrome (edema, frothy urine)	**UPCR**	Quantifies degree of protein loss
Suspected non-albumin protein (e.g., tubular disease, myeloma)	**UPCR**	Dipstick misses light chains
UTI or hematuria on UA	**Treat first, then repeat ACR**	False positives are common
Quick, low-cost initial screen in clinic	**Dipstick**	Fast and inexpensive
Discordant or unclear results	**Consider 24-hr urine**	Rarely, for clarification

How to Interpret ACR and UPCR Results?

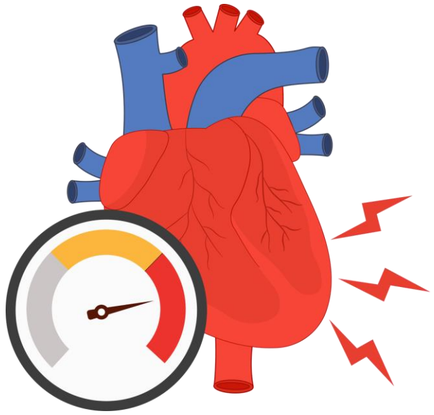
ACR (mg/g)	KDIGO Category	Interpretation
< 30	A1 – Normal to mildly increased	Normal albumin excretion
30–299	A2 – Moderately increased	**Albuminuria / early CKD**
≥ 300	A3 – Severely increased	High-risk CKD
≥ 3,000	Nephrotic-range albuminuria	Severe glomerular injury

UPCR (mg/g)	Type of Proteinuria	Interpretation	Clinical Significance
< 150	None	Normal protein excretion	Reassuring
150–500	Tubular OR mild glomerular	Low-level proteinuria	May suggest tubular injury (e.g., drug toxicity, interstitial disease) or early glomerular disease
500–3,500	Predominantly glomerular	Moderate–severe proteinuria	Significant kidney disease; evaluate cause ± referral
≥ 3,500	Glomerular (nephrotic-range)	Severe protein loss	Suggests nephrotic syndrome; refer to nephrology

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.
Brenner & Rector's The Kidney.

UTSouthwestern Medical Center

Most Common Causes of Persistent Proteinuria



Hypertension

Clues:

- Longstanding or poorly controlled hypertension
- History of hypertensive end-organ damage:
  - Left ventricular hypertrophy
  - Hypertensive retinopathy
- Low-grade to moderate proteinuria
- Slowly progressive decline in eGFR over years

✅ Often lower-grade albuminuria
✅ Commonly coexists with diabetes

Skorecki K, et al. Brenner & Rector's The Kidney. 11th ed. Elsevier; 2020.

Most Common Causes of Persistent Proteinuria

Diabetes

Clues:

- Longstanding diabetes (especially >5–10 years)
- Other diabetic complications:
  - Diabetic retinopathy
  - Peripheral neuropathy
- Gradual onset and progression of albuminuria

✅ Usually detected by ACR

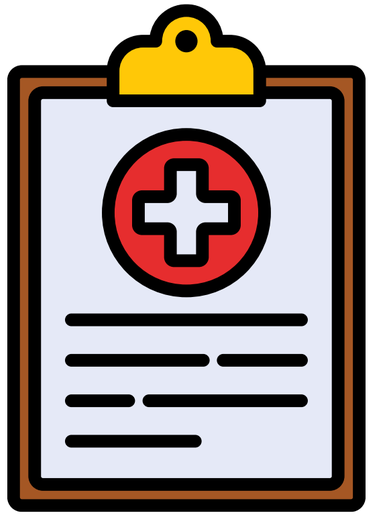
Hong J et al. Kidney Medicine. 2021; Penno G et al. (RIACE). Diabetes Care. 2012.

When to Question Diabetes or Hypertension as the Cause

Red flags suggesting an alternative diagnosis:

- Rapid onset of heavy proteinuria
- Nephrotic-range proteinuria early in disease
- Active urine sediment (hematuria, casts)
- Systemic symptoms (rash, joint pain, fevers)
- Unexplained AKI
- Age or timeline inconsistent with diabetes/HTN history

Key History Findings Suggesting Other Causes



- Rapid onset or sudden worsening of proteinuria

- Systemic symptoms:
  - Fevers, weight loss, night sweats
  - Rash, photosensitivity
  - Joint pain or swelling

- Gross hematuria or cola-colored urine
- Foamy urine with new-onset edema

- Medication or toxin exposure:
  - NSAIDs, antibiotics
  - Herbal supplements

- Recent contrast or chemotherapy
- Family history of kidney disease, dialysis, or early CKD

- Infections:
  - Chronic hepatitis
  - HIV
  - Recent streptococcal infection

Key Physical Exam Findings Suggesting Other Causes

- Edema (periorbital or lower extremities)
- Skin findings:
  - Rash, purpura, ulcers
- Joint swelling or tenderness
- Uncontrolled or malignant hypertension
- Signs of systemic disease:
  - Lymphadenopathy
  - Hepatosplenomegaly

Initiating Evidence-Based Therapies to Reduce Proteinuria

Goals of Treatment

- Reduce albuminuria/proteinuria
- Slow CKD progression
- Lower cardiovascular risk

Optimize Blood Pressure

KDIGO Recommendations:
Target systolic blood pressure (SBP) < 120 mmHg

Population	*Evidence*	*BP Target*
CKD + No Diabetes	ACC/AHA Guidelines	< 130/80
CKD + Diabetes	Sparse Data	< 130/80
CKD + Proteinuria > 1g/d	MDRD Study	< 125/75

Chang, A.R., et.al. Blood Pressure Goals in Patients with CKD: A Review of Evidence and Guidelines. *CJASN*. 2019.

Renin-angiotensin-system inhibitors (RASi)

- Recommendations
  - Start angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) for people with:
    - CKD + severely increased albuminuria (> 300 mg/g) without diabetes (1B).
    - CKD + moderately increased albuminuria (30-300 mg/g) without diabetes (2C).
    - CKD + moderately to severe albuminuria ***with*** diabetes (1B).

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Renin-angiotensin-system inhibitors (RASi)

- ACEi or ARB should be administered using the highest approved tolerated dose.
- Monitoring within 2-4 weeks of initiation or increase in dose.
  - Changes in BP, serum creatinine and serum potassium
- Continue medication even when eGFR falls below 30ml/min/1.73m².
- Continue medication unless serum creatinine increases more than 30%.
- Consider reducing dose or stopping RASi:
  - Symptomatic hypotension
  - Uncontrolled hyperkalemia
  - Reduce uremic symptoms (eGFR < 15)

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Sodium-glucose cotransporter-2 (SGLT2i)

- Recommendations
  - Start SGLT2i for people with:
    - DM2 + CKD with eGFR ≥ 20 ml/min/1.73m² (1A).
    - CKD with eGFR ≥ 20 ml/min/1.73m² + urine albumin-creatinine ratio (ACR) ≥ 200 (1A).
    - CKD + heart failure, irrespective of level of albuminuria (1A).
    - CKD with eGFR ≥ 20 to 45 ml/min/1.73m² + urine ACR < 200 (2B).

- Practice Points
  - Reversible decrease in eGFR on initiation is not an indication to discontinue therapy.

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Sodium-glucose cotransporter-2 (SGLT2i)

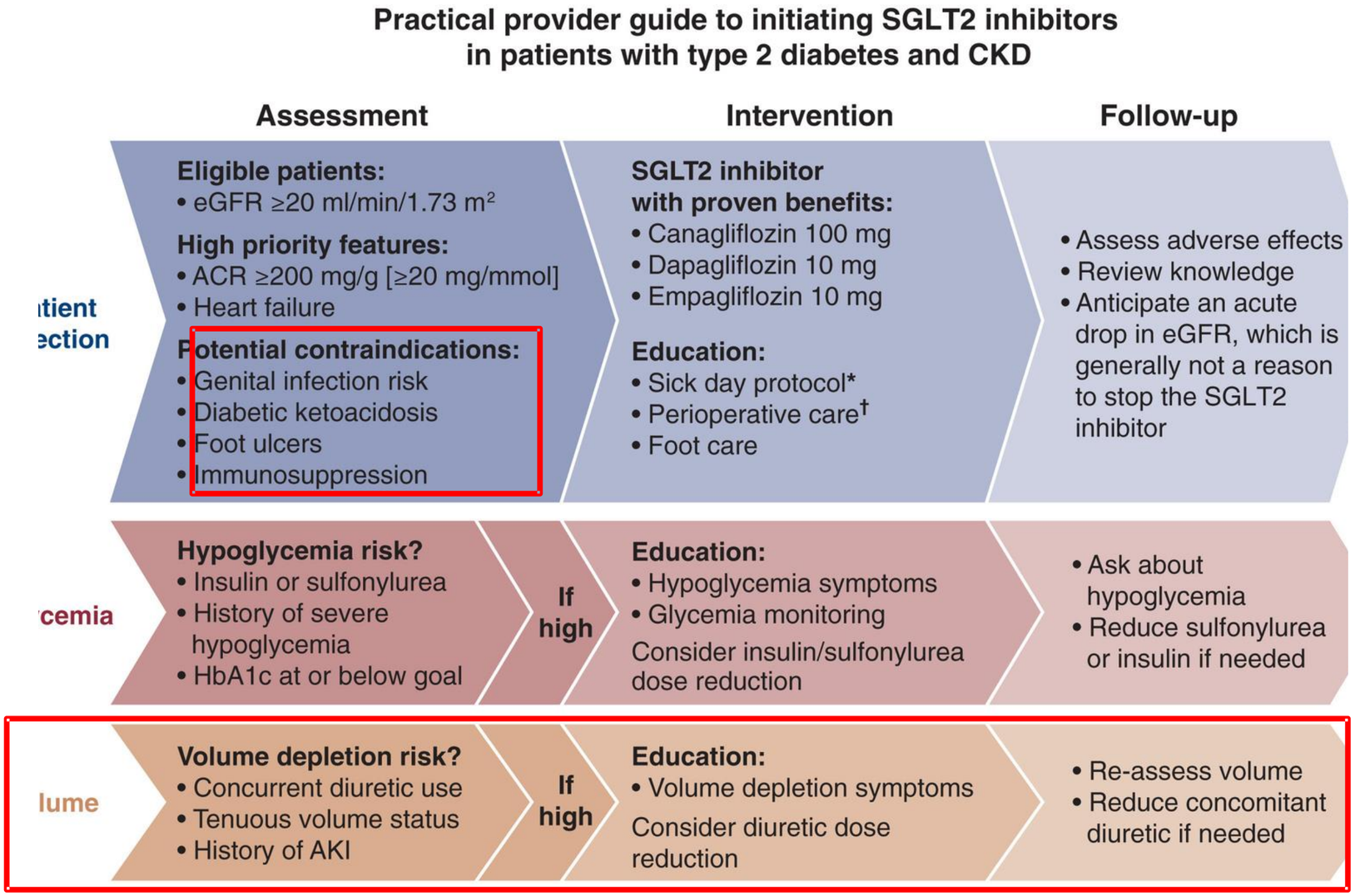
Practical provider guide to initiating SGLT2 inhibitors in patients with type 2 diabetes and CKD

	Assessment		Intervention	Follow-up
tient ection	**Eligible patients:** • eGFR ≥20 ml/min/1.73 m² **High priority features:** • ACR ≥200 mg/g [≥20 mg/mmol] • Heart failure **Potential contraindications:** • Genital infection risk • Diabetic ketoacidosis • Foot ulcers • Immunosuppression		**SGLT2 inhibitor with proven benefits:** • Canagliflozin 100 mg • Dapagliflozin 10 mg • Empagliflozin 10 mg **Education:** • Sick day protocol* • Perioperative care† • Foot care	• Assess adverse effects • Review knowledge • Anticipate an acute drop in eGFR, which is generally not a reason to stop the SGLT2 inhibitor
cemia	**Hypoglycemia risk?** • Insulin or sulfonylurea • History of severe hypoglycemia • HbA1c at or below goal	If high	**Education:** • Hypoglycemia symptoms • Glycemia monitoring Consider insulin/sulfonylurea dose reduction	• Ask about hypoglycemia • Reduce sulfonylurea or insulin if needed
lume	**Volume depletion risk?** • Concurrent diuretic use • Tenuous volume status • History of AKI	If high	**Education:** • Volume depletion symptoms Consider diuretic dose reduction	• Re-assess volume • Reduce concomitant diuretic if needed

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022.

UTSouthwestern Medical Center

Sodium-glucose cotransporter-2 (SGLT2i)



It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness.

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022.

UTSouthwestern Medical Center

Mineralocorticoid receptor antagonists (MRA)

- Recommendations
  - Suggest a nonsteroidal MRA with proven kidney or cardiovascular benefit for adults with:
    - DM2 + CKD with eGFR > 25 ml/min/1.73m² + normal serum potassium and albuminuria (> 30mg/g) despite maximum tolerated RASi dose (2A).

- Practice Points
  - A steroidal MRA may be used for treatment of:
    - Heart failure
    - Hyperaldosteronism
    - Refractory hypertension

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

UTSouthwestern Medical Center

Glucagon-like peptide-1 receptor agonists (GLP-1 RA)

- Recommendations
  - Start a long-acting GLP-1 RA for people with:
    - DM2 + CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2i or who are unable to use those medications (1B).

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Glucagon-like peptide-1 receptor agonists (GLP-1 RA)

- Prioritize agents with cardiovascular benefits
  - Liraglutide (Victoza), semaglutide (injectable - Ozempic), and dulaglutide (Trulicity).

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

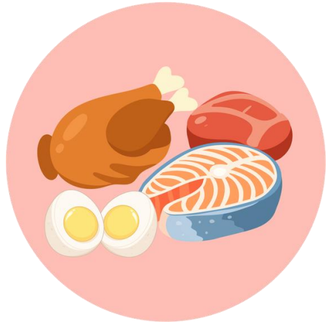
UTSouthwestern Medical Center

Initiating Evidence-Based Therapies to Reduce Proteinuria

Lifestyle & Risk Factor Modification

- Sodium restriction
- Weight management
- Smoking cessation
- Avoid NSAIDs

Dietary Protein Intake



Protein intake 0.8 g/kg/day

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

UTSouthwestern Medical Center

Monitoring Proteinuria Over Time

Why Monitor Proteinuria?

- Assess response to therapy
- Track disease progression
- Re-stratify kidney and cardiovascular risk
- Guide need for treatment escalation or referral

What to Monitor?

- Urine ACR (preferred for most patients)
- eGFR
- Blood pressure
- Serum potassium and creatinine (after RAASi or MRA changes)

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

Monitoring Proteinuria Over Time

How Often to Monitor?

Clinical Situation	Suggested Monitoring
No CKD, normal ACR	Annual screening
CKD with A2 albuminuria	Every 6–12 months
CKD with A3 albuminuria	Every 3–6 months
After starting or titrating ACEi/ARB, SGLT2i, or MRA	Check labs within 2–4 weeks, then periodic monitoring

What Constitutes Improvement?

- Reduction in ACR from baseline (even partial reduction is meaningful)
- Stabilization or slower decline in eGFR
- Improved BP control

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2024.

UTSouthwestern Medical Center

When to Refer to Nephrology?

Proteinuria-Based Criteria

- ACR ≥ 300 mg/g (A3) persistent proteinuria
- Nephrotic-range proteinuria
  - ACR ≥ 3,000 mg/g or
  - UPCR ≥ 3,500 mg/g
- Rapidly rising proteinuria despite optimized therapy

Kidney Function Criteria

- eGFR < 30 mL/min/1.73 m² (CKD G4–G5)
- Rapid decline in eGFR (>5 mL/min/1.73 m² per year or >25% drop)
- Recurrent or unexplained acute kidney injury

When to Refer to Nephrology?

Clinical or Diagnostic Red Flags

- Proteinuria not explained by diabetes or hypertension
- Active urine sediment (hematuria, casts)
- Systemic symptoms suggesting secondary disease (rash, joint pain, fevers, weight loss)
- Suspected glomerulonephritis or systemic disease

Management-Related Reasons

- Persistent albuminuria despite:
  - Optimized BP control
  - ACEi/ARB and SGLT2 inhibitor therapy
- Uncertainty about diagnosis or progression
- Need for biopsy consideration

Counseling Patients About Proteinuria

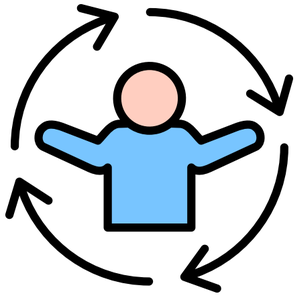
How to Explain Proteinuria

“Protein in the urine means the kidneys are under stress or damage”
“Often there are no symptoms early on”
“It can happen before kidney numbers change”

Key Reassurance Points

- Proteinuria does not automatically mean dialysis
- Many cases are manageable and treatable
- Early detection allows us to slow or even stop progression
- Small improvements in protein levels matter

Counseling Patients About Proteinuria



What Patients Can Do?

- Take medications consistently (BP meds, ACEi/ARB, SGLT2i)
- Control blood pressure and blood sugar
- Limit salt intake
- Avoid NSAIDs unless advised
- Keep follow-up and lab monitoring appointments

Set Expectations

- Proteinuria is something we monitor over time
- Goal is usually reduction, not always complete elimination
- Improvement may be gradual

When to Encourage Patients to Call?

- New swelling in legs or around eyes
- Sudden weight gain
- Changes in urine output

Key Take-Home Messages for Primary Care

- Proteinuria is an early, often silent marker of kidney and cardiovascular risk
- Albuminuria matters even when eGFR is normal
- ACR is the preferred test for screening, risk stratification, and monitoring
- Confirm persistence to distinguish benign from chronic disease
- Most proteinuria in primary care is due to diabetes or hypertension
- Proteinuria is modifiable:
  - Optimize blood pressure
  - Use ACE inhibitors/ARBs
  - Add SGLT2 inhibitors when appropriate
- Trends over time matter more than a single value
- Refer to nephrology for severe, progressive, or atypical cases
- Primary care plays a central role in changing kidney and cardiovascular outcomes