



MANAGEMENT OF

Chronic Kidney Disease (CKD)

2018 Update

This care process model (CPM) was developed by a multidisciplinary team of clinical experts from SelectHealth and Intermountain Healthcare using guidelines from Kidney International, the National Kidney Foundation, and the U.S. Veteran’s Administration/ Department of Defense. This CPM recommends screening, diagnosis, and treatment processes to improve care and outcomes for patients with chronic kidney disease (CKD) in primary care, along with nephrology consult/referral criteria to enhance quality outcomes.

► Why Focus ON CKD?

- **Prevalence.** Overall CKD prevalence rose from 12.3% to 14% between 1988 and 2010.^{USR1} According to the CDC, more than 30 million of all U.S. adults age 18 and older have CKD.^{CDC}
- **Underdiagnosis.** Research suggests that more than 70% of CKD cases go undiagnosed. In a large, 2007 study of outpatients with clinical indications of CKD, only 27% of actual CKD cases had been successfully screened and diagnosed.^{RYA}
- **Cardiovascular disease (CVD) risk.** Patients with an eGFR < 70 (CKD Stage G2) have a 51% greater risk of death from CVD than non-CKD patients.^{GOA} Patients with eGFR < 60 (CKD Stage G3) are more likely to die from CVD than progress to dialysis.^{NOG}
- **Increased hospitalization and medical expenditure.** In terms of all-cause hospitalization in patients over 65, those with CKD incur per person per year (PPPY) costs of over \$23,000, compared to \$8,000 for patients without end-stage renal disease (ESRD), CKD, diabetes, or congestive heart failure (CHF).^{USR1}
- **Impact.** Early identification and effective management of CKD by primary care physicians may reduce hospitalizations and prevent unnecessary morbidity and mortality. Early detection of progressive kidney disease is important because therapies, such as ACE-Is (angiotensin converting enzyme inhibitors) or ARBs (angiotensin II receptor blockers), can slow the rate of progression in many patients.

► GOALS AND MEASURES

This CPM is part of a comprehensive care management system for CKD.

Goals	Measures
<ul style="list-style-type: none"> • ↑ CKD screening rate for at-risk patients • ↑ Appropriate use of diagnostic testing • ↓ CVD mortality and overall treatment costs associated with CKD • Improve medical management, especially with ACE-I/ARB use • ↑ Referrals to RDN for CKD dietary management in all stages • Improve primary care/nephrology CKD co-management 	<ul style="list-style-type: none"> • Number of patients with a CKD diagnosis • Percent of patients who: <ul style="list-style-type: none"> – Are in each stage – Have appropriate labs done in recommended timeframes – Are treated with ACE-I/ARB medications when ACR > 300 (or ACR > 30 in patients with diabetes) – Have blood pressure in control (140 / 90) when ACR ≤ 300

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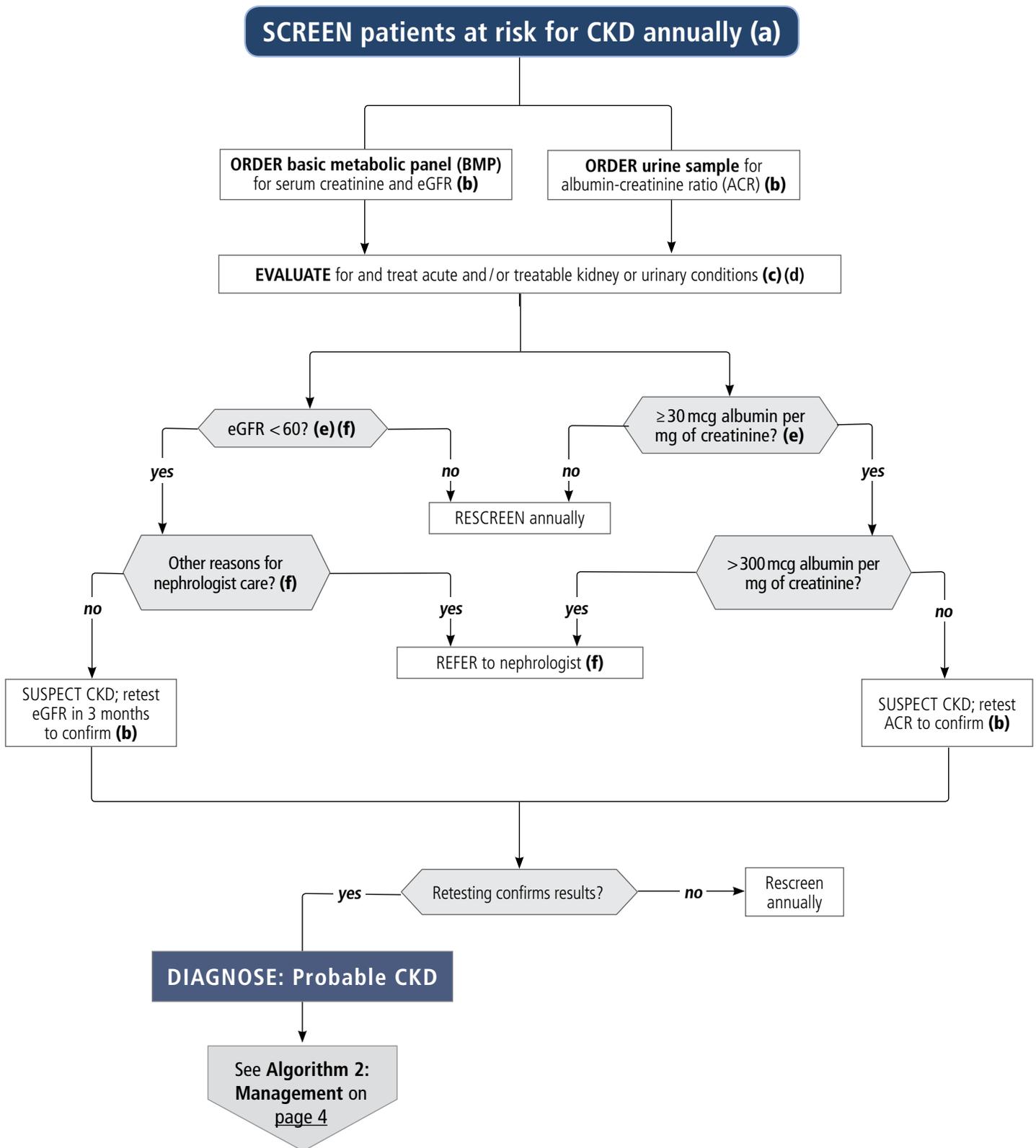
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What’s new in this update?

- Updated information on:
 - Phosphate binders
 - Hyperkalemia management
 - Bone density measurement
 - Home hemodialysis
 - Preemptive kidney transplant
- Additional patient resources (see [page 34](#))



ALGORITHM 1: SCREENING



See [page 3](#) for Algorithm 1 Notes

ALGORITHM 1 NOTES

(a) RISK FACTORS FOR CKD	
Screen patients who have ANY of these risk factors. ^{KDIGO}	
Chronic conditions	<ul style="list-style-type: none"> Diabetes type 1 (begin screening for CKD 5 years after diagnosis) Diabetes type 2 (begin screening for CKD at the time of diagnosis) Hypertension Cardiovascular disease (CVD) Structural renal tract disease Systemic illness affecting kidneys (HIV, lupus, vasculitis, rheumatoid arthritis, hyperuricemia, multiple myeloma)
History	<ul style="list-style-type: none"> Family history of kidney disease (dialysis, renal failure) History of acute renal failure
Urologic problems	<ul style="list-style-type: none"> Urinary obstruction, structural renal tract disease, urinary diversion surgery, or reflux nephropathy Recurrent urinary tract infections (UTIs) (> 3 in 1 year) Kidney stones
Medications	<ul style="list-style-type: none"> High dose or chronic treatment with nephrotoxic medications, including NSAIDs

(b) ANNUAL Screening FOR CKD	
These are the primary screening tests for CKD in order of preference. ^{KDIGO} A morning sample is preferred for urine samples.	
BMP For patients with risk factors, screen annually	<ul style="list-style-type: none"> Check eGFR (estimated glomerular filtration rate). If eGFR < 60, evaluate whether the patient needs nephrology care — see note (e). If urgent care is not needed, retest in 3 months to confirm chronic kidney disease. Use eGFR and ACR to help establish risk and severity if CKD is diagnosed (see page 6). The CKD-EPI equation is the primary equation used for estimating eGFR (see page 8).
UA: Albumin-creatinine ratio (ACR) For patients with risk factors, screen annually	<ul style="list-style-type: none"> If > 300 mcg of albumin to mg creatinine, refer to a nephrologist. If 30–300 mcg of albumin to mg creatinine, retest within 3 months. Two abnormal specimens are required before diagnosing CKD. Note: Vigorous exercise before the test, infection, fever, congestive heart failure (CHF), marked hyperglycemia, or marked hypertension may elevate albumin.
Urine dipstick If ACR test is not readily available	<ul style="list-style-type: none"> Spot urine collection is acceptable; no need for 24-hour urine sample. If protein is present (≥ 1+), order ACR to evaluate albuminuria (see above).

(c) CKD Indicators
The following conditions provide evidence of kidney damage: <ul style="list-style-type: none"> Diabetes with persistent moderate albuminuria Structural kidney abnormalities Persistent hematuria of renal origin Biopsy-proven kidney disease (e.g., glomerulonephritis or interstitial nephritis)

(d) Factors that affect kidney function
Patients with a recent decrease in renal function may be suffering from an underlying reversible process, which, if identified and corrected, may result in the recovery of function. In addition, certain drugs and substances affect kidney function or interfere with creatinine secretion.
<ul style="list-style-type: none"> Urinary tract obstruction or urinary tract infection (UTI). Decreased renal perfusion, caused by: <ul style="list-style-type: none"> Drugs that lower eGFR, such as NSAIDs and ACE inhibitors (ACE-Is) Hypovolemia, due to vomiting, diarrhea, diuretic use, bleeding, etc. Hypotension, due to myocardial dysfunction, excessive antihypertensive medications, or pericardial disease Infection, such as pneumonia Nephrotoxic drugs and substances, including: <ul style="list-style-type: none"> NSAIDs Radiographic contrast material, particularly in patients with diabetes Aminoglycoside antibiotics (particularly with unadjusted doses) False elevation of serum creatinine (sCr). Certain drugs and supplements interfere with creatinine secretion or with the assay used to measure sCr. With these drugs, sCr will be affected but there will be no change in eGFR; a clue that this is the case is the absence of an elevated blood urea nitrogen (BUN). Examples of medications with this effect: <ul style="list-style-type: none"> Cimetidine Flucytosine Trimethoprim Fenofibrates (ex: Tricor) Cefoxitin Creatine supplements

(e) Factors that may limit accuracy of eGFR
<ul style="list-style-type: none"> Pregnancy Age > 70 Unusual muscle mass Near-normal serum creatinine Rapidly changing serum creatinine Cirrhosis, nephrotic syndrome, or past transplant Medications listed in table (d) above
See page 7 for more information.

(f) Refer* to nephrologist for Consultation if: ^{KDIGO}
<ul style="list-style-type: none"> Acute kidney injury or abrupt sustained fall in eGFR eGFR ≤ 45 (GFR categories G3b–G5)— see Algorithm 2 on page 4 A consistent finding of significant albuminuria (ACR ≥ 300) Rapid progression of CKD (see page 5, table [ii]) Urinary red cell casts, RBC > 20 per high power field sustained and not readily explained CKD and hypertension refractory to treatment with 4 or more antihypertensive agents Persistent abnormalities of serum potassium Recurrent or extensive nephrolithiasis Hereditary kidney disease

* Referral may not be appropriate for patients whose life expectancy is limited.

ALGORITHM 2: MANAGEMENT

DIAGNOSIS: Probable CKD (a)

Recheck to exclude acute or reversible disease (see page 3, note [d])

ASSESS Testing Frequency and Need for Nephrology Consultation/Referral						
LEGEND ■ Deep Red: Extremely High Risk — Test 4+ times/yr ■ Red: Very High Risk — Test 3 times/yr ■ Orange: High Risk — Test 2 times/yr ■ Yellow: Moderately Increased Risk — Test once/yr ■ Green: Low or No Risk — Test 1 time/yr IF CKD				Persistent albuminuria categories description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mcg/mg <3 mg/mmol	30–300 mcg/mg 3–30 mg/mmol	>300 mcg/mg >30 mg/mmol
eGFR categories (ml/min/1.73 m ²) description and range	G1	Normal or high	>90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor/Refer**	Monitor/Refer*	Refer
	G4	Severely decreased	15–29	Refer	Refer	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

* Consider referral to nephrology service depending on local arrangements regarding monitoring or referring.
 ** Some Intermountain nephrologists recommend seeing patients at G3bA1, especially if diagnosis is unclear.

MANAGE CKD RISK (per items checked below)				
■ Red: Very High / Extremely High Risk ■ Orange: High Risk ■ Yellow: Moderately Increased Risk ■ Green: Low or No Risk	Low or no risk	Moderately increased risk	High risk	Very high / extremely high risk
	PCP management			PCP/nephrologist comanagement
Patient education on CKD (b)	✓	✓	✓	✓
Vaccinations (see sidebar page 14)	✓	✓	✓	✓
Albuminuria and hypertension management using ACE-I/ARB or other medications (c)	✓	✓	✓	✓
Lipid monitoring and management (d)	✓	✓	✓	✓
Diabetes management (e)	✓	✓	✓	✓
Avoidance or dose adjustment of nephrotoxic medications / substances (f)	✓	✓	✓	✓
Preservation of venous access (g)	✓	✓	✓	✓
Dietary management (h)	✓	✓	✓	✓
Hyperkalemia evaluation and treatment (j)	✓	✓	✓	✓
Metabolic acidosis evaluation and treatment (j)	✓	✓	✓	✓
Anemia evaluation and treatment (j)	✓	✓	✓	✓
Volume overload / edema evaluation and treatment (j)	✓	✓	✓	✓
Metabolic bone disease evaluation and treatment (j)	✓	✓	✓	✓
Patient education to prepare for dialysis (see page 16)	✓	✓	✓	✓

FOLLOW UP regularly: Reassess, reclassify, and adjust treatment every 3–12 months; assess progression (i)

*Adapted by permission from Macmillan Publishers Ltd: Official Journal of the International Society of Nephrology (Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Inter., Suppl.* 2013; 3: 1-150), copyright 2013.

ALGORITHM 2 MANAGEMENT NOTES

(a) CKD Staging (see page 6)

CKD is classified based on CGA – Cause, eGFR category, and Albuminuria.^{KDIGO} Staging and its defining language have changed since the previous versions of this CPM. The stages “G1–G5” roughly equate to the previous Stages 1 to 5, but the new staging system also accounts for albuminuria and cause. For example, Stage G2/A1 is low risk if there are no other markers of kidney disease; Stage G3a/A2 is high risk.

(b) Patient Education (see pages 15–17)

At diagnosis, patients need education on kidney function, expectations for living with CKD, treatment, and self-management to slow CKD progression. If the patient is low or no risk, provide education only if other markers of CKD are present.

(c) Albuminuria and hypertension management (see pages 18–19)

Albuminuria and hypertension are risk factors for CVD and can speed CKD progression. An ACE inhibitor (ACE-I) is the best management agent for most patients; carefully monitor creatinine and potassium during titration. If an ACE-I is not tolerated (usually due to a dry cough), switch to an ARB (combining an ACE-I and ARB is not recommended). Other medications may also be needed. See pages 18–19 for management targets, an algorithm, and medication details.

(d) Lipid Management (see pages 20–21)

Because dyslipidemias are prevalent in CKD and CKD patients are in the highest CVD risk category, lipid management is a key element of treatment. CKD patients can benefit from statins depending on their age, disease stage, and comorbidities. See pages 20–21 for information on unique aspects of dyslipidemia in CKD, a treatment algorithm, and medication tables.

(e) Diabetes Management (see pages 22–23)

In CKD patients with diabetes, a strong focus should be placed on glycemic control (HbA1c < 7%), albuminuria management (with an ACE-I/ARB), and robust blood pressure control (BP < 140/90 or in some cases even as low as 130/80). See pages 22–23 for risk factors that can speed the decline of renal function in these patients, tips on determining whether CKD is the result of diabetes or another cause, and key resources for diabetes management.

(f) Avoidance and/or dose adjustments of nephrotoxic medications and substances

These include NSAIDs, radiographic contrast (especially with diabetes patients), and aminoglycoside antibiotics (particularly with unadjusted doses).

(g) Preservation of venous access (see page 16)

At all CKD stages, patients should avoid venipuncture or IV placement in the nondominant arm. Starting at Stage G3b, patients should avoid subclavian central and PICC lines if at all possible.

(h) Dietary management (see pages 31–33)

All CKD patients should reduce their intake of sodium. Depending on the patient’s status, dietary management may also include management of potassium, phosphorus, calcium, and protein. (**Note:** A very low protein diet is not recommended.) See pages 31–33 for information and resources on dietary management; recommend referral to a registered dietitian nutritionist (RDN).

(i) CKD progression defined (see page 6)

Progression: Decline in eGFR category—a drop in eGFR category **OR** a > 25% drop in eGFR from baseline

Rapid progression: A sustained decline in eGFR of > 5 mL/year

(j) Monitoring and managing other comorbidities

Condition	Monitoring	Management	See Pg:
Hyperkalemia	Test for potassium: <ul style="list-style-type: none"> At regular follow-up appointments For ACE-I or ARB: Within 2 weeks of any dose change For the ARA (aldosterone receptor antagonist) spironolactone and eplerenone: At 4–7 days after adding or increasing dose if patient on ACE-I/ARB; between 7–10 days after adding or increasing dose if patient not on ACE-I/ARB If patient has hyperkalemia symptoms 	Manage/treat based on potassium (mmol/L): <ul style="list-style-type: none"> At 5.1 to 5.5: Review/adjust OTC meds, limit dietary potassium. At 5.5 to 6.0: Adjust prescription meds, check for other causes, refer to nephrologist if needed. At > 6.0: Consider urgent referral, hospitalization. 	<u>24–25</u>
Metabolic acidosis	Test for metabolic acidosis annually for moderately increased-risk patients, every 6 months for high-risk patients, and every 3 months for very high-risk patients.	<ul style="list-style-type: none"> Check for and address non-CKD causes. Treat with sodium bicarbonate. 	<u>26</u>
Anemia	<ul style="list-style-type: none"> Check for iron deficiency (CBC, serum iron, total iron-binding capacity, and serum ferritin) 1×/year (G3), 2×/year (G4), and 4×/year (G5). If anemia is present, screen for other causes such as GI bleeding. If eGFR < 60, you can assume EPO is deficient; checking levels is not recommended. 	<ul style="list-style-type: none"> Begin with a 3-month trial of oral iron therapy. Consider IV iron if oral iron isn’t tolerated or iron stores remain low. A nephrologist or hematologist should manage treatment with erythropoietin-stimulating agents (ESAs). 	<u>27</u>
Volume overload/ edema	<ul style="list-style-type: none"> Monitor weight and check for symptoms at every visit. Evaluate CVD risk; if eGFR > 30, volume overload often has a cardiac cause. Evaluate for CHF and metabolic concerns, and reevaluate medications. 	<ul style="list-style-type: none"> Restrict dietary sodium to < 2,000 mg per day. Treat with diuretics, preferably loop diuretics, adjusting dose/frequency based on patient response. Add a thiazide diuretic if necessary. 	<u>28</u>
Metabolic bone disease	<ul style="list-style-type: none"> Do a baseline measurement of iPTH, phosphorus, calcium, and calcium-phosphate product at stage G3 with follow-up testing based on baseline measures and stage. 	<ul style="list-style-type: none"> Reduce phosphate; regulate calcium and vitamin D. Consider phosphate binders. 	<u>29</u>

DEFINITION OF CKD

Chronic kidney disease (CKD) can be defined as abnormalities of kidney structure or function, present for more than 3 months, with implications for health.

PREDICTING PROGRESSION OF CKD

Understanding the risk for CKD progression supports clinical decisions about testing, treatment, and referral, as it supports shared decision making. It is important to explain to the patient that the goal is to slow disease progression and take measures to prevent or delay the need for ESRD and renal replacement therapy. KDIGO defines progression as follows:

- **Progression:** Decline in eGFR category—a drop in eGFR category OR a ≥ 25 % drop in eGFR from baseline
- **Rapid progression:** A sustained decline in eGFR of > 5 mL/year

In people with CKD progression, review current management, examine for reversible causes of progression, and consider referral to a specialist.^{KDIGO}

CONTROVERSY REGARDING OVERDIAGNOSIS

There has been some debate about whether relying on eGFR and albuminuria leads to overdiagnosis and overly aggressive treatment of CKD. Based on KDIGO guidelines, diagnosis of CKD has increased significantly (from approximately 1.7 % of the population before KDIGO to 14 % of the population after). This, combined with low rates of total kidney failure, suggest that many of those diagnosed will never progress to symptomatic forms of kidney disease.^{BMJ}

We recommend **monitoring change** over time to determine treatment and progression risk.

▶ DIAGNOSTIC CRITERIA AND STAGING

The 2012 Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guidelines for CKD clarify the definition and diagnosis of chronic kidney disease (CKD). Based on these guidelines, this section includes a best-practice definition of CKD (see sidebar), diagnostic criteria, and staging and progression guidelines.

Diagnostic criteria

The table below is adapted from the KDIGO guidelines. A patient should be diagnosed with CKD if markers of kidney disease (especially albuminuria) or decreased estimated glomerular filtration rate (eGFR) is present.

TABLE 1: Diagnostic criteria for CKD	
Either of the following present for > 3 months ^{KDIGO}	
Markers of kidney damage (1 or more)	<ul style="list-style-type: none"> • Albuminuria: ACR ≥ 30 mg/g • Urine sediment abnormalities • Electrolyte and other abnormalities due to tubular disorders • Abnormalities detected by histology • Structural abnormalities detected by imaging • History of kidney transplantation
Decreased eGFR	• eGFR < 60 ml/min/1.73 m ² (eGFR categories G3a–G5; see table 2 below)

Staging of CKD

KDIGO stages are based on CGA—Cause, eGFR category, and Albuminuria category. Assign cause based on the presence or absence of systemic disease and the location (observed or presumed) within the kidney (see table 2 below). KDIGO Patients with eGFR > 45 and without albuminuria are generally at lower risk for progressive kidney failure. However, those with mild impairment in renal function but with albuminuria are at higher risk.^{TON, LEV2}

See the management algorithm on [page 4](#) for eGFR and albuminuria category.

TABLE 2:* Classification of CKD based on cause ^{KDIGO}		
	Examples of systemic diseases affecting the kidney	Examples of primary kidney diseases (absence of systemic diseases affecting the kidney)
Glomerular diseases	Diabetes, systemic autoimmune diseases, systemic infections, drugs, neoplasia (including amyloidosis)	Diffuse, focal, or crescentic proliferative glomerulonephritis (GN); focal and segmental glomerulosclerosis, membranous nephropathy, minimal change disease
Tubulointerstitial diseases	Systemic infections; autoimmune diseases; sarcoidosis; drugs; urate; environmental toxins (lead, aristolochic acid); neoplasia (myeloma)	Urinary tract infections, stones, obstruction
Vascular diseases	Atherosclerosis, hypertension, ischemia, cholesterol emboli, systemic vasculitis, thrombotic microangiopathy, systemic sclerosis	Antineutrophil cytoplasmic antibody (ANCA)-associated renal limited vasculitis, fibromuscular dysplasia
Cystic/congenital diseases	Polycystic kidney disease, Alport syndrome, Fabry disease	Renal dysplasia, medullary cystic disease, podocytopathies

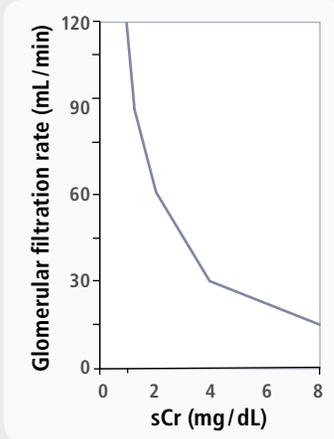
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✓ KEY RECOMMENDATION

Diagnosis of CKD requires a **basic metabolic panel (BMP)** for serum creatinine (sCr) to estimate the **estimated glomerular filtration rate (eGFR)** of the kidneys.

FIGURE 1. Relationship between eGFR and serum creatinine (sCr)

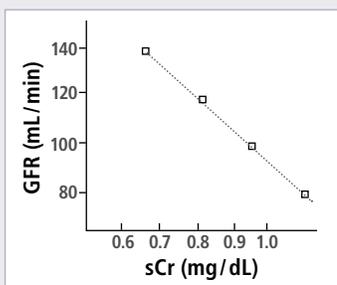
This graph shows the relationship between eGFR and serum creatinine (sCr).^{1NK1} As shown by the curve, an initial small rise in sCr (e.g., from 1 to 2) usually reflects a marked fall in eGFR. However, a marked rise in sCr (e.g., from 5 to 8) in patients with more advanced disease reflects a small absolute reduction in eGFR.



Adapted from UpToDate.^{1NK1}

FIGURE 2. Improved detection of sCr in early CKD

In early CKD, even small changes in serum creatinine can show disease progression.^{10F} Early detection of progressive kidney disease is important because therapies such as ACE-Is can slow the rate of progression in many patients. The technique for measuring sCr has recently been improved and standardized in most labs, so that small increases in sCr (about 0.05 mg/dL) can be detected even earlier in the disease process. As seen in the graph below, when small increases in sCr are plotted, the increase in creatinine correlates in a linear fashion with reduction in eGFR.



▶ BLOOD TESTING

This section describes the tests used to estimate kidney function (serum creatinine [sCr] and estimated glomerular filtration rate [eGFR]), the importance of detecting early changes, factors that may limit the accuracy of eGFR, and the equations used to calculate eGFR.

The importance of eGFR and initial small rises in sCr

The estimated glomerular filtration rate (eGFR) is an important measure of kidney function and is generally based on serum creatinine (sCr). The eGFR:

- Gives a rough measure of the number of functioning nephrons in a patient’s kidneys.
- Is expressed as a filtration rate of mL/min per 1.73 m² (though in this CPM, these units are often implied and not included).

A reduction in eGFR implies progression of CKD or the development of a superimposed and often reversible problem, such as decreased renal perfusion due to volume depletion.

In major guidelines, an eGFR below 60 indicates CKD.^{1NK2} However, even if the eGFR is over 60, a gradual increase in sCr over a period of time is one indicator of CKD. In fact, an initial small rise in sCr usually reflects a marked fall in eGFR (see figures at left). For example, a patient whose sCr increases on sequential measurements from 0.8 to 1.2 mg/dL likely will have lost 30% of eGFR (from 120 to 80). This patient may not yet have CKD complications, but it’s important to check for reversible causes of kidney dysfunction and start measures to slow CKD progression.

Limitations of eGFR calculations

The filtering units of the kidney, the glomeruli, filter approximately 180 liters daily (125 mL/min) of plasma. The normal value for eGFR is influenced by age, sex, ethnicity, and muscle mass/body size; it is approximately 130 for men and 120 for women, with considerable variation even among normal individuals.

The estimated glomerular filtration rate (eGFR) cannot be calculated exactly; it must be estimated using sCr and other factors (see page 8 for formulas used). However, sCr levels can be altered in some patients, which may limit the accuracy of the eGFR in some populations (see table 3 below).

Even though there are limits on accurately arriving at eGFR, exact knowledge of the eGFR is not required to provide appropriate treatment. What’s important to know is whether or not the eGFR (and therefore disease severity) is in a certain range and is changing or remains stable.

TABLE 3: Patients for whom the accuracy of eGFR may be limited

- Pregnant women, children, or elderly patients (> 70 years of age)
- Patients with:
 - Any unusual muscle mass due to cachexia, immobility, morbid obesity, or amputation (especially lower extremities)
 - Near-normal sCr (the equations grossly underestimate eGFR in this case)
 - Rapidly changing sCr (proper results require stable kidney function)
 - Cirrhosis or nephrotic syndrome, or post transplant
 - A vegetarian diet, or who are taking creatinine supplements or drugs that increase creatinine secretion — see note (d) on page 3

ONLINE CALCULATORS

Find eGFR and progression calculators at these websites:

- mdrd.com
CKD-EPI and MDRD, plus Cockcroft-Gault equation in the "Additional Information" window
- nkdep.nih.gov/lab-evaluation/gfr-calculators.shtml
MDRD calculator, plus pediatric calculator
- qxmd.com/calculate-online/nephrology/kidney-failure-risk-equation
QxMD Kidney Failure Risk Equation

For accurate drug dosing in overweight patients, use the Creatinine Clearance: Cockcroft-Gault equation calculator at: <https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation>

For further information, refer to the National Kidney Foundation 2014 publication:

[Frequently Asked Questions About GFR Estimates.](#)

Primary equations to estimate kidney function

The CKD-EPI equation is the primary equation used to estimate glomerular filtration rate for screening and diagnosing CKD. It is:

- Used by Intermountain Healthcare lab services to report an eGFR in the outpatient setting in persons age 18 and over.
- A modification of the MDRD for patients with normal or only mildly reduced kidney function.
- Based on a study that included people with and without kidney disease with a wide range of eGFRs.^{LEV1} In that study, the CKD-EPI was found to be as accurate as MDRD for people with eGFR <60 and had better accuracy and precision for patients with eGFR >60.
- Reported in ml/min/1.73 meters squared. By dividing by 1.73, the result is normalized or adjusted for body size and amount of available filtering renal tissue. This gives a single eGFR normalized for all body sizes.^{NKF5}

Cystatin C with CKD-EPI:

- More sensitive than serum creatinine in identifying mild reductions in kidney function and more accurate for eGFR in populations with lower creatinine production.^{INK2}
- Nephrologists may order this test for patients with eGFR between 45 and 59 who do not have markers of kidney damage. This test is used to confirm CKD.
- More costly than CKD-EPI equation alone.

Equations used to estimate creatinine clearance for drug dosing:

Using the eGFR for drug dosing can result in under dosing for a large individual or over dosing for a smaller individual. Therefore, the Cockcroft-Gault equation (reported in ml/min) provides an estimate of creatinine clearance that is used for drug dosing since it uses an individual's weight and is not adjusted for BSA. Creatinine clearance is used in determining drug dosing in clinical trials.

Intermountain Healthcare lab reports creatinine clearance in iCentra using either a weight or weight and height, when available. Use this value for drug dosing.

Furthermore, it is often recommended to use an adjusted body weight (ABW) with an adjustment of 40% for patients with a body weight more than 130% of their ideal weight (see sidebar link).^{WIN}

In obese patients, drug pharmacokinetics are highly variable.^{CHE} These patients require close monitoring of endpoints, toxicity, response, and serum drug levels.

TABLE 4: Other equations to estimate kidney function

	MDRD Equation	Cockcroft-Gault equation	Urine creatinine clearance
Use	Previously the standard for identifying CKD.	Medication metabolism is still based on this equation.	Not widely used because 2 major errors can limit creatinine clearance accuracy: inaccurate urine collection and increasing creatinine secretion.
Accuracy	Less accurate than the CKD-EPI equation.	May be influenced by body weight and BMI (see above).	In advanced CKD or nephrotic syndrome, 24-hour CrCl overestimates eGFR.
Results	Reported as an estimated glomerular filtration rate (eGFR).	Reported as a creatinine clearance (CrCl).	Reported as creatinine clearance (CrCl).
Factors Calculated	Serum creatinine (sCr), age, gender, and race	Serum creatinine, age, and lean body weight	24-hour urine collection (usually)

✓ KEY RECOMMENDATIONS

For all patients at risk for CKD, screen **ANNUALLY for albuminuria.**

- Test for albuminuria using a albumin-to-creatinine ratio (ACR).
- Retest by 3 months to confirm results; 2 specimens should be positive before diagnosing CKD.
- If ACR > 300 mg/g, refer the patient to a nephrologist.

If hematuria is present, see [page 10](#).

For more information on managing albuminuria, see [pages 18 to 19](#).

ASYMPTOMATIC BACTERIURIA

For patients with asymptomatic bacteriuria:

- Do not give an antibiotic.
- Try a first morning ACR (or 24-hour if significant concern exists).
- Use eGFR plus clinical judgment in treatment decision making.

► **URINARY PROTEIN TESTING**

The 2012 KDIGO Clinical Practice Guidelines place emphasis on measuring urinary albumin (rather than total protein) because albumin provides a more specific and sensitive measure of changes in glomerular permeability than total protein. In addition, relatively large increases in urine albumin excretion can occur without measurable increase in total protein.^{KDIGO}

Determining what tests to use

- **An albumin-to-creatinine ratio (ACR) is the preferred test**, as it gives the best estimate of daily albumin excretion and is the recommended test for CKD diagnosis and staging. Since urine creatinine excretion is relatively constant throughout the day and similar among individuals at 1 gram daily, a spot urine sample is effective (although an early morning sample is best).
- **Urinalysis** of a spot urine sample for **protein-to-creatinine ratio (PCR)** is only used in special circumstances. An ACR is generally recommended instead. Although PCR has a high variation in specificity and sensitivity for all proteins, PCR can be helpful in patients with suspected:^{KDIGO}
 - Tubular disease
 - Amyloidosis
 - Multiple myeloma
 - Monoclonal gammopathy of uncertain significance

Testing for albumin only (not total protein) may occasionally miss cases of tubular proteinuria. According to KDIGO, the significance of this problem is probably overestimated and should be the subject of further research.^{KDIGO}

TABLE 5: Albuminuria and proteinuria categories^{KDIGO}

MEASURE	Normal to mildly increased (A1)	Moderately increased (A2)	Severely increased (A3)
ACR (mg/g)	<30	30–300	>300
Protein reagent strip	Negative to trace	Trace to 1+	1+ or greater

- **A standard urine dipstick** can be used when urinalysis for ACR is unavailable. There are several limitations to urine dipstick results:
 - Dipsticks are inadequate to quantify daily protein excretion. Therefore, if the dipstick is positive (≥ 1+), urinalysis for ACR or PCR should be run (see above), preferably a first morning urine sample.
 - Dipsticks are not sensitive to the low concentrations of albumin that often occur early in CKD, particularly in patients with diabetes.
 - Dipsticks can result in false positives due to excessive urine concentration, infection, hematuria, exercise, or alkaline urine. (If any of these is present, address the issue and retest.)
- **24-hour urine collection** to check protein excretion is impractical and unnecessary, given the usefulness of calculating a ratio with creatinine (see above).

✓ KEY RECOMMENDATIONS

- **If microscopic hematuria is found:**
 - Evaluate and treat **infection**, evaluate for signs of a **glomerular cause**, and rule out **benign causes**. (See the algorithm below.)
 - If the above causes are ruled out, refer the patient to a urologist.

Blood in the urine (hematuria)

Hematuria is common, and in many patients (particularly young adults), it is transient and of no consequence. However, it can also indicate glomerular disease, renal stones, or malignancy. Cancer must be ruled out in patients over 40 with hematuria, even if it is transient, particularly in smokers.

Identifying hematuria

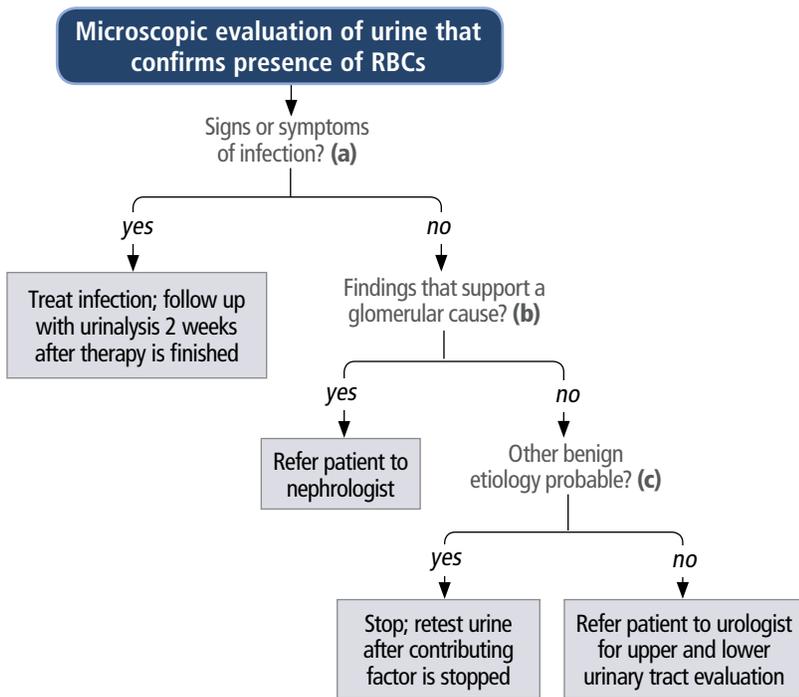
Hematuria may be grossly visible (macroscopic) or microscopic.

- Macroscopic hematuria may be indicated by red to brown urine. To evaluate, ensure that the color is present in the urine sediment in a centrifuged sample.
- Microscopic hematuria is defined as more than 2 red blood cells (RBCs) per high-power field in a spun urine sediment, in two out of three clean-catch, midstream samples. Heme dipsticks result in more false positive results than urine sediment examination, as they detect as little as one RBC per high-power field. Confirm a positive dipstick test with microscopic urine examination.

Evaluating microscopic hematuria

See the algorithm below for guidance on evaluating microscopic hematuria, adapted from AAFP (American Academy of Family Physicians) guidelines.^{MCD}

ALGORITHM 3: EVALUATING MICROSCOPIC HEMATURIA



ALGORITHM NOTES

- (a) Signs/symptoms of infection** include dysuria, frequency, flank/CVA pain, white blood cells (WBCs) or WBC esterase, nitrites, and bacteria
- (b) Findings that support a glomerular cause of hematuria** include:
 - Severely increased albuminuria (ACR > 300 mcg / mg)
 - Elevated serum creatinine
 - Red cell casts
- (c) Benign causes of microscopic hematuria** include:
 - Vigorous exercise
 - Trauma to urethra
 - Menstruation
 - Medications: penicillins, cephalosporins, diuretics, NSAIDs, cyclophosphamide (Cytosan), chlorpromazine (Thorazine), anticonvulsants

✓ KEY RECOMMENDATIONS

- Imaging tests are needed only for select patients.
- **Renal ultrasound** should always be the first imaging test considered.

► **IMAGING TESTS**

Imaging studies of the kidney are necessary only for select patients. Tests can be done alone or in combination to identify potentially treatable and reversible conditions of the kidney or to assess for possible urinary tract obstruction, kidney stones, renal cysts or masses, renal vascular diseases, or vesicoureteral reflux (in children and young adults).^{NKF2}

Determining appropriate tests

Renal ultrasound should always be the first imaging study performed on patients with kidney disease of unknown etiology. The table below summarizes imaging options, notes, and precautions for select patients and situations.

TABLE 6: Imaging options and precautions for select patients ^{NKF1}		
To evaluate:	Consider:	Notes and precautions
Any kidney disease of unknown etiology; obstructive uropathy; renal cysts	Renal ultrasound	Renal ultrasound should be the first study used for patients with kidney disease of unknown etiology or to assess for obstructive uropathy. In addition, though not as sensitive as a contrast-enhanced CT scan, ultrasound studies can identify renal cysts and assist in differentiating simple from complex cysts. Ultrasound is readily available and easy to perform, and it spares patients from radiation and exposure to contrast agents, which can aggravate patients with underlying renal dysfunction, especially those with disease at CKD Stage G3b to G5 (eGFR < 44 mL/min).
If renal ultrasound is inconclusive, consider the following for the reasons indicated:		
Kidney stones	NON-contrast CT scan	<p>Avoid contrast during CT scans if possible.^{NKF2} Contrast can be toxic to the kidneys, especially in dehydrated patients; see the next page for more information.</p> <p>Contrast-enhanced CT is appropriate only for renal cysts that cannot otherwise be identified as malignant, or for structural disorders. Consult a radiologist before ordering contrast.</p> <p>See the following pages for more information on preventing contrast-induced nephropathy (CIN) and evaluating renal cysts.</p>
Renal cyst (seen on ultrasound) that cannot be easily identified as simple or complex	CT scan—consult radiologist before using contrast	
Renal masses / cancer —identify and stage	CT scan—consult radiologist before using contrast	
Multiple cysts on ultrasound (also see p. 13 sidebar on polycystic kidney disease)	NON-contrast CT scan	
Structural disorders: medullary sponge kidney, papillary necrosis	CT scan—consult radiologist before using contrast	
Renal vein thrombosis	MRI—if MRI is not possible, consider renal venography or NON-contrast CT scan	<p>Avoid gadolinium during MRI in late-stage CKD. Gadolinium-enhanced MRI is contraindicated in patients with very high-risk CKD (eGFR < 30); it has been linked to an often severe disease called nephrogenic systemic fibrosis with very high morbidity and mortality.</p> <p>Expert opinion differs on whether it is appropriate to expose patients with eGFR 30–60 to gadolinium.^{PER2}</p>
Renal artery stenosis (see sidebar)	Duplex Doppler ultrasound; if inconclusive, MRI or CT angiography If necessary, use catheter-based renal angiogram (the most sensitive test)	<p>Renal arteriography / venography, radionuclide scans, intravenous pyelogram (IVP), voiding cystourethrogram, and retrograde or antegrade pyelography have a limited role.</p> <p>A urologist or nephrologist should decide whether any of these tests should be performed to evaluate for some etiologies of CKD.</p>

Radiation exposure in CT scanning

Abdominal CT scans involve more radiation exposure than many other imaging tests. According to the American College of Radiology, radiation exposure from an abdominal CT scan is an estimated 15 millisieverts (mSv) — equivalent to the estimated exposure from 150 chest x-rays.

Imaging radiation can increase a patient’s lifetime cancer risk. One patient in 100 will develop cancer from an exposure of 100 mSv, based on the BEIR VII report (the most widely cited report on radiation effects).^{NRC} The risk varies based on age and sex. The earlier the exposure, the higher the risk. Women are at higher risk than men.

To limit radiation exposure, use renal ultrasound first; if ultrasound is inconclusive, ensure that the test is appropriate (see table 6 on [page 11](#)). Check the patient’s record, and ask the patient about CT scans done elsewhere.

Testing FOR renal artery stenosis (RAS)^{TEX}

Testing should not be performed in patients who respond well to medical therapy or who have low or moderate likelihood of having RAS. The existing randomized trials conducted with these patients showed no evidence of benefit for adding revascularization to optimal medical therapy.

Testing should be considered if there is a high likelihood of having RAS and:

- A brief, significant blood pressure elevation prior to the evaluation of RAS (the strongest clinical predictor of a fall in blood pressure after renal revascularization)
- Failure of optimal medical therapy to control blood pressure
- Patient intolerance to optimal medical therapy
- Progressive renal insufficiency suspected to be due to RAS
- Suspected fibromuscular disease in a young person (to help limit the need for lifelong antihypertensive therapy)

Preventing contrast-induced nephropathy (CIN)

Contrast-induced nephropathy (CIN) is acute kidney injury that usually occurs within 48 to 72 hours after IV radiocontrast agents are administered. It is defined as a rise in serum creatinine of >25 % from baseline or >0.5 mg/dL. With CIN, fractional excretion of sodium (FENa) can be less than 1 %.

General precautions if contrast is used

With all CKD patients, take these precautions if contrast is ordered:

- **Manage medications.** Stop nephrotoxic medications, such as NSAIDs, for 48 hours before and after the procedure, and stop diuretics for 24 hours before the procedure.
- **Ensure adequate hydration.** Provide adequate fluids to achieve euvolemia; avoid “NPO after midnight” (ask for NPO approximately three hours before the procedure).
- **Order post procedure blood tests.** Check BUN/Cr (or BMP) 24 to 48 hours after CIN and before restarting metformin or other nephrotoxic drugs. Refer to the [Prevention of Contrast-induced Nephropathy CGL](#).

CIN mortality

CIN is associated with a significant risk for severe renal failure and death.

- In a study of 633 ED patients who received contrast-enhanced CT, incidence of CIN was 11 %; among the patients with CIN, mortality was 14 %.^{MIT}
- While most CIN cases resolve within several days, CIN in CKD patients poses a significantly increased risk for mortality within 1 year. A review of several studies revealed in-hospital mortality from CIN due to contrast during PCI was 7 % to 27.5 % and 1-year mortality was 12 % to 54.5 %.^{RUD}

When contrast is needed with CT scanning

According to consensus from radiology experts, contrast is necessary with CT scans only when evaluating for:

- An abscess
- Suspected appendicitis
- A strong suspicion of a tumor
- Suspected hepatic lesion

Note: Contrast with CT to evaluate diverticulitis is not recommended.

Precautions based on estimated CIN risk

The Mehran CIN risk score (see table 7 below) was designed to predict CIN risk after percutaneous coronary intervention (PCI) and was validated with more than 8,300 patients.^{MEH} While the Mehran Risk Score was developed with a focus on PCI patients, it may also be helpful in assessing CIN risk for contrast-based CT scans alone; the benefits have only been shown in conjunction with IV saline.

1. Calculate Risk Points		2. Follow Recommendations Based on Total Risk Score	
Factor	Points	TOTAL points	Actions to take
Hypotension	5	≤ 5 points	Ensure adequate hydration.
Intra-aortic balloon pump	5	6 to 16 points	<ul style="list-style-type: none"> • Give normal saline (NS) IV 500 mL (or oral equivalent) before study. • Consider NS IV 500 mL after study if patient is volume depleted. Note: Infuse each 500 mL over 1 to 2 hours if no history of heart failure; infuse over 3 to 4 hours if heart failure or potential volume overload.
CHF	5		
Age > 75 years	4		
Anemia	3	> 16 points	<ul style="list-style-type: none"> • AVOID contrast if at all possible. • If contrast is unavoidable: <ul style="list-style-type: none"> – Limit contrast volume. – Do careful volume loading with at least 500 mL NS before and after study. – Consider oral N-acetylcysteine (NAC, Mucomyst), 600 mg every 12 hours for 2 days before and 1 day after the study. Mucomyst should be used only in combination with IV saline.* – Check BUN / Cr 24 and 48 hours after the study.
Diabetes	3		
Contrast volume	1 for each 100 cm ³		
Serum creatinine > 1.5	4		
eGFR < 20	6		
20–40	4		
40–60	2		

* N-acetylcysteine (NAC, Mucomyst) is probably ineffective at preventing CIN.^{AMI} It may, however, be considered for patients with eGFR < 20. **NAC/Mucomyst should not be used alone;** the benefits have only been shown in conjunction with IV saline.

POLYCYSTIC KIDNEY DISEASE

The autosomal dominant form of polycystic kidney disease (ADPKD) accounts for 2.3 % of patients in end-stage renal disease.^{USR2} ADPKD often goes undiagnosed, but it can have serious consequences—extrarenal manifestations include heart valve disorders, coronary artery aneurysms, and cerebral aneurysms.

Screening and diagnosis.

Consider polycystic kidney disease if a patient has a **family history** of the condition and ultrasound reveals **multiple cysts**. If the patient meets the diagnosis criteria below, refer to nephrology for evaluation.

- **Age 15–29:** At least 2 cysts (unilateral or bilateral)
- **Age 30–59:** At least 2 cysts on each side
- **Age >60:** At least 4 cysts on each side

Management.

If polycystic kidney disease is not well managed, patients may progress to renal failure. Along with other standard CKD management methods, ADPKD management may also include:

- **Tighter blood pressure control for patients with ADPKD and left ventricular hypertrophy.**

A 7-year randomized study showed a goal of less than 120/80 provided cardiovascular benefits for these patients.^{5CH}

- **Increased fluid intake.**

Encourage liberal fluid intake, with a goal of more than 3 liters per day, to partially suppress serum ADH levels and help prevent nephrolithiasis.^{CHA}

- **Albuminuria management, using an ACE-I or ARB.**

Up to 30 % of patients with polycystic kidney disease may have moderately increased albuminuria. Control of albuminuria may prevent progression to ESRD (see pages 18 to 19).

Evaluating renal cysts

If imaging tests reveal renal lesions, evaluating their significance and determining when to refer to a specialist can be challenging. Such lesions are usually simple benign renal cysts, complex renal cysts, or neoplasms, although they can also be caused by inheritable conditions such polycystic kidney disease (see sidebar), medullary sponge kidney, von Hippel-Lindau disease, or tuberous sclerosis. Nephronophthisis and medullary cystic disease can also cause renal cysts.

Simple renal cysts are commonly found in normal kidneys and have an increased incidence with age. They are benign and only require treatment if they become symptomatic. Distinguishing a simple cyst from a complex cyst that may harbor a neoplasm is important.

The **Bosniak renal cyst classification system** was created to help diagnose and manage renal cysts.^{ISR} The system places cystic renal masses in five categories based on enhancement characteristics with CT scanning. Cysts meeting categories I, II, and IIF (“F” indicates that findings warrant follow-up) are typically benign. The presence of true contrast enhancement of the lesion (a minimum increased attenuation of 10 to 15 Hounsfield units) is the most important characteristic separating categories III and IV, which are associated with malignancy 40 % to 90 % of the time.

TABLE 8: Bosniak renal cyst classifications^{ISR}

Category	Characteristics	Management
Category I: Simple renal cyst	<ul style="list-style-type: none"> • Hairline thin wall. • No enhancement. Density less than 20 Hounsfield units (similar to water). • No septa, calcification, or solid components. 	Further evaluation generally not required.
Category II: Benign cyst	<ul style="list-style-type: none"> • A few hairline thin septa. • No measurement enhancement. • Uniformly high attenuation lesions <3 cm in diameter; well marginated; and do not enhance. 	Further evaluation generally not required. If unable to distinguish between a category II and IIF cyst, repeat ultrasound or enhanced CT in 6 to 12 months to ensure stability and correct diagnosis.
Category IIF: Minimally complicated cyst; doesn't neatly fall into Category II	<ul style="list-style-type: none"> • Multiple hairline thin septa or minimal smooth thickening of the wall or septa. “Perceived” enhancement of septa or wall may be present. • Thick and nodular calcification of the wall or septa, but no measurable contrast enhancement. • Totally intrarenal, nonenhancing, high attenuation lesions >3 cm in diameter. 	Category IIF cysts warrant follow-up imaging (hence the “F”) to document stability. Follow up with enhanced CT in 3 to 6 months: <ul style="list-style-type: none"> • No change suggests benign process. • Progression suggests neoplasia.
Category III: True indeterminate cystic mass	<ul style="list-style-type: none"> • Thickened irregular or smooth walls or septa in which measurable enhancement is present. 	Two approaches: <ol style="list-style-type: none"> 1. Immediate surgical referral for possible removal for resectable lesions (high false positive rate results in unnecessary surgery in up to 60 % of patients). 2. Order contrast-enhanced MRI and/or percutaneous biopsy; if still indeterminate, make surgical referral.
Category IV: Cyst that requires surgical referral	<ul style="list-style-type: none"> • Thickened irregular or smooth walls or septa in which measurable enhancement is present. • Enhancing soft-tissue components adjacent to, but independent of, the wall or septum. 	Surgical referral.

INTERMOUNTAIN PATIENT EDUCATION RESOURCES

See [page 34](#) for information on patient education resources available from Intermountain Healthcare.

OTHER RESOURCES

Other resources listed on [page 34](#) include:

- Web-based videos from the National Kidney Disease Education Program
- Web-based training modules (“Kidney School”) from the American Education Institute
- Booklets and handouts from the National Kidney Foundation and the Renal Support Network

► PATIENT EDUCATION AND SUPPORT

Education and support from a primary care provider (PCP) is vital in helping patients adhere to self-management strategies that can slow CKD progression, especially in the early stages of the disease. As CKD enters the later stages and the patient is comanaged with a nephrologist, the PCP also plays an important role in helping the patient learn to manage comorbidities, watch for complications, and weigh options for renal replacement if renal failure approaches. The long-term relationship between PCP and patient provides emotional support and motivation as patients make hard decisions.

Patient education at low or moderately increased risk CKD

Patients newly diagnosed with CKD will have questions about how the kidneys work and, even at the early stages, often fear that they will need to begin dialysis soon. In the early stages, educate the patient and family about what happens in CKD and the strategies that can slow its progression. (See [page 34](#) for Intermountain tools.)

Focus on the following areas:

- **Background on CKD.** Explain how the kidneys work, the main causes of CKD, and the fact that CKD moves through stages. This foundation can reassure patients, while at the same time motivating them to manage the disease. Patients should also have a basic understanding of kidney test results.
- **Medications for CKD.** Explain that prescribed medications, such as ACE-Is or ARBs, will help slow the progression of CKD. Without understanding the purpose of these medications, CKD patients can be tempted to stop taking them—because they don’t make a patient feel better.
- **Lifestyle changes to slow CKD progression, with a focus on managing blood pressure and blood glucose.** Stress the importance of weight control, increased physical activity, blood glucose control, smoking cessation, and/or dietary changes (such as reduced sodium), depending on the patient’s situation. Consider a referral to a registered dietitian nutritionist (RDN). See [page 33](#) for a list of Intermountain Healthcare RDN resources.
- **Vaccines.** Counsel patients to stay up to date on all vaccinations. CKD patients have a higher risk for infection. In addition, not being up to date on vaccines could delay transplant should the kidneys fail. Table 9 below summarizes vaccine recommendations. For CDC guidance on vaccine schedules, see cdc.gov/vaccines/schedules/hcp/adult.html.
- **Protecting the kidneys.** Explain that NSAIDs can damage the kidneys, and that these medications are in many over-the-counter preparations. Stress the importance of telling providers about ALL medications taken, including OTCs and supplements.
- **Cardiovascular risk.** Explain that CKD can increase the risk of heart problems as it progresses. Understanding the CV risk involved can help motivate patients to manage their CKD.

TABLE 9: Vaccines recommended for CKD patients^{KDIGO}

Influenza	All CKD patients
Prevnar 13 (PCV13)	All patients with eGFR < 30 or nephrotic syndrome
Pneumovax (PPSV23)	Give 1 year after Prevnar 13 for all adult patients with an eGFR < 30 or nephrotic syndrome
Hepatitis B*	Adults at risk of CKD progression with an eGFR < 30
Pediatric vaccines	All routine childhood vaccines are recommended for CKD patients, including Prevnar 13 and PSV23, unless a change is indicated due to altered immune status.

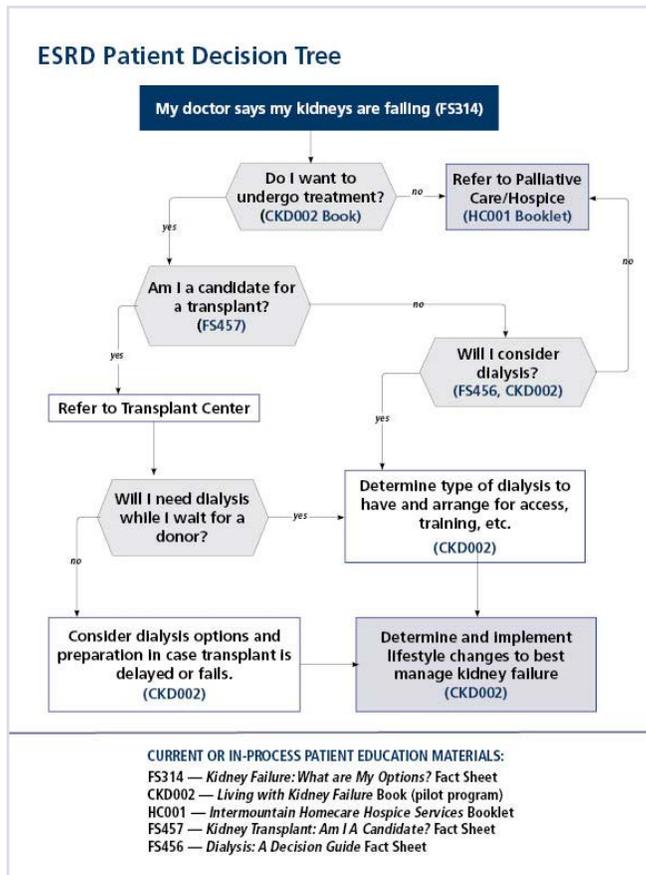
* The response rate for Hepatitis B is much higher if the vaccine is given before end-stage renal disease.

WHY PROTECT VENOUS ACCESS?

If a patient opts for hemodialysis but his or her veins are damaged, a central venous catheter will be used for access instead of a fistula or arteriovenous graft (AVG). Catheter-based access is far less safe for dialysis because it:

- Has high infection rates (15 times more than with a fistula)^{USR3}
- Has higher mortality rates (2 to 3 times higher than with a fistula)^{SIN}
- Is associated with more hospitalizations (average 35 days per year)^{BEA}

Use the ESRD Patient Decision Tree below to match Intermountain patient education best suited to patient shared decision making conversations. (See [page 34](#) for links to these resources.)



Patient education at high or very high-risk CKD

For patients who are newly diagnosed, provide basic information about CKD, treatment and lifestyle changes, and protecting the kidneys (see information on [page 15](#)). For all patients at stages 3b–5, provide additional information about:

- **Preventing or managing common comorbidities.** Explain that CKD can cause various other health problems, including too much potassium in the blood, acid/base problems in the blood, edema, anemia, and bone disease. Depending on the patient’s situation, provide additional information on potassium, phosphorus, vitamin D supplementation, calcium, and iron therapy. Consider referral to a registered dietitian nutritionist (RDN), especially if multiple dietary restrictions are needed.
- **Checking for symptoms of edema.** Educate patients to weigh themselves routinely and schedule an appointment if they gain five pounds or more in less than a week
- **Protecting venous access for fistula or arteriovenous graft (AVG).** Explain to patients that protecting their veins will give them the option of using the safest method for hemodialysis (see sidebar at left), should they ever go into renal failure. Patients should avoid:
 - Venipuncture or IV lines in the nondominant arm
 - Subclavian central lines or PICC lines (use instead a small-caliber IJ line), starting at Stage G3b (eGFR <45)

It is important that patients understand that:

- Damage to the veins in the nondominant arm may make placing a fistula or AVG difficult or impossible.
- Emphasizing that a fistula or AVG is the safest form of access for hemodialysis can help motivate patients to protect their veins.

- **Addressing renal replacement therapy (RRT) options, as the patient reaches Stage G4.** RRT options include dialysis (hemodialysis and peritoneal dialysis) and transplantation in those with good expected survival. Table 10 (on page 17) presents an overview of the pros and cons of these options. When a patient’s eGFR drops below 30, provide this basic information on RRT and refer the patient to a nephrologist for more detailed education and preparation. The recommended education focus based on the anticipated option is as follows:
 - **If hemodialysis is anticipated:** Education at this stage should be early enough to give time for a fistula to be placed and have a chance to mature. (Note: The KDOQI guidelines call for fistula placement at least six months before the anticipated need for hemodialysis.^{VAWG} However, predicting this timing is complicated and imprecise.)
 - **If peritoneal dialysis is anticipated:** Patients should be counseled on how peritoneal dialysis (PD) compares with hemodialysis (HD) according to the 2012 USRDS Annual Data Report, which indicated that the:^{USR1}
 - Overall cost of care for PD patients was \$5,885 to \$6,334 less per year than matched HD patients.
 - Rates of PD patient hospital admissions have fallen 13.9% since 1993.
 - Survival probability is similar for PD and HD patients; since 1997, survival probability has improved for PD patients and remained stable for HD patients.

OVERCOMING BARRIERS TO FISTULA OR AVG PLACEMENT

A fistula or AVG is the safest access for hemodialysis. However, some patients may want catheter-based access, even though it can lead to serious infections, because they want to avoid fistula or AVG placement. Below are tips for helping patients work through common barriers:

- **“I’m afraid of the surgery—I hate hospitals.”** Explain that a fistula can help prevent hospitalizations in the long run because it reduces infection risk.
- **“Fistula dialysis means needles every time.”** Reassure patients that numbing medication can be used before each treatment. Needle anxiety can be reduced through relaxation exercises and dialysis team support.
- **“People will see the fistula and ask questions, or it will remind me that my health isn’t good.”** Remind patients that a fistula is their lifeline to effective, safe treatment. Patients who use a fistula report perceptions of greater overall general health compared to patients who use a catheter.^{USR3}

– **If transplantation is anticipated:** It is important to have a conversation with patients about RRT when eGFR is in the 20–30 mL/mn range as this gives time for patients to have critical conversations with prospective living donors. The new kidney allocation system allows patients to be listed preemptively for kidney transplantation. Stress that preemptive kidney transplants are associated with superior outcomes and that donor matching is easier than in the past. Blood group and/or tissue compatibility with the prospective donor is no longer a constraint given the availability of paired-donor exchanges (see table 10 below for pros and cons).

- **Palliative care and hospice.** During end-stage CKD, the goal is to minimize symptoms and provide education. Discuss how the disease will affect the patient over time (disease progression); ask patients to discuss their wishes; encourage them to create a Physician Order for Life Sustaining Treatment (POLST)/advanced directive; and encourage them to share their wishes with family and caregivers.

The decision not to undergo RRT should largely be determined by baseline quality of life. For patients with multiple medical problems in addition to kidney failure, transplantation may not be possible, and dialysis may prolong suffering. In very debilitated nursing home patients, dialysis did not improve functional status.^{KUR} Patients with stage G5 CKD (eGFR < 15) who elect not to undergo RRT qualify for hospice. Time to death is quite variable if kidney failure is advanced, but is likely less than six months.

Option	Pros	Cons
In-center hemodialysis (HD)	<ul style="list-style-type: none"> • Facilities widely available (more limited in rural areas) • Trained professionals are with the patient at all times • Interaction with other patients • Patients can live alone, don’t need home equipment 	<ul style="list-style-type: none"> • Treatments scheduled by center; times relatively fixed • Patients must travel to the center 3 days per week • Potentially more frequent ups and downs • Patients may require a few hours to feel better after a dialysis session
Home hemodialysis (HHD)	<ul style="list-style-type: none"> • Hemodialysis treatments done in patients home, giving patient more control over timing. • Short daily sessions— 2 to 3 hours, 5 to 6 days a week or nocturnal (overnight)— 6 to 8 hours, 3 to 6 nights a week) • Much fewer diet restrictions 	<ul style="list-style-type: none"> • Requires dedicated home storage space for supplies and equipment • Patient’s home may need minor electrical or plumbing changes • Patient and caregiver training required
Peritoneal dialysis (PD)	<ul style="list-style-type: none"> • Can be done alone, at home; schedule not as fixed • Equipment not necessarily required • Not as many ups and downs (PD is done every day) • Diet is much less restricted • Better Medicare coverage 	<ul style="list-style-type: none"> • Must be done daily (can disrupt daily schedule) • Bathing or swimming not allowed due to catheter • Protein loss associated with PD may worsen malnutrition • Home storage space needed for supplies
Preemptive kidney transplant	<ul style="list-style-type: none"> • A transplanted kidney works like a normal kidney • Patients may feel healthier and more “normal” • Very few diet restrictions • Patients with transplant generally live longer than similar patients who remain on dialysis 	<ul style="list-style-type: none"> • Requires major surgery • Wait times for donors can be long • Transplants may be rejected and generally do not last a lifetime • Potential side effects of antirejection medications, including weight gain, development or worsening of diabetes, and an impaired immune system

✓ KEY RECOMMENDATIONS

- **Screening:** Get an accurate blood pressure at every visit (see [page 34](#) for resources). Obtain home blood pressure readings if elevated. Check ACR as noted on [page 4](#).
- **Management (see algorithm 4):**
 - Counsel lifestyle changes.
 - Prescribe ACE-I; if ACE-I not tolerated, switch to ARB.
 - If ACE-I or ARB not effective, add other medications based on guidance in [High Blood Pressure CPM](#).

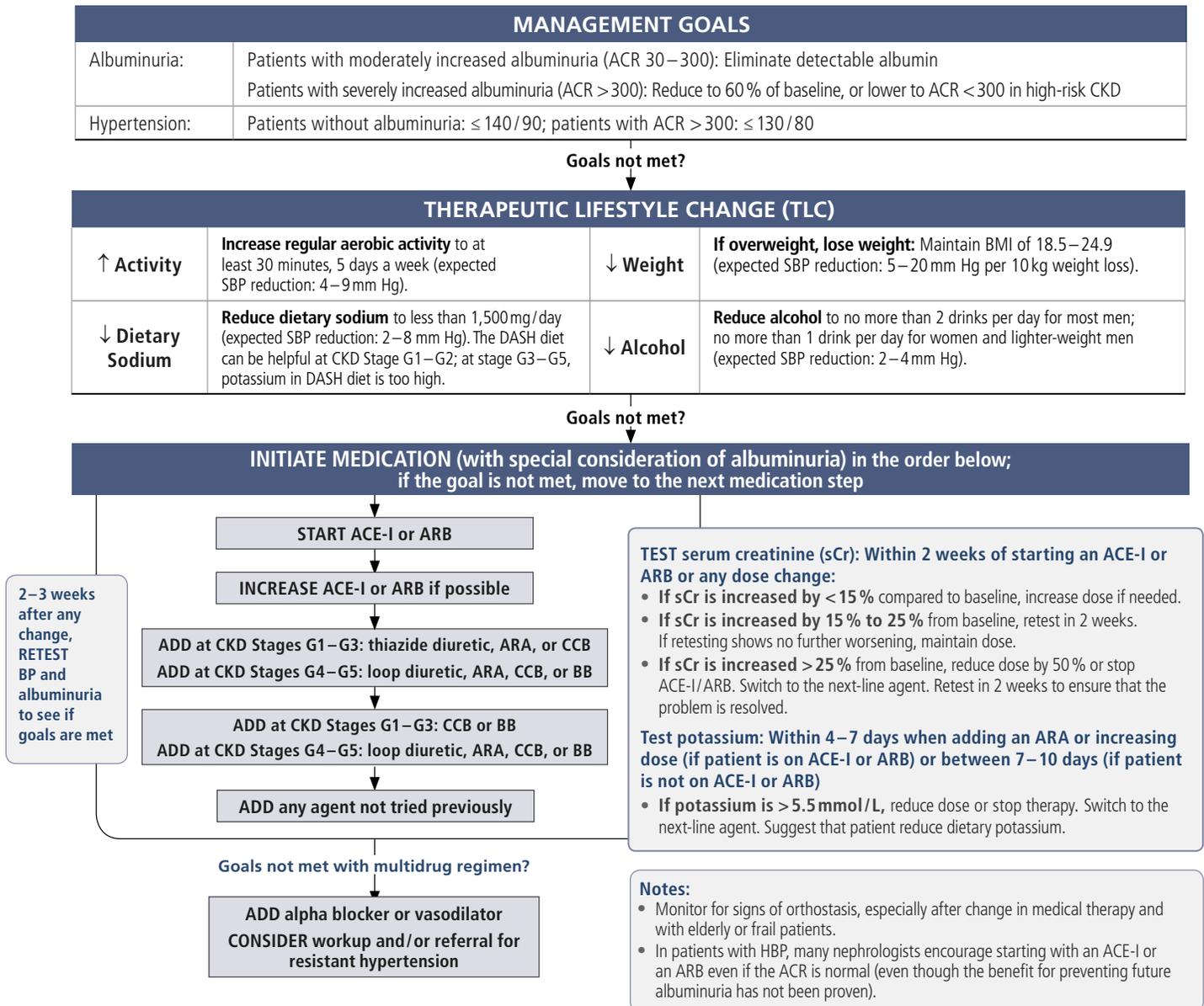
▶ **ALBUMINURIA AND HYPERTENSION**

Albuminuria is a marker of kidney damage as well as an important prognostic finding. A high level of albumin is associated with all-cause and cardiovascular mortality, independent of cardiovascular risk factors.^{VAN}

Hypertension, a common complication of CKD, is also a risk factor for faster CKD progression and for cardiovascular disease (CVD).^{NKF1} Reaching a target blood pressure goal is the key to managing albuminuria. Though all antihypertensive agents can be used to lower blood pressure in CKD, some agents (such as ACE-Is and ARBs) also slow the progression of kidney disease by blocking the renin-angiotensin-aldosterone system (RAAS) (see sidebar on [page 19](#)). When setting a blood pressure goal, individualize targets and agents according to age, proteinuria status, CVD, comorbidities, risk of progression, retinopathy, and tolerance to treatment.

ALGORITHM 4: ALBUMINURIA / HYPERTENSION MANAGEMENT

Abbreviations used in this algorithm: ACR=albumin-creatinine ratio; SBP=systolic blood pressure; ARA=aldosterone receptor antagonist; BB=beta blocker; CCB=calcium channel blocker



ACE-I/ARB SIDE EFFECTS

- **Decrease in eGFR:** A rise in serum creatinine (sCr) usually begins a few days after starting or increasing ACE-I/ARB dose. Check sCr and/or eGFR within 2 weeks of initiation or dose change.
- **Hypotension:** If patient is volume depleted, avoid starting and ACE-I or ARB (which has higher rates of hypotensive symptoms). Start the ACE-I or ARB at a low dose to minimize first-dose hypotension.
- **Hyperkalemia:** If a patient's initial potassium is >5, reduce dietary potassium (refer patient to a dietician), start ACE-I/ARB at a low dose, and monitor carefully (also if increasing dose). Discontinue ACE-I/ARB if potassium is >5.5 despite dose reduction.
- **Cough (dry, hacking):** Occurs in 5–20% of patients treated with an ACE-I. Cough (much less common with ARBs) usually resolves a few days after stopping therapy, but resolution can take up to 4 weeks. Cough generally recurs with rechallenge with any ACE-I.
- **Angioedema (causes swelling of mouth, tongue, pharynx, and eyelids):** A rare but potentially fatal complication (0.1–0.7% of ACE-I-treated patients). Discontinue ACE-I or ARB (although these have lower rates of complication); symptoms usually resolve within 24–48 hours. Protect the airway; tongue swelling can cause asphyxiation.

MANAGING LOW BLOOD PRESSURE (BP) AND CKD

Decreased renal perfusion due to low blood pressure can be much more serious in CKD patients and increase risk of acute kidney injury and subsequent worsening of CKD.

There is no evidence that "lower is better" for a BP target. Once BP is controlled below a target goal, there is no benefit to increasing medication further to reach an even lower BP.

Be especially aware of symptoms of low blood pressure in patients with CKD. Consider titrating BP medications as indicated to allow the blood pressure to rise (while still remaining below recommended targets) if symptoms (such as light-headedness, fainting, increasing fatigue, or exercise intolerance) suggest low blood pressure. **Also check for orthostatic changes in blood pressure.**

While symptoms are more helpful in managing hypotension than targets, a systolic BP less than 90–100 or mean BP less than 65 would often be associated with these symptoms and, in general, should be avoided.

ACE-Is and ARBs

- **An ACE inhibitor (ACE-I) is the drug class of choice for hypertension and albuminuria management.** Better outcomes are associated with agents that address the RAAS system and lower both albuminuria and blood pressure. ACE-I or ARB therapy can result in a 35% to 45% reduction in urinary proteins, with a dose-related effect.^{NKF1}
- **Begin with an ACE-I, and if the patient doesn't tolerate ACE-I treatment, switch to an ARB.** Recent evidence suggests that increased adverse events may outweigh any benefits of combining an ACE-I and ARB.^{YUS} Begin at a low dose and titrate to the maximum tolerated dose (see the [High Blood Pressure CPM](#)) while monitoring and managing side effects (see algorithm on the previous page and the sidebar at right).
- **Contraindications — Do NOT prescribe ACE-Is or ARBs with:**
 - Pregnancy (contraception is recommended with ACE-I/ARB therapy for women of reproductive age as these drugs can cause fetal toxicity)^{MER}
 - Bilateral renal artery stenosis

Other medications

Multi-drug regimens are necessary in many CKD patients. This CPM recommends the following medications (see the [High Blood Pressure CPM](#) for side effects and precautions):

- **Diuretics:** Thiazide diuretics are useful when added to an ACE-I or ARB for albuminuria and hypertension management. Loop diuretics are preferred in patients with Stage G4–G5 CKD (eGFR < 30).
- **Aldosterone receptor antagonists (ARAs):** ARAs have been found effective for patients with refractory hypertension.
- **Calcium channel blockers (CCBs):** Either type of CCB—dihydropyridine (e.g., amlodipine) or nondihydropyridine (e.g., verapamil and diltiazem)—can be used to manage albuminuria, but the nondihydropyridine CCBs have demonstrated more significant and consistent reductions in albuminuria. Avoid combining nondihydropyridine CCBs with beta blockers, due to the risk of bradycardia.
- **Beta blockers (BBs):** Beta blockers can be part of combination therapy for most patients as a third- or fourth-line agent. Carvedilol may be one of the best choices due to its favorable effects on lipids, renal albumin excretion, and insulin sensitivity. Once a patient's heart rate is < 80 bpm, increasing BB dosage will have limited effectiveness; add other medications instead.
- **Alpha blockers, vasodilators:** These drugs should not be used unless previous therapies have been exhausted, and should not be used alone, due to a higher incidence of side effects (leg edema, orthostasis) and a lack of outcome data.
- **Direct renin inhibitors (DRIs):** Aliskiren (Tekturna) is not recommended with an ACE-I or an ARB.

Note: Avoid combining CCBs and beta blockers. Nondihydropyridine CCBs combined with beta blockers can lead to severe bradycardia, especially when used with digoxin.

► LIPID MANAGEMENT

Cardiovascular disease (CVD) is one of the most common CKD comorbidities, and CKD patients should be considered in the high CVD risk category, similar to patients with coronary artery disease. CVD is the major cause of mortality in CKD.^{WEI} Patients with early CKD are more likely to die of CVD disease than progress to Stage G5 CKD.^{NOG} In addition, dyslipidemias may contribute directly to CKD progression.^{NKF4} Lower serum HDL cholesterol is an independent predictor of a faster decline in eGFR.^{BAK}

Prevalence and profile of dyslipidemia in patients with CKD. Dyslipidemias are prevalent in CKD due to a variety of factors, including changes in proteinuria, eGFR, and CKD treatments. The following are typical findings in CKD patients; however, this profile may differ across patients, reflecting the pattern seen with comorbidities (such as diabetes and nephrotic syndrome) or with use of steroids and cyclosporine:

- Triglycerides, VLDL, LDL, Lipoprotein(a), and apoprotein B are often elevated.
- As CKD progresses, especially into Stage G5, total cholesterol, HDL, and LDL may decline (see below). Despite this decline, coronary risk remains high.
- LDL decreases in hemodialysis, but increases in peritoneal dialysis.

Use of lipid-lowering drugs (LLDs) in patients with CKD. Because those in earlier stages of CKD have a higher risk from elevated lipids, start statins as early as recommended by guidelines. Despite the issues complicating the picture of dyslipidemia and CVD risk in patients with CKD, major guidelines as well as a review of LLD trials with CKD patients advise the following:^{NKF2, NOG,}

- Only statins (or statins with ezetimibe) have been shown to improve clinical outcomes. (See management guidelines on [page 19](#).) Multiple LLD trials have been reassuring on the risk of statins used in CKD. (See the [Cardiovascular Risk and Cholesterol CPM](#) for safety notes and precautions.)
- Recent trials have shown that the use of statins is beneficial, particularly for reducing vascular events when used in CKD Stages G1 to G4.^{NOG} These trials include the pravastatin pooling project, Heart Protection study (simvastatin), ASCOT LLA (atorvastatin), and SHARP (ezetimibe + simvastatin).
- Statins have not been proven to improve morbidity and mortality in CKD Stage G5 or end-stage renal failure.^{NOG} Deciding whether to use statins in these patients should be based on consultation with a nephrologist. The SHARP and 4D trials showed questionable benefit from statins in Stage G5 and dialysis; the ALERT trial showed no measurable benefit from statins in transplant patients. However, in patients with coronary artery disease or peripheral vascular disease, statins may still be indicated.

Lifestyle weight management and therapeutic lifestyle changes (TLC). For all CKD patients, management of dyslipidemia should include recommending lifestyle weight management and therapeutic lifestyle changes. Counsel patients to:

- See a registered dietitian nutritionist (RDN) for nutrition counseling to manage lipids (see [page 33](#)). Tailored nutrition therapy can be very effective for lowering LDL and triglycerides, but has little influence on HDL.
- Increase regular aerobic activity to > 150 minutes a week. A recent study found that with an exercise therapy program, HDL levels increased and triglyceride levels decreased, and that these changes are correlated significantly with an improvement in eGFR.^{TOY}
- If overweight, lose weight: Maintain BMI of 18.5–24.9 (expected SBP reduction: 5–20 mm Hg per 10 kg weight loss).
- Reduce alcohol to < 2 drinks a day for most men; < 1 drink a day for women and lighter-weight men; abstain if high triglycerides.

ASPIRIN RISK

Balance risk for atherosclerotic events and bleeding when prescribing aspirin to CKD patients.

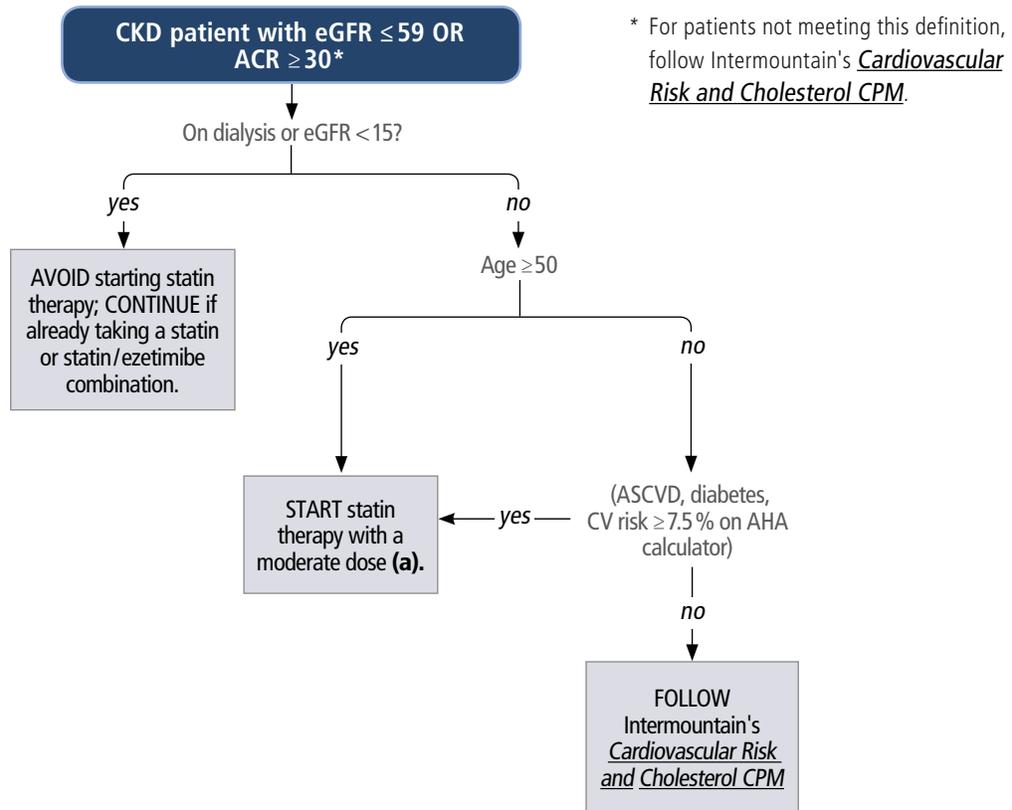
CVD RISK, DYSLIPIDEMIA, AND CKD

CKD patients have unique factors that lead to a higher risk for developing CVD. While many CKD patients have the traditional CVD risk factors (hypertension, diabetes, and dyslipidemia), several other factors increase the risk of developing CVD:^{NOG}

- Inflammation
- Oxidative stress
- Volume overload
- Malnutrition
- Anemia
- Albuminuria

ALGORITHM 5: DYSLIPIDEMIA MANAGEMENT

Triglyceride measurement is based on a fasting lipid profile. Very high (> 500 mg/dL) fasting triglycerides are unusual in CKD Stage G1 to G3, but are more common in Stages G4 to G5 or dialysis. If not corrected by removing a secondary cause, treatment to reduce the risk of pancreatitis takes precedence over treatment of LDL cholesterol. There are no LDL treatment goals for patients with CKD, and follow-up blood tests are not generally recommended, except to evaluate compliance.



Algorithm adapted from KDOQI clinical practice guidelines for dyslipidemia management in patients with CKD.^{NKF4}

(a) Recommended doses (mg / d) of statins in adults with CKD (stages 3–5)	
Moderate Doses from Intermountain's <i>Cardiovascular Risk and Cholesterol CPM</i>	
Medication	Dose (mg / d)
atorvastatin	10
simvastatin ¹	20–40
pravastatin	40
fluvastatin	40 bid
pitavastatin	2–4
rosuvastatin	10

1. Combined simvastatin/ezetimibe also has been shown to be effective in reducing CV risk in patients with CKD, but has not been found to be superior to statins alone; dose: 20/10mg/d.

2. **Bold type** indicates preferred medications; lovastatin omitted as generally not used in stages 3–5 due to lack of studies.

✓ KEY RECOMMENDATIONS

- **Screening.** Screen diabetes patients annually for CKD, with the following distinctions based on DM type:
 - **With type I DM,** screening should begin 5 years after diagnosis.
 - **With type II DM,** screening should begin at diagnosis.
- **Management.** Focus is shifting to individualized care for blood pressure and glycemic control. Emphasis on treating high blood pressure and ASCVD prevention with lipid management may be especially helpful in reducing mortality among diabetes patients with CKD.

General guidelines:

 - **Glycemic control:** HbA1c < 7 % for most patients
 - **ACE-I or ARB if ACR ≥ 30:** Most effective way to reduce albuminuria; see [page 19](#). (Avoid dual use of ACE-I and ARB.)
 - **BP control:** BP goal < 140/90 for patients with diabetes and CKD unless ACR > 300; then goal < 130/80.

▶ DIABETES MANAGEMENT

CKD is common in patients who have been diagnosed with diabetes mellitus (DM). Approximately 40 % of patients with type I DM and 20 % to 40 % of patients with type II DM will develop chronic kidney disease. Diabetes is the most common cause of end-stage renal disease, accounting for 45 % of patients on dialysis. For patients with comorbid diabetes and CKD, mortality risk is two times greater and nonfatal complications (such as CHF, nonfatal MI, nonfatal stroke) occur 1.5 to 3 times more frequently than for those with diabetes alone.^{PAP}

CKD risk factors for patients with diabetes

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines for CKD evaluation and classification identify key risk factors shown to cause early or more rapid worsening of renal function in patients with diabetes.^{NKF²} These risk factors include being of African American, Hispanic, or Pima Indian descent or having:

- A sibling or parent with diabetes and CKD
- Elevated blood pressure
- Glomerular hyperfiltration
- High / elevated HbA1c
- High BMI
- Tobacco use
- Diabetic retinopathy

CKD can usually be attributed to diabetes if albuminuria is either severely increased (ACR > 300 mg/g) OR moderately increased (ACR 30 to 300 mg/g) in a patient with DM retinopathy or type I DM of > 10 years duration.

In a patient with diabetes, consider another cause for CKD and resulting treatment decisions if any of these factors are present:

- Absence of diabetic retinopathy
- Low or rapidly decreasing eGFR
- Rapidly increasing albuminuria or nephrotic syndrome
- Refractory hypertension
- Presence of an active urinary sediment
- Signs or symptoms of another systemic disease
- Type I DM of less than 10 years duration

RESOURCES FOR DIABETES MANAGEMENT

- Intermountain's Care Process Model **Adult Diabetes Mellitus** provides thorough guidance on diabetes treatment. It can be found on the Clinical Programs page at intermountain.net and intermountainphysician.org.
- Referral to a registered dietitian nutritionist (RDN) for help with education, nutritional planning, and motivation on managing their diabetes and CKD. See page 33 for a list of RDNs.



To access renal dosing for all medications, visit:

- **Lexicomp**—
<http://online.lexi.com/lco/action/home>
- **Clinical Key**—
<https://www.clinicalkey.com//pharmacology/?representedOrganization.id.root=UTD191860&assignedAuthorizedPerson.id.root=13059110656>

Management focus

Focus is shifting to individualized care for managing patients with diabetes and CKD. Follow these general guidelines:

- **Glycemic control.** Keeping HbA1c at 7.0% or lower in DM patients reduces the risk of developing albuminuria. While there are no large, long-term trials on the effect of glycemic control on established CKD progression, most experts recommend a 7.0% HbA1c goal for most patients with diabetes and CKD. Individualization is recommended as indicated clinically.
- **Use of an ACE-I or ARB.** Albuminuria (ACR >30 mg/g) is an early marker for renal dysfunction in diabetes patients and a strong risk factor for CVD. ACE-I/ARB medications have been shown to be the most effective in DM patients to reduce albuminuria—even in DM patients with normal blood pressure. (Based on current evidence, dual use of an ACE-I and ARB should be avoided.) See [page 19](#).
- **Blood pressure control.** To reduce mortality risk, focus on meeting blood pressure goals in patients with albuminuria (ACR >300 mg/g) of BP <130/80 and BP <140/90 for those without albuminuria.

Diabetes medications in CKD patients

Intermountain's *Adult Diabetes Mellitus Care Process Model* provides comprehensive guidance on treatment of hyperglycemia with insulin and oral medications. In that CPM, medication tables include usual dosing, SelectHealth formulary status, cost, and notes. As CKD progresses beyond Stage G2, dose adjustments are needed to account for the renal clearance of some medications.^{LUB} See resources at right for help with renal dosing.

Insulin therapy

For insulin, the evidence doesn't support specific dosage changes for patients with CKD, but careful monitoring is required. As renal function declines, the effect of insulin is prolonged and risk for hypoglycemia increases.

Metformin use in high-risk patients

KDIGO recommends that metformin be continued in people with eGFR ≥ 45 (eGFR categories G1–G3a); its use should be reviewed in those with GFR 30–44 (eGFR category G3b); and it should be discontinued in people with eGFR <30 (eGFR categories G4–G5).^{KDIGO}

Glycemic control goal

We recommend individualized therapy with a goal of 7.0% HbA1c. For example, the target may be extended above 7.0% for patients with comorbidities or limited life expectancy and risk of hypoglycemia.

✓ KEY RECOMMENDATIONS

- **Educate patients at high risk for hyperkalemia** to watch for severe muscle weakness or fatigue and to contact your office if it occurs.
- **Educate all CKD patients on potassium and their diet.** See [page 30](#). Consider referral to a registered dietitian nutritionist (RDN).
- **Obtain potassium level:**
 - When changing ACE-I/ARB dose or adding/increasing ARA dose based on information at right.
 - If the patient has any symptoms of hyperkalemia and at regular CKD follow-up appointments.
- **If you identify hyperkalemia, redraw blood and retest** to rule out hemolysis or a lab error.
- **Consider medication-induced hyperkalemia or other causes indicated at right.**
- **If results are confirmed,** follow the guidance on the next page for management, based on the severity of hyperkalemia.

MORE ON POTASSIUM AND CKD

- **How potassium is excreted.** In healthy patients, an increased potassium load is typically excreted, without complications, in a process that depends in part on aldosterone, insulin, beta-2 adrenergic receptors, and Na-K-ATPase activity in cell membranes.^{MOU2}
- **How CKD complicates potassium.** Both CKD and medications used to treat CKD (see list at right) impair the excretion process in multiple ways. CKD comorbidities, such as metabolic acidosis, can also affect potassium clearance.
- **Why it matters.** Because potassium is involved in cellular membrane potential and conduction, hyperkalemia interferes with all electrically active cells—neurons, voluntary muscles, and involuntary muscles. The most prominent effect is on myocardial cell conduction, which is why hyperkalemia can cause fatal arrhythmias.

▶ OTHER COMORBIDITIES

Hyperkalemia

Hyperkalemia is defined as a serum potassium level greater than 5 mmol/L. Since the kidneys are responsible for excreting potassium, impaired renal function is a major cause of hyperkalemia.^{KAH,ROS2} In fact, impaired renal function was present in up to 83% of patients requiring hospitalization due to hyperkalemia.^{MOO}

Evaluation and monitoring

Always test patients with any symptoms of hyperkalemia and at regular CKD follow-up appointments. Testing should also be done when changing medication doses as follows:

- For patients on ACE-I/ARBs, within:
 - 2 weeks of any dose change
 - 4–7 days when adding an aldosterone receptor antagonist (ARA) or increasing ARA dose
- For patients NOT on ACE-I/.ARBs, within 7–10 days if adding ARA or increasing ARA dose

If hyperkalemia found or concerning results, evaluate first for a medication-induced cause. With the following commonly prescribed medicines, consider either dosage reduction or elimination to improve hyperkalemia.^{PER1}

- ACE-Is, ARBs, or direct renin inhibitors ([see page 18](#) for algorithm with guidance on ACE-I/ARB dosage reductions)
- Potassium supplements
- Potassium-sparing diuretics (ARAs)
- NSAIDs, including OTC preparations
- Bactrim (trimethoprim / sulfamethoxazole)
- Digoxin
- Nonselective beta blockers (such as atenolol and propranolol)
- Cyclosporine and tacrolimus
- Heparin
- OTC herbal supplements and vitamins, such as alfalfa, dandelion, horsetail, nettle, or multivitamins containing potassium
- **Other causes.** Once medications have been eliminated, consider other causes of hyperkalemia, such as:^{EVA}
 - Lab error or hemolysis during the blood drawing process (recheck results) or pseudohyperkalemia in the setting of marked WBC elevation (CML, etc.).
 - Increased potassium release from cells and/or decreased tissue uptake: Metabolic acidosis, insulin deficiency, hyperglycemia, hyperosmolality, increased tissue catabolism (rhabdomyolysis, major surgery, radiation therapy).
 - Reduced urinary excretion: Hypoaldosteronism (most common in diabetics), renal failure, low urine flow, decreased effective circulating volume depletion, obstruction.
 - Dietary potassium in patients with renal insufficiency: CKD patients should control their potassium intake; see sidebar at left and dietary section on [page 30](#).

Impact: Hyperkalemia may result in muscle weakness, paralysis, cardiac conduction abnormalities, or dysrhythmias. If hyperkalemia is not recognized and treated early, it can lead to fatal cardiac arrhythmias.^{EVA} Patients requiring hospitalization from hyperkalemia have a mortality rate up to 41%.^{MOO}

Management

Management should be based on the patient’s potassium level and expert consensus of the CKD CPM Development Team (summarized in table 11 below). Eliminating medications and OTC substances that increase potassium, along with tighter restrictions on dietary potassium, often resolves the condition if K⁺ is 5.1 to 6.0. K⁺ >6.0 requires emergency/urgent treatment.

Patiromer (Veltassa) is a new potassium binder approved by the FDA in 2015 for hyperkalemia management. It is a nonabsorbed cation exchange polymer that binds to potassium and prevents its absorption, thereby leading to increased fecal potassium excretion and lower serum potassium levels. Widespread use is currently limited by cost and prior authorization requirements.

Key prescribing information is as follows:

- Available as a powder (either 8.4, 16.8, and 25.2 g packets) to be mixed in a 1/3 glass of water and taken once a day with food
- Taken at least 3 hours before or after other medications (can interfere with other drug absorption)
- Not indicated for acute hyperkalemia management as slow in action and potassium levels go down significantly only after two to three days
- Dose titration at seven-day intervals
- Main side effects: disturbance of bowel motility (e.g., constipation, diarrhea and hypomagnesemia)

TABLE 11: Hyperkalemia prevention and management approach*		
K ⁺ level (mmol/L)	Physician management	Patient education “zone”
3.5 to 5.0	<ul style="list-style-type: none"> • No management needed; provide general education about potassium (see Intermountain fact sheet, <i>Kidney Disease and Potassium</i>). 	<p>SAFETY ZONE</p> <p>Patients should limit high-potassium foods to keep potassium from getting too high.</p>
5.1 to 5.5	<ul style="list-style-type: none"> • Review the patient’s use of over-the-counter substances that may be causing the problem (see previous page). Consider tighter limits on dietary potassium. See the dietary advice on page 30. • Retest potassium within 2 weeks to see if the problem is resolved. 	<p>CAUTION ZONE</p> <p>Patients need stricter dietary limits and possibly medication changes or medical treatments.</p>
5.5 to 6.0	<ul style="list-style-type: none"> • Along with the steps above, review and adjust the dose of prescribed medications. Begin with medications other than ACE-I/ARB therapy. Retest potassium within 2 weeks after any change in therapy. • Reduce or stop ACE-I/ARB therapy if other medications are not present and ACE-I/ARB therapy is the likely cause. See page 19. • Look for other causes if medications are reduced/stopped without positive results. • Consider prescribing patiromer (Veltassa), and counsel patient as to side effects and costs.. • Refer the patient to a nephrologist if hyperkalemia persists despite efforts to manage. 	
> 6.0	<ul style="list-style-type: none"> • Consider hospitalization or make an emergency referral for cardiac monitoring and urgent treatment. • If the patient can’t or won’t go for emergency treatment, use all the measures described above and consider the following treatment options: <ul style="list-style-type: none"> – Loop diuretics (or increasing the dose if they are already used). For dosing of diuretics, see the <i>Hypertension CPM</i>. – Sodium polystyrene sulfonate (Kayexalate). Sodium polystyrene sulfonate is generally dosed at 15 to 30 grams orally, with subsequent doses given every 4 to 6 hours as needed to lower potassium levels.^{MOU1} Use caution with sodium polystyrene sulfonate, especially postoperatively, as bowel necrosis has been reported in post-op patients using this medication.^{GRUY} – Fludrocortisone (Florinef). The usual fludrocortisone dosage is 0.1 mg daily, although more will be needed in some patients. Primary side effects are hypertension and fluid retention, which may respond to an added diuretic.^{HOL} – Insulin with glucose. Administer insulin therapy with glucose if the patient is diabetic. A common regimen is 10 units of regular insulin in 500 mL of 10 % dextrose, given over 60 minutes. Another regimen is a bolus injection of 10 units of regular insulin, followed immediately by 50 mL of 50 % dextrose (25 g of glucose).^{MOU1} 	<p>DANGER ZONE</p> <p>Patient requires urgent treatment and may require a hospital stay to get potassium levels back to normal.</p>

* For patient with chronic serum potassium levels of 5.5-6.5 mmol/L, attempts could be made to lower the potassium with diuretics or by lowering the dose of medications that may increase potassium. Dietary consults for limiting potassium intake may also help.

✓ KEY RECOMMENDATIONS

- **Screen** BMP at the following intervals, based on CKD stage:
 - Every 12 months at Stages G1 and G2
 - Every 6 months at stage G3
 - Every 3–4 months at Stages G4 and G5
- **Manage:** Treat to maintain bicarb > 22 mEq/L by giving sodium bicarbonate or baking soda.
- **Consider other causes.** Treating the cause may help prevent further problems.

OTHER CAUSES OF ACIDOSIS

- **It's helpful to know whether acidosis is non-anion gap or anion gap.** An anion-gap calculator is available at: mdcalc.com/anion-gap.
- **Other causes of non-anion gap acidosis:**
 - Diarrhea
 - Renal tubular acidosis
 - Medications: acetazolamide, spironolactone
- **Causes of anion gap acidosis:**
 - Medications: Isoniazid, salicylates, paraldehyde
 - Alcohol or methanol poisoning
 - Diabetic or alcoholic ketoacidosis
 - Lactic acidosis
 - Rhabdomyolysis and/or uremia in renal failure

Metabolic Acidosis

Metabolic acidosis (serum bicarbonate < 22 mEq/L) is common in patients with CKD—particularly patients with diabetes—and can become apparent when the patient's eGFR drops below 50. Metabolic acidosis in CKD is typically non-anion gap acidosis (see sidebar) and is chronic and mild.

How CKD causes metabolic acidosis: The kidneys maintain acid-base balance by excreting hydrogen ions, reabsorbing filtered bicarbonate from tubular fluid, and ammoniogenesis. When eGFR is below 50, ammonium (NH_4^+) excretion per nephron is three to four times higher than normal rates. Despite this compensation, CKD leads to progressive retention of hydrogen ions and the development of metabolic acidosis.

Evaluation and monitoring

Metabolic acidosis is evaluated by a basic metabolic panel. KDOQI guidelines for bone metabolism and disease in CKD recommend testing for metabolic acidosis at the intervals indicated on [page 4](#).^{NKF3}

Management

Treatment for metabolic acidosis is inexpensive and effective. Over-the-counter sodium bicarbonate does not aggravate hypertension or lead a patient to need diuretics, despite the increased sodium load. In fact, new studies suggest that correction of metabolic acidosis may also slow the progression of CKD.^{DEB, MAH}

KDOQI guidelines recommend maintaining serum bicarbonate levels above 22 mEq/L by giving sodium bicarbonate.^{NKF3} Sodium bicarbonate is preferred over sodium citrate (with the exception of patients with kidney stones), due to the potential for increased passive absorption of aluminum with sodium citrate.

Usual daily dosing is 0.5 mEq (42 mg bicarbonate)/kg. Usual dosing of sodium bicarbonate tablets is 1,300 mg, twice daily—begin with 650 mg twice daily and titrate the dose as needed. However, baking soda is an inexpensive option:

- For a 150 lb patient, 1 teaspoon of baking soda daily
- For a 200 lb patient, 1.25 teaspoons of baking soda daily

Impact: Chronic metabolic acidosis can lead to muscle wasting and weakness, impaired albumin synthesis, and loss of bone minerals. It can also exacerbate hyperkalemia. If severe, metabolic acidosis can result in coma and death.

✓ KEY RECOMMENDATIONS

- **Regularly monitor iron stores** (ferritin and/or transferrin saturation) based on CKD stage.
- **Begin with a 3-month trial of oral iron** therapy.
- If the patient does not tolerate oral iron, or iron stores remain low after 3 months, **consider IV iron therapy**.
- **Use ESAs for low EPO only if absolutely necessary.**

USE OF ERYTHROPOIETIN STIMULATING AGENTS (ESAs)

There is no clear recommended target Hgb level for ESA therapy, and ESAs should not be administered in an attempt to normalize Hgb.

Recent evidence on use of ESAs suggests no clear benefit and possible increased risk for adverse events, including stroke. Studies have shown increased risk for adverse events if target Hgb > 11.5. ESA therapy is best managed by a nephrologist or hematologist.

The 2012 KDIGO guidelines for using ESAs (e.g., Procrit, Epogen, or Aranesp) to treat anemia in patients with CKD recommend:

- Initiating only for patients not on dialysis with severe anemia (Hgb < 10 g/dL)
- Starting therapy for patients in CKD stage 5 (not on dialysis) when Hgb is between 9 and 10
- Only using to prevent the need for blood transfusion
- Determining appropriateness based on rate of fall of Hgb concentration, prior response to iron therapy, risks of needing a transfusion and related to ESA therapy, and symptoms that can be attributed to anemia

Anemia

Anemia is a common complication of CKD as a consequence of the loss of erythropoietin (EPO) production by the impaired kidneys.

The risk for anemia increases as eGFR drops below 60; more than 80 % of patients with Stage G4 CKD will have some degree of anemia. Patients with diabetes may develop EPO deficiency at earlier stages of CKD. (Note: Polycystic kidney disease patients tend to retain EPO production and not become anemic, in spite of marked reduction in eGFR.)

Impact: There is a high risk for cardiovascular disease among patients with CKD, in part as a result of anemia, which has been found to be an independent predictor of left ventricular hypertrophy (LVH) and heart failure (HF).^{AST,MCC} Additionally, severe anemia may hasten disease progression in earlier stages of the CKD, accelerating the onset of end-stage renal disease (ESRD).^{BER}

Evaluation and monitoring

Diagnose anemia in adults and children over 15 with CKD when the Hb concentration is 13.0 g/dL (130 g/L) in males and 12.0 g/dL (120 g/L) in females.^{KDIGO} While iron deficiency is common in CKD, rule out other causes of anemia such as GI bleeding.

If serum creatinine (sCr) is < 1.5 mg/dL, check the EPO level. If renal function is impaired (sCr > 1.5 mg/dL or eGFR < 60 mL/min), checking EPO is unnecessary, as EPO deficiency can be assumed.

Monitor for anemia in ALL CKD Stages G3–G5 patients as shown in table 13:

TABLE 12: Annual Monitoring for Anemia (more often when clinically indicated)

CKD Stage	3	4 (no dialysis)	5 (dialysis)
CKD patients WITHOUT anemia			
Recommended Hgb testing frequency	≥ 1/year	≥ 2/year	≥ 4/year
CKD patients WITH anemia (not treated with an ESA—see info on ESAs at right)			
Recommended Hgb testing frequency	≥ 4/year (not on dialysis)	≥ 4/year	≥ 12/year

Management

Consider iron supplementation (see table below) for relative iron deficiency, beginning with a one- to three-month trial of oral iron therapy. **Do not supplement with iron if ferritin > 800 ng/mL, due to the possibility of iron overload.** Consider IV iron therapy if patient does not tolerate oral iron or if patient is compliant, but iron stores remain low after three months.

TABLE 13: Recommendations for Iron Supplementation Therapy

Oral (initial 3-month trial recommended)	IV* — ONLY WHEN: Oral therapy unsuccessful Patient not on dialysis or ESA therapy
Usual dosing: 65 mg elemental iron, 3 times daily Take only on empty stomach Do not take within 2 hours of consuming: <ul style="list-style-type: none"> • Bran, fiber, grains, nuts, soy, and vegetables • Tea, coffee, and caffeine • Red grape juice and wine • Dairy and egg • Thyroid medications, phosphate binders, carbonate antacids, or copper supplements 	Usual dosing: <ul style="list-style-type: none"> • 1 gram IV iron sucrose (Venofer) in divided doses as follows: • 200 mg IV injected undiluted over 2 to 5 minutes • Injected on 5 different occasions within a 14-day period • Total cumulative dose of 1,000 mg

* To protect the patient’s venous access, minimize the number of transfusions if possible and avoid the nondominant arm.

✓ KEY RECOMMENDATIONS

- **Screen at every visit:** Check for weight change and other signs, such as shortness of breath, refractory hypertension, or peripheral edema.
- **Evaluate cardiac risk:** Especially if eGFR > 30, edema may have a cardiac cause.
- **Manage volume overload:**
 - Discontinue or reduce medications that can cause edema.
 - Restrict dietary sodium to 1,500 mg per day.
 - Prescribe diuretics, starting with a loop diuretic.

EDUCATE PATIENTS TO AVOID OVERHYDRATION

Patients newly diagnosed with kidney disease may hold to the myth that they should drink large amounts of water daily to “flush the kidneys.” As this behavior can cause volume overload, it’s important to correct this misconception during discussions about kidney disease with patients at Stage G3b or later.

ADJUSTING LOOP DIURETICS

Loop diuretics have a dose-response curve; you may need to increase the dose beyond the typical maximum to treat volume overload. To decide whether to adjust the dose or the frequency of a loop diuretic, ask the patient whether the current dose prompts urination.

- **If a single dose does not prompt urination, increase the dose** rather than giving the same dose twice daily. For example, if a patient doesn’t respond to 40 mg of furosemide (Lasix), the single dose may need to increase to 80 mg.
- **If a single dose prompts urination, increase the frequency** of that dose to twice daily.

Volume Overload and Edema

Volume overload is a frequent complication of CKD at Stages G4 and G5, or with severe nephrotic syndrome at any CKD stage. The kidneys typically balance sodium and intravascular volume until eGFR falls below 15. However, even at earlier CKD stages (eGFR below 40), the kidneys are less able to respond to sodium, and these patients can be prone to volume overload.

Evaluation and monitoring

- **Monitor patients regularly** for signs and symptoms of volume overload:
 - Check a patient’s weight at every visit. An increase in weight may be a sign of salt and water retention. Educate patients to weigh themselves routinely and schedule an appointment if they experience a weight gain of 5 lb or more in less than 1 week.
 - Check for other signs, including refractory hypertension, shortness of breath, or peripheral edema. (Please note that peripheral edema does not always indicate volume overload.) Patients with volume overload may also have jugular venous distension, hepatojugular reflux, pulmonary crackles, chest discomfort, and progressive decrease in exercise tolerance.
- **In patients with signs or symptoms, evaluate CV risk and check for cardiac causes.** In patients with eGFR > 30, volume overload is often caused by a cardiac condition such as heart failure. If eGFR < 30, CKD is more likely to be the cause.

Management

- **Discontinue or reduce the dose of medications** that can cause edema:
 - NSAIDs
 - Thiazolidinediones (e.g., rosiglitazone / Avandia, pioglitazone / Actos)
 - Calcium channel blockers
 - Direct vasodilators (e.g., minoxidil / Loniten, hydralazine / Apresoline)
 - GABA analogues (e.g., gabapentin / Neurontin and pregabalin / Lyrica)
 - Pramipexole (Mirapex)
 - Corticosteroids
 - Estrogens
- **Restrict dietary sodium to 1,500 mg per day.** Dietary sodium is a contributor to volume overload and edema. See [page 32](#) for more details on sodium restriction.
- **If volume overload persists, prescribe diuretics.**
 - Begin with a loop diuretic. See the [High Blood Pressure CPM](#).
 - If volume overload does not respond, adjust the loop diuretic dose or frequency. See the sidebar for tips on adjusting loop diuretic therapy.
 - If volume overload still does not respond, try a different loop diuretic. For example, if oral absorption is impaired (such as in bowel edema), switching from furosemide (Lasix) to another loop diuretic, such as torsemide (Demadex), may be helpful.
 - If volume overload does not respond with a loop diuretic alone, consider adding a thiazide diuretic. Follow up to monitor the patient for hypokalemia or prerenal azotemia. See [page 19](#).

If these measures are not effective, refer the patient to a nephrologist.

Impact: Volume overload and edema can lead to decompensated heart failure in dialysis patients and is a strong predictor of mortality.^{HEN, HUN}

✓ KEY RECOMMENDATIONS

- **Monitor:** Annually measure serum levels based on CKD stage (see [table 15](#)).
- **Reduce phosphate; regulate calcium and vitamin D.**

OSTEOPOROSIS AND BISPSPHONATES

- Diagnosis of osteoporosis in patients in CKD stages 3b–5 becomes increasingly challenging. Rule out other forms of osteodystrophy before treating with bisphosphonates.
- In CKD stage 4–5 patients, bisphosphonate safety and efficacy has not been well-studied in CKD populations, and IV bisphosphonates have been implicated in nephrotoxicity.^{KDIGO}

VITAMIN D

Evaluate patients with levels of iPTH above the upper normal limit of the assay for vitamin D deficiency. See [page 30](#) for information about treating vitamin D deficiency.

Metabolic Bone Disease

Early in the course of CKD, changes in bone mineral metabolism and calcium and phosphate homeostasis occur (resulting in renal osteodystrophy, extraskeletal calcifications, etc.). These changes progress as kidney function declines.^{KDIGO}

Controversy exists about treatment targets for serum concentrations of calcium, phosphate, and intact parathyroid hormone (iPTH) and the impact of vitamin D on these mineral metabolites. Recent research on the role of fibroblast growth factor 23 (FGF-23) (an important molecule in phosphate, iPTH, and vitamin D homeostasis) has caused many to question the previous focus on iPTH.^{KDIGO1} The optimal iPTH value for CKD stages 3b–5 is unknown.

Impact: Metabolic bone disease results in both skeletal and extraskeletal consequences, including cardiovascular calcification, which can progress rapidly and lead to adverse outcomes such as stroke, ischemic heart disease, and peripheral arterial disease.^{MAR,OHT}

Evaluation and monitoring

KDIGO monitoring and evaluation guidelines for CKD Stages 3–5 recommend:^{KDIGO2}

- Measuring serum levels of calcium, phosphate, iPTH, and alkaline phosphatase for baseline values and subsequent retesting as indicated in [table 15](#) below.
- Not routinely performing bone mineral density (DXA) testing — Unless DXA results will aid in treatment decisions about fracture risk reduction. Otherwise, the information may be misleading or unhelpful because DXAs neither assess bone quality nor help predict fractures.

TABLE 14: Monitoring frequency for metabolic bone disease^{KDIGO}

		Annual Testing Frequency**			
		Serum Calcium	Phosphorus	iPTH	Alkaline Phosphatase Activity
CKD Stage	3	1–2	1–2	1–2	Based on baseline level and CKD progression
	4	2–4	2–4	1–2	≥ 1*
	5	4–12	4–12	2–4	≥ 1*

*For stages 4–5D, retest more frequently in presence of elevated iPTH
 ** The frequency of testing is determined by severity of disease, the rate of progression, and current treatment

Management

TABLE 15: Management of metabolic bone disease — Goals and recommendations

Goals	Recommendations (serum calcium <9.5)	Recommendations (serum calcium >9.5)
1. Reduce phosphate* unless phosphate is already low. Target: Within age-appropriate limits. (Maintain serum phosphate concentration in the normal range based on local laboratory reference values.) 2. Regulate calcium. Target: 8.4 to 9.5 mg/dL 3. Regulate vitamin D. Target: 30 to 50 ng/mL	Limit dietary phosphorus to 800 to 1,000 mg daily. (See pages 31–33 for details on dietary management of phosphorous, calcium, and vitamin D.) Consider calcium phosphate binders as initial therapy. Follow patient’s calcium levels, and do not exceed 2,000 mg per day of total elemental calcium. Products include: <ul style="list-style-type: none"> • Calcium carbonate antacids, such as Tums or Rolaids. Tablet weight is 40 % elemental calcium; some patients need 1 to 3 tablets with each meal. • Calcium acetate (PhosLo) by prescription. • Avoid hypercalcemia. 	Consider noncalcium phosphate binders. These are more expensive than calcium-based medications and can cause GI upset. Product choice depends on preferred formulation: <ul style="list-style-type: none"> • Sevelamer (Renagel or Renvela): Available in tablet or powder to be sprinkled on food. Usual dosing is 0.8 or 1.6 grams, 3 times daily with meals. • Lanthanum (Fosrenol): Available as large tablet (chewable or crushed to sprinkle on food). Initial dose is 1,500 mg per day, with doses up to 4,500 mg per day. • Iron-based binders (taken with meals): <ul style="list-style-type: none"> – Velphoro (sucroferric oxyhydroxide): Available as 500 mg chewable tablet. Initial dose is 1 tablet, 3 times a day – Auryxia (ferric citrate): Available as 210 mg tablet. Initial dose is 2 tablets, 3 times/day

*Phosphate and phosphorus are used interchangeably.

✓ KEY RECOMMENDATIONS

- **For patients with eGFR < 60,** take a baseline measurement of serum vitamin D 25 hydroxy (OH) levels. Retest yearly or more often if clinically indicated.
- Correct vitamin D deficiency and insufficiency using treatment strategies recommended for the general population.
- Nephrologists may recommend treating patients with vitamin D who have normal levels to help treatment of hyperparathyroidism.

DOSING FOR CKD PATIENTS

Correct vitamin D deficiency and insufficiency using treatment strategies recommended for the general population.^{KDIGO}

Note: In mild vitamin D deficiency, **OTC supplements** are generally as effective as and less expensive than prescription supplements. The benefit of a prescription form is it can be taken less frequently. If a patient does not respond to OTC vitamin D, consider a prescription supplement.

SAFETY

Vitamin D₂ and vitamin D₃ are safe, even at high doses. Hypercalcemia and hyperphosphatemia related to supplementation are rare.^{BAS,TRA} However, during vitamin D supplementation, monitor calcium and phosphorus levels quarterly in patients in stages 4 or 5:

- **Calcium:** If serum Ca is > 9.5 mg/dL, reduce the vitamin D dose. If serum Ca is > 10.2 mg/dL, stop vitamin D therapy.
- **Phosphorus:** If serum P is > 4.6 mg/dL, initiate or increase a phosphate binder and/or restrict dietary phosphate.

▶ VITAMIN D AND CKD

This section reviews general principles about vitamin D deficiency in CKD, but is not meant to be a complete overview of vitamin D deficiency. The supplement dosage information is intended for CKD patients and should not be considered a general guide for all patients.

Why is it important?

Vitamin D plays an important role in bone mineral metabolism, which is altered in CKD patients. Treating vitamin D deficiency in patients with metabolic bone disease may improve secondary hyperparathyroidism. Vitamin D also potentially regulates many cellular functions; deficiency may be linked to increased risk for many diseases, including diseases of the immune and cardiovascular systems.

Who's at highest risk?

Vitamin D deficiency is prevalent at all stages of CKD. Deficiency increases in the winter months as sun exposure decreases. Dietary intake is typically insufficient in vitamin D, but is particularly inadequate in the presence of common renal dietary restrictions. Vitamin D deficiency is even more prevalent in patients who have other risk factors:

- Patients living at a latitude north of Arizona, especially for patients with nephrotic-range albuminuria (loss of vitamin D binding protein)
- Patients who are obese
- Patients with darker skin
- Elderly patients (the body's ability to produce vitamin D from the sun decreases with age)
- Patients with malabsorption
- Institutionalized patients

What serum 25(OH)D level is desirable?

Vitamin D deficiency is defined as a serum 25(OH)D level < 20 ng/mL; whereas insufficiency is defined as a 25(OH)D level < 30 ng/mL. The goal recommended in the KDOQI guideline for bone disease is > 30 ng/mL (normal levels).^{MAH} Serum levels above 50 ng/mL should be avoided; studies have shown increased all-cause mortality in patients with serum 25(OH)D over 60 ng/mL.^{MEL}

What vitamin supplements should be used in CKD?

Both ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃) are effective forms of vitamin D supplementation in all stages of CKD. However, some recent studies (not in CKD patients) suggest that vitamin D₃ (as compared to vitamin D₂) may be more effective and is also more readily available than vitamin D₂ (see the sidebar for information on dosing and safety).^{RUC}

Active 1,25 (OH) vitamin D analogs (calcitriol, paricalcitol, doxercalciferol, alfacalcidol) should NOT be used to treat vitamin D deficiency. Active analogs are likely more effective when 25(OH)D levels are normal. Because they have a narrow margin of safety, active vitamin D analogs should only be prescribed by a nephrologist.

✓ KEY RECOMMENDATIONS

- **Referral to an RDN** is recommended to tailor diet information to fit a particular patient’s disease stage and status.
- **In the early stages of CKD**, primary dietary management should focus on diet related to diabetes, hypertension, lipid management, and obesity. These conditions will accelerate loss of kidney function.
- **As CKD progresses**, loss of appetite and taste aversions are common, along with the development of malnutrition. **Malnutrition must be avoided** because it increases the patient’s risk of mortality. Dietary restrictions should be liberalized if malnutrition is present.
- **Use of the DASH diet** is appropriate in the early stages of CKD, but is generally high in potassium and phosphorus, and its use may need to be reassessed in the later stages.

▶ DIETARY MANAGEMENT

In patients with CKD, nutritional needs and interventions change based on the stage and progression of the disease. Nutritional goals must be individualized to maintain the best health possible of each patient and maintain serum blood levels within appropriate levels. Referral to a registered dietitian nutritionist (RDN) is suggested. Dietary strategies are helpful in managing sodium, potassium, phosphorus, calcium, and protein. However, the need for diet restrictions should be assessed regularly, and the patient should be provided with the most liberal diet possible—imposing only those restrictions necessary based on the patient’s current condition.

Dietary concern	Recommendations and tips
Malnutrition	<p>Guidelines from the Academy of Nutrition and Dietetics and the American Society of Parenteral and Enteral Nutrition (ASPEN) have defined updated clinical criteria for malnutrition, listed below.^{5K1} Refer a patient to an RDN for nutritional management if two or more of these criteria are present:</p> <ul style="list-style-type: none"> • Weight loss: <ul style="list-style-type: none"> – > 5% in 1 month – > 7.5% in 3 months – > 10% in 6 months – > 20% in 1 year • Reduced dietary intake for ≥ 1 month • Muscle loss • Fluid accumulation • Loss of subcutaneous fat • Reduced grip strength <p>Note: While serum albumin may help in screening for malnutrition, it is not diagnostic because of multiple limitations. However, reduced serum albumin is a predictor of mortality in CKD.</p>
Protein intake	<ul style="list-style-type: none"> • Recommend a moderate protein intake of 0.8 to 1 g per kg of weight daily. A very low protein diet (<0.6 g protein per kg of weight daily) to preserve kidney function is not recommended. It’s important to discourage excessive protein intake (e.g., the Atkins diet and similar high-protein diets). However, very little evidence exists to support the traditional wisdom that tightly restricting dietary protein is important in CKD. • Tips: Encourage patients to focus on high biologic value proteins (mainly animal proteins). These provide all of the essential amino acids and allow patients to consume less total protein while still meeting their amino acid needs. <ul style="list-style-type: none"> – 1 ounce of meat contains 7 grams high biologic value protein. – The protein in 1 egg or 1 cup of milk = approximately 1 ounce of meat. – 3 ounces of meat is about the size of a deck of cards. • Examples of a 0.8 g/kg protein diet with about 50% of protein from high biologic value sources: <ul style="list-style-type: none"> – For a man with an ideal weight of 180 pounds: 65 grams of protein daily, with about 35 grams being high biologic value (5 ounces of meat) and the other 30 grams from protein in other foods (breads, vegetables, etc.). – For a woman with an ideal weight of 140 pounds: 50 grams of protein daily, with 28 grams being high biologic value (4 ounces of meat) and the rest from protein in other foods.

VEGETARIANS AND PROTEIN

- A vegetarian diet is fine for CKD patients, but diet counseling would be appropriate. To get the necessary amino acids, vegetarians must combine proteins from multiple sources, including:
 - Milk or eggs, for lacto-ovo vegetarians
 - Soy (tofu, soy milk, etc.)
 - Beans, lentils, peas, and other legumes
 - Nuts and seeds
 - Whole grains (wheat, oats, rice, etc.)
- To get the necessary amino acids, vegetarians may need to consume more protein than these guidelines recommend. However, a vegetarian diet may bring other health benefits that slow CKD progression. If a potassium restriction is indicated, it may become very difficult to meet protein needs on a vegetarian diet, as most vegetarian sources of protein are high in potassium.

PROMOTING POSITIVE CHANGE

While limits on specific nutrients can be important for CKD patients, they can also be challenging. Imposing strict dietary limits—with no room for compromise—is an approach that may backfire. Some patients react by concluding that the goal can't be met and it's not worth the effort to try managing their diet.

Remember that any positive change in a patient's diet is worthwhile.

If your patient needs to manage one or more nutrients, explain why, provide resources to help (see the list below), provide encouragement to keep working toward the goal, and refer the patient to a registered dietitian nutritionist (RDN). See [page 33](#) for a list of Intermountain RDNs and phone numbers.

NATIONAL KIDNEY FOUNDATION RESOURCES

The NKF has produced a variety of patient education resources, available in an A to Z index at kidney.org/atoz.

Topics covered include general nutrition for CKD patients and topics on nutrition for dialysis or transplantation (look under N), plus specific nutrients including carbohydrates, cholesterol, potassium, phosphorus, and sodium (look under the appropriate letter).

INTERMOUNTAIN RESOURCES

Intermountain has these fact sheets on managing key nutrients in CKD:

- [Kidney Disease and Potassium](#)
- [Kidney Disease and Your Bones](#)
- [Kidney Disease, High Blood Pressure, and Urine Proteins](#)

See [page 34](#) for additional information, including ordering directions.

TABLE 16: Dietary management of CKD, continued

Dietary concern	Recommendations and tips
<p>Sodium</p> <p>Sodium is an extracellular electrolyte involved in fluid balance. Increased sodium intake can cause increased intravascular volume; this increases the work load for the kidneys and the heart. A high-sodium diet can also impede ACE-I/ARB therapy. Decreased sodium intake may help slow CKD progression by lowering intraglomerular pressure. Hyponatremia may not indicate a need for additional salt in the diet, but may be related to overhydration, hyperglycemia, or starvation.</p>	<ul style="list-style-type: none"> • Recommendation: KDIGO guidelines recommend that CKD patients limit sodium to 2,000 mg daily (or 1,500 mg daily if edema/fluid retention).^{KDIGO} This goal may be difficult for many patients to meet, and requires overall dietary changes that will take time to achieve. • Tips for limiting sodium intake: <ul style="list-style-type: none"> – Make foods from scratch; restaurant meals and packaged foods are often high in sodium. Use NO salt in cooking (just herbs and spices), and don't add salt after food is prepared. – Limit salted snacks like chips and pretzels. – Avoid convenience food, packaged seasonings, and cured meats. Avoid frozen meals; even those labeled "healthy" often have high levels of sodium. Avoid canned foods and/or rinse canned foods before use. – Use herbal blends (such as Mrs. Dash), pepper, garlic, lemon or lime juice, and vinegar to season foods; check the labels and avoid those that contain salt. Check the labels of salt substitutes and avoid those with potassium.
<p>Potassium</p> <p>Potassium is an intracellular electrolyte with key function involved in muscle contraction. When a patient with renal disease can maintain both aldosterone secretions and distal flow, potassium excretion is usually maintained within normal limits. Hyperkalemia usually becomes apparent if the patient has low urine output, hypoaldosteronism, or increased tissue breakdown. If an ACE-I is prescribed, dietary potassium will likely need to be limited.</p>	<ul style="list-style-type: none"> • Recommendation: If a patient's serum potassium level increases to more than 5 mEq/L, dietary potassium should be restricted to 2,000 to 4,000 mg daily, depending on the patient's level of hyperkalemia. The need for potassium restriction can change rapidly. (Note: Patients on diuretics may require a high-potassium diet with additional potassium supplementation.) • Tips for limiting potassium intake: <ul style="list-style-type: none"> – Significantly limit potatoes, tomatoes and tomato-based sauces, bananas, oranges and orange juice, prunes and prune juice, cooked spinach and chard, winter squash, and avocados. – Avoid multiple high-potassium foods in 1 meal or 1 day. – Limit dairy products to 1 serving daily. – Avoid salt substitutes—they often are high in potassium. – Avoid noni juice, alfalfa, dandelion, horsetail, and nettle (and combination supplements containing them).
<p>Phosphorus</p> <p>As eGFR falls, phosphorus retention can begin, and high phosphorus levels contribute to CKD progression.</p>	<ul style="list-style-type: none"> • Recommendation: Phosphorus management targets depend on the stage of CKD: <ul style="list-style-type: none"> – At Stage G3 and G4, serum phosphate should be kept to normal limits: <4.6 mg/dL. – At Stage G5 CKD, serum phosphate should be kept at <5.5 mg/dL. • Tips for managing phosphorus: <ul style="list-style-type: none"> – Limit dietary phosphorus to 800 to 1,000mg daily when a patient's serum phosphate is above the levels listed above. Patients can limit phosphorus by decreasing intake of legumes, nuts, organ meats, dairy products, colas, and chocolate (or taking a phosphorus binder when these foods are consumed). – Consider phosphorus binder therapy when hyperphosphatemia exists at the above levels or once eGFR falls below 30. Calcium carbonate (e.g., Tums[®]) is generally the first-line phosphorus binder. Other options include calcium acetate (PhosLo), sevelamer (Renvela), and lanthanum (Fosrenol).

REFERRAL TO A REGISTERED DIETITIAN NUTRITIONIST (RDN)

Patients should be referred to a registered dietitian nutritionist (RDN) when any new diet restriction is ordered or when lack of diet understanding is apparent. Balancing diet restrictions for multiple chronic conditions can be frustrating to patients, as they sometimes seem to contradict each other.

An RDN can help tailor diet information to fit a particular patient, helping the patient get the most benefit from these restrictions while still finding some joy in eating. See the list below for contact information. Many insurers cover consultations with RDNs for patients with CKD and/or diabetes; patients should check with their health plans.

RDN RESOURCES AT INTERMOUNTAIN

Patients can be referred to see an outpatient RDN at the facilities listed below. Note that some medical group regions have RDNs employed by the medical group.

- Alta View Hospital: 801-507-3253
- American Fork Hospital: 801-855-3461
- Bear River Valley Hospital: 435-716-5310
- Budge Clinic: 435-716-1710
- Cassia Regional Hospital: 208-677-6035
- Delta Community Hospital: 435-864-5591
- Dixie Regional Medical Center: 435-251-3793
- Fillmore Community Hospital: 435-743-5591
- Heber Valley Hospital: 435-657-4311
- Intermountain Medical Center: 801-507-3253
- LDS Hospital: 801-507-3253
- Logan Regional Hospital: 435-716-5310
- McKay-Dee Hospital Center: 801-387-7539
- North Ogden Clinic: 801-786-7500
- Park City Hospital: 435-658-7119
- Primary Children’s Hospital: 801-662-1601
- Riverton Hospital: 801-507-3253
- Sanpete Valley Hospital: 435-462-4620
- Sevier Valley Hospital: 435-893-0569
- Sunset Clinic: 435-634-6010
- Utah Valley Hospital: 801-357-8143
- Valley View Medical Center: 435-251-3793

TABLE 16: Dietary management of CKD, continued

Dietary concern	Recommendations and tips
<p>Calcium</p> <p>Calcium levels are often low in patients with CKD. Changes in Vitamin D, metabolism, elevated phosphorus, and limiting high calcium foods (e.g., limiting dairy products on low potassium and low phosphorus diets) can result in hypocalcemia.</p>	<ul style="list-style-type: none"> • Recommendation: Normal serum calcium is 8.5 to 10.2 mg/dL; assess calcium status concurrently with vitamin D deficiency and phosphorus. Note: For patients with hypoalbuminemia, the calcium measurement needs to be corrected using this formula: $\text{Corrected calcium} = \text{measured serum calcium} + (0.8 \times [4.5 - \text{serum albumin}])$ • Tips: <ul style="list-style-type: none"> – The use of calcium supplements may be indicated. Patients should be supplemented with 1,200 to 1,500 mg elemental calcium daily, in divided doses. The total elemental calcium of supplements and calcium-based phosphorus binders should not exceed 2,000 mg. – Calcium supplements should be taken in between meals on an empty stomach and should not be taken with iron supplements. – Calcium carbonate contains 40 % elemental calcium and is the recommended calcium source. – Calcium citrate is not recommended in CKD because it may increase risk of aluminum toxicity.
<p>Supplements and herbal remedies</p> <p>Many supplements and herbal remedies are touted to improve kidney function, while some may actually be harmful to the kidneys or worsen other areas of concern with CKD.</p>	<ul style="list-style-type: none"> • Educate CKD patients to use caution with all complementary and alternative medicine (CAM) supplements. Patients should avoid supplements that may harm the kidneys, as well as supplements that are erroneously touted by the CAM community to improve kidney function. • Strongly discourage the following supplements, as they may be nephrotoxic or worsen other areas of concern in CKD: Herbs containing aristolochic acid (in some weight-loss supplements), high-dose capsicum (cayenne, pepper sauces such as Tabasco, chili pepper), chromium nicotinate, comfrey, creatine, lobelia, L-lysine, noni juice or extract, pennyroyal, piracetam, sarsaparilla, uva-ursi, and yohimbe. (This list is not all inclusive.) • Caution patients about use of black licorice to treat hyperkalemia. Though black licorice is touted as a natural treatment for hyperkalemia in the CAM community, no level of intake has been studied. • Caution patients about CAM remedies often used for urinary problems. Patients may believe that some CAM remedies used to treat upper urinary tract problems, particularly cranberry extract, can be transferred to kidney disease. Caution patients that these CAM remedies do not apply to kidney disease, and that high amounts of these supplements will not improve kidney function.
<p>Iron</p>	<ul style="list-style-type: none"> • Recommendation: A high iron diet is generally not recommended to help treat anemia in CKD patients due to poor dietary absorption, medication interactions, and the complexity of existing diet restrictions. • See page 27 for information on anemia and iron therapy.
<p>Vitamin D</p>	<p>For those at risk for vitamin D deficiency, dietary intake is typically insufficient. See page 30 for a full discussion of vitamin D in CKD, including supplementation and monitoring recommendations.</p>

OTHER WEB RESOURCES

For providers:

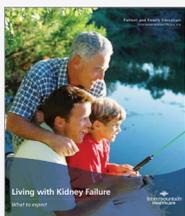
- Intermountain CKD provider website: IntermountainHealthcare.net/kidney
- National Kidney Disease Education Program, an initiative of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the NIH, and the U.S. Department of Health & Human Services (DHHS): NKDEP.NIH.gov
- Full clinical practice guidelines from Kidney Disease Improving Global Outcomes (KDIGO): kdigo.org
- Full clinical practice guidelines from the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI): www.kidney.org/professionals

For patients:

- Intermountain CKD patient website: IntermountainHealthcare.org/kidney
- NKF Cares site from the National Kidney Foundation, with articles, videos, and links to support groups: kidney.org/patients
- Kidney School, web-based training modules provided by the Medical Education Institute: KidneySchool.org
- The Renal Support Network, a nonprofit, patient-focused, patient-run organization that provides non-medical services to those affected by CKD: RSNhope.org

LIVING WITH KIDNEY FAILURE BINDER

To provide comprehensive, early education for patients in Stage 3b–Stage 5 CKD, the Dialysis Services team has developed the *Living with Kidney Failure* binder. This binder



is currently part of a pilot educational program at Logan Regional Hospital with plans to expand the program to other facilities later on.

Geared to helping patients make critical treatment decisions and take an active role in preventing and/or managing disease progression, the binder includes extensive information on staging, ways to slow progression, key information on transplant and dialysis services, and support resources (including understanding costs and Medicare coverage).

For more information on the pilot program and copies of the binder, contact Ray Morales, AVP Dialysis Services at Ray.Morales@imail.org.

RESOURCES

Intermountain provider resources

To find this CPM and Best Practice Flash Cards, clinicians can go to intermountainphysician.org/clinicalprograms and select Chronic Kidney Disease from the topic list on the right side of the screen.



To access renal dosing for all medications, visit:

- Lexicomp— <http://online.lexi.com/lco/action/home>
- Clinical Key— <https://www.clinicalkey.com//pharmacology/?representedOrganization.id.root=UTD191860&assignedAuthorizedPerson.id.root=13059110656>

Intermountain patient education

Clinicians can order Intermountain patient education booklets and fact sheets for distribution to their patients from Intermountain’s Online Library and Print Store, iprintstore.org.

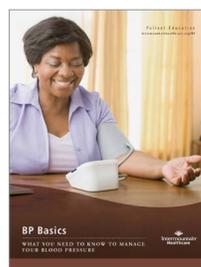
In addition, an array of booklets, trackers, and fact sheets are available to help patients manage related hypertension and blood glucose.

Fact sheets:

- [Understanding Chronic Kidney Disease](#)
- [Kidney Disease and Your Bones](#)
- [Kidney Disease and Potassium](#)
- [Kidney Disease and Anemia](#)
- [Kidney Disease, High Blood Pressure, and Urine Proteins](#)
- [Kidney Failure: Your Options](#)
- [Dialysis: What's the Right Option for Me?](#)
- [Transplant: Am I a Candidate?](#)



BP Tracker



BP Basics Booklet



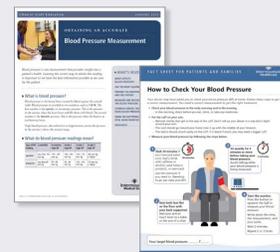
BG Tracker



Diabetes Care Handbook

RESOURCES TO IMPROVE BP MEASUREMENT

- Office measurement (clinical staff): Intermountain University training and pamphlet [Obtaining an Accurate Blood Pressure Measurement](#)
- Home measurement (patients): Fact sheet [How to Check Your Blood Pressure](#)



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This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Paula Haberman, MD, CKD Development Team Lead (paula.haberman@imail.org).