VA/DoD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF CHRONIC KIDNEY DISEASE IN PRIMARY CARE

Department of Veterans Affairs

Department of Defense

GUIDELINE SUMMARY

Key Elements Addressed by the Guideline

1. Diagnostic criteria and identification of early disease.
2. Identification of susceptibility factors (adult patients at increased risk for developing CKD).
3. Identification of progression factors (adult patients at high risk for worsening kidney damage and subsequent loss of kidney function).
4. Evaluation of patients with kidney disease (estimate of GFR, blood pressure, and assessment of proteinuria as a marker of kidney damage).
5. Slowing the progression of CKD and prevention of conditions that exacerbate chronic disease.
6. Management of comorbidities.
7. Indication for consultation and referral to a nephrologist.
8. Outline of patient education and preparation for kidney replacement therapy.

Key Changes in the Update to the 1999 VA/DoD Guideline for ESKD

The revised guideline recommendations continue to support the approach initially advocated in the 1999 version of the VA/DoD guideline for ESKD; however, a goal of the current update is to provide guidance to primary care providers in the management of CKD in the primary care setting. The emphasis of the current guideline has thus shifted away from the management of severe CKD (eGFR <30 ml/min/1.73m^2) and toward the management of earlier stage CKD (eGFR $\geq$ 30 ml/min/1.73m^2). In addition, the evidence published from randomized trials in recent years allowed the Working Group to make firmer recommendations in the following areas:

- Diagnostic Workup:
    - Classification of CKD based on eGFR rather than levels of serum creatinine.
- A unified approach to management of common aspects of kidney disease that is not dependent on the underlying etiology of the CKD:
    - Complications of CKD (anemia, cardiovascular disease, dyslipidemia).
    - Strategies to slow the decline of eGFR.

Scope of Guideline

Target population:

Adult patients with CKD: This guideline applies to both patients presenting for the first time with CKD and to patients already being followed for CKD. In both instances, CKD is defined as the presence of decreased eGFR or proteinuria or structural renal damage as determined by radiologic imaging or kidney biopsy, which can occur together or independently.

Audiences:

The guideline is relevant to all healthcare professionals who have direct contact with patients with CKD, and make decisions about their care. This version of the guideline was specifically tailored to provide what would be of greatest value to the primary care provider.

Evidence

Evidence Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.*
B	A recommendation that clinicians provide (the service) to eligible patients. *At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.*
C	No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.*
D	Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.*
I	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Lack of Evidence – Consensus of Experts

Where existing literature was ambiguous or conflicting, or where scientific data were lacking on an issue, recommendations were based on the clinical experience of the Working Group. These recommendations are indicated in the evidence tables as based on "Working Group Consensus."

This Guideline is the product of many months of diligent effort and consensus-building among knowledgeable individuals from the VA, DoD, and academia, and a guideline facilitator from the private sector. An experienced moderator facilitated the multidisciplinary Working Group. The draft document was discussed in 3 face-to-face group meetings. The content and validity of each section was thoroughly reviewed in a series of conference calls. The final document is the product of those discussions and has been approved by all members of the Working Group.

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Algorithm and Annotations

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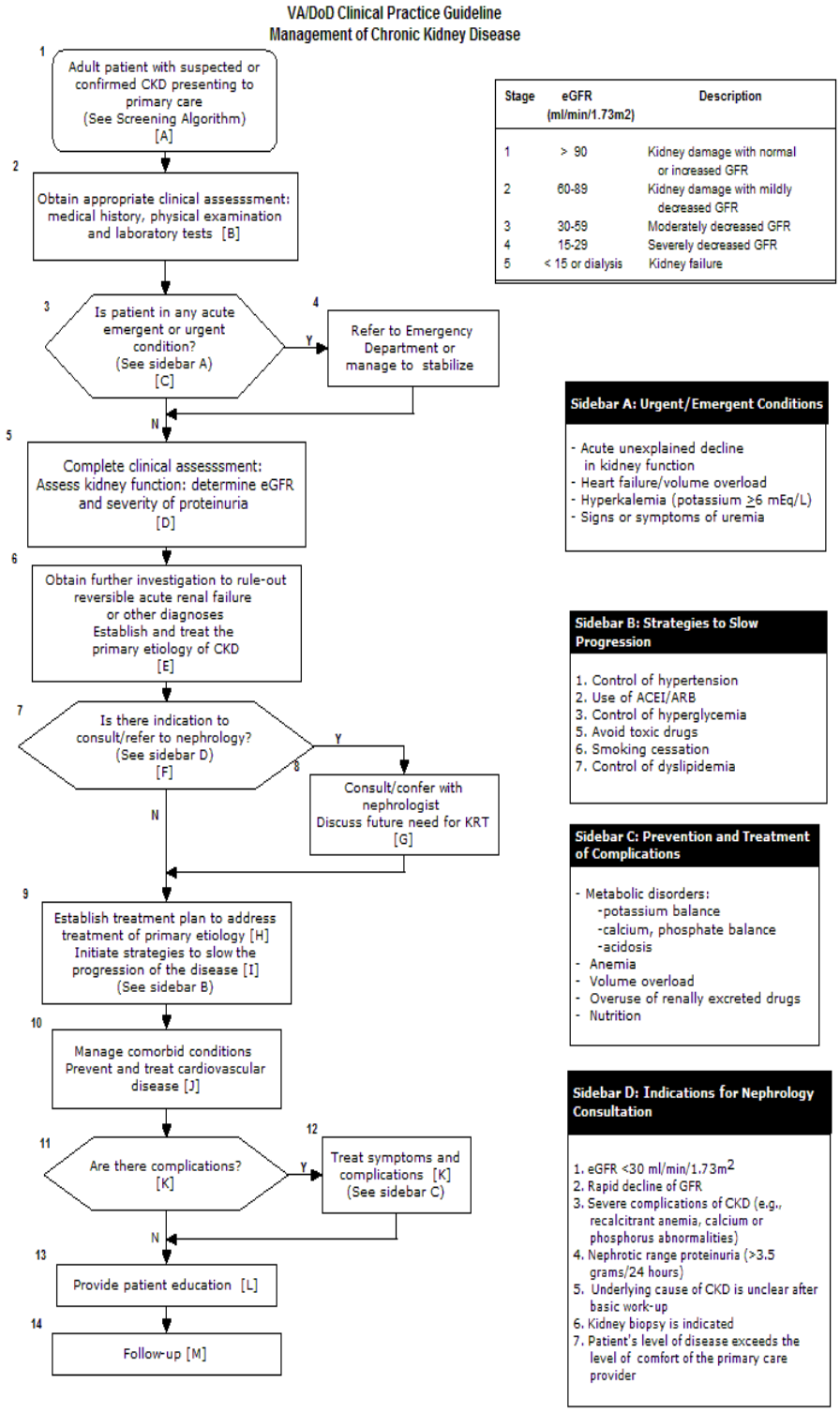
VA/DoD Clinical Practice Guideline
Management of Chronic Kidney Disease
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2 | 60-89 | Kidney damage with mildly decreased GFR
3 | 30-59 | Moderately decreased GFR
4 | 15-29 | Severely decreased GFR
5 | < 15 or dialysis | Kidney failure
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5. Underlying cause of CKD is unclear after basic work-up
6. Kidney biopsy is indicated
7. Patient's level of disease exceeds the level of comfort of the primary care provider
ACEI - Angiotensin-Converting Enzyme Inhibitor , ARB - Angiotensin II Receptor Blockers , DM - Diabetes Mellitus, eGFR - Estimated Glomerular Filtration Rate, KRT - Kidney Replacement Therapy.
6/2/2008

Annotations

Annotation A	*Adult Patient with Suspected or Confirmed CKD Presenting to Primary Care*

1. DEFINITION OF CHRONIC KIDNEY DISEASE

1.1. Patient with Suspected or Confirmed Chronic Kidney Disease (CKD)

This guideline should be used for patients in need of further diagnostic work-up and follow-up. These patients present to primary care and are found to have one of the following (see Table 1.1):

Table 1.1 Definitions of Chronic Kidney Disease

- Persistent decreased eGFR < 60 ml/min/1.73m² on two tests at least three months apart

or

- Proteinuria (> 1+) on dipstick or urine protein-to-creatine ratio > 0.2, confirmed on two tests at least three months apart

or

- Microalbuminuria defined as albumin-to-creatine ratio > 30, confirmed on two out of three urine tests in patients with diabetes mellitus (DM)

or

- Known structural kidney disease defined by imaging or pathologic examination (e.g., polycystic kidney disease [PCKD])

Estimated glomerular filtration rate (eGFR) is the preferred method to assess kidney function.

DEFINITIONS

This guideline is intended to apply both to patients presenting for the first time with CKD and to patients with existing CKD. In both instances, CKD is defined as the presence of decreased eGFR or proteinuria, which can occur together or independently, or the presence of microalbuminuria in patients with diabetes or structural kidney disease. The presence of proteinuria may indicate kidney disease even with a normal eGFR. Any of these patients has a potentially serious kidney disease that might progress to kidney failure.

Note: Pure hematuria without proteinuria is usually a urologic problem. If a referral is needed after the initial work-up by primary care, it should be to urology and not nephrology.

1.2. CKD Classification

- **The most common criterion for chronic kidney disease** is an eGFR < 60 ml/min/1.73m² for at least 3 months.

- **In patients with eGFR > 60 ml/min/1.73m²**, the presence of CKD should be established based on the presence of kidney damage indicated by pathological abnormalities on kidney biopsy, proteinuria (or microalbuminuria in patients with diabetes), or imaging studies.

- **Patients who meet criteria for** CKD may be assigned to a CKD stage based on the presence or absence of abnormalities on urinalysis or imaging and their estimated level of glomerular filtration rate (eGFR).

- **Classification System** of Chronic Kidney Disease (see Table 1.2): Defining stages of CKD requires "categorization" of continuous measures of kidney function, and the "cut-off levels" of eGFR for each stage are inherently arbitrary. Nonetheless, staging of CKD may facilitate the application of clinical

practice guidelines (CPG), clinical performance measures, and quality improvement efforts to the evaluation and management of CKD.

Table 1.2 Classification of Chronic Kidney Disease Stages (based on KDOQI, 2002)

Stage	Description	eGFR (ml/min/1.73m^2)	Common complications
1	Kidney damage with normal eGFR	Normal or $\geq$ 90 ml/min/1.73m^2 with other evidence of chronic kidney damage *	Hypertension more frequent than amongst patients without CKD
2	Mild impairment	60 - 89 ml/min/1.73m^2 with other evidence of chronic kidney damage *	Hypertension frequent
3	Moderate impairment	30 - 59 ml/min/1.73m^2	Hypertension common Decreased dietary calcium absorption Reduced renal phosphate excretion Elevation of parathyroid hormone Altered lipoprotein metabolism Reduced spontaneous protein intake Anemia Left ventricular hypertrophy Salt and water retention Decreased renal potassium excretion
4	Severe impairment	15 - 29 ml/min/1.73 m^2	As above but more pronounced plus: Metabolic acidosis
5	Established renal failure	< 15 ml/min/1.73m^2 or on dialysis	All the above (with greater severity) plus: Salt and water retention causing edema and apparent heart failure Anorexia Nausea, Vomiting Pruritus (itching without skin disease) Neuropathy, altered mental status

* The "other evidence of chronic kidney damage" may be one of the following:
- Persistent microalbuminuria in a diabetic
- Persistent proteinuria
- Persistent hematuria of renal origin
- Structural abnormalities of the kidneys demonstrated on ultrasound scanning or other radiological tests, e.g., polycystic kidney disease, reflux nephropathy
- Biopsy-proven chronic kidney disease such as glomerulonephritis or interstitial nephritis (most of these patients will have microalbuminuria or proteinuria, hematuria or low eGFR)

2. EARLY DETECTION OF KIDNEY DISEASE

2.1. Case Identification/Screening

1. Patients with hypertension, diabetes, cardiovascular disease, or a family history of kidney disease should be screened annually for the presence of kidney disease. [C]
2. Screening for CKD may be considered in patients with other conditions that have shown high incidence of CKD. [C]
    a. Persistent hematuria (after exclusion of other causes, e.g., urological disease)
    b. Recurrent urinary tract infections or urinary obstruction
    c. Systemic illness that can affect the kidney (e.g., Human Immunodeficiency Virus (HIV), Systemic Lupus Erythematosis, hyperuricemia, multiple myeloma).
3. Testing for kidney disease includes urinalysis and estimation of the glomerular filtration rate (eGFR). [B]
4. Patients with diabetes who have a negative urine protein by dipstick should be tested for the presence of microalbuminuria. [B]

(See **Appendix B-1: Screening Algorithm for CKD)**

Screening can be performed using a microalbumin-sensitive dipstick or measurement of microalbumin-to-creatinine ratio in a morning urine sample.)

Annotation B	*Obtain Appropriate Clinical Assessment: Medical History, Physical Examination, and Laboratory Tests*

3. EVALUATION OF PATIENTS WITH CKD

For every newly discovered patient with kidney disease and those with acute worsening of CKD, the history, physical examination, and basic laboratory evaluation remain the cornerstone for establishing etiology and ruling out reversible causes. Clinical assessment will help identify the clinical markers that indicate kidney disease and outline basic diagnostic testing required in all patients.

Once CKD has been identified, goals include determining the severity of the disease, establishing the most likely cause (or causes), and evaluating associated complications and comorbid conditions.

3.1. Medical History

1. The patient with CKD should be evaluated for underlying (causative or contributory) medical conditions. A targeted history to detect the presence and possible contribution of conditions present in a patient with new or established CKD includes: [I]
    a. History of diabetes, hypertension, cardiovascular disease, lower urinary tract symptoms suggestive of urinary obstruction, hepatitis B or C, HIV, kidney stones, urinary tract infections, symptoms suggestive of a systemic vasculitis (e.g., rash, arthritis, serositis), or chronic pain syndrome (raising suspicion for analgesic abuse), genito-urinary malignancy, history of abdominal/pelvic surgery or radiation, exposure to environmental toxins.
    b. There are no symptoms that are specific to and diagnostic of CKD itself. When patients develop the following symptoms in the presence of renal failure (eGFR<15 ml/min/1.73m^2) these symptoms are usually attributed to their CKD.
        - Sleep disturbance
        - Decreased attentiveness
        - Nausea, vomiting, anorexia, weight change
        - Dyspnea, orthopnea, leg swelling
        - Fatigue, muscle cramps, restless legs, peripheral neuropathy
        - Pruritus.
    c. Medications should be reviewed to identify those that may be contributing to renal impairment including: nonsteroidal anti-inflammatory drugs (NSAIDs), other analgesics, diuretics, lithium, cyclosporine, tacrolimus, antiviral agents, chemotherapeutic agents, antibiotics, allopurinol, and dietary and herbal supplements (see Appendix D-2).

        Note: Angiotensin-converting enzyme inhibitors (ACEI) and Angiotensin II Receptor Blockers (ARB), which are generally preferred agents in CKD due to their renoprotective effects, may cause an acute decline in the eGFR due to hemodynamic effects in some cases requiring discontinuation of the drug.
    d. Family history of ESKD or of a particular kidney disease (e.g., polycystic kidney disease [PCKD]).

3.2. Physical Examination

1. The physical examination should include the following: [I]
    a. Height, weight, and body mass index
    b. Vital signs, including orthostatic blood pressure and pulse
    c. Volume assessment (rales, jugular venous distension, peripheral edema, and cardiac heave/gallop/rub)
    d. Abdominal findings (mass, bruit, palpable bladder, and flank tenderness)
    e. Integument (rash, stigmata of atheroembolic disease, or ischemia)
    f. Extremities: foot examination, femoral artery (bruit), joints (arthritis).

3.3. Laboratory Tests

1. Routine laboratory testing for diagnosis and routine follow-up of patients with CKD should include: [I]
    a. Urinalysis and examination of urinary sediment as indicated
    b. Random microalbumin-to-creatinine ratio in patients with diabetes (urine protein-to-creatinine ratio is acceptable if there is overt proteinuria on dipstick)
    c. Sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), creatinine (S_{Cr}) and eGFR, glucose, calcium, phosphorous, albumin, total protein, and lipid profile
    d. Complete blood count with differential
    e. Additional tests may be indicated depending on the differential diagnosis for CKD or particular complications in a given patient.

    See Appendix B-3 – Specialized Laboratory Studies for the Diagnosis of Kidney Disease.
    See Section 4.4 for the recommendation regarding ultrasound.

Annotation D	*Complete Clinical Assessment: Assess Kidney Function: Determine eGFR and Severity of Proteinuria (Rate of Decline*

4. ASSESSMENT OF KIDNEY FUNCTION

4.1. Measuring Disease Progression

Table 4.1. Stages of Chronic Kidney Disease (CKD)

Stage	eGFR (ml/min/1.73m^2)	Description	Action*
1	≥ 90	Kidney damage with normal or increased GFR	Diagnosis and treatment. Treatment of comorbid conditions, slowing progression, CVD risk reduction
2	60-89	Kidney damage with mildly decreased GFR	Estimating progression
3	30-59	Moderately decreased GFR	Evaluating and treating complications
4	15-29	Severely decreased GFR	Preparation for kidney replacement therapy
5	< 15 or dialysis	Kidney failure	Replacement (if uremia present)

** Includes action from the preceding stages*

The eGFR is a measure of the filtering capacity of the kidneys. In patients with CKD eGFR declines over time and is associated with an increased risk of adverse outcomes including death. Thus, both the baseline level of eGFR and the rate of change in eGFR are key pieces of information that should inform the management of patients with CKD.

While not a perfect reflection of true GFR, eGFR calculated using the MDRD equation has the advantage of being easily communicable to patients who might be encouraged to "know their number." Staging provides a systematic and uniform classification of CKD (see Table 4.1). Patients in more advanced stages are more likely to progress to the point of needing dialysis and are also more likely to experience complications related to CKD, which are relatively uncommon at earlier stages. To accommodate the fact that at any stage of CKD there can be considerable variability in disease progression between individuals, the rate of loss of eGFR should also be incorporated into the clinical management of patients with CKD of any stage.

Note: The term end-stage kidney disease (ESKD) refers to patients on dialysis or with a kidney transplant, similar to the term end stage renal disease (ESRD) used elsewhere. ESRD is an administrative term used in the U.S., where the Medicare program finances the care of most dialysis and transplant patients. ESRD overlaps with but is not identical to CKD Stage 5.

4.2. Estimating GFR

1. The severity of CKD should be classified based on the level of the estimated glomerular filtration rate (eGFR) (see Table 4.2).
2. Kidney function in patients with CKD should be assessed by formula-based estimation of GFR (eGFR), preferably using the 4-variable Modification of Diet in Renal Disease (MDRD) equation. [A]
3. Serum creatinine alone should NOT be used as a measure of kidney function. [B]
4. All clinical laboratories should report an estimate of GFR (4-variable MDRD, 6-variable MDRD, or Cockroft-Gault equations) alongside a measurement of serum creatinine. [Expert Opinion]
5. In clinical laboratories without the ability to automatically incorporate race into the MDRD calculation, adjusted values for race should be determined (multiply by 1.21 for African-Americans). [B]
6. There is no need to collect 24-hour urine samples to measure creatinine clearance. [D]

Clinicians without access to automated reporting of eGFR can:

1. Use a web-based tool at : http://www.nkdep.nih.gov/professionals/gfr_calculators/index.htm
2. Calculate eGFRs using the actual MDRD equation:

$$eGFR = 186 \times [S_{Cr}]^{-1.154} \times [age]^{-0.203} \times [0.742 \text{ if female}] \times [1.210] \text{ if black}$$

Key: GFR=glomerular filtration rate; MDRD=Modification of Diet in Renal Disease; S_{Cr}=Serum creatinine concentration

3. For laboratories using an isotopic dilution mass spectrometry (IDMS) traceable measurement of serum creatinine the following formula should be used:

$$eGFR = 175 \times [S_{Cr}]^{-1.154} \times [age]^{-0.203} \times [0.742 \text{ if female}] \times [1.210] \text{ if black}$$

Key: GFR=glomerular filtration rate; MDRD=Modification of Diet in Renal Disease; S_{Cr}=Serum creatinine concentration

Table 4.2. Classification of Chronic Kidney Disease (eGFR)

Stage	eGFR (ml/min/1.73m²)
1	≥ 90
2	60 – 89
3	30 – 59 Known to be stable [a] Newly diagnosed or progressive [b]
4	15 – 29 Known to be stable [a] Newly diagnosed or progressive [b]
5	< 15

[a] Stable kidney function is defined as a change of eGFR of <15% (< 2 ml/min/1.73m²) over 6 months or more

[b] Progressive decline in kidney function is defined as 15% fall in eGFR (> 2 ml/min/1.73m²) over 6 - 12 months or longer

4.3. Assessing Proteinuria

1. Proteinuria should initially be assessed using a conventional dipstick. A first morning specimen is preferred, but random urine specimens are acceptable (see Table 4.3 and Table 4.4).
    a. If the dipstick is 1+ or greater, a quantitative test should be performed using the random urine protein-to-creatinine ratio
    b. A protein-to-creatinine ratio of > 0.2 is considered abnormal (> 200 mg protein/g creatinine).
2. Microalbuminuria – in patients with diabetes – should be assessed using a laboratory method expressed as an albumin-to-creatinine ratio. If dipsticks designed to detect urinary microalbumin are used, positive tests should be followed by laboratory confirmation.
3. The diagnosis of microalbuminuria cannot be reliably made in the presence of an acute medical condition. As far as it is practicable, the best possible metabolic control of diabetes should be achieved before evaluating for microalbuminuria. Patients should not be screened during intercurrent illness or after heavy exercise.
4. It is important to consider other causes of increased albumin excretion, especially in the case of Type 1 diabetes present for < 5 years. In addition to the previously mentioned conditions, other causes can include menstrual contamination, vaginal discharge, uncontrolled hypertension, and heart failure.
5. A 24-hour urine collection for protein and creatinine is not needed for quantitation of proteinuria, as it is more cumbersome for patients and prone to collection errors.

    24-hour urine collection may be considered for: pregnant women, extreme age and weight, malnutrition, skeletal muscle disease, paraplegia or quadriplegia, patients with a vegetarian diet and rapidly changing kidney function.

Table 4.3. Urine Dipstick: Interpretation

Protein	Blood	Consider
Negative	Negative	Rule-out false negative, microalbuminuria, multiple myeloma and other paraproteinuria Heart failure, volume depletion or obstruction, ischemic nephropathy
Positive	Negative	Rule-out false positive, benign, or orthostatic proteinuria Consider diabetes, HTN, tubulo-interstitial diseases, nephrotic syndrome Quantitate proteinuria
Positive	Positive	UTI, pyelonephritis, RPGN, GN, HIV, vasculitis, pulmonary-kidney syndrome, HUS, TTP, malignant HTN, nephrotic syndrome, nephrolithiasis with obstruction, atypical DM, PCKD
Negative	Positive	Look for urologic cause of hematuria

Key: DM: Diabetes Mellitus; GN: Glomerulonephritis; HTN: Hypertension; HUS: Hemolytic Uremic Syndrome; PCKD: Polycystic Kidney Disease; RPGN: Rapidly Progressive Glomerulonephritis; TTP: Thrombotic Thrombocytopenic Purpura; UTI: Urinary Tract Infection

Table 4.4. Evaluation of Proteinuria

A	Random urine protein-to-creatinine ratio estimates 24-hour excretion of protein in grams/24 hours. To perform the test, a random urine sample is submitted to the laboratory for protein concentration (in mg/dL) and creatinine concentration (in mg/dL). The protein concentration is divided by the creatinine concentration, and the unit-less number is the estimated daily protein excretion in gm/24 hours.
B	Further define cause based on the degree of proteinuria/albuminuria: Normal: < 150 mg/24 hours or < 0.2 protein-to creatinine ratio Microalbuminura: 30 – 300 mg/24 hours (specifically albumin; usually measured in diabetics) Nephrotic range proteinuria: > 3 g/24 hours
C	Degree of proteinuria and differential diagnosis 1. Overflow proteinuria: Trace or negative dipstick protein but a disproportionate larger amount on a 24-hour test. Its presence suggests: light-chain proteinuria as seen in multiple myeloma or lymphoproliferative process, or hemolysis (only if dip also blood +), since dipstick only measures albumin not globulins, such as light chains. 2. Proteinuria: 150 mg – 2000 mg/24 hours. a. May occur with interstitial diseases as well as glomerular disease b. Interstitial diseases resulting in proteinuria include analgesic nephropathy, collagen vascular diseases (Sjogren's syndrome, lupus), heavy metal toxicity, interstitial nephritis (drugs or infectious), or granulomatous diseases 3. Proteinuria greater than 3,500 mg/24 hours suggests glomerular proteinuria and these patients should be referred to a nephrologist. Rule-out diabetes nephropathy, hepatitis, HIV, vasculitis, malignancy, and GN 4. Massive proteinuria (> 6 gm/24 hours). Focus history and physical to rule out HIV, severe focal glomerulosclerosis or minimal change disease. Refer to a nephrologist.
Key: GN: Glomerulonephritis; IEP: Immuno-Electrophoresis; UPEP: Urine Protein Electrophoresis; UTI: Urinary Tract Infection	

4.4. Imaging the Kidney

1. Consider kidney ultrasound in cases of unknown etiology to evaluate for kidney size, anatomical abnormality, or urinary tract obstruction.

Annotation C	*Is Patient in Any Acute Emergent or Urgent Condition?*

5. URGENT/EMERGENT CONDITIONS

1. Evaluation should identify complications of CKD that may require immediate treatment. These may include:
    a. Acute renal failure
    b. Fluid overload, especially pulmonary edema
    c. Hyperkalemia (potassium $\geq$ 6.0 mEq/L)
    d. Metabolic acidosis (bicarbonate $\leq$ 16 mEq/L)
    e. Pericarditis
    f. Encephalopathy
    g. Uremic symptoms, such as nausea, vomiting, and anorexia.

Annotation E	*Obtain Further Investigation to Rule-Out Reversible Acute Renal Failure or Other Diagnoses; Establish and Treat the Primary Etiology of CKD*

6. REVERSIBLE CONDITIONS

1. Any rapid reduction in eGFR in a patient with CKD should be considered acute kidney failure and evaluated promptly. [I]
2. Before ascribing deterioration in kidney function to progression of the patient's underlying chronic disease, evaluate for reversible causes such as: [I]
    a. Volume depletion
    b. Severe heart failure
    c. Urinary tract obstruction
    d. Acute tubular necrosis occurring in the setting of hypotension or nephrotoxic agents, such as radiocontrast or antibiotics
    e. Acute interstitial nephritis, often due to drugs such as NSAIDs or antibiotics.

7. PRIMARY ETIOLOGY OF KIDNEY DISEASE

1. Use history, physical examination, laboratory tests, and imaging procedures to establish the most likely etiology. [I]
2. Patients with CKD not related to hypertension or diabetes or in whom the etiology is uncertain may benefit from a referral to a nephrologist for evaluation and treatment. [I]
3. A kidney biopsy should be considered in patients with nephrotic range proteinuria (urine protein-to-creatinine ratio > 3.5) particularly in the absence of diabetes to determine the etiology of the kidney disease.
4. Urology should be consulted for patients with urinary tract obstructions. [I]

Annotation F	*Is there Indication to Consult/Refer to Nephrology?*

8. CONSULTATION WITH/REFERRAL TO NEPHROLOGY

Indications for a nephrology referral in CKD:

- Underlying cause is unclear after the basic work-up
- Kidney biopsy is indicated
- eGFR < 30 ml/min/1.73m^2
- Rapid progression of CKD
- Superimposed acute kidney failure
- Management is beyond the comfort of the individual provider

Nephrology consultation for help in diagnosis and treatment is indicated in:

1. Patients with eGFR < 30 ml/min/1.73m^2) to facilitate education and planning for renal replacement therapy (dialysis or kidney transplant).
2. Patients with kidney function that is deteriorating rapidly (e.g., eGFR decline of 50 percent eGFR from previous measure over 6 months or less).
3. Patients with metabolic complications of CKD (e.g., anemia, secondary hyperparathyroidism).
4. Patients with CKD of unclear etiology after the initial work up, or a known or suspected kidney condition requiring specialized care (e.g., a glomerulonephritis).

Annotation G	*Discuss Future Need for KRT*

1. ESKD and kidney replacement therapy (KRT) should be discussed with patients by the primary care provider while referring to nephrology for assistance in evaluation and treatment:
    a. Discuss the progression of kidney disease to ESKD, in general terms
    b. Explain why the patient needs to see the nephrologist
    c. Reinforce and review the information provided to the patient by the nephrologist
    d. Discuss the principles of dialysis (peritoneal dialysis or hemodialysis) and transplantation, in general terms
    e. Maintain consistency of information between the primary care provider and the nephrologist.

Annotation H	*Establish Treatment Plan to Address Treatment of Primary Etiology*

9. MANAGEMENT OF CKD – PROMOTION OF GENERAL HEALTH

1. Treatment plan for patients diagnosed with CKD should include routine monitoring of kidney function and promotion of general health, addressing cardiovascular risk factors as related to CKD. These may include:
    a. Regular measurement of kidney function (eGFR) to assess the severity of kidney impairment (see Section 4)

b. Management of the primary etiology
c. Initiation of strategies to slow the progression of the disease
d. Prevention and management of complications
e. Management of co-existing comorbid conditions (e.g., diabetes, hypertension, cardiovascular disease).

2. There is insufficient evidence to support a particular management strategy for reducing cardiovascular risk in patients with CKD, although the prevalence of cardiovascular disease is high in this population. In the absence of evidence to support a tailored approach in patients with renal insufficiency, strategies applicable to the general population should be considered.

Annotation I	*Initiate Strategies to Slow the Progression of the Disease*

10. STRATEGIES TO SLOW THE PROGRESSION OF THE DISEASE

The progression of kidney disease may be slowed with the use of non-invasive interventions.

10.1 Control of hypertension
10.2 Use of an ACEI or ARB
10.3 Protein restriction
10.4 Control of hyperglycemia in patients with diabetes
10.5 Avoidance of nephrotoxic drugs and adjusting medication doses as indicated
10.6 Smoking cessation
10.7 Control of dyslipidemia

10.1. Control of Hypertension

1. Blood pressure should be closely monitored in all patients with CKD and checked at each visit. [I]
2. Blood pressure measurement should conform to published standards (see VA/DoD CPG for Management of Hypertension). [C]
3. Treatment of high blood pressure in CKD should include identification of target blood pressure levels, nonpharmacologic therapy, and specific antihypertensive agents for the prevention of progression of kidney disease and development of cardiovascular disease.
4. Antihypertensive therapy should be adjusted to achieve blood pressure of < 130/80 mm Hg. [C]

Non Pharmacologic Interventions

5. All patients with CKD with hypertension should be offered life-style advice, including maintenance of normal body weight (body mass index 18.5 to 24.9 kg/m^2), reduction in dietary sodium intake (< 2 g/day), regular aerobic physical exercise, smoking cessation, and limitation of alcohol intake. [B]

Pharmacologic Interventions

6. ACEIs or ARBs are the preferred agent for patients with kidney disease and hypertension. ACEIs may be preferred based on cost. ARBs may be substituted for patients with an ACEI induced cough. [A]
7. Many patients will require two or more medications to achieve their target blood pressure control. A diuretic should be used when a second blood pressure medication is needed, or if hyperkalemia occurs. Thiazide diuretics may be used if estimated GFR > 30 ml/min/1.73m^2, but loop diuretics are usually needed for patients with lower eGFR. Potassium-sparing diuretics should be used with caution in patients with CKD. (see Table 10.1)
8. An increase of serum creatinine, as much as 30 percent above baseline after ACEI or ARB initiation, may be tolerated. ACEIs or ARBs should not be discontinued for this situation, since these medications are renoprotective.
9. Patients with refractory hypertension, defined as inability to achieve goal blood pressure despite combination therapy with three drugs from complementary classes (including a diruetic), may benefit from an evaluation by a specialist in hypertension.

Table 10.1. Summary of Number of Antihypertensive Agents Required to Reach Target Blood Pressure

Study, Year	Target Blood Pressure (mm Hg)	Achieved Blood Pressure	Mean Number of Agents
IDNT, 2001	Systolic < 135	Systolic 138	2.6
RENAAL, 2001	Systolic < 140	Systolic 141	2.7
ABCD, 2000	Diastolic < 75 or 80-89[a]	132/78 and 138/86[a]	2.4
CSG Captopril Trial, 1993	Systolic < 140, Diastolic < 90	Mean arterial pressure 96±8 and 100±8[b]	1-3[b]

[a] Denotes intensive blood pressure control group and moderate blood pressure control group, respectively.
[b] Denotes captopril and placebo groups, respectively, number of agents inferred from report; there were approximately 25% normotensive participants.
Source: KDOQI Diabetes and CKD, 2007

10.2. Use of an ACEI or ARB

1. Patients with non-DM CKD with hypertension or diabetes with macroalbuminuria should be treated with an ACEI or ARB to slow the progression of kidney disease [A] and reduce proteinuria [A].
(See VA/DoD CPG for Management of Diabetes Mellitus)
2. Patients with diabetes and microalbuminuria should be treated with an ACEI or ARB to slow the progression from microalbuminuria to macroalbuminuria, considered a surrogate for progression to CKD. [A]
3. ACEIs and ARBs should be initiated at low doses and titrated to moderate to high doses as used in clinical trials. [A]
4. There is insufficient evidence to recommend combination therapy with an ACEI and ARB to slow the progression of kidney disease except in a limited population of non-DM CKD. [C]
5. Creatinine and potassium levels should be monitored one to two weeks after initiation or after a change in dose of ACEI or ARB therapy and periodically to maintain a normal range. [C]
6. Treatment with an ACEI or ARB should not be initiated in patients with hyperkalemia (> 5.5). [D]
7. People who develop cough on an ACEI should be switched to an ARB. Some people who develop angioedema on an ACEI may be switched to an ARB but require careful monitoring since some may also develop angioedema on an ARB. [C]
8. In most patients, an ACEI or ARB should be continued unless:
    a. There is an acute GFR decline of > 30 percent within the first two weeks after initiation. [B]
    b. Serum potassium is ≥ 6 mEq/L, despite appropriate treatment. [B]
9. If ACEIs and ARBs are not tolerated, a nondihydropyridine calcium channel blocker, either verapamil or diltiazem, may be considered to reduce proteinuria. [B]

10.3. Protein Restriction

1. There is insufficient evidence to recommend the routine implementation of a low protein diet (≤ 0.6g/kg/day) to slow the loss of GFR in patients with CKD. [D]
2. A low protein diet may delay the onset of uremic symptoms in patients close to needing dialysis but this benefit must be weighed against the risk of protein malnutrition. [B]

10.4. Control of Hyperglycemia in Patients with Diabetes

1. In patients with diabetes, glycemic control should be managed according to the VA/DoD CPG for Management of Diabetes Mellitus.

2. In patients with CKD, the use of antidiabetic agents should be reviewed and modified since several are renally excreted (see Appendix D).

10.5. Avoidance of Nephrotoxic Drugs and Adjustment of Medication Doses as Indicated

1. Use of prescription and over-the-counter drugs, including herbal supplements, should be reviewed and doses modified or adjusted to the level of kidney function (per CrCl or sCr) in patients with CKD. [C]
2. Avoid or limit exposure to nephrotoxic drugs. [D]
3. Patients with CKD should preferentially undergo imaging studies that do not require the use of iodinated contrast. If iodinated contrast cannot be avoided, low- or iso-osmolar non-ionic agents should be used. Consider the use of measures to prevent contrast nephropathy, including intravenous fluids. [B]

   Clinicians should also be aware of recent FDA warnings on the risk for nephrogenic systemic fibrosis with the use of gadolinium-based contrast agents in patients with acute or severe chronic kidney disease.

   (See Appendix D-2)

10.6. Smoking Cessation

1. Patients should be advised to stop smoking to reduce cardiovascular risk [A] and slow the progression of kidney disease [C].
   (See the VA/DoD Guideline for Management of Tobacco Use.)

10.7. Control of Dyslipidemia

1. Patients with CKD or diabetic nephropathy who have dyslipidemia should be treated to reduce cardiovascular risk [A] and slow progression of kidney disease [B].

   (See VA/DoD CPG for Management of Dyslipidemia.)
2. Statin and fibrate therapies have a higher frequency of adverse events in patients with CKD that warrants careful monitoring. Lower statin doses may be necessary to reduce the risk of myopathy. [I]

Annotation K	*Treat Symptoms and Complications*

11. COMPLICATIONS OF CKD

Metabolic abnormalities:

- **11.1** Disorders of potassium balance
- **11.2** Disorders of calcium and phosphate metabolism (bone mineral)
- **11.3** Acid based abnormalities
- **11.4** Hematologic abnormalities (anemia)
- **11.5** Volume overload
- **11.6** Disorders of nutrition
- **11.7** Adjustment of medication doses
- **11.8** Immunization

11.1. Disorders of Potassium Balance

1. Patients with high levels of potassium (> 6 mEq/L) should be referred to the emergency department.

2. Treatment of high levels of potassium should be guided by balancing the benefit and harm to address the most likely etiology:
    a. Dietary restriction of potassium intake considering a consultation with a dietitian (see Table 11.1)
    b. Increase urinary potassium excretion using loop diuretics in the absence of volume depletion
    c. Lower dose or withdraw of ACEI/ARBs if the potassium is > 6 mEq/L
    d. Treating acidosis with oral sodium-bicarbonate
    e. Increase fecal potassium excretion using sodium polystyrene sulfonate (Kayexalate®) (with sorbitol) 30 to 60 g daily or every other day
    f. Refer to nephrology if etiology is unknown.

Table 11.1. Potassium Content of Foods

Highest content (> 25 mEq/100 g)	Dried figs, molasses, seaweed
Very high content (>12.5 mEq/100 g)	Dried fruit (dates, prunes), nuts, avocados, bran cereals, wheat germ, lima beans
High content (> 6.2 mEq/100 g)	Vegetables: spinach, tomatoes, broccoli, winter squash, beets, carrots, cauliflower, potatoes Fruits: bananas, cantaloupes, kiwi, oranges, mango

11.2. Disorders of Bone Mineral Metabolism

1. Serum phosphorus, calcium, and intact parathyroid hormone (PTH) should be checked at least annually in patients with eGFR < 45 ml/min/1.73 m^2 and at least every 6 months if abnormal.
2. Goal calcium levels should be within "normal" limits (8.4 - 10.5mg/dL). Phosphorus should be maintained within the range of 2.7 to 4.6 mg/dL, though this goal may not be achievable in patients with very advanced CKD (eGFR < 15 ml/min/1.73 m^2).
3. Serum phosphorus above the target should be treated initially with dietary phosphorus restriction and phosphorus binders.
    a. Calcium carbonate or calcium acetate should be used as first line binders except in patients with a serum calcium level close to the upper limit of normal (e.g., 10.2 mg/dL) or above the normal range.
    b. If hypercalcemia or hypocalcemia occur after correction of hyperphospatemia, patients should be referred to nephrology.
4. Patients in whom hyperphosphatemia or hypocalcemia cannot be controlled with phosphate binders and those with intact parathyroid hormone (PTH) levels greater than twice the normal value should be referred to nephrology.

11.3. Acid Based Abnormalities

1. Serum bicarbonate (measured as plasma total CO_2) should be monitored at least annually and should be maintained at or above 22 mEq/L. [C]
2. Oral bicarbonate replacement in the form of sodium bicarbonate tablets is indicated when the serum total CO_2 falls below 22 mEq/L. [C]
3. Caution should be used when administering bicarbonate to patients with uncontrolled hypertension or heart failure. [C]

11.4. Hematologic Abnormalities (Anemia)

1. Hemoglobin is the preferred test for evaluation of anemia.
2. Hemoglobin should be measured at least annually in patients with CKD.

3. Anemia should be diagnosed when the hemoglobin is < 13.5 g/dL in males and < 12.0 g/dL in females.
4. Evaluation of anemia should consist of measurement of at least the following:
    a. Hemoglobin
    b. Complete blood count including white blood cell and platelet count
    c. Red blood cell indices (mean corpuscular volume, mean corpuscular hemoglobin concentration)
    d. Absolute reticulocyte count
    e. Iron parameters:
        - Serum iron
        - Total Iron Binding Capacity (TIBC)
        - Percent transferrin saturation (serum iron × 100 divided by TIBC) [TSAT]
        - Serum ferritin
        - Content of hemoglobin in reticulocytes (CHr) if available
    f. Other tests as indicated by clinical situation (e.g., test for occult blood in stool).
5. Supplemental iron should be provided to anemic CKD patients whose serum ferritin < 100 ng/ml or TSAT < 20 percent or CHr < 29 pg/cell [A]. Hemoglobin and iron parameters should be monitored at least every 6 months in patients receiving supplemental iron. [I]
6. Consider treatment of anemia in patients with CKD with an erythropoietic stimulating agent if the hemoglobin is less than < 10 g/dL and after appropriate evaluation and ruling out other possible causes. Such treatment may require referral to nephrology or hematology and more frequent monitoring of hemoglobin values. [I]
7. For patients receiving erythropoietic stimulating agents, the target hemoglobin should not exceed 12 g/dL. [B]
8. Supplements of Vitamin C, androgens, or carnitine should not be administered as adjuvants to the treatment of anemia of CKD. [D]

Adverse effects of therapy with erythropoietic stimulating agents:

- Hypertension occurs in 20 to 30 percent of patients and is easily treatable
- Vascular access thrombosis
- Hyperkalemia
- Myalgia and flu-like symptoms
- Injection pain and skin irritation around the injection site
- Pure red cell aplasia is very rare and is associated with anti-erythropoietin antibodies.

11.5. Volume Overload

RECOMMENDATIONS

1. Patients with symptoms consistent with volume overload should be evaluated for cardiac causes, and cardiovascular risk should be assessed (see VA/DoD CPG for Management of Chronic Heart Failure). [I]
2. Patients with CKD and eGFR < 30 ml/min/1.73m^2 and symptoms consistent with volume overload may be considered as a complication of the kidney disease and managed accordingly. [I]
3. The following interventions should be considered in managing volume overload: [B]
    a. Obtain weight at every visit
    b. Restrict dietary sodium to 2 g/day; on occasion, consider measuring urinary sodium concentration to assess compliance with dietary restriction
    c. Use loop diuretics (divided doses may be preferred); if refractory to twice a day dosing, consider adding thiazide-type diuretics with careful follow-up to avoid severe pre-renal azotemia or hypokalemia.

d. If volume overload is refractory to therapy, consider referral to nephrology.

11.6. Disorders of Nutrition

1. Patients may benefit from a dietary evaluation by a medical nutrition therapist and should be advised about a healthy diet and the preferred range of sodium, phosphate, and potassium in their diet (see Annotation L – Patient Education). [C]
2. Additional assessment and dietary counseling should be initiated if body mass index or other biomarker tests indicate deterioration of nutrition status. [I]
3. Diet modifications may be indicated in patients presenting with metabolic disorders in any of the following: [B]
    a. Limiting dietary potassium intake between 50 to 70 mEq/day (1950 – 2730 mg/day) in patients with hyperkalemia
    b. Sodium restrictions in patients with hypertension (< 2 g/day)
    c. Phosphate restriction is indicated in patients with CKD when:
        - Serum phosphorus levels are above 4.6 mg/dl (1.49 mmol/L)
        - Parathyroid hormone (PTH) levels are above normal
    d. Limiting dietary protein to < 0.8 g protein/kg/day may be considered in patients with severe CKD (eGFR < 30 ml/min/1.73m^2). A restricted protein diet should include at least 50 percent being from high biologic value protein sources and ensure sufficient energy level intake to compensate for restriction and avoid malnutrition. There is insufficient evidence to recommend dietary protein restriction for all patients with CKD. (see Table 11.2)

Table 11.2. Recommended Intake of Protein, Energy, and Minerals in CKD

	Protein	Energy	Phosphorus	Sodium
Mild to Moderate CKD (eGFR 25 – 60 ml/min/1.73m^2)	No restriction	No restriction	600 – 800 mg/day	< 2 g/day [a]
Advanced CKD (eGFR < 25 ml/min/1.73m^2)	0.60 – 0.75 g/kg/day [b]	35 kcal/kg/day [c]	600 – 800 mg/day [d] 8 gr/KG	< 2 g/day
a. If hypertensive edema or history of heart failure b. With close supervision and frequent dietary counseling c. 30 kcal/kg/day for individuals 60 years or older d. Along with phosphate binders, as needed				

11.7. Adjustment of Medication Doses

1. Evaluate the patient's drug therapy for potential dosage modification based on kidney dysfunction (i.e., per CrCl or sCr) at each visit. [I]
2. Avoid medications contraindicated in patients with impaired kidney function. [I]

11.8. Immunization

1. *Influenza* immunization is recommend for adults less than age 50 with chronic illness (i.e., heart, lung or kidney disease; asthma; diabetes; anemia or other blood disorders; HIV/AIDS; patients with weakened immune systems) and all adults age 50 and older. [A]
2. *Pneumococcal* immunization should be administered to all adults age 65 and older, and those less than age 65 with chronic illness that places them at the highest risk for serious pneumococcal infection (HIV/AIDS; sickle cell disease; immunosuppressive treatment with radiation, chemotherapy or long-term steroids;

anatomic or functional asplenia; status post organ or bone marrow transplant; nephrotic syndrome, or renal failure). [B]

3. *Patients with CKD should* receive the pneumococcal vaccine, including previously unvaccinated persons and persons who have not received the vaccine within 5 years (and were less than 65 years of age at the time of vaccination). All persons who have unknown vaccination status should receive one dose of the vaccine. [B]
4. Hepatitis B vaccine should be administered to patients receiving hemodialysis. [C]
5. Adults age 60 years and older should be vaccinated with the zoster/shingles vaccine to reduce the occurrence of herpes zoster (shingles). [C]

Annotation J	*Prevent and Treat Cardiovascular Disease*

12. THE RISK FOR CARDIOVASCULAR DISEASE

1. Patients with CKD should be evaluated for risk stratification of cardiovascular disease. Patients with CKD should be assessed for cardiovascular risk including fasting lipid profile, blood pressure, tobacco use (smoking) history, family history of premature cardiovascular disease, obesity, and physical activity level. Strategies to reduce cardiovascular risk factors should be implemented.
    a. For the treatment of hypertension – see VA/DoD Guideline for Management of Hypertension.
    b. For control of dyslipidemia – see VA/DoD Guideline for Management of Dyslipidemia. (Dosage adjustment of statins and careful monitoring is required in patients with CKD)
    c. For the treatment of smoking cessation – see VA/DoD CPG for Management of Tobacco Use.
2. For treatment of ischemic heart disease – see the VA/DoD CPG for Management of Ischemic Heart Disease.
3. For the treatment of congestive heart failure – see the VA/DoD CPG for Management of Chronic Heart Failure.
4. Although the risk of bleeding from anticoagulants/antiplatelets agents is higher in patients with CKD, there is insufficient evidence to recommend a different approach to secondary prevention using aspirin or clopidogrel in patients with CKD. However, there is insufficient evidence to support the use of aspirin for primary prevention of cardiovascular events in all patients with CKD because it is unclear whether the benefits outweigh the risks. [I]

Annotation L	*Provide Patient Education*

13. PATIENT EDUCATION

1. Patient education should begin soon after the diagnosis of CKD. The importance of strategies to delay the progression of kidney disease and avoid further kidney injury must be highlighted. [I]
2. Assessment of adherence to therapy and strategies to overcome barriers should be discussed with all patients. [I]
3. Patients should be provided with information about: [I]
    a. The risk factors, natural history, and health consequences of CKD
    b. Lifestyle changes including smoking cessation, exercise, and dietary modifications needed to prevent progression of kidney disease
    c. Educate patients about receiving annual vaccinations
    d. Inform patients with eGFR < 30 ml/min/1.73m^2 about renal replacement therapy options (hemodialysis, peritoneal dialysis, and transplantation)

e. Patients who are considering hemodialysis in the future should be advised about protecting their non-dominant arm for dialysis vascular access placement.

Annotation M	*Follow-Up*

14. FOLLOW-UP

1. Patients with CKD and an eGFR > 30 ml/min/1.73m^2 with no associated co-morbidities should be followed up every 6 to 12 months.
2. Patients with more advanced CKD should be referred to a nephrologist for consultation and/or continued follow-up.
   (See Table 14.1)

Table 14.1. Classification of CKD and Follow-Up Frequency by Primary Care

Stage	Description	eGFR (ml/min/1.73m^2)	Follow-up Frequency by Primary Care
1	Kidney damage with normal or increased GFR	≥ 90	Not more than routine
2	Kidney damage with mildly decreased GFR	60 - 89	12 months *
3	Moderately decreased GFR	30 -59	6 – 12 months *
4	Severely decreased GFR	15 - 29	3 – 6 months * Refer to Nephrology
5	Kidney failure	< 15 or dialysis	Refer to Nephrology

** Patients who are newly diagnosed or in whom kidney disease is progressing rapidly should be seen more frequently.*

Kidney function should also be checked during intercurrent illness and peri-operatively in all patients with Stage 2 to 5 CKD.

Appendix A: Guideline Development Process

Table A-1: Quality of Evidence (QE)	
I	At least one properly done randomized controlled trial (RCT)
II-1	Well-designed controlled trial without randomization
II-2	Well-designed cohort or case-control analytic study, preferably from more than one source
II-3	Multiple time series evidence with/without intervention, dramatic results of uncontrolled experiment
III	Opinion of respected authorities, descriptive studies, case reports, and expert committees

Table A-2: Overall Quality	
Good	High grade evidence (I or II-1) directly linked to health outcome
Fair	High grade evidence (I or II-1) linked to intermediate outcome; *or* Moderate grade evidence (II-2 or II-3) directly linked to health outcome
Poor	Level III evidence or no linkage of evidence to health outcome

Table A-3: Net Effect of the Intervention	
Substantial	More than a small relative impact on a frequent condition with a substantial burden of suffering; *or* A large impact on an infrequent condition with a significant impact on the individual patient level.
Moderate	A small relative impact on a frequent condition with a substantial burden of suffering; *or* A moderate impact on an infrequent condition with a significant impact on the individual patient level.
Small	A negligible relative impact on a frequent condition with a substantial burden of suffering; *or* A small impact on an infrequent condition with a significant impact on the individual patient level.
Zero or Negative	Negative impact on patients; *or* No relative impact on either a frequent condition with a substantial burden of suffering; or an infrequent condition with a significant impact on the individual patient level.

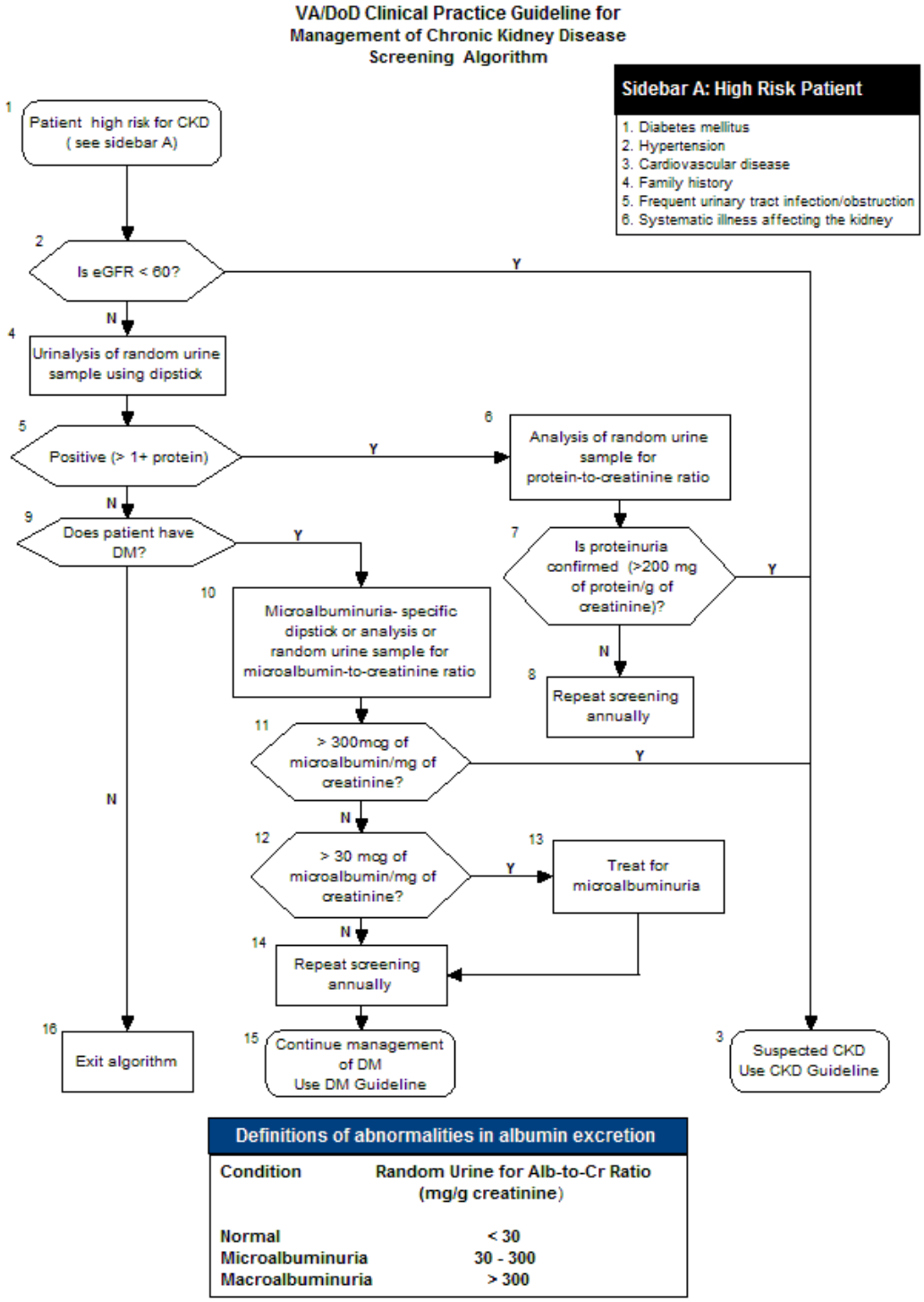
Table A-4: Final Grade of Recommendation				
	The net benefit of the intervention			
Quality of Evidence	**Substantial**	**Moderate**	**Small**	**Zero or Negative**
Good	A	B	C	D
Fair	B	B	C	D
Poor	I	I	I	I

Evidence Rating System

A	A strong recommendation that the clinicians provide the intervention to eligible patients. *Good evidence was found that the intervention improves important health outcomes and concludes that benefits substantially outweigh harm.*
B	A recommendation that clinicians provide (the service) to eligible patients. *At least fair evidence was found that the intervention improves health outcomes and concludes that benefits outweigh harm.*
C	No recommendation for or against the routine provision of the intervention is made. *At least fair evidence was found that the intervention can improve health outcomes, but concludes that the balance of benefits and harms is too close to justify a general recommendation.*
D	Recommendation is made against routinely providing the intervention to asymptomatic patients. *At least fair evidence was found that the intervention is ineffective or that harms outweigh benefits.*
I	The conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention. *Evidence that the intervention is effective is lacking, or poor quality, or conflicting, and the balance of benefits and harms cannot be determined.*

Appendix B: Assessment

Appendix B-1: Screening Algorithm for CKD



Appendix B-2: Etiologic Evaluation

	CLUES	URINE SEDIMENT	RANGE of PROTEINURIA	SPECIAL TESTS
Essential Hypertension	▪ Look for other signs of end organ damage	No formed elements	Trace→Moderate	N/A
Diabetes Mellitus	▪ Frequently associated with retinopathy	< 25% have microscopic hematuria	Microalbuminuria→ Nephrotic	N/A
Glomerulo-nephritis	▪ Use history and physical to focus serological evaluation	Dysmorphic RBCs or RBC casts	Trace→Nephrotic	C_3, C_4, ASO, ANCA, HIV, HEP B & C, ANA, RPR, Blood cultures, Cryoglobulin, anti-GBM, SPEP, UPEP
Interstitial Nephritis	▪ Medication history, fever, rash, and eosinophilia ▪ Classic triad of fever, rash, and eosinophilia is present in a minority only	Pyuria, white blood cell (WBC) casts, eosinophiluria	Trace→Moderate	Galium scanning
Pre-Renal	▪ Clinical diagnosis ▪ Volume depletion, hypotension ▪ Congestive heart failure, sepsis, liver disease	Hyaline casts may be present	None →Trace	FE_{Na} < 1% FE_{Urea} < 35%
Urinary Tract Obstruction	▪ Suggested by history and physical exam ▪ May or may not be oliguric	Benign or may have hematuria	None	Kidney ultrasound, bladder scan, other imaging studies may be necessary
Paraproteinemia	▪ Globulin > albumin; constitutional symptoms, anemia out of proportion to kidney failure	May have hematuria, RBC casts, granular casts	May have false negative dipstick, trace to nephrotic range by spot protein/creatinine	SPEP/UPEP, serum free light chain ratio IEP or immunofixation to confirm, hypercalcemia may be present, ESR
Polycystic Kidney Disease	▪ Palpable kidneys ▪ +/- family history ▪ Flank pain	May have hematuria	Trace→Moderate	Kidney ultrasound or CT
Renovascular Disease	▪ Late onset or refractory hypertension ▪ Smoking history ▪ Clinical evidence of atherosclerotic disease	Benign	None →Trace	Asymmetric kidney size on ultrasound; abnormal duplex of kidney arteries.; additional investigation (e.g., captopril radionucleotide scan, MRA) may be indicated
Vasculitis	▪ Constitutional symptoms, fever, peripheral neuropathy, rash, may have respiratory involvement	Hematuria; granular casts	Trace →Nephrotic	C_3, C_4, ANA, ANCA; HepBsurface Ag; HepC Ab; cryoglobulins; ESR, CRP; RF; HIV
Acute Tubular Necrosis	▪ Medication history ▪ History of hypotension, crush injury, IV contrast	Muddy brown granular casts; renal tubular epithelial cells; crystalluria	Trace	FE_{Na} > 2%; Uosm < 350 mOsm/l FE_{Urea} > 35% CPK, urine myoglobin
Atheroembolic Disease	▪ "Stuttering" GFR loss, stigmata of emboli ▪ History of endovascular procedure	Hematuria and/or eosinophiluria may be present	Trace →Moderate	Eosinophilia; low complements

Appendix B-3. Specialized Laboratory Studies for the Diagnosis of Kidney Disease

Laboratory Test	Significance
Serum complement levels (C_3,C_4)	May be decreased in: o Post-streptococcal glomerulonephritis o Post-infectious glomerulonephritis o Membranoproliferative glomerulonephritis o Lupus nephritis o Cryoglobulinemia o Atheroembolic disease
Anti-nuclear antibody (ANA)	Positive in: o Lupus nephritis
Anti-neutrophil cytoplasmic antibody (ANCA)	Positive in: o Wegener's granulomatosis (C-ANCA) o Microscopic polyangiitis (P-ANCA) o Pauci-immune rapidly progressive glomerulonephritis (RPGN) (P-ANCA)
Anti-glomerular basement membrane antibodies (anti-GBM)	Positive in: o Goodpasture's syndrome o Anti-GBM associated RPGN
Serum protein electrophoresis (SPEP) Urine protein electrophoresis (UPEP) Serum free light chain ratio	Positive for monoclonal immunoglobulin in: o Multiple myeloma o Amyloid o Light-chain deposition disease
Cryoglobulins	Positive in: o Cryoglobulinemia
Hepatitis B surface antigen	Associated with: o Membranous nephropathy o Polyarteritis nodosa o Membranoproliferative nephritis
Hepatitis C serologies	Associated with: o Mixed cryoglobulinemia o Membranoproliferative glomerulonephritis o Membranous nephropathy
HIV serologies	Associated with: o Focal and segmental glomerulosclerosis (FSGS)
Eosinophiluria	Associated with: o Acute interstitial nephritis o Atheroembolic disease o May be positive in any condition with eosinophilia or pyuria

Appendix B-4. Kidney Imaging Studies

Imaging study	Significance
Kidney ultrasound	Diagnosis of: o Obstructive kidney disease o Polycystic kidney disease o Assessment of kidney size: ▪ Enlarged in diabetic nephropathy, amyloid ▪ Small in chronic kidney disease ▪ Asymmetric in renovascular disease
Kidney Doppler	Diagnosis of: o Renovascular disease o Renal vein thrombosis
Radioisotope kidney scan	Diagnosis of: o Renovascular disease o Obstructive uropathy o Assessment of split kidney function
CT scan	Assessment of: o Kidney masses o Atypical kidney cysts o Kidney stones
Magnetic resonance angiography	Diagnosis of: o Renovascular disease
Renal angiography	Diagnosis of: o Renovascular disease (gold standard) o Kidney artery thrombosis/thromboembolism o Polyarteritis nodosa
Retrograde ureterogram	Diagnosis of: o Upper-tract obstruction
Intravenous pyelogram	Not indicated in kidney disease

Appendix C: Slowing Progression of CKD (see full guideline)

Appendix D: Pharmacotherapy

Appendix D-1. Dosing Recommendations for ACEIs and ARBs in Patients with CKD[a-c]

DRUG	USUAL DOSE RANGE	COMMENTS/CAUTIONS
Angiotensin Converting Enzyme Inhibitors (ACEIs)		
Benazepril	10 – 40 mg divided once or twice daily	o Start with lower or less frequent doses in patients with CKD (except fosinopril as partial compensation by hepatobiliary elimination) or in patients currently being treated with a diuretic. o Use with caution in patients with renal artery stenosis. o Monitor potassium and renal function after initiation. o Concomitant therapy with potassium-sparing diuretics and/or potassium supplements may result in hyperkalemia. o Due to the potential risk for fetal morbidity and mortality in patients taking ACEIs during pregnancy, it is recommended that therapy be discontinued as soon as a woman becomes pregnant; alternate therapy should be considered. ACEIs should only be prescribed in pregnant women when the benefit clearly outweighs the potential risk for fetal abnormalities. o Contraindicated in patients with a history of angioedema on an ACEI
Captopril[d]	25 – 150 mg divided two to three times daily	
Enalapril	5 – 40 mg divided once or twice daily	
Fosinopril	10 – 40 mg once daily	
Lisinopril	10 – 40 mg once daily	
Moexipril[d]	7.5 – 30 mg divided once or twice daily	
Perindopril	4 – 8 mg divided once or twice daily	
Quinapril	10 – 80 mg divided once or twice daily	
Ramipril	2.5 – 20 mg divided once or twice daily	
Trandolapril	1 – 4 mg once daily	
Angiotensin II Receptor Blockers (ARBs)		
Candesartan	8 – 32 mg once daily	o Alternative to ACEIs in patients unable to tolerate an ACEI. o Consider lower doses in patients with intravascular volume depletion (e.g., patients currently being treated with a diuretic). o Use with caution in patients with renal artery stenosis. o Monitor potassium and renal function after initiation. o Concomitant therapy with potassium-sparing diuretics and/or potassium supplements may result in hyperkalemia. o Contraindicated in 2nd and 3rd trimesters of pregnancy due to potential neonatal/fetal morbidity and death. o Use with caution in patients with a history of angioedema on an ACEI.
Eprosartan	400 – 800 mg divided once or twice daily	
Irbesartan	150 – 300 mg once daily	
Losartan	50 – 100 mg divided once or twice daily	
Olmesartan	20 – 40 mg once daily	
Telimisartan	40 – 80 mg once daily	
Valsartan	80 – 320 mg once daily	

Refer to www.pbm.va.gov or http://vaww.pbm.va.gov for a current list of medications on the One VA National Formulary

[a] Adapted from KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Guideline 11: Use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in CKD at http://www.kidney.org/professionals/kdoqi/guidelines_bp/guide_11.htm

[b] Adapted from McEvoy GK, ed. American Hospital Formulary Service Drug Information, Bethesda, MD: American Society of Health-System Pharmacists, Inc., 2006.

[c] Adapted from Hebel SK ed. Drug Facts and Comparisons, St. Louis, Missouri: Facts and Comparisons Inc., May 2006.

[d] One hour before meals, on an empty stomach

Appendix D-2: Cautions in the Use of Selected Medications in Patients with CKD

DRUG	COMMENTS
Analgesics/Antipyretics	
NSAIDs	In general, all NSAIDs (including COX-2 inhibitors) should be used with extreme caution, if at all, in patients with kidney disease. Patients with preexisting kidney dysfunction are at increased risk for acute kidney failure, which may occur within several days following administration of NSAIDs. In addition, metabolites are primarily eliminated by the kidneys. If used, monitor kidney function prior to initiating therapy and during chronic administration; use lowest possible dose. May also cause fluid retention or edema, worsening of hypertension, or hyperkalemia.
Opioid Analgesics	**Hydromorphone:** Accumulation may occur with severe kidney impairment; use with caution. **Meperidine:** Possible accumulation of meperidine and/or normeperidine in patients with kidney impairment. **Oxycodone:** Patients with CrCl < 60 ml/min had higher concentrations compared to patients without kidney impairment; monitor for increased sedation. **Tramadol:** If CrCl < 30 ml/min, increase dosing interval to 12 hours with a maximum dose 200 mg per day.
Anorexiant Medications	
Sibutramine	Do not use in patients with severe kidney impairment as the drug has not been adequately studied in this patient population.
Anticoagulants	
Heparin	Use with caution in patients with kidney impairment as hyperkalemia may develop.
Enoxaparin	Although no dosage adjustment is recommended for patients with mild or moderate kidney impairment, patients should be monitored carefully for signs or symptoms of bleeding. Dose adjustments are recommended for patients with severe kidney impairment (CrCl < 30mL/min).
Antidiabetic Agents	
Alpha-Glucosidase Inhibitors	**Acarbose:** Increased plasma concentrations of acarbose seen in patients with kidney impairment; not recommended in patients with serum creatinine > 2 gm/dL as has not been studied in this patient population. **Miglitol:** Safety of using miglitol in patients with CrCl < 25 ml/min unknown.
Exenatide	Not recommended for use in patients with severe kidney impairment (CrCl clearance < 30 ml/min).
Insulin	Half-life may be prolonged in patients with kidney function impairment, decrease insulin dose accordingly.
Repaglinide	Patients with severe kidney impairment should be initiated at a dose of 0.5 mg and carefully titrated; not studied in patients with CrCl < 20 ml/min.
Metformin	Use with caution in patients with decreased GFR due to risk of lactic acidosis (risk increases as kidney function decreases). Metformin is contraindicated in patients with kidney dysfunction as indicated by serum creatinine levels > 1.5 g/dL (males) or 1.4 g/dL (females), or abnormal CrCl. CKD prolongs the half-life and decreases the clearance of metformin.
Sitagliptan	Dosage adjustment recommended for patients with moderate-severe CKD: 50mg once daily if CrCl ≥ 30 to <50 ml/min or serum creatinine > 1.7 to ≤ 3.0 mg/dl for males >1.5 to ≤ 2.5 mg/dl females; 25 mg once daily if CrCl < 30 ml/min or serum creatinine > 3.0 mg/dl for males or > 2.5 mg/dl for females.

Sulfonylureas	Decreased elimination in patients with kidney impairment may lead to hypoglycemia; use with caution and monitor kidney function and glucose levels. Acetohexamide, chlorpropamide, glyburide, tolazamide should be avoided in patients with impaired kidney function as these agents are eliminated unchanged or as active compounds dependent on the kidney for elimination; glipizide or tolbutamide are preferred as these agents are metabolized to inactive or weakly active compounds.
Antigout Agents	
Allopurinol	Decrease dose or adjust regimen based on kidney function due to increased potential for toxicity and rash (suggested doses according to CrCl: 60 ml/min 200 mg daily; 40 ml/min 150 mg daily; 20 ml/min 100 mg daily; 10 ml/min 100 mg every other day; < 10 ml/min 100 mg three times/week). Colchicine should be used with caution in patients with combined kidney and hepatic disease to avoid neutropenia and gastrointestinal side effects.
Anti-infective Agents	
Antibiotics, Antifungals, Antivirals	Dosage adjustments frequently required in kidney disease. Certain infections will require more aggressive dosing (e.g., endocarditis, meningitis, etc.); therefore, consultation with infectious diseases is recommended. **Aminoglycosides** are nephrotoxic and dose adjustment is required based on CrCl or sCr. Trimethoprim can cause hyperkalemia. Accumulation of the IV vehicle of the parenteral formulation of voriconazole may occur in patients with kidney function impairment; consult the package insert for further information. Acyclovir, other antivirals, and sulfa drugs may cause crystaluria. The acyclovir/gancyclovir dose must be decreased to avoid encephalopathy. The dose and/or dosing interval of adefovir and entecavir should be adjusted in patients with kidney function impairment. Consult individual product information or alternate sources on dosing in kidney function impairment.
Bisphosphonates	
Alendronate	Although not adequately studied, it is anticipated that impaired kidney function would result in accumulation of alendronate in bone. No dosage adjustment is required in patients with mild to moderate kidney dysfunction (CrCl 35 to 60 ml/min); not recommended in patients with CrCl < 35 ml/min as the safety and efficacy in this patient population has not been studied.
Etidronate	Only use if potential benefit outweighs risk for worsening kidney function; if used, reduce dose if serum creatinine is 2.5 to 4.9mg/dL.
Ibandronate	Not recommended in patients with CrCl < 30 ml/min.
Pamidronate	If kidney function deteriorates, withhold treatment until the patient's kidney function returns to baseline.
Risedronate	Not recommended in patients with CrCl < 30 ml/min.
Zoledronic acid	Single doses should not exceed 4 mg (and the infusion not less than 15 minutes) due to potential deterioration in kidney function, possibly resulting in kidney failure.
Cardiovascular and Antilipemic Agents	
ACEI/ARB	Refer to Annotation 10.2
Atenolol	Decrease dose or regimen based on kidney function (initiate therapy at 25 mg daily with a maximum dose of 50 mg daily in patients with CrCl 15 to 35 ml/min or 50 mg every other day if CrCl < 15 ml/min). Dosage adjustment in patients with kidney impairment also recommended for bisoprolol, nadolol, and timolol, and for sotalol (used as an antiarrhythmic agent).

Digoxin	Half-life prolonged with impaired kidney function and may take longer to achieve steady state; decrease dose or adjust regimen based on level of kidney function (in general, patients with a CrCl < 50 ml/min will require a reduction in maintenance dose).
Diuretics	Thiazide diuretics may not be effective in patients with advanced kidney disease, although metolazone may be used in addition to a loop diuretic, if required to obtain clinical response. Spironolactone and other potassium sparing diuretics should be used with caution to avoid hyperkalemia.
Fibric Acid Derivatives	**Gemfibrozil:** has been associated with worsening kidney function in patients with creatinine levels > 2 gm/dL; consider alternative therapy. **Fenofibrate:** Accumulation of fenofibrate may occur in patients with CrCl < 50 ml/min; minimize dose.
HMG-CoA Reductase Inhibitors (statins)	Kidney impairment may predispose patients to myopathy while on statins.–**Lovastatin:** Lower doses should be considered; doses > 20 mg/day not generally recommended if CrCl < 30 ml/min. **Pravastatin:** starting dose of 10 mg/day in significant kidney dysfunction. **Rosuvastatin:** starting dose of 5mg/day with maximum 10mg daily if CrCl < 30 ml/min. **Simvastatin:** initiate therapy at 5 mg/day and closely monitor patients with severe kidney impairment due to increased plasma concentrations.
Erectile Dysfunction Agents	
PDE Inhibitors	**Sildenafil:** Initial dose 25 mg if CrCl < 30ml/min. **Tadalafil:** Initial dose 5 mg if CrCl 31-50 ml/min; maximum dose 10 mg.
Gastrointestinal Drugs	
H2 Antagonists	Adjust dose based on level of kidney function impairment. **Cimetidine:** 300 mg every 12 hours or lowest possible dose in severe kidney dysfunction. **Famotidine:** reduce the dose by half or prolong dosing interval to 36 to 48 hours in moderate to severe kidney impairment. **Nizatidine:** 150 mg/day for acute or 150 mg every other day for maintenance if CrCl is 20 to 50 ml/min or 150 mg every other day for acute or 150 mg every 3 days for maintenance if CrCl < 20 ml/min. **Ranitidine:** 150 mg every 24 hours if CrCl < 50 ml/min.
Psychotropic and Central Nervous System Agents	
Anticonvulsants	**Gabapentin:** Decrease dose or adjust regimen based on kidney function (recommended total daily doses according to CrCl: 30 to 59 ml/min 400-1400 mg; 15 to 29 ml/min 200-700 mg; 15 ml/min 100-300 mg). **Levitiracetam:** Reduce dose depending on level of kidney impairment (CrCl 50-80 ml/min 500 to 1000 mg every 12 hours; CrCl 30-50 ml/min 250 to 750 mg every 12 hours; CrCl < 30 ml/min 250 to 500 mg every 12 hours).

Antidepressants	**Paroxetine:** Reduce initial dose (10 mg/day immediate-release or 12.5 mg/day controlled-release) in patients with CrCl < 30 ml/min, due to increased plasma concentrations. **Citalopram or Escitalopram:** Use with caution in patients with severe kidney impairment; no dosage adjustment necessary in mild to moderate impairment. **Duloxetine:** Not recommended in patients with CrCl < 30 ml/min due to increased plasma concentrations and accumulation of major metabolites. **Venlafaxine:** Reduce total daily dose of extended-release by 25 to 50% in patients with GFR 10 to 70 ml/min and by 25% for the immediate-release product in patients with mild to moderate kidney impairment due to reduced clearance and prolonged half-life. **Bupropion:** Use with caution in patients with kidney impairment; consider reduction in dose or frequency of administration due to potential accumulation of the drug and its metabolites.
Antipsychotic Agents	**Lithium:** Increased risk of toxicity in patients with severe kidney impairment; use with extreme caution, if at all. Risk of toxicity also increased in patients with dehydration or sodium depletion. Nephrogenic diabetes insipidus can occur in up to 30 to 50% of patients and may persist in 10 to 25% of patients after 1 to 2 years of continued therapy. **Risperidone:** Reduce initial dose in patients with severe kidney disease (oral 0.5 mg twice daily with gradual increases in dose as indicated) due to reduced clearance of the drug and its metabolites. **Paloperidone (active metabolite of risperidone):** Reduce dose (CrCl $\geq$ 50 to 79 ml/min maximum 6 mg per day; CrCl 10 to < 50 ml/min maximum 3 mg per day).
Memantine	Dosage adjustments may be necessary in patients with a CrCl < 50 ml/min (CrCl 15 to 29 ml/min target dose 5 mg twice daily) due to increased plasma concentrations and half-life.

Appendix E: Complications of Kidney Disease

Parameter	Abnormality	Issues/Needs/Recommendations	Treatment
Potassium	> 6.5 mEq/L	Emergency room treatment	Instruct patient to present to the emergency room
	5.5-6.4 mEq/L	Precipitants:	General treatment: ▪ Sodium polystyrene sulfonate30 – 60 g qd or qod ▪ Loop diuretics to increase potassium secretion ▪ Restrict dietary potassium intake ▪ Refer if etiology is unknown
		▪ Drugs: ACEI, ARBs, potassium-sparing diuretics, NSAIDs, trimethoprim-sulphamethoxazole	▪ Discontinue offending drug
		▪ Other: Volume depletion	▪ Correct dehydration
		▪ High intake of potassium-rich foods	▪ Restrict dietary potassium (2 – 3 g/d)
		▪ Acidosis/Renal Tubular acidosis	▪ Treat cause, bicarb if < 20
		▪ Hyperglycemia or starvation in DM	▪ Control hyperglycemia & ensure adequate nutrition
		▪ Urinary tract obstruction	▪ Assess and intervene to relieve
	< 3.5 mEq/L	Precipitants:	General treatment: ▪ Supplement potassium only cautiously with close follow-up
		▪ Diuretics	▪ Discontinue/reduce dose of diuretics
		▪ Diarrhea	▪ Treat diarrhea
		▪ Malnutrition	▪ Provide nutritional counseling
		▪ High renin/aldosterone states	▪ Referral to endocrine or nephrology
Calcium	< 8 mg/dL	▪ Rare in CKD unless the eGFR is < 30 ml/min/1.73m^2 ▪ Results from hyperphosphatemia and decreased production and activity of 1,25,dihydroxyvitamin D_3 ▪ If low serum albumin, check ionized calcium	Serum phosphorous >4.6 mg/dL: ▪ Dietary phosphorous restriction ▪ Calcium acetate or carbonate with meals Serum phosphorous normal: ▪ Calcium acetate or carbonate between meals Refractory hypocalcemia: ▪ Consider use 1,25,dihydroxyvitamin D_3 or other active vitamin D
	> 11 mg/dL	▪ Usually related to the use of calcium supplements or Vitamin D	▪ Reduce calcium supplements, Vitamin D
		▪ Consider conditions such as myeloma, granulomas, neoplasms	▪ Specific treatment of the underlying condition

Parameter	Abnormality	Issues/Needs/Recommendations	Treatment
Phosphorus	> 4.5 mg/dL	▪ Hyperphosphatemia usually begins to occur when the eGFR is < 30ml/min/1.73 m^2	▪ Restrict dietary phosphorous to 0.6 – 1.2 g/d ▪ Use phosphorous binders (calcium acetate or carbonate) with meals
Albumin	< 3.5 g/dL	▪ Associated with increased mortality ▪ General causes of hypoalbuminemia include abnormal metabolism, chronic inflammation, and liver disease. ▪ Specific causes that could be addressed are: o Nephrotic syndrome o Acidosis o Poorly controlled diabetes o Reduced intake	▪ Assess urinary protein, refer if worse ▪ Assess and treat acidosis ▪ Maximize diabetic control ▪ Nutritional assessment supplementation
Anemia	HCT < 33% Hgb <11g/dL (Pre-menopausal female) HCT < 37% Hgb <12g/dL (Male & post-menopausal female)	▪ Usual causes of anemia must be excluded before attributing to kidney disease ▪ Common causes in CKD: o Inadequate erythropoiesis o Reduced RBC half-life o Bleeding	▪ Erythropoietin levels are not helpful for diagnosis of suspected anemia of kidney disease ▪ Initiate oral iron treatment if the transferrin saturation is < 20% and/or the ferritin is < 100 ng/ml ▪ If the patient is symptomatic, or the Hgb is < 10 g/dL despite iron therapy, refer to nephrology or hematology for consideration of erythropoietin therapy
HCO_3	< 22 mEq/L	▪ Other causes of acidosis must be considered prior to ascribing to kidney disease, especially if the HCO_3 is < 15 mEq/L ▪ Common in CKD. Kidney causes include: o Impaired kidney acidification o Accumulation of organic acids	▪ $NaHCO_3$ tablets when the serum bicarbonate falls below 22 mEq/L ▪ Usual starting dose: 0.4 mEq/kg/day in divided doses ▪ One 650 mg $NaHCO_3$ tablet contains 7.7 mEq sodium/7.7 mEq HCO_3

Key: *ACEI-I: Angiotensin-Converting Enzyme-Inhibitor; ARB: Angiotensin Receptor Blockers; CKI: Chronic Kidney Insufficiency; DM: Diabetes Mellitus; eGFR: Estimated Glomerular Filtration Rate; Hgb: Hemoglobin; NSAIDs: Nonsteroidal Anti-inflammatory Drugs; RBC: Red Blood Cell*

Appendix F: Nutrition (see full guideline)

Appendix G: Patient Education

RESOURCES FOR PATIENT EDUCATION

Education materials are available through a number of resources. Below is a listing of organizations that provide information including videos, pamphlets, fact sheets, and books.

Resource	Contact
American Association of Kidney Patients	800-749-AAKP www.aakp.org
National Kidney Foundation (Series of patient education booklets are free online)	800-622-9010 http://www.kidney.org/patients/
American Kidney Fund	800-638-8299 http://www.akfinc.org
Baxter Healthcare Renal Division	http://www.kidneydirections.com/
Fresenius Medical Care North America	http://www.fmcna.com
National Kidney and Urologic Disease Information Clearinghouse • "Kidney Disease Dictionary" • "ESRD & Choosing a Treatment that is Right for You" • "Your Kidneys and How They Work " • "Vascular Access for Hemodialysis" • "Eat Right to Feel Right on Hemodialysis"	http://kidney.niddk.nih.gov/
The Nephron Information Center • "How the Kidney Works" • "Early Renal Insufficiency" • ESRD diet books and brochures	http://www.nephron.com
R &D Laboratories	http://www.ikidney.com/
Renalnet	http://www.renalnet.org/
Kidney School: tailored, interactive self-management learning center with 16 modules. Provided by Life Options. Supported by an unrestricted educational grant from Amgen Inc ®: The Medical Education Institute, Inc.	http://www.kidneyschool.org/pdfs/KSIdeaGuide.pdf

The above list of sites is not all-inclusive. Some of the sites have links to other sites as well.

Appendix H: Follow-up for Chronic Kidney Disease

Category	Issue		When
History	Nephrotoxic medications	Ask about use of medications such as NSAIDs, aminoglycoside, contrast agents	Each visit
	Fluid overload	Ask about ankle swelling, dyspnea, orthopnea	
	Uremia	Ask about anorexia, nausea, vomiting (More likely to be apparent when GFR < 30 ml/min/1.73m^2)	
	Malnutrition	Ask about weight, dietary history, food recall records for protein and energy intake; do subjective global assessment	
	Neuropathy	Ask about paresthesias, mental-status abnormalities, sleep disturbances, restless legs	
Physical exam	Fluid overload	Look for jugular venous distension, rales, S3 gallop, ankle edema	Each visit
	Uremia	Look for asterixis, pericardial rub	Each visit for eGFR < 30 ml/min/1.73m^2
Labs	Renal function eGFR	Use the Modification of Diet in Renal Disease (MDRD) equation to estimate GFR	Each CKD visit
	Anemia	Hemoglobin	Each year and as clinically indicated
	Iron deficiency	Serum iron, total iron binding capacity (TIBC), and ferritin	Each year and as clinically indicated
	Proteinuria	Spot urine for protein and creatinine	Each year and as clinically indicated
	Metabolic abnormalities	Electrolytes	Each CKD visit
	Bone disease	Calcium, phosphorus, parathyroid hormone (PTH)	Each year, if abnormal every 6 months and as clinically indicated
	Malnutrition	24-hour urine for urea nitrogen excretion	As clinically indicated
	Obstruction	Renal ultrasound	At initial evaluation and for acute decline in GFR
Non-drug therapy	Dietary modification	Advise about diet, protein, salt restriction Aim for weight to be within 30% of ideal through diet and exercise	Each visit
Drug therapy	Blood pressure	Antihypertensive drug therapy	Each visit
	Glycemic control	Oral hypoglycemic agents or insulin	
	Anemia and other metabolic consequences of CKD	Erythropoietin, iron, if iron deficient, or both	
	Hyperkalemia	Sodium polystyrene sulfonate and bicarbonate as needed	
	Fluid overload	Diuretics	
	Calcium and phosphorus metabolism	Phosphate binders and Vitamin D	
Patient education	Overall management	Patient education about complexity of management, minimizing risk factors, importance of adherence to medical regimen and follow-up, preparation for possible future need for dialysis	Ongoing

Appendix I: Acronym List

ACEI	Angiotensin-Converting Enzyme Inhibitor
ANA	Anti-Nuclear Antibody
ANCA	Anti-Neutrophil Cytoplasmic Antibody
ARB	Angiotensin II Receptor Blocker
BUN	Blood Urea Nitrogen
CHr	Content of Hemoglobin in Reticulocytes
CKD	Chronic Kidney Disease
CPG	Clinical Practice Guideline
DM	Diabetes Mellitus
eGFR	Estimated Glomerular Filtration Rate
ESKD	End-Stage-Kidney Disease
GBM	Glomerular Basement Membrane
GFR	Glomerular Filtration Rate
GN	Glomerulonephritis
HIV	Human Immunodeficiency Virus
HTN	Hypertension
HUS	Hemolytic Uremic Syndrome
IEP	Immuno-Electrophoresis
MDRD	Modification of Diet in Renal Disease
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
PCKD	Polycystic Kidney Disease
PTH	Parathyroid Hormone
RBC	Red Blood Cell
RCT	Randomized Controlled Trial
S_{Cr}	Serum Creatinine Concentration
SPEP	Serum Protein Electrophoresis
TIBC	Total Iron Binding Capacity
TSAT	Transferrin Saturation
TTP	Thrombotic Thrombocytopenic Purpura
UPEP	Urine Protein Electrophoresis
UTI	Urinary Tract Infection
WBC	White Blood Cell

Appendix J: Participant List (see full guideline)

Appendix K: Bibliography (see full guideline)