Content for *Chronic Kidney Disease 2006: A Guide to Select NKF-KDOQI Guidelines and Recommendations* was edited by Nephrology Pharmacy Associates, Inc., by George R. Bailie, PharmD, PhD; Curtis A. Johnson, PharmD; Nancy A. Mason, PharmD; and Wendy L. St. Peter, PharmD.

This publication was made possibe through an unrestricted educational grant from American Regent, Inc., Shirley, NY.

DISCLAIMER

Chronic Kidney Disease 2006: A Guide to Select NKF-KDOQI Guidelines and Recommendations is offered as a general summary for physicians, pharmacists, nurses and other health care professionals. It is designed to facilitate access to the many published clinical practice guidelines and recommendations relevant to people with chronic kidney disease. Appropriate application of these guidelines and recommendations can only be identified by medical professionals. Depending on the circumstances, the risks of misapplication can be serious and can include severe injury, including death. These guidelines and recommendations cannot identify medical risks specific to individual patients or recommend patient treatment. These guidelines are not to be used as a substitute for professional training. The absence of typographical and other errors cannot be guaranteed. Use of these guidelines and recommendations indicates acknowledgement that neither the National Kidney Foundation, Inc., Nephrology Pharmacy Associates, Inc., nor American Regent, Inc. will be held responsible for any loss or injury, including death, sustained in connection with or as a result of their use. Readers should consult complete information available in published guidelines and recommendations before determining their application in a specific clinical situation.

Guides such as *Chronic Kidney Disease 2006: A Guide to Select NKF-KDOQI Guidelines and Recommendations* can only draw from information available as of the date of publication. Nephrology Pharmacy Associates, Inc., American Regent, Inc. and the National Kidney Foundation, Inc. are under no obligation to update information contained herein. Future medical advances or product information may affect or change the information provided. Original guidelines may be updated at any time. Health care professionals using this reference are responsible for monitoring ongoing development of practice guidelines and recommendations.

This booklet is for general reference. It contains a synopsis only of each of the guidelines and recommendations. In addition, because of limitations of space, reference to whether the recommendations are evidence- or opinion-based has been omitted. Readers should refer to the original published recommendations to gain further background information, literature citations and descriptions of the processes involved in the generation of the guidelines and recommendations.

PREFACE

An estimated 20 million adults in the United States have chronic kidney disease (CKD) — about one in nine adults. The prevalence of CKD may be increasing for several reasons. The incidences of the two greatest causes of CKD, diabetes mellitus and hypertension, are on the increase and are worsened by obesity, smoking and other risk factors.

Until recently, there were few standardized, published clinical practice guidelines specifically for kidney diseases. A number of authoritative bodies, such as the American Diabetes Association, the Department of Veterans Affairs and the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, have periodically issued position statements in general areas that had relevance to kidney disease, although not specifically designed for that purpose. The advent of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI™) in recent years was the first initiative that specifically and systematically attempted to address the need for clinical practice guidelines for use in people with CKD. Since its inception, KDOQI has produced a large number of these clinical practice guidelines.

The accompanying text and tables have been prepared as a consolidated reference for clinical practice guidelines and recommendations that address many aspects of the care of people with CKD. Clinicians must use their best judgment when utilizing these guidelines and recommendations. Please note that all guidelines, recommendations, tables and figures included in this resource are numbered according to the original KDOQI publications for easy cross-referencing.

Table of Contents

SECTION 1

ANEMIA

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease*. Am J Kidney Dis 47:S1–S146, 2006 (Suppl 3). Available at: **http://www.kidney.org/professionals/kdoqi/guidelines_anemia/index.htm**

Based on the strength of available evidence, the new guidelines have been segregated into either clinical practice guidelines (CPGs) or clinical practice recommendations (CPRs). CPGs are those where there is robust evidence (generally from prospective, randomized controlled trials [RCTs]), while CPRs are those where the evidence is less strong, and are based on the opinions of the work group. To further identify CPGs, they are enclosed within a text box. The original document is subdivided into five sections containing eight CPGs or CPRs for chronic kidney disease (CKD) in adults, eight CPRs for CKD in children, and a review of CPRs for CKD in transplant recipients. Selected CPGs and CPRs are included here. Guidelines, recommendations, tables and figures are numbered according to the original document.

CPGs AND CPRs FOR ANEMIA IN CKD IN ADULTS

CPR 1.1: IDENTIFYING PATIENTS AND INITIATING EVALUATION

1.1.1 Stage and cause of CKD:
In the opinion of the Work Group, hemoglobin (Hb) testing should be carried out in all people with CKD, regardless of stage or cause.

1.1.2 Frequency of testing for anemia:
In the opinion of the Work Group, Hb levels should be measured at least annually.

1.1.3 Diagnosis of anemia:
In the opinion of the Work Group, diagnosis of anemia should be made and further examination should be undertaken at the following Hb concentrations:
- **<13.5 g/dL in adult males**
- **<12.0 g/dL in adult females**

CPR 1.2: EVALUATION OF ANEMIA IN CKD

1.2.1 In the opinion of the Work Group, initial assessment of anemia should include the following tests:

1.2.1.1 A complete blood count (CBC) — in addition to the Hb concentration — including red blood cell indices (mean corpuscular Hb [MCH], mean corpuscular Hb concentration [MCHC]), white blood cell count and differential and platelet count

1.2.1.2 Absolute reticulocyte count

1.2.1.3 Serum ferritin to assess iron stores

1.2.1.4 Serum transferin saturation (TSAT) *or* content of Hb in reticulocytes (CHr) to assess adequacy of iron for erythropoiesis

CPG AND CPR 2.1: Hb RANGE

2.1.1 Lower limit of Hb:
In people with CKD, Hb should be ≥11.0 g/dL.

2.1.2 Upper limit of Hb:
In the opinion of the Work Group, there is insufficient evidence to recommend routinely maintaining Hb levels at ≥13.0 g/dL in people treated with an erythropoiesis-stimulating agent (ESA).

CPR 3.1: USING ESAs

3.1.1 Frequency of Hb monitoring:

3.1.1.1 In the opinion of the Work Group, the frequency of Hb monitoring in people treated with ESAs should be at least monthly.

3.1.2 ESA dosing:

3.1.2.1 In the opinion of the Work Group, the initial ESA dose and ESA dose adjustments should be determined by the individual's Hb level, the target Hb level, the observed rate of rise in Hb level and clinical circumstances.

3.1.2.2 In the opinion of the Work Group, ESA doses should be decreased, but not necessarily withheld, when a downward adjustment of Hb level is needed.

3.1.2.3 In the opinion of the Work Group, scheduled ESA doses that have been missed should be replaced at the earliest possible opportunity.

3.1.2.4 In the opinion of the Work Group, ESA administration in ESA-dependent people should continue during hospitalization.

3.1.2.5 In the opinion of the Work Group, hypertension, vascular access occlusion, inadequate dialysis, history of seizures or compromised nutritional status are not contraindications to ESA therapy.

3.1.3 Route of administration:

3.1.3.1 In the opinion of the Work Group, the route of ESA administration should be determined by the CKD stage, treatment setting, efficacy, safety and class of ESA used.

3.1.3.2 In the opinion of the Work Group, convenience favors subcutaneous (SC) administration in people with non-hemodialysis-dependent-CKD (HD-CKD).

3.1.3.3 In the opinion of the Work Group, convenience favors intravenous (IV) administration in people with HD-CKD.

3.1.4 Frequency of administration:

3.1.4.1 In the opinion of the Work Group, frequency of administration should be determined by the CKD stage, treatment setting, efficacy considerations and class of ESA.

3.1.4.2 In the opinion of the Work Group, convenience favors less frequent administration, particularly in people with non-HD-CKD.

CPG AND CPR 3.2: USING IRON AGENTS

3.2.1 Frequency of iron status tests:

In the opinion of the Work Group, iron status tests should be performed as follows:

3.2.1.1 Every month during initial ESA treatment

3.2.1.2 At least every three months during stable ESA treatment or in people with HD-CKD not treated with ESA

3.2.2 Interpretation of iron status tests:

In the opinion of the Work Group, results of iron status tests, Hb, and ESA dose should be interpreted together to guide iron therapy.

3.2.3 Targets of iron therapy:

In the opinion of the Work Group, sufficient iron should be administered to generally maintain the following indices of iron status during ESA treatment:

3.2.3.1 HD-CKD:

- **Serum ferritin >200 ng/mL**

AND

- **TSAT >20%, or CHr >29 pg/cell**

3.2.3.2 Nondialysis-dependent-CKD (ND-CKD) and peritoneal dialysis-dependent-CKD (PD-CKD):

- **Serum ferritin >100 ng/mL**

AND

- **TSAT >20%**

3.2.4 Upper level of ferritin:

In the opinion of the Work Group, there is insufficient evidence to recommend routine administration of IV iron if serum ferritin level is >500 ng/mL. When serum ferritin is >500 ng/mL, decisions regarding IV iron administration should weigh ESA responsiveness, Hb and TSAT level and the individual's clinical status.

3.2.5 Route of administration:

3.2.5.1 The preferred route of administration is IV in people with HD-CKD.

3.2.5.2 In the opinion of the Work Group, the route of iron administration can be either IV or oral in people with ND-CKD or PD-CKD.

3.2.6 Hypersensitivity reactions:

In the opinion of the Work Group, resuscitative medication and personnel trained to evaluate and resuscitate anaphylaxis should be available whenever a dose of iron dextran is administered.

CPG AND CPR 3.3: USING PHARMACOLOGICAL AND NONPHARMACOLOGICAL ADJUVANTS TO ESA TREATMENT IN HD-CKD

3.3.1 L-Carnitine:

In the opinion of the Work Group, there is insufficient evidence to recommend the use of L-carnitine in the management of anemia in people with CKD.

3.3.2 Vitamin C:

In the opinion of the Work Group, there is insufficient evidence to recommend the use of vitamin C (ascorbate) in the management of anemia in people with CKD.

3.3.3 Androgens:

Androgens should not be used as an adjuvant to ESA treatment in people with anemia and CKD.

CPR 3.4: TRANSFUSION THERAPY

3.4.1 In the opinion of the Work Group, no single Hb concentration justifies or requires transfusion. In particular, the target Hb recommended for chronic anemia management (see Guideline 2.1) *should not serve as a transfusion trigger*.

CPR 3.5: EVALUATING AND CORRECTING PERSISTENT FAILURE TO REACH OR MAINTAIN INTENDED HB.

3.5.1 Hyporesponse to ESA and iron therapy:

In the opinion of the Work Group, people with anemia and CKD should undergo evaluation for specific causes of hyporesponse whenever the Hb level is inappropriately low for the ESA dose administered. Such conditions include, but are not limited to:

- **A significant increase in the ESA dose requirement to maintain a certain Hb level or a significant decrease in Hb level at a constant ESA dose**
- **A failure to increase the Hb level to >11.0 g/dL despite an ESA dose equivalent to epoetin greater than 500 IU/kg/wk.**

3.5.2 Evaluation for pure red blood cell aplasia (PRCA):

In the opinion of the Work Group, evaluation for antibody-mediated PRCA should be undertaken when a person receiving ESA therapy for more than four weeks develops each of the following:

- **Sudden rapid decrease in Hb level at the rate of 0.5 to 1.0 g/dL/wk, *OR* requirement of red blood cell transfusions at the rate of approximately one to two per week, *AND***
- **Normal platelet and white blood cell counts, *AND***
- **Absolute reticulocyte count less than 10,000/μL**

CPR FOR ANEMIA IN CKD IN CHILDREN

All statements in the pediatric section are CPRs because there is insufficient evidence in this population to support CPGs. When the adult guideline statement applies equally well to adults and children, the statement is accompanied by the following: (*FULLY APPLICABLE TO CHILDREN*). When the adult guideline statement needs modification for children, the following instruction is given, followed by the pediatric-specific guideline statement: (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*)

CPR FOR PEDIATRICS 1.1: IDENTIFYING PATIENTS AND INITIATING EVALUATION

1.1.1 Stage and cause of CKD (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, Hb testing should be carried out in all people with CKD, regardless of stage or cause.

1.1.2 Frequency of testing for anemia (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, Hb levels should be measured at least annually.

1.1.3 Diagnosis of anemia (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*):

Adult CPR

In the opinion of the Work Group, diagnosis of anemia should be made and further evaluation should be undertaken at the following Hb concentrations:

- **<13.5 g/dL in adult males**
- **<12.0 g/dL in adult females**

Pediatric CPR

In the opinion of the Work Group, in the pediatric patient, diagnosis of anemia should be made and further evaluation should be undertaken whenever the observed Hb concentration is less than the fifth percentile of normal when adjusted for age and sex.

CPR FOR PEDIATRICS 1.2: EVALUATION OF ANEMIA IN CKD

1.2.1 In the opinion of the Work Group, initial assessment of anemia should include the following tests (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*):

1.2.1.1 A CBC including – in addition to the Hb concentration – red blood cell indices (MCH, MCHC), white blood cell count and differential and platelet count.

1.2.1.2 Absolute reticulocyte count

1.2.1.3 Serum ferritin to assess iron stores

1.2.1.4 Adult CPR:

- **Serum TSAT *or* CHr to assess adequacy or iron for erythropoiesis.**

Pediatric CPR:

- **In the pediatric patient, serum TSAT to assess adequacy of iron for erythropoiesis.**

CPR FOR PEDIATRICS 2.1: Hb RANGE

2.1.1 Lower limit of Hb (*FULLY APPLICABLE TO CHILDREN*):
In people with CKD, Hb level should be ≥11.0 g/dL.

2.1.2 Upper limit of Hb (*FULLY APPLICABLE TO CHILDREN*):
In the opinion of the Work Group, there is insufficient evidence to recommend routinely maintaining Hb levels at ≥13.0 g/dL in people treated with ESAs.

CPR FOR PEDIATRICS 3.1: USING ESAs

3.1.1 Frequency of Hb monitoring (*FULLY APPLICABLE TO CHILDREN*):

3.1.1.1 In the opinion of the Work Group, the frequency of Hb monitoring in people treated with ESAs should be at least monthly.

3.1.2 ESA dosing (*FULLY APPLICABLE TO CHILDREN*):

3.1.2.1 In the opinion of the Work Group, the initial ESA dose and ESA dose adjustments should be determined by the individual's Hb level, the target Hb level, the observed rate of rise in Hb level and clinical circumstances.

3.1.2.2 In the opinion of the Work Group, ESA doses should be decreased, but not necessarily withheld, when a downward adjustment of Hb level is needed.

3.1.2.3 In the opinion of the Work Group, scheduled ESA doses that have been missed should be replaced at the earliest possible opportunity.

3.1.2.4 In the opinion of the Work Group, ESA administration in ESA-dependent people should continue during hospitalization.

3.1.2.5 In the opinion of the Work Group, hypertension, vascular access occlusion, inadequate dialysis, history of seizures or compromised nutritional status are not contraindications to ESA therapy.

3.1.3 Route of administration (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*):

3.1.3.1 Adult CPR:

In the opinion of the Work Group, the route of ESA administration should be determined by the CKD stage, treatment setting, efficacy, safety and class of ESA used.

Pediatric CPR:

In the opinion of the Work Group, in the pediatric patient, the route of administration should be determined by the CKD stage, treatment setting, efficacy considerations, the class of ESA used and the anticipated frequency and pain of administration.

3.1.3.2 In the opinion of the Work Group, convenience favors SC administration in people with non-HD-CKD.

3.1.3.3 In the opinion of the Work Group, convenience favors IV administration in people with HD-CKD.

3.1.4 Frequency of administration (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*):

3.1.4.1 Adult CPR:

In the opinion of the Work Group, frequency of administration should be determined by the CKD stage, treatment setting, efficacy considerations and class of ESA.

Pediatric CPR:

In the opinion of the Work Group, in the pediatric patient, the frequency of administration should be determined by the CKD stage, treatment setting, efficacy considerations and class of ESA; as well, consideration should be given to the anticipated frequency of administration and pain on administration of each agent and their potential effects on the child and family.

3.1.4.2 In the opinion of the Work Group, convenience favors less frequent administration, particularly in people with non-HD-CKD.

CPR FOR PEDIATRICS 3.2: USING IRON AGENTS

3.2.1 Frequency of iron status tests (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, iron status tests should be performed as follows:

3.2.1.1 Every month during initial ESA treatment

3.2.1.2 At least every three months during stable ESA treatment or in people with HD-CKD not treated with ESAs.

3.2.2 Interpretation of iron status tests (*FULLY APPLICABLE TO CHILDREN*):
In the opinion of the Work Group, results of iron status tests, Hb, and ESA dose should be interpreted together to guide iron therapy.

3.2.3 Targets of iron therapy (*APPLICABLE TO CHILDREN, BUT NEEDS MODIFICATION*):
In the opinion of the Work Group, sufficient iron should be administered to generally maintain the following indices of iron status during ESA treatment:

3.2.3.1 Adult CPR HD-CKD:
- **Serum ferritin >200 ng/mL**

AND
- **TSAT >20% or CHr >29 pg/cell**

Pediatric CPR HD-CKD:
- **Serum ferritin >100 ng/mL**

AND
- **TSAT >20%**

3.2.3.2 ND-CKD and PD-CKD:
- **Serum ferritin >100 ng/mL**

AND
- **TSAT >20%**

3.2.4 Upper level of ferritin (*FULLY APPLICABLE TO CHILDREN*):
In the opinion of the Work Group, there is insufficient evidence to recommend routine administration of IV iron if serum ferritin level is >500 ng/mL. When serum ferritin is >500 ng/mL, decisions regarding IV iron administration should weigh ESA responsiveness, Hb and TSAT levels and the individual's clinical status.

3.2.5 Route of administration (*FULLY APPLICABLE TO CHILDREN*):

3.2.5.1 The preferred route of administration is IV in people with HD-CKD. (*STRONG RECOMMENDATION*)

3.2.5.2 In the opinion of the Work Group, the route of iron administration can be either IV or oral in people with ND-CKD or PD-CKD.

3.2.6 Hypersensitivity reactions (*FULLY APPLICABLE TO CHILDREN*):
In the opinion of the Work Group, resuscitative medication and personnel trained to evaluate and resuscitate anaphylaxis should be available whenever a dose of iron dextran is administered.

CPR FOR PEDIATRICS 3.3: USING PHARMACOLOGICAL AND NONPHARMACOLOGICAL ADJUVANTS TO ESA TREATMENT IN HD-CKD

3.3.1 L-Carnitine (*FULLY APPLICABLE TO CHILDREN*):
In the opinion of the Work Group, there is insufficient evidence to recommend the use of L-carnitine in the management of anemia in people with CKD.

3.3.2 Vitamin C (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, there is insufficient evidence to recommend the use of vitamin C (ascorbate) in the management of anemia in people with CKD.

3.3.3 Androgens (*FULLY APPLICABLE TO CHILDREN*):

Androgens should not be used as an adjuvant to ESA treatment in people with anemia and CKD.

CPR FOR PEDIATRICS 3.4: TRANSFUSION THERAPY

3.4.1 (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, no single Hb concentration justifies or requires transfusion. In particular, the target Hb recommended for chronic anemia management (see Guideline 2.1) should not serve as a transfusion trigger.

CPR FOR PEDIATRICS 3.5: EVALUATING AND CORRECTING PERSISTENT FAILURE TO REACH OR MAINTAIN INTENDED HB

3.5.1 Hyporesponse to ESA and iron therapy (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, people with anemia and CKD should undergo evaluation for specific causes of hyporesponse whenever the Hb level is inappropriately low for the ESA dose administered. Such conditions include, but are not limited to:

- **A significant increase in the ESA dose requirement to maintain a certain Hb level or a significant decrease in Hb level at a constant ESA dose**
- **A failure to increase the Hb level to greater than 11.0 g/dL despite an ESA dose equivalent to epoetin >500 IU/kg/wk**

3.5.2 Evaluation for PRCA (*FULLY APPLICABLE TO CHILDREN*):

In the opinion of the Work Group, evaluation for antibody-mediated PRCA should be undertaken when a person receiving ESA therapy for more than four weeks develops each of the following:

- **Sudden rapid decrease in Hb level at the rate of 0.5 to 1.0 g/dL/wk *OR* requirement of red blood cell transfusions at the rate of approximately one to two per week *AND***
- **Normal platelet and white blood cell counts *AND***
- **Absolute reticulocyte count <10,000/μL**

ADDENDUM

Major changes that appear in the 2006 update, compared with previous versions of the anemia guidelines, include:

- Lower and upper limit of Hb in adults and children (CPG and CPR 2.1).

- Omission of specific initial dosing for ESAs in adults and children (CPR 3.1).
- Targets for iron therapy, preferred route of administration of iron in people with HD-CKD and hypersensitivity reactions to iron in adults and children (CPG and CPR 3.2).
- Use of adjuvants to ESA treatment in people with HD-CKD in adults and children (CPG and CPR 3.3).

Use of specific abbreviations to distinguish the CKD patient populations to which anemia CPGs and CPRs apply. *These abbreviations are not classifications of patients according to stage of CKD; rather, they are used to show the clinician where literature/evidence and best practice recommendations have a distinct focus on dialysis or nondialysis CKD populations, for example, those CPGs and CPRs related to ESA use and iron therapy.* The abbreviations, along with an operational definition, are:

ND-CKD: used to refer to patient populations in CKD stages 1–4, and those in stage 5 not on dialysis.

PD-CKD: used to refer to CKD stage 5 patient populations that are receiving peritoneal dialysis (PD) therapy.

HD-CKD: used to refer to CKD stage 5 patient populations that are receiving hemodialysis (HD) therapy.

Non-HD-CKD: used to refer to either CKD patient populations receiving PD or CKD stages 1–5 populations receiving no HD.

SECTION 2

NUTRITION

Source: National Kidney Foundation. *Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines for Nutrition in Chronic Renal Failure*. Am J Kidney Dis 35:S1–140, 2000 (Suppl 2).

Available at: **http://www.kidney.org/professionals/kdoqi/guidelines_updates/doqi_nut.html**

These guidelines provide recommendations regarding the assessment of protein–energy nutritional status and the desirable dietary energy and protein intake for adults undergoing maintenance dialysis (MD). Guidelines, tables and figures are numbered according to the original document for easy cross-referencing. Guidelines regarding nutritional issues in children are beyond the scope of this handbook. The reader is referred to the KDOQI guidelines for more information on nutrition in children with CKD.

MD: EVALUATION OF PROTEIN–ENERGY NUTRITIONAL STATUS

GUIDELINE 1: USE OF PANELS OF NUTRITIONAL MEASURES

Nutritional status in people undergoing MD should be assessed with a combination of valid, complementary measures rather than any single measure alone.

1. There is no single measure that provides a comprehensive indication of protein–energy nutritional status.
2. Measures of energy and protein intake, visceral protein pools, muscle mass, other dimensions of body composition and functional status identify different aspects of protein–energy nutritional status.
3. Malnutrition may be identified with greater sensitivity and specificity using a combination of factors.

GUIDELINE 2: PANELS OF NUTRITIONAL MEASURES FOR PEOPLE ON MD

For people undergoing MD, nutritional status should be routinely assessed by predialysis or stabilized* serum albumin, percent of usual body weight, percent of standard (National Health and Nutrition Evaluation Survey [NHANES]) body weight, subjective global assessment (SGA), dietary interviews and diaries and protein equivalent of total nitrogen appearance normalized to body weight (nPNA).

* A predialysis serum measurement is obtained from an individual immediately before the initiation of a HD or intermittent PD treatment. A stabilized serum measurement is obtained after the individual has stabilized on a given dose of continuous ambulatory PD (CAPD).

1. These parameters should be measured routinely (as indicated in Table 1) because they provide a valid and clinically useful characterization of the protein–energy nutritional status of people on MD.

Table 1. Recommended Measures for Monitoring Nutritional Status of Maintenance Dialysis Patients

Category	Measure	Minimum Frequency of Measurement
I. Measurements that should be performed routinely in all patients	• Predialysis or stabilized serum albumin	Monthly
	• Percent of usual postdialysis (MHD) or post-drain (CPD) body weight	Monthly
	• Percent of standard (NHANES II) body weight	Every four months
	• Subjective global assessment	Every six months
	• Dietary interview and/or diary	Every six months
	• nPNA	Monthly for MHD; every three to four months for CPD
II. Measures that can be useful to confirm or extend the data obtained from the measures in Category I	• Predialysis or stabilized serum pre-albumin	As needed
	• Skinfold thickness	As needed
	• Mid-arm muscle area, circumference, or diameter	As needed
	• Dual-energy X-ray absorptiometry	As needed
III. Clinically useful measures, which, if low, might suggest the need for a more rigorous examination of protein–energy nutritional status	• Predialysis or stabilized serum	As needed
	• Creatinine	
	• Urea nitrogen	
	• Cholesterol	
	• Creatinine index	As needed

Abbreviations: CPD, chronic peritoneal dialysis; MHD, maintenance HD; nPNA, protein equivalent of total nitrogen appearance normalized to body weight.

GUIDELINE 3: SERUM ALBUMIN

Serum albumin is a valid and clinically useful measure of protein–energy nutritional status in people undergoing MD.

1. The predialysis or stabilized serum albumin is a measure of visceral protein pool size.
2. The serum albumin at the time of initiation of chronic dialysis therapy or during the course of MD is an indicator of future mortality risk.
3. A predialysis or stabilized serum albumin equal to or greater than the lower limit of the normal range (approximately 4.0 g/dL for the bromcresol green method) is the outcome goal.
4. Individuals with a predialysis or stabilized serum albumin that is low should be evaluated for protein–energy malnutrition.
5. The presence of acute or chronic inflammation limits the specificity of serum albumin as a nutritional marker.

GUIDELINE 4: SERUM PRE-ALBUMIN

Serum pre-albumin is a valid and clinically useful measure of protein–energy nutritional status in people on MD.

1. The predialysis or stabilized serum pre-albumin is a measure of visceral protein pool size.
2. The serum pre-albumin level at the time of initiation of dialysis or during MD is an indicator of future mortality risk.
3. An individual with predialysis or stabilized serum pre-albumin <30 mg/dL should be evaluated for protein–energy malnutrition.
4. The presence of acute or chronic inflammation limits the specificity of serum pre-albumin as a nutritional marker.
5. There is insufficient evidence to conclude that pre-albumin is a more sensitive index of nutritional status than albumin.

GUIDELINE 5: SERUM CREATININE AND THE CREATININE INDEX

The serum creatinine (SCr) and creatinine index are valid and clinically useful markers of protein–energy nutritional status in people on MD.

1. The predialysis or stabilized SCr and the creatinine index reflect the sum of dietary intake of foods rich in creatine and creatinine (e.g., skeletal muscle) and endogenous (skeletal muscle) creatinine production minus the urinary excretion, dialytic removal and endogenous degradation of creatinine.
2. Individuals with low predialysis or stabilized SCr (less than approximately 10 mg/dL) should be evaluated for protein–energy malnutrition and wasting of skeletal muscle.
3. A low creatinine index and, in the absence of substantial endogenous urinary creatinine clearance, a low SCr concentration suggest low dietary protein intake (DPI) and/or diminished skeletal muscle mass and are associated with increased mortality rates.

GUIDELINE 6: SERUM CHOLESTEROL

Serum cholesterol is a valid and clinically useful marker of protein–energy nutritional status in people on maintenance HD (MHD).

1. Low or declining serum cholesterol concentrations are predictive of increased mortality risk.
2. Hypocholesterolemia is associated with chronic protein–energy deficits and/or the presence of comorbid conditions, including inflammation.
3. Individuals with low, low-normal (less than approximately 150–180 mg/dL), or declining serum cholesterol levels should be investigated for possible nutritional deficits.

GUIDELINE 7: DIETARY INTERVIEWS AND DIARIES

Dietary interviews and/or diaries are valid and clinically useful for measuring DPI and dietary energy intake (DEI) in people undergoing MD.

GUIDELINE 8: PROTEIN EQUIVALENT OF TOTAL NITROGEN APPEARANCE

Protein equivalent of total nitrogen appearance (PNA) or protein catabolic rate (PCR) is a valid and clinically useful measure of net protein degradation and protein intake in people on MD.

1. When nitrogen balance is zero in the steady state, the difference between nitrogen intake and total nitrogen losses is zero or only slightly positive (i.e., up to about 0.5 g nitrogen/d because of unmeasured nitrogen losses). Hence, in the clinically stable individual, PNA provides a valid estimate of protein intake.
2. The PNA can be estimated from interdialytic changes in urea nitrogen concentration in serum and the urea nitrogen content of urine and dialysate.
3. Because both net protein breakdown under fasting conditions and dietary protein requirements are strongly influenced by body mass, PNA (or PCR) is often normalized to a function of body weight (Guideline 12).

GUIDELINE 9: SUBJECTIVE GLOBAL NUTRITIONAL ASSESSMENT

SGA is a valid and clinically useful measure of protein–energy nutritional status in people on MD.

GUIDELINE 10: ANTHROPOMETRY

Anthropometric measurements are valid and clinically useful indicators of protein–energy nutritional status in people on MD.

1. These measures include percent usual body weight, percent standard body weight, body mass index, skinfold thickness, estimated percent body fat, and midarm muscle area, circumference or diameter.

GUIDELINE 11: DUAL-ENERGY X-RAY ABSORPTIOMETRY

Dual-energy X-ray absorptiometry (DXA) is a valid and clinically useful technique for assessing protein–energy nutritional status.

1. Accurate data on body composition are helpful to assess long-term adequacy of protein–energy nutritional status.
2. Whole body DXA provides an accurate method to assess body composition, which is less influenced by the abnormalities in hydration status common in people on MD.

GUIDELINE 12: ADJUSTED EDEMA-FREE BODY WEIGHT

The body weight to be used for assessing or prescribing protein or energy intake is the adjusted edema-free body weight. For people on HD, this should

be obtained postdialysis. For people on PD, this should be obtained after drainage of dialysate.

1. The adjusted edema-free body weight should be used for people undergoing MD who have an edema-free body weight less than 95% or >115% of the median standard weight, as determined from the NHANES II data.
2. For individuals whose edema-free body weight is between 95 and 115% of the median standard weight, the actual edema-free body weight may be used.
3. For DXA measurements of total body fat and fat-free mass, the actual edema-free body weight obtained at the time of the DXA measurement should be used.
4. For anthropometric calculations, the postdialysis (for MHD) or post-drain (for CPD) actual edema-free body weight should be used.

MD: MANAGEMENT OF ACID–BASE STATUS

GUIDELINE 13: MEASUREMENT OF SERUM BICARBONATE

Serum bicarbonate should be measured in people on MD once monthly.

GUIDELINE 14: TREATMENT OF LOW SERUM BICARBONATE

Predialysis or stabilized serum bicarbonate levels should be maintained ≥22 mmol/L.

MD: MANAGEMENT OF PROTEIN AND ENERGY INTAKE

GUIDELINE 15: DPI IN MHD

The recommended DPI for clinically stable people on MHD is 1.2 g/kg body weight/d.

1. At least 50% of the dietary protein should be of high biological value.

GUIDELINE 16: DPI FOR CPD

The recommended DPI for clinically stable people on CPD is 1.2 to 1.3 g/kg body weight/d.

1. DPI should be no less than 1.2 g/kg/d.
2. Unless an individual has demonstrated adequate protein nutritional status on a 1.2-g protein/kg/d diet, 1.3 g protein/kg/d should be prescribed.
3. At least 50% of the dietary protein should be of high biological value.

GUIDELINE 17: DAILY ENERGY INTAKE FOR PEOPLE ON MD

The recommended daily energy intake for people on MHD or CPD is 35 kcal/kg body weight/d for those who are less than 60 years of age and 30 to 35 kcal/kg body weight/d for individuals 60 years or older.

1. Energy expenditure of people undergoing MHD or CAPD is similar to that of normal, healthy individuals.

2. Metabolic balance studies of people undergoing MHD indicate that a total daily energy intake of about 35 kcal/kg/d induces neutral nitrogen balance and is adequate to maintain serum albumin and anthropometric indices.
3. Because individuals more than 60 years of age tend to be more sedentary, a total energy intake of 30 to 35 kcal/kg is acceptable.

MD: NUTRITIONAL COUNSELING AND FOLLOW-UP

GUIDELINE 18: INTENSIVE NUTRITIONAL COUNSELING WITH MD

Every person on MD should receive intensive nutritional counseling based on an individualized plan of care developed before or at the time of commencement of MD therapy.

1. A plan of care for nutritional management should be developed before or during the early phase of MD care and modified frequently based on the individual's medical and social conditions.
2. The plan of care should be updated at least every three to four months.
3. Nutrition counseling should be intensive initially and provided thereafter every one or two months and more frequently if inadequate nutrient intake or malnutrition is present or if adverse events or illnesses occur that may cause deterioration in nutritional status.

GUIDELINE 19: INDICATIONS FOR NUTRITIONAL SUPPORT

Individuals undergoing MD who are unable to meet their protein and energy requirements with food intake for an extended period of time should receive nutrition support.

1. The period of inadequate intake after which nutritional support should be instituted ranges from days to two weeks, depending on the severity of the individual's clinical condition, degree of malnutrition (if any) and the degree of inadequacy of their nutritional intake.
2. Before considering nutrition support, the individual should receive a complete nutritional assessment.
3. Any potentially reversible or treatable condition or medication that might interfere with appetite or cause malnutrition should be eliminated or treated.
4. For nutrition support, the oral diet may be fortified with energy and protein supplements.
5. If oral nutrition (including nutritional supplements) is inadequate, tube feeding should be offered if medically appropriate.
6. If tube feeding is not used, intradialytic parenteral nutrition (IDPN; for HD) or intraperitoneal amino acids (IPAA; for PD) should be considered if either approach in conjunction with existing oral intake meets the protein and energy requirements.
7. If the combination of oral intake and IDPN or IPAA does not meet protein and energy requirements, daily total or partial parenteral nutrition should be considered.

8. The dialysis regimen should be regularly monitored and modified to treat any intensification of the individual's uremic state that is caused by superimposed illness or increased protein intake.

GUIDELINE 20: PROTEIN INTAKE DURING ACUTE ILLNESS

The optimum protein intake for a person on MD who is acutely ill is at least 1.2 to 1.3 g/kg/d.

1. People on MHD who are acutely ill should receive at least 1.2 g protein/kg/d.
2. People on CPD who are acutely ill should receive at least 1.3 g protein/kg/d.

GUIDELINE 21: ENERGY INTAKE DURING ACUTE ILLNESS

The recommended energy intake for a person on MD who is acutely ill is at least 35 kcal/kg/d for those who are less than 60 years of age and at least 30 to 35 kcal/kg/d for those who are 60 years of age or older.

MD: CARNITINE

GUIDELINE 22: L-CARNITINE FOR PEOPLE ON MD

There are insufficient data to support the routine use of L-carnitine for people undergoing MD.

1. Although the administration of L-carnitine may improve subjective symptoms such as malaise, muscle weakness, intradialytic cramps and hypotension and quality of life (QOL) in selected people on MD, the totality of evidence is insufficient to recommend its routine provision for any proposed clinical disorder without prior evaluation and attempts at standard therapy.
2. The most promising of proposed applications is treatment of erythropoietin-resistant anemia.

ADVANCED CHRONIC RENAL FAILURE WITHOUT DIALYSIS

GUIDELINE 23: PANELS OF NUTRITIONAL MEASURES FOR NONDIALYZED PATIENTS

For individuals with chronic renal failure (CRF; glomerular filtration rate [GFR] <20 mL/min) protein–energy nutritional status should be evaluated by serial measurements of a panel of markers including at least one value from each of the following clusters: (1) serum albumin; (2) edema-free actual body weight, percent standard (NHANES II) body weight or SGA; and (3) nPNA or dietary interviews and diaries.

1. It is recommended that serum albumin and actual or percent standard body weight and/or SGA be measured every one to three months.
2. Dietary interviews and diaries and/or nPNA should be performed every three to four months.

3. For people with more advanced CRF (i.e., GFR ≤15 mL/min), concomitant illness, inadequate nutrient intake, deteriorating nutritional status or frank malnutrition, more frequent monitoring may be necessary.

GUIDELINE 24: DPI FOR NONDIALYZED PATIENTS

For individuals with CRF (GFR <20 mL/min) who are not undergoing MD, the institution of a planned low-protein diet providing 0.60 g protein/kg/d should be considered. For individuals who will not accept such a diet or who are unable to maintain adequate DEI with such a diet, an intake of up to 0.75 g protein/kg/d may be prescribed.

1. When properly implemented and monitored, low-protein, high-energy diets maintain nutritional status while limiting the generation of potentially toxic nitrogenous metabolites, the development of uremic symptoms, and the occurrence of other metabolic complications.
2. Evidence suggests that low-protein diets may retard the progression of renal failure or delay the need for dialysis therapy.
3. At least 50% of the dietary protein should be of high biological value.
4. When people with CRF consume uncontrolled diets, a decline in protein intake and in indices of nutritional status is often observed.

GUIDELINE 25: DEI FOR NONDIALYZED PATIENTS

The recommended DEI for individuals with CRF (GFR <25 mL/min) who are not undergoing MD is 35 kcal/kg/d for those who are younger than 60 years old and 30 to 35 kcal/kg/d for individuals who are 60 years of age or older. Because individuals more than 60 years of age tend to be more sedentary, a lower total energy intake of 30 to 35 kcal/kg/d is acceptable.

1. Energy expenditure of nondialyzed individuals with CRF is similar to that of healthy individuals.
2. Metabolic balance studies of such individuals indicate that a diet providing about 35 kcal/kg/d engenders neutral nitrogen balance and maintains serum albumin and anthropometric indices.
3. Because individuals more than 60 years of age tend to be more sedentary, a lower total energy intake of 30 to 35 kcal/kg/d is acceptable.

GUIDELINE 26: INTENSIVE NUTRITIONAL COUNSELING FOR CRF

The nutritional status of individuals with CRF should be monitored at regular intervals.

1. A spontaneous reduction in DPI and a progressive decline in indices of nutritional status occur in many nondialyzed patients with CRF.
2. The presence of protein–energy malnutrition at the initiation of MD is predictive of future mortality risk.

3. Interventions that maintain or improve nutritional status during progressive renal failure are likely to be associated with improved long-term survival after commencement of MD.
4. Because evidence of protein–energy malnutrition may develop before individuals require renal replacement therapy, regular monitoring (e.g., at one- to three-month intervals) of the individual's nutritional status should be a routine component of the care for the person with CRF.
5. Nutritional status should be assessed more frequently if there is inadequate nutrient intake, frank protein–energy malnutrition or the presence of an illness that may worsen nutritional status.

GUIDELINE 27: INDICATIONS FOR RENAL REPLACEMENT THERAPY

In people with CRF (e.g., GFR <15–20 mL/min) who are not undergoing MD, if protein–energy malnutrition develops or persists despite vigorous attempts to optimize protein and energy intake and there is no apparent cause for malnutrition other than low nutrient intake, initiation of MD or a renal transplant is recommended.

SECTION 3

2006 UPDATES HEMODIALYSIS ADEQUACY, PERITONEAL DIALYSIS ADEQUACY AND VASCULAR ACCESS

Source: National Kidney Foundation. *KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for 2006 Updates: Hemodialysis Adequacy, Peritoneal Dialysis Adequacy and Vascular Access*. Am J Kidney Dis 48:S1–S322, 2006 (Suppl 1). Available at: http://www.kidney.org/professionals/KDOQI/guideline_upHD_PD_VA/index.htm

The original document is subdivided into three major sections, one each for HD adequacy, PD adequacy and vascular access. Each section includes CPGs and CPRs for adults and children. Guidelines, recommendations, tables and figures are numbered according to the original document for easy cross-referencing.

CPGs FOR HD ADEQUACY

GUIDELINE 1: INITIATION OF DIALYSIS

1.1 People who reach CKD stage 4 (estimated GFR <30 mL/min/1.73 m^2) should receive timely education about kidney failure and options for its treatment, including kidney transplantation, PD, HD in the home or in-center and conservative treatment. Patients' family members and caregivers also should be educated about treatment choices for kidney failure.

1.2 Estimation of kidney function:
Estimation of GFR should guide decision making regarding dialysis therapy initiation. GFR should be estimated by using a validated estimating equation (Table 1) or by measurement of creatinine and urea clearances, not simply by measurement of SCr and urea nitrogen. Refer to the original guideline for a summary of special circumstances in which GFR estimates should be interpreted with particular care.

1.3 Timing of therapy:
When people reach stage 5 CKD (estimated GFR <15 mL/min/1.73 m^2), nephrologists should evaluate the benefits, risks and disadvantages of beginning kidney replacement therapy (KRT). Particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5.

GUIDELINE 2: METHODS FOR MEASURING AND EXPRESSING THE HD DOSE

Quantifying HD is the first step toward assessment of its adequacy. Fortunately, the intermittent rapid decrease in urea concentration during HD allows a relatively easy measurement of the dose.

Table 1. Validated GFR-Estimating Equations

Age ≥18 years
Cockcroft-Gault equation[1]
MDRD 4-Variable equation[2]
MDRD 6-Variable equation[3]
Age ≤18 years
Schwartz formula[4]

References:

[1] Cockcroft DW, Gault MH. *Prediction of creatinine clearance from serum creatinine*. Nephron 16:31–41, 1976.

[2] Levey AS, Grenne T, Kusek JW, et al. *A simplified equation to predict glomerular filtration rate from serum creatinine*. J Am Soc Nephrol 11:155A (abst), 2000.

[3] Levey AS, Bosch JP, et al. *A more accurate method to estimate glomerular filtration from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group*. Ann Intern Med 130:461–470, 1999.

[4] Schwartz GJ, Brion LP, Spitzer A. *The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children and adolescents*. Pediatr Clin North Am 34:571–590, 1987.

MDRD, modification of diet in renal disease.

2.1 The delivered dose of HD should be measured at regular intervals no less than monthly.

2.2 The frequency of treatments should be included in the expression of dose.

2.3 The dose of HD should be expressed as $(K_{urea} \times T_d)/V_{urea}$ (abbreviated as Kt/V),where K_{urea} is the effective (delivered) dialyzer urea clearance in milliliters per minute integrated over the entire dialysis, T_d is the time in minutes measured from beginning to end of dialysis, and V_{urea} is the patient's volume of urea distribution in milliliters.

2.4 The preferred method for measurement of the delivered dose is formal urea kinetic modeling. Other methods may be used provided they give similar results and do not significantly overestimate the modeled dose.

2.5 Several methods can be used to add the continuous component of residual urea clearance to the intermittent dialysis single-pool delivered Kt/V (spKt/V) to compute an adjusted intermittent Kt/V. Laboratories reporting adjusted session Kt/V values should clearly identify such measurements by a different name (e.g., "adjusted"Kt/V or "total" Kt/V).

GUIDELINE 3: METHODS FOR POSTDIALYSIS BLOOD SAMPLING

When dialysis adequacy is assessed by using predialysis and postdialysis blood urea nitrogen (BUN) measurements, blood samples should be drawn by using certain acceptable procedures.

3.1 Both samples (predialysis and postdialysis) should be drawn during the same treatment session.

3.2 The risk of underestimating predialysis BUN level because of saline dilution or by sampling the blood after treatment has begun should be avoided.

3.3 The risk of underestimating the postdialysis BUN level because of access recirculation (AR) should be avoided by first slowing the blood flow through the dialyzer to a rate at which AR is expected to be minimal (100 mL/min) for a period long enough to ensure that unrecirculated blood has advanced to below the sampling port (usually 15 s).

3.4 An alternative method is to stop the dialysate flow for a period long enough to increase the dialysate outlet BUN level close to that of the blood inlet BUN level (3 min) before obtaining the postdialysis sample.

GUIDELINE 4: MINIMALLY ADEQUATE HD

4.1 Minimally adequate dose:
The minimally adequate dose of HD given three times per week to people with residual native kidney urea clearance (Kr) less than 2 mL/min/1.73 m^2 should be an spKt/V (excluding residual kidney function [RKF]) of 1.2 per dialysis. For treatment times less than five hours, an alternative minimum dose is a urea reduction ratio (URR) of 65%.

4.2 Target dose:
The target dose for HD given three times per week with Kr less than 2 mL/min/1.73 m^2 should be an spKt/V of 1.4 per dialysis not including RKF, or URR of 70%.

4.3 In people with Kr ≥2 mL/min/1.73 m^2, the minimum session spKt/V can be reduced. One method of minimum dose reduction is described in CPR 4.4. In such people, the target spKt/V should be at least 15% greater than the minimum dose.

4.4 Missed and shortened treatments:
Efforts should be made to monitor and minimize the occurrence of missed or shortened treatments.

GUIDELINE 5: CONTROL OF VOLUME AND BLOOD PRESSURE

There is ample evidence in the non-CKD population that optimal control of blood pressure influences mortality. In the HD population, available evidence indicates that control of an individual's fluid volume influences outcome. Volume and blood pressure are linked; thus, it is important to optimize ultrafiltration and dry weight to control blood pressure in an effort to improve patient outcome.

5.1 The ultrafiltration component of the HD prescription should be optimized with a goal to render the patient euvolemic and normotensive. This includes counseling the patient on sodium and fluid restriction, adequate ultrafiltration, and the use of diuretics in people with RKF.

5.2 Daily dietary sodium intake should be restricted to no more than 5 g of sodium chloride (2.0 g or 85 mmol of sodium).

5.3 Increasing positive sodium balance by "sodium profiling" or using a high dialysate sodium concentration should be avoided.

GUIDELINE 6: PRESERVATION OF RKF

Prospective randomized trials and observational studies have confirmed that the presence of RKF is one of the most important predictors of a patient's survival.

6.1 One should strive to preserve RKF in people on HD.

6.2 Methods for preserving RKF differ among patients (see CPR 6).

GUIDELINE 7: QUALITY IMPROVEMENT PROGRAMS

The continuous quality improvement (CQI) process has been shown to improve clinical outcomes in many disciplines, including CKD. It presently is conducted at both the facility and local network level.

7.1 For HD adequacy, each dialysis clinic should continue to monitor the processes related to the delivery of dialysis, such as Kt/V, reuse standards, etc.

7.2 Consideration should be given to providing resources and training for expanding the assessment of clinical outcomes beyond mortality to include hospitalization rates, QOL, patient satisfaction, and transplantation rates, recognizing that without adequate resources and training, these outcomes are unlikely to be valid, and the efforts to collect such information may adversely affect patient care.

7.3 Quality improvement programs should include representatives of all disciplines involved in the care of people on HD, including physicians, physician assistants, nurse practitioners, nurses, social workers, dietitians and administrative staff.

GUIDELINE 8: PEDIATRIC HD PRESCRIPTION AND ADEQUACY

8.1 Initiation of HD:

8.1.1 Dialysis initiation considerations for the pediatric patient should follow the adult patient guideline of a GFR <15 mL/min/1.73 m^2.

8.1.2 For pediatric patients, GFR can be estimated by using either a timed urine collection or the Schwartz formula.

8.1.3 Dialysis therapy initiation should be considered at higher estimated GFRs when the individual's clinical course is complicated by the presence of the signs and symptoms listed in Table 2, CPR 1 for adults, as well as malnutrition or growth failure for pediatric patients. Before dialysis is undertaken, these conditions should be shown to be refractory to medication and/or dietary management.

8.2 Measurement of HD adequacy:

8.2.1 spKt/V, calculated by either formal urea kinetic modeling or the second-generation natural logarithm formula, should be used for month-to-month assessment of delivered HD dose.

8.2.2 Assessment of nutrition status is an essential component of HD adequacy measurement. Normalized PCR should be measured monthly by using either formal urea kinetic modeling or algebraic approximation.

8.2.3 Principles and statements regarding slow-flow methods for post-dialysis sampling and inclusion of RKF (or lack thereof) outlined in the adult guidelines also pertain to pediatric patients.

8.3 Prescription of adequate HD:

8.3.1 Children should receive at least the delivered dialysis dose as recommended for the adult population.

8.3.2 For younger pediatric patients, prescription of higher dialysis doses and higher protein intakes at 150% of the recommended nutrient intake for age may be important.

8.4 Non-dose-related components of adequacy:

Accurate assessment of intravascular volume during the HD treatment should be provided to optimize ultrafiltration.

CPRs FOR HD ADEQUACY

CPR FOR GUIDELINE 1: INITIATION OF DIALYSIS

Certain complications of kidney failure justify initiation of dialysis treatment in people for whom estimated GFR has not yet decreased to15 mL/min/1.73 m^2 (Table 11).

Table 11. Complications That May Prompt Initiation of Kidney Replacement Therapy

Intractable ECV overload
Hyperkalemia
Metabolic acidosis
Hyperphosphatemia
Hypercalcemia or hypocalcemia
Anemia
Neurological dysfunction (eg, neuropathy, encephalopathy)
Pleuritis or pericarditis
Otherwise unexplained decline in functioning or well-being
Gastrointestinal dysfunction (eg, nausea, vomiting, diarrhea, gastroduodenitis)
Weight loss or other evidence of malnutrition
Hypertension

CPR FOR GUIDELINE 2: METHODS FOR MEASURING AND EXPRESSING THE HD DOSE

For people managed with HD, both dialyzer and native kidney function can be measured periodically to assess the adequacy of replacement therapy. Urea clearance is the preferred measure of both (see Guideline 2).

2.1 Kr is measured best from a timed urine collection.

2.2 For purposes of quality assurance (QA), the delivered dose should be measured and compared with the prescribed dose each month.

CPR FOR GUIDELINE 4: MINIMALLY ADEQUATE HD

4.1 High-Flux Membrane:
When methods to achieve good dialysate water quality are available, high-flux HD membranes should be used, defined as those providing β_2-microglobulin (β2M) clearance of at least 20 mL/min under conditions of actual use.

4.2 Minimum dose with hemofiltration or hemodiafiltration:
The recommended minimum delivered dose target, measured by using pretreatment and post treatment BUN levels, is the same as that for HD.

4.3 Minimum spKt/V levels for different dialysis schedules:

4.3.1 Two to six treatments per week are appropriate for certain people.

4.3.2 Twice-weekly HD is not appropriate for people with Kr less than 2 mL/min/1.73 m^2.

4.3.3 Minimum spKt/V targets for two-, four-, and six-times-per-week dialysis schedules logically should be different from that for the thrice-weekly schedule. In the absence of dose-ranging outcomes data, minimum spKt/V targets for different schedules can be based on achieving a minimum standard Kt/V of 2.0 per week.

4.3.4 The target spKt/V dose should be at least 15% higher than the listed minimum dose because of the variability in measuring Kt/V, as discussed in Guideline 4.

4.4 RKF (measured by Kr):

4.4.1 The minimally adequate dose of dialysis can be reduced in people with Kr >2 mL/min/1.73 m^2.

4.4.2 In the absence of dose-ranging outcomes data, the minimum spKt/V target for people with substantial RKF can be reduced, but the reduced target should be no lower than 60% of the minimum target for people with no residual renal function (the reduction depends on dialysis frequency), per values provided in Table 13.

Table 13. Minimum spKt/V[a] Values Corresponding to a stdKt/V[b] of Approximately 2.0 per week

Schedule	K_r <2 mL/min/1.73 m²	K_r >2 mL/min/1.73 m²
2x/wk	Not recommended	2.0[c]
3x/wk	1.2	0. 9
4x/wk	0.8	0.6
6x/wk (short daily)	0.5	0.4

a. Dialyzer clearance only, expressed per dialysis
b. Calculated using a 2-compartment mathematical model. Assumptions: patient with V = 35 L (should not matter); T_d is constant; K_d varies; ultrafiltration is 7 L/wk; nPCR is 1 g/kg/d (should not matter); dialyzed compartment is 1/3 of total V; K_r(urea) is 0 or 2 mL/min; symmetric schedule.
c. Not recommended unless Kr > 3
It is important to note that the minimum values for spKt/V shown in this table do not take into account reported improvements in outcome from increasing Kt/V when dialysis frequency is increase to more than 3x/week.

4.4.3 When the minimally adequate dose is reduced because of substantial RKF, Kr should be monitored at least quarterly and as soon as possible after any event that might have acutely reduced RKF.

4.5 Increase in minimally adequate dose for women and smaller individuals: An increase in the minimally adequate dose of dialysis should be considered for the following groups of people:

4.5.1 Women of any body size.

4.5.2 Smaller individuals, for example, people with values for anthropometric or modeled V ≤25 L.

4.6 Dialysis adequacy for people who are malnourished and/or losing weight:

An increase in the minimally adequate dose of dialysis and/or a change to a more frequent dialysis schedule should be considered for the following groups of patients:

4.6.1 People whose weights are 20% less or lower than their peer body weights.

4.6.2 People with recent otherwise unexplained and unplanned weight loss.

4.7 Dialysis adequacy for people with hyperphosphatemia or chronic fluid overload and other categories of patients who might benefit from more frequent dialysis:

A change to a more frequent dialysis schedule should be considered for the following groups of patients:

4.7.1 People with hyperphosphatemia.

4.7.2 People with chronic fluid overload with or without refractory hypertension.

4.8 A change to a more frequent dialysis schedule may be beneficial to a broader group of patients in terms of improving QOL and quality of sleep, reducing sleep apnea and improving sensitivity to erythropoietin.

4.9 Minimum dialysis treatment time for thrice-weekly schedules: The minimum HD treatment time for thrice-weekly dialysis in people with Kr <2 mL/min should be at least three hours.

CPR FOR GUIDELINE 5: DIALYZER MEMBRANES AND REUSE

Selection of dialyzer membranes and reuse practices are not included in the prescription of small-solute clearance, yet they can be important determinants of patient survival and QOL.

5.1 When dialyzers are reused, they should be reprocessed following the Association for the Advancement of Medical Instrumentation *Standards and Recommended Practices* for reuse of hemodialyzers.

5.2 Dialyzers intended for reuse should have a blood compartment volume not less than 80% of the original measured volume or a urea (or ionic) clearance not less than 90% of the original measured clearance.

5.3 The use of poorly biocompatible, unmodified cellulose dialyzer membranes for HD is discouraged.

CPR FOR GUIDELINE 6: PRESERVATION OF RKF

Several actions and precautions are recommended to preserve and enhance RKF.

6.1 Angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARBs) are agents of choice in people on HD with significant RKF and who need antihypertensive medication. Other measures to protect native kidneys are listed in Table 15.

6.2 Insults known to be nephrotoxic (e.g., see Table 16) in people with normal or impaired kidney function should be assumed, in the absence of direct evidence, to be nephrotoxic for the remnant kidney in people on HD and therefore should be avoided.

6.3 Prerenal and postrenal causes of decrease in RKF should be considered in the appropriate clinical setting.

Table 15. Efforts To Protect RKF

Avoidance of nephrotoxic agents, especially aminoglycosides, nonsteroidal anti-inflammatory drugs, COX-2 inhibitors and radiocontrast media
Avoidance of excessive ultrafiltration and hypotension during treatment
Routine use of biocompatible dialyzer membranes
Routine use of bicarbonate-based dialysate
Aggressive treatment of severe hypertension
Use of ACE inhibitors and/or ARBs
Use of ultrapure dialysate

COX-2: Cyclooxygenase-2

Table 16. Potential Insults to RKF

Radiographic contrast dye administered intravenously or intra-arterially
Aminoglycoside antibiotics
Nonsteroidal anti-inflammatory drugs, including COX-2 inhibitors
ECF volume depletion
Urinary tract obstruction
Hypercalcemia
Severe hypertension
Withdrawal of immunosuppressive therapy from a transplanted kidney

CPGs FOR PD ADEQUACY

GUIDELINE 1: INITIATION OF DIALYSIS

1.1 Preparation for kidney failure:
People who reach CKD stage 4 (estimated GFR <30 mL/min/1.73 m^2) should receive timely education about kidney failure and options for its treatment, including kidney transplantation, PD, HD in the home or in-center and conservative treatment. Patients' family members and caregivers also should be educated about treatment choices for kidney failure.

1.2 Estimation of kidney function:
Estimation of GFR should guide decision making regarding dialysis therapy initiation. GFR should be estimated by using a validated estimating equation (Table 1) or by measurement of creatinine and urea clearances, not simply by measurement of SCr and urea nitrogen. Refer to the original guideline for a summary of special circumstances in which GFR estimates should be interpreted with particular care.

1.3 Timing of therapy:
When people reach stage 5 CKD (estimated GFR <15 mL/min/1.73 m^2), nephrologists should evaluate the benefits, risks and disadvantages of beginning KRT. Particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5.

GUIDELINE 2: PD SOLUTE CLEARANCE TARGETS AND MEASUREMENTS

Data from RCTs suggested that the minimally acceptable small-solute clearance for PD is less than the prior recommended level of a weekly Kt/V_{urea} of 2.0. Furthermore, increasing evidence indicates the importance of RKF as opposed to peritoneal small-solute clearance with respect to predicting patient survival. Therefore, prior targets have been revised as indicated next.

2.1 For people with RKF (considered to be significant when urine volume is >100 mL/d):

2.1.1 The minimal "delivered" dose of total small-solute clearance should be a total (peritoneal and kidney) Kt/V_{urea} of at least 1.7 per week.

2.1.2 Total solute clearance (residual kidney and peritoneal, in terms of Kt/V_{urea}) should be measured within the first month after initiating dialysis therapy and at least once every four months thereafter.

2.1.3 If the individual has >100 mL/d of residual urine volume and residual kidney clearance is being considered as part of the total weekly solute clearance goal, a 24-hour urine collection for urine volume and solute clearance determinations should be obtained at a minimum of every two months.

2.2 For people without RKF (considered insignificant when urine volume is ≤100 mL/d):

2.2.1 The minimal "delivered" dose of total small-solute clearance should be a peritoneal Kt/V_{urea} of at least 1.7 per week measured within the first month after starting dialysis therapy and at least once every four months thereafter.

GUIDELINE 3: PRESERVATION OF RKF

Prospective randomized trials of dialysis adequacy and many observational studies have confirmed a strong association between the presence of RKF and reduction of mortality in people on PD therapy.

3.1 It is important to monitor and preserve RKF.

3.2 In the individual with RKF who needs antihypertensive medication, preference should be given to the use of ACE inhibitors or ARBs.

3.3 In the normotensive person with RKF, consideration should be given to the use of ACE inhibitors or ARBs for kidney protection.

3.4 Insults to RKF (see Table 7) in people with CKD also should be considered insults to RKF in people on PD and should be avoided when possible.

GUIDELINE 4: MAINTENANCE OF EUVOLEMIA

Volume overload is associated with congestive heart failure (CHF), left ventricular hypertrophy (LVH) and hypertension; therefore, it is important to monitor ultrafiltration volume, dry weight, sodium intake and other clinical assessments of volume status.

4.1 Each facility should implement a program that monitors and reviews peritoneal dialysate drain volume, RKF and blood pressure on a monthly basis.

4.2 Some of the therapies one should consider to optimize extracellular water and blood volume include, but are not limited to, restricting dietary sodium and water intake, use of diuretics in people with RKF and optimization of peritoneal ultrafiltration volume and sodium removal.

Table 7. Potential Insults to RKF in Patients on Dialysis

Radiocontrast dye administered intravenously or intra-arterially
Aminoglycoside antibiotics
NSAIDS, including cox-2 inhibitors
ECF volume depletion
Urinary tract obstruction
Hypercalcemia
Withdrawal of immunosuppressive therapy from a transplanted kidney

GUIDELINE 5: QUALITY IMPROVEMENT PROGRAMS

The CQI process has been shown to improve outcomes in many disciplines, including CKD stage 5.

5.1 Each home-training unit should establish quality improvement programs with the goal of monitoring clinical outcomes and implementing programs that result in improvements in patient care.

5.2 Quality improvement programs should include representatives of all disciplines involved in the care of the person on PD, including physicians, midlevel practitioners, nurses, social workers, dietitians and administrators.

5.3 Suggested domains of clinical activities one should consider monitoring are listed in Table 9.

Table 9. Various Domains To Be Considered for CQI Studies

1.	Peritonitis rates
2.	Exit-site infection rates
3.	Technique failure rates
4.	Patient satisfaction
5.	QOL
6.	Catheter-related problems and catheter survival rates
7.	Other domains, outlined in other parts of these guidelines, such as adequacy measures, anemia and bone and mineral metabolism management, blood pressure and volume control, lipid control, etc.

GUIDELINE 6. PEDIATRIC PD

6.1 Recommended laboratory measurements for peritoneal membrane function:

6.1.1 The peritoneal equilibration test is the preferred approach to the clinical assessment of peritoneal membrane transport capacity in pediatric patients and should be performed to aid in the prescription process.

6.2 Maintenance of euvolemia and normotension:

6.2.1 The frequent presence of hypertension and associated cardiac abnormalities in children receiving PD requires strict management of blood pressure, including attention to fluid status.

6.3 Quality improvement programs:

6.3.1 The CQI process has been shown to improve outcomes in many disciplines, including CKD stage 5.

6.3.1.1 Each home training unit should establish quality improvement programs with the goal of monitoring clinical outcomes and implementing programs that result in improvements in patient care. In children, growth and school attendance/performance are clinical activities to be monitored in addition to those recommended for adult patients.

6.3.1.2 Quality improvement programs should include representatives of all disciplines involved in the care of the pediatric individual on PD, including physicians, nurses, social workers, dietitians, play therapists, psychologists and teachers.

6.3.1.3 Single-center trends in pediatric clinical outcomes should be compared with national and international data.

CPRs FOR PD ADEQUACY

CPR FOR GUIDELINE 1: INITIATION OF DIALYSIS

Certain complications of kidney failure justify initiation of dialysis treatment in people for whom estimated GFR has not yet decreased to 15mL/min/1.73m^2 (Table 10).

Table 10. Complications That May Prompt Initiation of Kidney Replacement Therapy

Intractable ECV overload
Hyperkalemia
Metabolic acidosis
Hyperphosphatemia
Hypercalcemia or hypocalcemia
Anemia
Neurological dysfunction (eg, neuropathy, encephalopathy)
Pleuritis or pericarditis
Otherwise unexplained decline in functioning or well-being
Gastrointestinal dysfunction (eg, nausea, vomiting, diarrhea, gastroduodenitis)
Weight loss or other evidence of malnutrition
Hypertension

CPR FOR GUIDELINE 2: PD PRESCRIPTION TARGETS AND MEASUREMENTS

In a PD prescription, there are certain general considerations.

2.1 Regardless of delivered dose, if an individual is not thriving and has no other identifiable cause other than possible kidney failure, consideration should be given to increasing dialysis dose (see Table 11).

Table 11. Possible Indications To Consider Increasing the Dose of Dialysis

Uremic neuropathy
Uremic pericarditis
Nausea or vomiting otherwise unexplained
Sleep disturbance
Restless leg syndrome
Pruritus
Uncontrolled hyperphosphatemia
Evidence of volume overload
Hyperkalemia
Metabolic acidosis unresponsive to oral bicarbonate therapy
Anemia

2.2 In a person with minimal RKF, a continuous (rather than intermittent) 24 h/d of PD dwell PD prescription should be used to maximize middle-molecule clearance.

2.3 If either peritoneal Kt/V_{urea} is at least 1.7 or 24-hour urine output is <100 mL, monitoring of RKF is not required for monitoring the dose of PD. However, periodic measurement of RKF may be of value in this group of patients for the reasons noted in Table 12.

2.4 All measurements of peritoneal solute clearance should be obtained when the person is clinically stable and at least one month after resolution of an episode of peritonitis.

2.5 More frequent measurements of either peritoneal urea clearance or RKF should be obtained when clinically indicated (see Table 13).

2.6 When calculating Kt/V_{urea}, one should estimate V from either the Watson or Hume equation in adults. In the absence of evidence, use of the individual' ideal or standard (rather than actual) weight should be considered in the calculation of V.

2.7 The determination of peritoneal C_{Cr} is of little added value for predicting risk for death; therefore, for simplicity, adequacy targets are based on urea kinetics only. Peritoneal creatinine excretion rate may be used to monitor estimates of muscle mass over time.

2.8 During the monthly evaluation of people on PD, nutritional status should be estimated. Serum albumin levels should be monitored, and when obtaining 24-hour total solute clearances, estimations of DPI (such as nPNA) should be measured.

Table 12. Possible Clinical Indications for Obtaining a 24-Hour RKF Collection

Small-solute clearance measurement
24-hour urine volume
24-hour urine sodium excretion
Creatinine generation rate

Table 13. Clinical Indications for Measurement of Peritoneal or Kidney Clearance

Routine monitoring of total solute clearance
Documentation of delivered total solute clearance after a prescription change
Patient who has failure to thrive
Patient who is hypertensive or volume-overloaded
During an occasional evaluation of any other unsuspected clinical problem

CPR 3: RECOMMENDED LABORATORY MEASUREMENTS FOR PERITONEAL MEMBRANE FUNCTION AND ULTRAFILTRATION VOLUME

Total solute clearance and peritoneal effluent volume ultimately are influenced by peritoneal membrane transport characteristics. Multiple tests are documented to be efficacious for determining peritoneal membrane transport. None of these tests has been shown to be clinically superior to the others (see Table 14).

3.1 Each center should choose one of these tests to use when characterizing peritoneal transport in their patients.

3.2 Baseline peritoneal membrane transport characteristics should be established after initiating a daily PD therapy.

3.3 Data suggest that it would be best to wait four to eight weeks after starting dialysis to obtain this baseline measurement.

3.4 Peritoneal membrane transport testing should be repeated when clinically indicated (see Table 15).

3.5 All measurements of peritoneal transport characteristics should be obtained when the individual is clinically stable and at least one month after resolution of an episode of peritonitis.

Table 14. Standardized Tests for Evaluating Peritoneal Membrane Transport/Function

	Method of Peritoneal Function Testing		
Aspect of Peritoneal Function	**PET**	**SPA**	**PDC**
Small solute transport	D/P* creatinine	MTAC creatinine	Area permeability
Ultrafiltration capacity	Drain volume	Drain volume	Estimates ultrafiltration coefficient
Ultrafiltration via water channels	D/P Na	Model for Na channel	—
Fluid absorption	—	Dextran 70	Derived
Peritoneal blood flow	—	—	—
Permeability to macromolecules	—	Restriction coefficients	Large-pore flow

Abbreviations: SPA, standard peritoneal permeability analysis; MTAC, mass transfer area coefficient.
* Ratio of concentration of solutes in dialysate (D) to plasma (P).

Table 15. Clinical Indications for Repeat Peritoneal Membrane Transport Testing

Presence of unexplained volume overload
Decreasing drain volume (DV) on: overnight dwell (CAPD), or daytime dwell (APD)
Increasing clinical need for hypertonic dialysate dwells to maintain DV
Worsening of hypertension
Change in measured peritoneal solute removal (Kt/V_{urea})
Unexplained signs or symptoms of uremia

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis;
APD, automated peritoneal dialysis

CPR 4: WRITING THE PD PRESCRIPTION

The PD modality has an impact on adherence and QOL, which are important considerations in writing a PD prescription. Ultrafiltration, which is important in optimizing volume control and thus patient survival, is dependent on the prescription and peritoneal membrane characteristics. Clearance of middle molecules, although not proved to influence patient survival, should be an important consideration in the prescription.

4.1 The individual's schedule and QOL should be taken into account when prescribing PD.

4.2 To optimize middle-molecule clearance in people who have minimal RKF, the PD prescription should preferentially include dwells for the majority of the 24-hour day. This is recommended even if small-molecule clearance is above target without the longer dwell.

4.3 As tolerated by the patient, to optimize small-solute clearance and minimize cost, one should first increase instilled volume per exchange before increasing the number of exchanges per day. The exchange volume of the supine exchange(s) should be increased first because this position has the lowest intra-abdominal pressure.

4.4 The person's record of PD effluent volume should be reviewed monthly, with particular attention to the drain volume from the overnight dwell(s) of CAPD and the daytime dwell(s) of automated peritoneal dialysis (APD).

4.5 A number of techniques can be used to optimize volume and blood pressure control.

- **4.5.1 To achieve the desired volume status, the lowest possible dialysate dextrose concentration should be used.**
- **4.5.2 When appropriate, implement dietary sodium and fluid restriction.**
- **4.5.3 To achieve dry weight in people with RKF, diuretics may be preferred to increasing dialysate dextrose concentration.**
- **4.5.4 Drain volume should be optimized during the overnight dwell(s) of CAPD and the daytime dwell(s) of APD to maximize solute clearance and ultrafiltration volume.**
- **4.5.5 In people who are hypertensive or who show evidence of volume overload, ultrafiltration generally should not be negative (i.e., no absorption) for any daytime or nighttime exchanges.**

CPR FOR GUIDELINE 6: PEDIATRIC PD

6.1 Dialysis initiation:

- **6.1.1 Dialysis initiation should be considered for the pediatric patient when GFR is 9 to 14 mL/min/1.73 m^2 body surface area (BSA) and should be recommended when GFR is ≤8 mL/min/1.73 m^2. GFR can be estimated by either averaging the measured creatinine and**

urea clearances by using a timed urine collection, the Schwartz formula or a timed urine collection to determine C_{Cr} after a dose of cimetidine. Dialysis therapy initiation should be considered at the greater estimated GFR levels when the individual's clinical course is complicated by the presence of malnutrition, fluid overload, hypertension, hyperkalemia, hyperphosphatemia, acidosis, growth failure/decreasing height velocity or neurological consequences of uremia. Before dialysis is undertaken, these conditions should be shown to be persistent and refractory to medication and/or dietary management.

6.2 Modality selection:

6.2.1 The decision regarding the selection of PD as a dialysis modality for the pediatric patient should take a variety of factors into account, including patient/family choice, patient size, medical comorbidities and family support.

6.3 Solute clearance targets and measurements:

6.3.1 In the absence of definitive data correlating solute removal and clinical outcome in children, current recommendations for solute clearance in pediatric patients receiving PD are as follows:

6.3.1.1 The pediatric patient's clinical status should be reviewed at least monthly, and delivery of the prescribed solute clearance should render the individual free of signs and symptoms of uremia.

6.3.1.2 All measurements of peritoneal solute clearance should be obtained when the individual is clinically stable and at least one month after resolution of an episode of peritonitis.

6.3.1.3 More frequent measurements of peritoneal solute clearance and RKF should be considered when clinical events are likely to have resulted in decreased clearance or when new/worsening signs or symptoms of uremia develop.

6.3.1.4 Regardless of the delivered dose of dialysis, if a person is not doing well and has no other identifiable cause other than kidney failure, a trial of increased dialysis is indicated.

6.3.2 For people with RKF (defined as urine Kt/V_{urea} >0.1/wk):

6.3.2.1 The minimal "delivered" dose of total (peritoneal and kidney) small-solute clearance should be a Kt/V_{urea} of at least 1.8/wk.

6.3.2.2 Total solute clearance should be measured within the first month after initiating dialysis and at least once every six months thereafter.

6.3.2.3 If the individual has RKF and residual kidney clearance is being considered as part of the individual's total weekly solute clearance goal, a 24-hour urine collection for urine volume and solute clearance determinations should be obtained at a minimum of every three months.

6.3.3 For people without RKF (defined as urine $Kt/V_{urea} < 0.1$/wk) or for those in whom RKF is unable to be measured accurately:

6.3.3.1 The minimal "delivered" dose of small-solute clearance should be a peritoneal Kt/V_{urea} of at least 1.8/wk.

6.3.3.2 The peritoneal solute clearance should be measured within the first month after starting dialysis and at least once every six months thereafter.

6.3.4 When calculating Kt/V_{urea}, one should estimate V or total body weight (TBW) by using the sex-specific nomograms based on the following equations:

Males: $TBW = 0.010 \cdot (\text{height} \times \text{weight})^{0.68} - 0.37 \times \text{weight}$

Females: $TBW = 0.14 \cdot (\text{height} \times \text{weight})^{0.64} - 0.35 \times \text{weight}$

6.4 Preservation of RKF:

6.4.1 Techniques that may contribute to the preservation of RKF in pediatric patients receiving PD should be incorporated as a component of dialysis care whenever possible.

6.4.1.1 Nephrotoxic insults in those with normal or impaired kidney function should be assumed, in the absence of direct evidence, to also be nephrotoxic in people on PD therapy who have RKF and therefore should be avoided.

6.4.1.2 Aminoglycoside antibiotics should be avoided whenever possible to minimize the risk for nephrotoxicity, as well as ototoxicity and vestibular toxicity.

6.4.1.3 "Prekidney" and "postkidney" causes of a decrease in RKF should be considered in the appropriate clinical setting.

6.4.1.4 Infections of the urinary tract should be treated promptly.

6.4.1.5 Diuretics should be used to maximize urinary salt and water excretion.

6.4.1.6 ACE inhibitors or ARBs should be considered in people on PD who require antihypertensive medications and have RKF.

6.5 Writing the PD prescription:

6.5.1 In addition to solute clearance, QOL, ultrafiltration/volume control and possibly the clearance of middle molecules should be considered when writing the PD prescription.

6.5.1.1 The individual's dialysis schedule and QOL as it relates to such issues as school and work attendance/performance should be taken into account when designing the dialysis prescription.

6.5.1.2 To optimize small-solute clearance, minimize cost and possibly decrease the frequency of exchanges, one should first increase the instilled volume per exchange (target range, 1,000 to 1,200 mL/m^2 BSA; maximum, 1,400 mL/m^2 BSA), as tolerated by the individual, before increasing the number of exchanges per day. The volume of the supine exchange(s) should be increased first because this position has the lowest intra-abdominal pressure. Objective evidence of patient tolerance may require assessment of intraperitoneal pressure.

6.5.1.3 The individual's record of PD effluent volume should be reviewed monthly, with particular attention to the drain volume from the overnight dwell of CAPD and daytime dwell of continuous cycling PD (CCPD).

6.5.1.4 Factors to be considered when attempting to optimize total body volume include:

- Dietary sodium and fluid restriction may be implemented in people unable to maintain euvolemia/normotension with dialysis alone.
- In people with RKF, diuretics may be preferred over increasing the dialysate dextrose concentration to achieve euvolemia.
- Drain volume should be optimized after the overnight dwell of CAPD and the daytime dwell(s) of CCPD to maximize solute clearance and ultrafiltration volume.
- In people who are hypertensive or in whom there is evidence of volume overload, ultrafiltration generally should be positive for all daytime or nighttime exchanges.
- An effort should be made to determine the lowest possible dialysate dextrose concentration required to achieve the desired ultrafiltration volume.

6.5.1.5 To optimize middle-molecule clearance in people who have minimal RKF, the PD prescription should preferentially include the use of CCPD with dwells 24 h/d or CAPD. This is recommended even if small-molecule clearance is above target without the longer dwell.

6.5.1.6 The use of nightly intermittent PD (i.e., no daytime dwell) can be considered in pediatric patients who are clinically well, whose combined dialysis prescription and RKF achieves or exceeds the target solute clearance and who are without evidence of hyperphosphatemia, hyperkalemia, hypervolemia or acidosis.

6.6 Other aspects of the care of the pediatric PD patient:

6.6.1 All children on PD therapy with anemia should follow the *KDOQI Guidelines for Management of Anemia* that pertain to pediatrics.

6.6.2 Management of dyslipidemias for prepubertal children on PD therapy should follow recommendations by the National Cholesterol Expert Panel in Children and Adolescents. Post-pubertal children or adolescents on PD therapy should follow the pediatric recommendations provided in the *KDOQI Clinical Practice Guidelines for Managing Dyslipidemia in CKD.*

6.6.3 All children on PD therapy should follow the pediatric-specific recommendations provided in the *KDOQI Clinical Practice Guidelines for CVD in Dialysis Patients* and the *KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in CKD.*

6.6.4 All children on PD therapy should follow the recommendations provided in the *KDOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure.*

CPGs FOR VASCULAR ACCESS

GUIDELINE 1: PATIENT PREPARATION FOR PERMANENT HD ACCESS

Appropriate planning allows for the initiation of dialysis therapy at the appropriate time with a permanent access in place at the start of dialysis therapy.

1.1 People with a GFR <30 mL/min/1.73 m^2 (CKD stage 4) should be educated on all modalities of KRT options, including transplantation, so that timely referral can be made for the appropriate modality and placement of a permanent dialysis access, if necessary.

1.2 In people with CKD stage 4 or 5, forearm and upper-arm veins suitable for placement of vascular access should not be used for venipuncture or for the placement of IV catheters, subclavian catheters, or peripherally inserted central catheter lines.

1.3 People should have a functional permanent access at the initiation of dialysis therapy.

1.3.1 A fistula should be placed at least six months before the anticipated start of HD treatments. This timing allows for access evaluation and additional time for revision to ensure a working fistula is available at initiation of dialysis therapy.

1.3.2 A graft should, in most cases, be placed at least three to six weeks before the anticipated start of HD therapy. Some newer graft materials may be cannulated immediately after placement.

1.3.3 A PD catheter ideally should be placed at least two weeks before the anticipated start of dialysis treatments. A backup HD access does not need to be placed in most people. A PD catheter may be used as a bridge for a fistula in "appropriate" patients.

1.4 Evaluations that should be performed before placement of a permanent HD access include:

1.4.1 History and physical examination.

1.4.2 Duplex ultrasound of the upper-extremity arteries and veins.

1.4.3 Central vein evaluation in the appropriate patient known to have a previous catheter or pacemaker.

GUIDELINE 2: SELECTION AND PLACEMENT OF HD ACCESS

A structured approach to the type and location of long-term HD accesses should help optimize access survival and minimize complications. The access should be placed distally and in the upper extremities whenever possible. Options for fistula placement should be considered first, followed by prosthetic grafts if fistula placement is not possible. Catheters should be avoided for HD and used only when other options listed are not available.

2.1 The order of preference for placement of fistulae in people with kidney failure who choose HD as their initial mode of KRT should be (in descending order of preference):

2.1.1 Preferred: Fistulae.

2.1.1.1 A wrist (radiocephalic) primary fistula.

2.1.1.2 An elbow (brachiocephalic) primary fistula.

2.1.1.3 A transposed brachial basilic vein fistula.

2.1.2 Acceptable: Arteriovenous graft (AVG) of synthetic or biological material, such as:

2.1.2.1 A forearm loop graft, preferable to a straight configuration.

2.1.2.2 Upper-arm graft.

2.1.2.3 Chest wall or "necklace" prosthetic graft or lower extremity fistula or graft; all upper-arm sites should be exhausted.

2.1.3 Avoid if possible: Long-term catheters.

2.1.3.1 Short-term catheters should be used for acute dialysis and for a limited duration in hospitalized patients. Noncuffed femoral catheters should be used in bed-bound patients only.

2.1.3.2 Long-term catheters or dialysis port catheter systems should be used in conjunction with a plan for permanent access. Catheters capable of rapid flow rates are preferred. Catheter choice should be based on local experience, goals for use and cost.

2.1.3.3 Long-term catheters should not be placed on the same side as a maturing AV access, if possible. Special attention should be paid to consideration of avoiding femoral catheter access in people on HD who are current or future kidney transplant candidates. Magnetic resonance angiography (MRA) imaging of both arteries and veins is the diagnostic procedure of choice for evaluating central vessels for possible chest wall construction.

2.1.4 Individuals should be considered for construction of a primary fistula after failure of every dialysis AV access.

2.1.5 Although this order of access preference is similar for pediatric patients, special considerations exist that should guide the choice of access for children receiving HD. Please refer to CPG 9 for specific recommendations.

2.1.6 In the person receiving PD who is manifesting signs of modality failure, the decision to create a backup fistula should be individualized by periodically reassessing need. In individuals at high risk for failure (see the PD Adequacy Guidelines), evaluation and construction should follow the procedures in CPG 1 for people with CKD stage 4.

2.2 Fistulae:

2.2.1 Enhanced maturation of fistulae can be accomplished by selective obliteration of major venous side branches in the absence of a downstream stenosis.

2.3 Dialysis AVGs:

2.3.1 The choice of synthetic or biological material should be based on the surgeon's experience and preference. The choice of synthetic or biological conduits should consider local experience, technical details and cost.

2.3.2 There is no convincing evidence to support tapered versus uniform tubes, externally supported versus unsupported grafts, thick- versus thin-walled configurations, or elastic versus nonelastic material.

2.3.3 Although the majority of past experience with prosthetic grafts has been with the use of polytetrafluoroethylene, other prosthetics (e.g., polyurethane) and biological conduits (bovine) have been used recently with similar outcomes.

2.3.4 People with swelling that does not respond to arm elevation or that persists beyond two weeks after dialysis AV access placement should receive an imaging study or other noncontrast study to evaluate central venous outflow (see CPG 1).

2.4 Catheters and port catheter systems:

2.4.1 The preferred insertion site for tunneled cuffed venous dialysis catheters or port catheter systems is the right internal jugular vein. Other options include the right external jugular vein, left internal and external jugular veins, subclavian veins, femoral veins and translumbar and transhepatic access to the IVC. Subclavian access should be used only when no other upper-extremity or chest wall options are available.

2.4.2 Ultrasound should be used in the placement of catheters.

2.4.3 The position of the tip of any central catheter should be verified radiologically.

GUIDELINE 3: CANNULATION OF FISTULAE AND GRAFTS AND ACCESSION OF HD CATHETERS AND PORT CATHETER SYSTEMS

The use of aseptic technique and appropriate cannulation methods, the timing of fistula and graft cannulation, and early evaluation of immature fistulae are all factors that may prevent morbidity and may prolong the survival of permanent dialysis accesses.

3.1 Aseptic techniques:

3.1.1 For all vascular accesses, aseptic technique should be used for all cannulation and catheter accession procedures.

3.2 Maturation and cannulation of fistulae:

3.2.1 A primary fistula should be mature, ready for cannulation with minimal risk for infiltration and able to deliver the prescribed blood flow throughout the dialysis procedure.

3.2.2 Fistulae are more likely to be useable when they meet the Rule of 6s characteristics: flow >600 mL/min, diameter at least 0.6 cm, no more than 0.6 cm deep, and discernible margins.

3.2.3 Fistula hand-arm exercise should be performed.

3.2.4 If a fistula fails to mature by six weeks, a fistulogram or other imaging study should be obtained to determine the cause of the problem.

3.3 Cannulation of AVGs:

Grafts generally should not be cannulated for at least 2 weeks after placement and not until swelling has subsided so that palpation of the course of the graft can be performed. The composite polyurethane graft should not be cannulated for at least 24 hours after placement and not

until swelling has subsided so that palpation of the course of the graft can be performed. Rotation of cannulation sites is needed to avoid pseudoaneurysm formation.

3.4 Dialysis catheters and port catheter systems:

Infection-control measures that should be used for all HD catheters and port catheter systems include the following:

3.4.1 The catheter exit site or port cannulation site should be examined for proper position of the catheter/port catheter system and absence of infection by experienced personnel at each HD session before opening and accessing the catheter/port catheter system.

3.4.2 Changing the catheter exit-site dressing at each HD treatment, using either a transparent dressing or gauze and tape.

3.4.3 Using aseptic technique to prevent contamination of the catheter or port catheter system, including the use of a surgical mask for staff and patient and clean gloves for all catheter or port catheter system connect, disconnect and dressing procedures.

GUIDELINE 4: DETECTION OF ACCESS DYSFUNCTION: MONITORING, SURVEILLANCE, AND DIAGNOSTIC TESTING

Prospective surveillance of fistulae and grafts for hemodynamically significant stenosis, when combined with correction of the anatomic stenosis, may improve patency rates and may decrease the incidence of thrombosis. The Work Group recommends an organized monitoring/surveillance approach with regular assessment of clinical parameters of the AV access and HD adequacy. Data from the clinical assessment and HD adequacy measurements should be collected and maintained for each patient's access and made available to all staff. The data should be tabulated and tracked within each HD center as part of a QA/CQI program.

4.1 Physical examination (monitoring):

Physical examination should be used to detect dysfunction in fistulae and grafts at least monthly by a qualified individual.

4.2 Surveillance of grafts:

Techniques, not mutually exclusive, that may be used in surveillance for stenosis in grafts include:

4.2.1 Preferred:

4.2.1.1 Intra-access flow by using one of several methods using sequential measurements with trend analysis. Refer to original guideline for details.

4.2.1.2 Directly measured or derived static venous dialysis pressure by one of several methods. Refer to original guideline for details.

4.2.1.3 Duplex ultrasound.

4.2.2 Acceptable:

4.2.2.1 Physical findings of persistent swelling of the arm, presence of collateral veins, prolonged bleeding after needle withdrawal, or altered characteristics of pulse or thrill in a graft.

4.2.3 Unacceptable:

4.2.3.1 Unstandardized dynamic venous pressures should not be used.

4.3 Surveillance in fistulae:

Techniques, not mutually exclusive, that may be used in surveillance for stenosis in AVFs include:

4.3.1 Preferred:

4.3.1.1 Direct flow measurements.

4.3.1.2 Physical findings of persistent swelling of the arm, presence of collateral veins, prolonged bleeding after needle withdrawal or altered characteristics of pulse or thrill in the outflow vein.

4.3.1.3 Duplex ultrasound.

4.3.2 Acceptable:

4.3.2.1 Recirculation using a non-urea-based dilutional method.

4.3.2.2 Static pressures, direct or derived.

4.4 When to refer for evaluation (diagnosis) and treatment:

4.4.1 One should not respond to a single isolated abnormal value. With all techniques, prospective trend analysis of the test parameter has greater power to detect dysfunction than isolated values alone.

4.4.2 Persistent abnormalities in any of the monitoring or surveillance parameters should prompt referral for access imaging.

4.4.3 An access flow rate <600 mL/min in grafts and <400–500 mL/min in fistulae.

4.4.4 A venous segment static pressure (mean pressures) ratio >0.5 in grafts or fistulae.

4.4.5 An arterial segment static pressure ratio >0.75 in grafts.

GUIDELINE 5: TREATMENT OF FISTULA COMPLICATIONS

Appropriate interventions for access dysfunction may result in an increased duration of survival of the AVF.

5.1 Problems developing in the early period after AVF construction (first six months) should be promptly addressed.

5.1.1 Persistent swelling of the hand or arm should be expeditiously evaluated and the underlying pathology should be corrected.

5.1.2 A program should be in place to detect early access dysfunction, particularly delays in maturation. The patient should be evaluated no later than six weeks after access placement.

5.2 Intervention:

Intervention on a fistula should be performed for the presence of:

5.2.1 Inadequate flow to support the prescribed dialysis blood flow.

5.2.2 Hemodynamically significant venous stenosis.

5.2.3 Aneurysm formation in a primary fistula. Postaneurysmal stenosis that drives aneurysm also should be corrected. The aneurysmal segment should not be cannulated.

5.2.4 Ischemia in the access arm.

5.3 Indications for pre-emptive percutaneous angioplasty (PTA):

A fistula with a >50% stenosis in either the venous outflow or arterial inflow, in conjunction with clinical or physiological abnormalities, should be treated with PTA or surgical revision.

5.3.1 Abnormalities include reduction in flow, increase in static pressures, AR pre-empting adequate delivery of dialysis or abnormal physical findings.

5.4 Stenosis, as well as the clinical parameters used to detect it, should return to within acceptable limits following intervention.

5.5 Thrombectomy of a fistula should be attempted as early as possible after thrombosis is detected, but can be successful even after several days.

5.6 Access evaluation for ischemia:

5.6.1 People with an AVF should be assessed on a regular basis for possible ischemia.

5.6.2 People with new findings of ischemia should be referred to a vascular access surgeon emergently.

5.7 Infection:

Infections of primary AVFs are rare and should be treated as subacute bacterial endocarditis with six weeks of antibiotic therapy. Fistula surgical excision should be performed in cases of septic emboli.

GUIDELINE 6: TREATMENT OF AVG COMPLICATIONS

Appropriate management and treatment of AVG complications may improve the function and longevity of the vascular access.

6.1 Extremity edema:

People with extremity edema that persists beyond two weeks after graft placement should undergo an imaging study (including dilute iodinated contrast) to evaluate patency of the central veins. The preferred treatment for central vein stenosis is PTA. Stent placement should be considered in the following situations:

6.1.1 Acute elastic recoil of the vein (>50% stenosis) after angioplasty.

6.1.2 The stenosis recurs within a three-month period.

6.2 Indicators of risk for graft rupture:

Any of the following changes in the integrity of the overlying skin should be evaluated urgently:

6.2.1 Poor eschar formation.

6.2.2 Evidence of spontaneous bleeding.

6.2.3 Rapid expansion in the size of a pseudoaneurysm.

6.2.4 Severe degenerative changes in the graft material.

6.3 Indications for revision/repair:

6.3.1 AVGs with severe degenerative changes or pseudoaneurysm formation should be repaired in the following situations:

6.3.1.1 The number of cannulation sites are limited by the presence of a large (or multiple) pseudoaneurysm(s).

6.3.1.2 The pseudoaneurysm threatens the viability of the overlying skin.

6.3.1.3 The pseudoaneurysm is symptomatic (pain, throbbing).

6.3.1.4 There is evidence of infection.

6.3.2 Cannulation of the access through a pseudoaneurysm must be avoided if at all possible and particularly so if the pseudoaneurysm is increasing in size.

6.4 Treatment of stenosis without thrombosis:

Stenoses that are associated with AVGs should be treated with angioplasty or surgical revision if the lesion causes >50% decrease in the luminal diameter and is associated with the following clinical/physiological abnormalities:

6.4.1 Abnormal physical findings.

6.4.2 Decreasing intragraft blood flow (<600 mL/min).

6.4.3 Elevated static pressure within the graft.

6.5 Outcomes after treatment of stenosis without thrombosis:

After angioplasty or surgical revision of a stenosis, each institution should monitor the primary patency of the AVG. Reasonable goals are as follow:

6.5.1 Angioplasty:

6.5.1.1 The treated lesion should have <30% residual stenosis and the clinical/physiological parameters used to detect the stenosis should return to acceptable limits after the intervention.

6.5.1.2 A primary patency of 50% at six months.

6.5.2 Surgical revision:

6.5.2.1 The clinical/physiological parameters used to detect the stenosis should return to acceptable limits after the intervention.

6.5.2.2 A primary patency of 50% at one year.

6.6 If angioplasty of the same lesion is required more than two times within a three-month period, the individual should be considered for surgical revision if he or she is a good surgical candidate.

6.6.1 If angioplasty fails, stents may be useful in the following situations:

6.6.1.1 Surgically inaccessible lesion.

6.6.1.2 Contraindication to surgery.

6.6.1.3 Angioplasty-induced vascular rupture.

6.7 Treatment of thrombosis and associated stenosis:

Each institution should determine which procedure, percutaneous thrombectomy with angioplasty or surgical thrombectomy with AVG revision, is preferable based on expediency and physician expertise at that center.

6.7.1 Treatment of AVG thrombosis should be performed urgently to minimize the need for a temporary HD catheter.

6.7.2 Treatment of AVG thrombosis can be performed by using either percutaneous or surgical techniques. Local or regional anesthesia should be used for the majority of patients.

6.7.3 The thrombectomy procedure can be performed in either an outpatient or inpatient environment.

6.7.4 Ideally, the AVG and native veins should be evaluated by using intraprocedural imaging.

6.7.5 Stenoses should be corrected by using angioplasty or surgical revision.

6.7.6 Methods for monitoring or surveillance of AVG abnormalities that are used to screen for venous stenosis should return to normal after intervention.

6.8 Outcomes after treatment of AVG thrombosis:

After percutaneous or surgical thrombectomy, each institution should monitor the outcome of treatment on the basis of AVG patency. Reasonable goals are as follows:

6.8.1 A clinical success rate of 85%; clinical success is defined as the ability to use the AVG for at least one HD treatment.

6.8.2 After percutaneous thrombectomy, primary patency should be 40% at three months.

6.8.3 After surgical thrombectomy, primary patency should be 50% at six months and 40% at one year.

6.9 Treatment of AVG infection:

Superficial infection of an AVG should be treated as follows:

6.9.1 Initial antibiotic treatment should cover both Gram-negative and Gram-positive microorganisms.

6.9.1.1 Subsequent antibiotic therapy should be based on culture results.

6.9.1.2 Incision and drainage may be beneficial.

6.9.2 Extensive infection of an AVG should be treated with appropriate antibiotic therapy and resection of the infected graft material.

GUIDELINE 7: PREVENTION AND TREATMENT OF CATHETER AND PORT COMPLICATIONS

Catheters and ports are essential tools for providing urgent and, in some cases, long-term vascular access. Prevention and early treatment of complications should greatly reduce associated morbidity and mortality.

7.1 Catheters and ports should be evaluated when they become dysfunctional. Dysfunction is defined as failure to attain and maintain an extracorporeal blood flow of ≥300 mL/min at a prepump arterial pressure more negative than −250 mm Hg.

7.2 The exception is pediatric or smaller adult catheters that are not designed to have flows in excess of 300 mL/min.

7.3 Methods that should be used to treat a dysfunctional or nonfunctional catheter or port include:

7.3.1 Repositioning of a malpositioned catheter.

7.3.2 Thrombolytics, using either an intraluminal lytic, intradialytic lock protocol, intracatheter thrombolytic infusion or interdialytic lock.

7.3.3 Catheter exchange with sheath disruption, when appropriate.

7.4 Treatment of an infected HD catheter or port should be based on the type and extent of infection.

7.4.1 All catheter-related infections, except for catheter exit-site infections, should be addressed by initiating parenteral treatment with an antibiotic(s) appropriate for the organism(s) suspected.

7.4.2 Definitive antibiotic therapy should be based on the organism(s) isolated.

7.4.3 Catheters should be exchanged as soon as possible and within 72 hours of initiating antibiotic therapy in most instances, and such exchange does not require a negative blood culture result before the exchange. Follow-up cultures are needed one week after cessation of antibiotic therapy (standard practice).

7.4.4 Port pocket infections should be treated with systemic antibiotics and irrigation, in conjunction with the manufacturers' recommendations.

GUIDELINE 8: CLINICAL OUTCOME GOALS

8.1 Goals of access placement:

8.1.1 Each center should establish a database and CQI process to track the types of accesses created and complication rates for these accesses.

8.1.2 The goals for permanent HD access placement should include:

8.1.2.1 Prevalent functional AVF placement rate of >65% of patients.

8.1.2.2 Cuffed catheter for permanent dialysis access (i.e., not as a bridge) in <10% of patients. Long-term catheter access is defined as the use of a dialysis catheter for more than three months in the absence of a maturing permanent access (i.e., graft or fistula).

8.2 The primary access failure rates of HD accesses in the following locations and configurations should not be more than the following:

8.2.1 Forearm straight grafts: 15%.

8.2.2 Forearm loop grafts: 10%.

8.2.3 Upper-arm grafts: 5%.

8.2.4 Tunneled catheters with blood flow <300 mL/min: 5%.

8.3 Access complications and performance:

8.3.1 Fistula complications/performance should be as follows:

8.3.1.1 Fistula thrombosis: fewer than 0.25 episodes/patient-year at risk.

8.3.1.2 Fistula infection: <1% during the use-life of the access.

8.3.1.3 Fistula patency >3.0 years (by life-table analysis).

8.3.2 Graft complications/performance should be as follows:

8.3.2.1 Graft thrombosis: fewer than 0.5 thrombotic episodes/patient-year at risk.

8.3.2.2 Graft infection: <10% during the use-life of the access.

8.3.2.3 Graft patency greater than two years (by life-table analysis).

8.3.2.4 Graft patency after PTA: longer than four months.

8.3.3 Catheter complications/performance should be as follows:

8.3.3.1 Tunneled catheter-related infection <10% at three months and <50% at one year.

8.3.3.2 The cumulative incidence of the following insertion complications should not exceed 1% of all catheter placements:

- Pneumothorax requiring a chest tube.
- Symptomatic air embolism.
- Hemothorax.
- Hemomediastinum.
- Hematoma requiring evacuation.

8.3.4 Cumulative patency rate of tunneled cuffed catheters: Not specified.

8.4 Efficacy of corrective intervention:

The rate of certain milestones after correction of thrombosis or stenosis should be as follows:

8.4.1 AVF patency after PTA: >50% unassisted patency at six months (and <30% residual stenosis post-procedure or lack of resolution of physical findings post-procedure).
AVF patency following surgery: >50% unassisted patency at one year.

8.4.2 AVG patency after PTA: please refer to CPG 6.5.1.
AVG patency after surgery: please refer to CPG 6.5.2.
AVG after either PTA or surgery: >90% with post-procedure restoration of blood flow and >85% post-procedure ability to complete one dialysis treatment. Please refer to guideline 6.8.

8.4.3 Surgical correction is set to a higher standard because of the use of venous capital.

CPRs FOR VASCULAR ACCESS

CPR FOR GUIDELINE 1: PATIENT PREPARATION FOR PERMANENT HD ACCESS

Factors that may be helpful in preparing the individual for placement of a permanent HD access include the following:

1.1 The veins of the dorsum of the hand should be the preferred site for IV cannulation.

1.2 Sites for venipuncture should be rotated if arm veins need to be used.

1.3 People with CKD stage 5 should be educated on the risks and benefits associated with catheters and strongly encouraged to allow the evaluation for and creation of a fistula for long-term access when appropriate. Such discussions with the patient should be initiated months before the anticipated start of dialysis therapy.

1.4 Alternative imaging studies for central veins include duplex Doppler ultrasound (DDU) and magnetic resonance imaging (MRI)/MRA.

CPR FOR GUIDELINE 2: SELECTION AND PLACEMENT OF HD ACCESS

Recommendations for fistulae:

2.1 When a new native fistula is infiltrated (i.e., presence of hematoma with associated induration and edema), it should be rested until the swelling is resolved.

CPR FOR GUIDELINE 3: CANNULATION OF FISTULAE AND GRAFTS AND ACCESSION OF DIALYSIS CATHETERS AND PORTS

3.1 Cannulation skill:
Staff should be appropriately trained and observed for technical mastery before cannulating any AV access. Only those with said technical

mastery should be allowed to cannulate a new fistula. A protocol for minimizing vessel damage should be used for cannulation failure. Re-cannulation should be attempted only when the cannulation site is healed and the vessel is assessed to be normal and appropriate for cannulation. Heparin management should be reviewed on a case-by-case basis to minimize postdialysis bleeding.

3.2 Self-cannulation:

People who are capable and whose access is suitably positioned should be encouraged to self-cannulate. The preferred cannulation technique is the buttonhole.

3.3 Buttonhole:

People with fistula access should be considered for buttonhole (constant-site) cannulation.

3.4 Elevation of arm for swelling:

The AVG access arm should be elevated as much as possible until swelling subsides, which may take as long as three to six weeks. Increase in symptoms requires urgent evaluation.

CPR FOR GUIDELINE 4: DETECTION OF ACCESS DYSFUNCTION: MONITORING, SURVEILLANCE, AND DIAGNOSTIC TESTING

4.1 Monitoring the access:

4.1.1 Access patency should be ensured before each treatment before any attempts to cannulate the access.

4.1.2 All caregivers, including fellows in training, should learn and master the methods for examining a vascular access.

4.1.3 Access characteristics, such as pulsatility and presence of thrill, as well as flow and pressure, should be recorded and tracked in a medical record and be available to all caregivers of the vascular access team.

4.2 Frequency of measurement is dependent on the method used:

4.2.1 It is not clear that access flow measurements performed at a monthly frequency provide sufficient data stability to make decisions. Until additional studies are performed to determine the optimal frequency, more frequent measurements are recommended.

4.2.2 Static pressure measurements require less technology and should be made more frequently than flow measurements. Direct measurements of static pressure ratios should be made every two weeks. Less direct measurements should be made weekly. Dynamic pressures, if used (see CPG 4.2.3), should be measured with each dialysis treatment, but derivation of a static pressure should be attempted, rather than using the raw numbers.

4.2.3 Measurement of recirculation is not recommended as a surveillance technique in grafts.

4.3 Frequency of measurement for access complications:

4.3.1 Thrombosis in fistulae develops more slowly than in grafts. Flow measurements performed at a monthly frequency appear to be adequate. Until additional studies are performed to determine the optimal frequency, less frequent measurements are not recommended.

4.3.2 Because static pressure measurements are inherently less accurate in detecting access stenosis in fistulae, the frequency should not be less than in grafts. Direct measurements of static pressure ratios should be made every two weeks. Less direct measurements should be made weekly. Dynamic pressures should be measured with each dialysis. Increased recirculation can indicate reduced effective blood pump flow, resulting in inadequate dialysis.

4.4 Diagnostic testing:

4.4.1 Characteristics of access (see CPR 4.1), as well as blood pump flow and pressure performance, should be recorded and tracked in medical records.

4.4.2 Data should be analyzed at least monthly to evaluate access dysfunction.

4.4.3 After intervention, the surveillance parameter should be restored to normal.

4.4.4 Data should be analyzed to improve success rates and ensure that interventions are appropriately assessed. For example, PTA and surgical revision rates, recurrence rates, and number of procedures per patient-year should be systematically analyzed in a CQI process.

4.4.5 A multidisciplinary team should be involved.

4.4.6 Pre-emptive correction of hemodynamically significant stenoses should remain the standard of care.

CPR FOR GUIDELINE 5: TREATMENT OF FISTULA COMPLICATIONS

5.1 If a new fistula access has vein margins that are difficult to discern on physical examination and cannulation frequently is associated with aspiration of clot, the patient should be referred for access marking by means of DDU to define the center of the vessel and depth of the fistula. A diagram of these findings should be sent to the dialysis unit.

5.1.1 The patient should be taught to examine his or her access daily, while at home, for thrombosis.

CPR FOR GUIDELINE 7: PREVENTION AND TREATMENT OF CATHETER AND PORT COMPLICATIONS

7.1 Treatment of catheter dysfunction:

Catheter dysfunction should be treated when a dialyzer blood flow of 300 mL/min is not being attained in a catheter previously able to deliver >350 mL/min at a prepump pressure of −250 torr.

7.1.1 A dysfunctional catheter (blood flow <300 mL/min) for two consecutive treatments should be treated in the HD unit by using an intraluminal interdialytic thrombolytic lock protocol between two dialysis treatments (i.e., 35 to 69 hours).

7.2 Radiological evaluation:

Any dysfunction that cannot be managed in the dialysis unit should be sent for radiographic study to diagnose dysfunction and document the condition of the vessel.

7.2.1 Catheter imaging with contrast infusion can identify other correctable problems (e.g., residual lumen thrombus, external fibrin catheter sheath, malpositioned catheter tip). Appropriate interventions may follow, such as:

7.2.1.1 Repositioning of the catheter.

7.2.1.2 Angioplasty of a vessel.

7.2.1.3 Replacement of a malpositioned catheter over guide wire.

7.2.1.4 Higher-dose lytic infusion for occlusive thrombus (e.g., right atrial) or fibrin sheath.

7.3 Choice of thrombolytic and use of other modalities:

7.3.1 A special brush is used to remove thrombus from the lumens of a conventional catheter by using a protocol specific to this procedure.

7.4 Treatment of infection:

7.4.1 Catheter exit-site infections, in the absence of a tunnel infection, should be treated with topical and/or oral antibiotics, ensuring proper local exit-site care. In general, it should not be necessary to remove the catheter.

7.4.2 If a person with bacteremia is afebrile within 48 hours and is clinically stable, catheter salvage might be considered by using an interdialytic antibiotic lock solution and three weeks of parenteral antibiotics in appropriate situations. A follow-up blood culture one week after completion of the course of antibiotics should be performed.

7.4.3 Antibiotic lock with antibiotic to which the organism is sensitive is indicated when follow-up cultures indicate reinfection with the same organism in a person with limited catheter sites.

7.4.4 Short-term catheters should be removed when infected. There is no conclusive evidence to support a rationale for scheduled replacement except for those in the femoral area.

CPR 8: VASCULAR ACCESS IN PEDIATRIC PATIENTS

8.1 Choice of access type:

8.1.1 Permanent access in the form of a fistula or graft is the preferred form of vascular access for most pediatric patients on MHD therapy.

8.1.2 Circumstances in which a central venous catheter may be acceptable for pediatric long-term access include lack of local surgical expertise to place permanent vascular access in small children, patient size too small to support a permanent vascular access, bridging HD for PD training or PD catheter removal for peritonitis, and expectation of expeditious kidney transplantation.

8.1.3 If surgical expertise to place permanent access does not exist in the patient's pediatric setting, efforts should be made to consult vascular access expertise among local adult-oriented surgeons to either supervise or place permanent vascular access in children.

8.1.4 Programs should evaluate their patients' expected waiting times on their local deceased-donor kidney transplant waiting lists. Serious consideration should be given to placing permanent vascular access in children >20 kg in size who are expected to wait more than one year for a kidney transplant.

8.2 Stenosis surveillance:

An AVG stenosis surveillance protocol should be established to detect venous anastomosis stenosis and direct patients for surgical revision or PTA.

8.3 Catheter sizes, anatomic sites, and configurations:

8.3.1 Catheter sizes should be matched to patient sizes with the goal of minimizing intraluminal trauma and obstruction to blood flow while allowing sufficient blood flow for adequate HD.

8.3.2 External cuffed access should be placed in the internal jugular with the distal tip placed in the right atrium.

8.3.3 The blood flow rate of an external access should be minimally 3–5 mL/kg/min and should be adequate to deliver the prescribed HD dose.

SECTION 4

CHRONIC KIDNEY DISEASE

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification*. Am J Kidney Dis 39:S1–S266, 2002 (Suppl 1). Available at: **http://www.kidney.org/professionals/kdoqi/guidelines_ckd/toc.htm**

This series is divided into several parts containing 15 CPGs. Selected CPGs are included here. Guidelines, tables and figures are numbered according to the original document for easy cross-referencing.

DEFINITION AND CLASSIFICATION OF STAGES OF CKD

GUIDELINE 1: DEFINITION AND STAGES OF CKD

- The presence of CKD should be established, based on presence of kidney damage and level of kidney function (GFR), irrespective of diagnosis.
- Among people with CKD, the stage of disease should be assigned based on the level of kidney function, irrespective of diagnosis, according to the KDOQI classification (see Table 33).

Table 33. Stages of Chronic Kidney Disease: A Clinical Action Plan

GUIDELINE 2. EVALUATION AND TREATMENT

- People with CKD should be evaluated to determine:
  - Diagnosis (type of kidney disease).
  - Comorbid conditions.
  - Severity, assessed by level of kidney function.
  - Complications, related to level of kidney function.

- Risk for loss of kidney function.
- Risk for cardiovascular disease (CVD).

- Treatment of CKD should include:
  - Specific therapy, based on diagnosis.
  - Evaluation and management of comorbid conditions.
  - Slowing the loss of kidney function.
  - Prevention and treatment of CVD.
  - Prevention and treatment of complications of decreased kidney function.
  - Preparation for kidney failure and KRT.
  - Replacement of kidney function by dialysis and transplantation, if signs and symptoms of uremia are present.
- A clinical action plan should be developed for each patient, based on the stage of disease as defined by the KDOQI CKD classification (see Table 1).
- Review of medications should be performed at all visits for the following:
  - Dosage adjustment based on level of kidney function.
  - Detection of potentially adverse effects on kidney function or complications of CKD.
  - Detection of drug interactions.
  - Therapeutic drug monitoring, if possible.
- Self-management behaviors should be incorporated into the treatment plan at all stages of CKD.
- People with CKD should be referred to a specialist for consultation and co-management if the clinical action plan cannot be prepared, the prescribed evaluation of the patient cannot be carried out or the recommended treatment cannot be carried out. In general, people with GFR <30 mL/min/1.73 m^2 should be referred to a nephrologist.

GUIDELINE 3: INDIVIDUALS AT INCREASED RISK FOR CKD

Some individuals without kidney damage and with normal or elevated GFR are at increased risk for development of CKD.

- All individuals should be assessed, as part of routine health encounters, to determine whether they are at increased risk of developing CKD, based on clinical and sociodemographic factors (see Table 40).
- Individuals at increased risk of developing CKD should undergo testing for markers of kidney damage, and to estimate the level of GFR.
- Individuals found to have CKD should be evaluated and treated as specified in Guideline 2.
- Individuals at increased risk, but found not to have CKD, should be advised to follow a program of risk factor reduction, if appropriate, and undergo repeat periodic evaluation.

Table 40. Potential Risk Factors for Susceptibility to and Initiation of Chronic Kidney Disease

EVALUATION OF LABORATORY MEASUREMENTS FOR CLINICAL ASSESSMENT OF KIDNEY DISEASE

GUIDELINE 4: ESTIMATION OF GFR

Estimates of GFR are the best overall indices of the level of kidney function.

- The level of GFR should be estimated from prediction equations that take into account the SCr concentration and some or all of the following variables: age, gender, race, and body size. The following equations provide useful estimates of GFR:
  - In adults, the Modification of Diet in Renal Disease (MDRD) study (see equation 1) and Cockcroft-Gault (see equation 2) equations.
  - In children, the Schwartz (see equation 3) and Counahan-Barratt (see equation 4) equations.
- The SCr concentration alone should not be used to assess the level of kidney function.
- Clinical laboratories should report an estimate of GFR using a prediction equation, in addition to reporting the SCr measurement.
- Autoanalyzer manufacturers and clinical laboratories should calibrate SCr assays using an international standard.

- Measurement of creatinine clearance using timed (e.g, 24-hour) urine collections does not improve the estimate of GFR over that provided by prediction equations. A 24-hour urine sample provides useful information for:
  - Estimation of GFR in individuals with exceptional dietary intake (vegetarian diet, creatine supplements) or muscle mass (amputation, malnutrition, muscle wasting).
  - Assessment of diet and nutritional status.
  - Need to start dialysis.

Equation 1: MDRD equation:

$$GFR = 186 \times (SCr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$$

GFR is expressed in mL/min/1.73 m^2, SCr is expressed in mg/dL, and age is expressed in years.

Equation 2: Cockcroft-Gault equation:

$$\text{Creatinine clearance (mL/min)} = [(140 - \text{Age}) \times \text{weight}] \times (0.85 \text{ if female}) / (72 \times \text{SCr})$$

SCr is expressed in mg/dL, weight in kilograms, age in years.

Equation 3: Schwartz equation:

$$\text{Creatinine clearance (mL/min)} = (k \times \text{length}) / \text{SCr}$$

Where k is defined by the age group (infant 1–52 weeks = 0.45, child 1–13 years = 0.55, adolescent male = 0.7, adolescent female = 0.55), length is in centimeters, SCr is mg/dL.

Equation 4:. Counahan-Barratt equation:

$$GFR \text{ (ml/min/1.73 } m^2) = (0.43 \times \text{length}) / \text{SCr}$$

Where length is in centimeters, SCr is in mg/dL.

GUIDELINE 5: ASSESSMENT OF PROTEINURIA

Guidelines for Adults and Children

- Under most circumstances, untimed ("spot") urine samples should be used to detect and monitor proteinuria in children and adults.
- It is usually not necessary to obtain a timed urine collection (overnight or 24-hour) for these evaluations in either children or adults.
- First morning specimens are preferred, but random specimens are acceptable if first morning specimens are not available.
- In most cases, screening with urine dipsticks is acceptable for detecting proteinuria:
  - Standard urine dipsticks are acceptable for detecting increased total urine protein.
  - Albumin-specific dipsticks are acceptable for detecting albuminuria.
- People with a positive dipstick test (≥1+) should undergo confirmation of proteinuria by a quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio) within three months.

- People with two or more positive quantitative tests temporally spaced by one to two weeks should be diagnosed as having persistent proteinuria and undergo further evaluation and management for CKD as stated in Guideline 2.
- Monitoring proteinuria in people with CKD should be performed using quantitative measurements.

Specific Guidelines for Adults

- When screening adults at increased risk for CKD, albumin should be measured in a spot urine sample using either:
  - Albumin-specific dipstick.
  - Albumin-to-creatinine ratio.
- When monitoring proteinuria in adults with CKD, the protein-to-creatinine ratio in spot urine samples should be measured using:
  - Albumin-to-creatinine ratio.
  - Total protein-to-creatinine ratio is acceptable if albumin-to-creatinine ratio is high (>500–1,000 mg/g).

Specific Guidelines for Children Without Diabetes

- When screening children for CKD, total urine protein should be measured in a spot urine sample using either:
  - Standard urine dipstick.
  - Total protein-to-creatinine ratio.
- Orthostatic proteinuria must be excluded by repeat measurement on a first morning specimen if the initial finding of proteinuria was obtained on a random specimen.
- When monitoring proteinuria in children with CKD, the total protein-to-creatinine ratio should be measured in spot urine specimens.

Specific Guidelines for Children With Diabetes

- Screening and monitoring of post-pubertal children with diabetes for five or more years should follow the guidelines for adults.
- Screening and monitoring other children with diabetes should follow the guidelines for children without diabetes.

GUIDELINE 6: MARKERS OF CKD OTHER THAN PROTEINURIA

- Urine sediment examination or dipstick for red blood cells and white blood cells should be performed in people with CKD and in individuals at increased risk of developing CKD.

- Imaging studies of the kidneys should be performed in people with CKD and in selected individuals at increased risk of developing CKD.
- Although several novel urinary markers (such as tubular or low-molecular-weight proteins and specific mononuclear cells) show promise of future utility, they should not be used for clinical decision making at present.

ASSOCIATION OF LEVEL OF GFR WITH COMPLICATIONS IN ADULTS

GUIDELINE 7: HYPERTENSION

- Blood pressure should be closely monitored in all people with CKD.
- Treatment of high blood pressure in CKD should include specification of target blood pressure levels, nonpharmacological therapy, and specific antihypertensive agents for the prevention of progression of kidney disease and development of CVD.

GUIDELINE 8: ANEMIA

- People with GFR <60 mL/min/1.73 m^2 should be evaluated for anemia. The evaluation should include measurement of Hgb level. **Note: This guideline has been recently updated (see *2006 Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease,* page x). CPR 1.1.1 states "In the opinion of the Work Group, Hb testing should be carried out in all patients with CKD, regardless of stage or cause."**
- Anemia in CKD should be evaluated and treated.

GUIDELINE 9: NUTRITIONAL STATUS

- People with GFR <60 mL/min/1.73 m^2 should undergo assessment of dietary protein and energy intake and nutritional status (see *K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure*, Guidelines 23 and 26, page x):
  Guideline 23. Panels of Nutritional Measures for Nondialyzed Patients: "For individuals with CRF (GFR <20 mL/min) protein-energy nutritional status should be evaluated by serial measurements of a panel of markers including at least one value from each of the following clusters:
  (1) Serum albumin;
  (2) Edema-free actual body weight, percent standard (NHANES II) body weight, or subjective global assessment (SGA); and
  (3) Normalized protein nitrogen appearance (nPNA) or dietary interviews and diaries."
  Guideline 26. Intensive Nutritional Counseling for CRF: "The nutritional status of individuals with CRF should be monitored at regular intervals."
- People with decreased dietary intake or malnutrition should undergo dietary modification, counseling, and education or specialized nutrition therapy (see *K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure (CRF)*, Guidelines 24 and 25, page x.

Guideline 24. Dietary Protein Intake for Nondialyzed Patients: "For individuals with chronic renal failure (GFR <25 mL/min) who are not undergoing maintenance dialysis, the institution of a planned low-protein diet providing 0.60 g protein/kg/d should be considered. For individuals who will not accept such a diet or who are unable to maintain adequate dietary energy intake with such a diet, an intake of up to 0.75 g protein/kg/d may be prescribed."

Guideline 25. Dietary Energy Intake (DEI) for Nondialyzed Patients: "The recommended DEI for individuals with chronic renal failure (GFR <25 mL/min) who are not undergoing maintenance dialysis is 35 kcal/kg/d for those who are younger than 60 years old and 30–35 kcal/kg/d for individuals who are 60 years of age or older."

GUIDELINE 10: BONE DISEASE AND DISORDERS OF CALCIUM AND PHOSPHORUS METABOLISM

- People with GFR <60 mL/min/1.73 m^2 should be evaluated for bone disease and disorders of calcium and phosphorus metabolism.
- People with bone disease and disorders of bone metabolism should be evaluated and treated.

GUIDELINE 11: NEUROPATHY

- People with CKD should be periodically assessed for central and peripheral neurological involvement by eliciting symptoms and signs during routine office visits or exams.
- Specialized laboratory testing for neuropathy in people with CKD is indicated only in the presence of symptoms.

GUIDELINE 12: INDICES OF FUNCTIONING AND WELL-BEING

- People with GFR <60 mL/min/1.73 m^2 should undergo regular assessment for impairment of functioning and well-being:
  - To establish a baseline and monitor changes in functioning and well-being over time.
  - To assess the effect of interventions on functioning and well-being.

STRATIFICATION OF RISK FOR PROGRESSION OF KIDNEY DISEASE AND DEVELOPMENT OF CARDIOVASCULAR DISEASE

GUIDELINE 13: FACTORS ASSOCIATED WITH LOSS OF KIDNEY FUNCTION IN CKD

- The rate of GFR decline should be assessed in people with CKD to:
  - Predict the interval until the onset of kidney failure.
  - Assess the effect of interventions to slow the GFR decline.
- Among people with CKD, the rate of GFR decline should be estimated by:

- Computing the GFR decline from past and ongoing measurements of SCr.
- Ascertaining risk factors for faster versus slower GFR decline, including type (diagnosis) of kidney disease, nonmodifiable and modifiable factors.

- Interventions to slow the progression of kidney disease should be considered in all people with CKD.
  - Interventions that have been proven to be effective include:
    1. Strict glucose control in diabetes.
    2. Strict blood pressure control.
    3. ACE inhibition or angiotensin-2 receptor blockade.
  - Interventions that have been studied, but the results are inconclusive, include:
    1. Dietary protein restriction.
    2. Lipid-lowering therapy.
    3. Partial correction of anemia.
- Attempts should be made to prevent and correct acute decline in GFR. Frequent causes of acute decline in GFR include:
  - Volume depletion.
  - IV radiographic contrast.
  - Selected antimicrobial agents (for example, aminoglycosides and amphotericin B).
  - Nonsteroidal anti-inflammatory agents, including cyclo-oxygenase type 2 inhibitors.
  - ACE inhibition and angiotensin-2 receptor blockers.
  - Cyclosporine and tacrolimus.
  - Obstruction of the urinary tract.
- Measurements of SCr for estimation of GFR should be obtained at least yearly in people with CKD, and more often in people with:
  - GFR <60 mL/min/1.73 m^2.
  - Fast GFR decline in the past (≥ 4 mL/min/1.73 m^2 per year).
  - Risk factors for faster progression.
  - Ongoing treatment to slow progression.
  - Exposure to risk factors for acute GFR decline.

GUIDELINE 14: ASSOCIATION OF CKD WITH DIABETIC COMPLICATIONS

- Prevention, detection, evaluation and treatment of diabetic complications in people with CKD should follow published guidelines and position statements.
- Guidelines regarding ACE inhibitors or ARBs and strict blood pressure control are particularly important because these agents may prevent or delay some of the adverse outcomes of both kidney and CVD.
- Application of published guidelines to diabetic people with CKD should take into account their "higher-risk" status for diabetic complications.

GUIDELINE 15: ASSOCIATION OF CKD WITH CVD

- All people with CKD should be considered in the "highest risk" group for CVD, irrespective of levels of traditional CVD risk factors.
- All people with CKD should undergo assessment of CVD risk factors (see Table 130) including:
  - Measurement of "traditional" CVD risk factors in all patients.
  - Individual decision making regarding measurement of selected "CKD-related" CVD risk factors in some patients.
- Recommendations for CVD risk factor reduction should take into account the "highest-risk" status of people with CKD.

Table 130. Traditional vs. Chronic Kidney Disease-Related Factors Potentially Related to an Increased Risk for Cardiovascular Disease

ADDENDUM

- There are national initiatives to routinely report GFR when an SCr has been ordered.
- Another initiative is to standardize the national laboratory assay for calibration of SCr values.
- The equations given in the guidelines are for the estimation of stable kidney function. They are not valid for use when there are rapid changes in kidney function, such as with acute renal failure. There have been recent questions about the applicability of the MDRD equation in all patient populations with kidney disease.

SECTION 5

BONE METABOLISM AND DISEASE

Source: National Kidney Foundation. *K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease*. Am J Kidney Dis 42:S1–S202, 2003 (Suppl 3). Available at: **http://www.kidney.org/professionals/kdoqi/guidelines_bone/index.htm**

These CPGs address the complications of secondary hyperparathyroidism and renal osteodystrophy and their treatment. Included are guidelines for the assessment and treatment of disorders related to calcium and phosphorus metabolism, renal bone diseases, amyloidosis, aluminum toxicity and metabolic acidosis. Guidelines, tables and figures are numbered according to the original document for easy cross-referencing.

GUIDELINE 1: EVALUATION OF CALCIUM AND PHOSPHORUS METABOLISM

1.1 Serum levels of calcium, phosphorus, and intact plasma parathyroid hormone (PTH) should be measured in all people with CKD and GFR <60 mL/min/1.73 m^2. The frequency of these measurements should be based on the stage of CKD (Table 14).

1.2 These measurements should be made more frequently if the individual is receiving concomitant therapy for the abnormalities in the serum levels of calcium, phosphorus or PTH, as detailed in Guidelines 4, 5, 7 and 8, and in transplant recipients, Guideline 16.

1.3 Measurement of plasma PTH levels may be done less frequently for those with levels within the low end of the target levels (Table 15).

1.4 The target range of plasma levels of intact PTH in the various stages of CKD are denoted in Table 15.

Table 14. Frequency of Measurement of PTH and Calcium/Phosphorus by Stage of CKD

CKD Stage	GFR Range (mL/min/1.73 m^2)	Measurement of PTH	Measurement of Calcium/Phosphorus
3	30-59	Every 12 months	Every 12 months
4	15-29	Every 3 months	Every 3 months
5	<15 or dialysis	Every 3 months	Every month

Table 15. Target Range of Intact Plasma PTH by Stage of CKD

CKD Stage	GFR Range (mL/min/1.73 m^2)	Target "intact" PTH (pg/mL [pmol/L])
3	30-59	35-70 [3.85-7.7 pmol/L] (OPINION)
4	15-29	70-110 [7.7-12.1 pmol/L] (OPINION)
5	<15 or dialysis	150-300 [16.5-33.0 pmol/L] (EVIDENCE)

GUIDELINE 2: ASSESSMENT OF BONE DISEASE ASSOCIATED WITH CKD

2.1 The most accurate diagnostic test for determining the type of bone disease associated with CKD is iliac crest bone biopsy with double tetracycline labeling and bone histomorphometric analysis.

2.2 It is not necessary to perform bone biopsy for most situations in clinical practice. However, a bone biopsy should be considered in people with kidney failure (stage 5) who have:

2.2a Fractures with minimal or no trauma (pathological fractures).

2.2b Intact plasma PTH levels between 100 and 500 pg/mL (11.0–55.0 pmol/L; in CKD stage 5) with co-existing conditions such as unexplained hypercalcemia, severe bone pain or unexplained increases in bone alkaline phosphatase activity.

2.2c Suspected aluminum bone disease, based on clinical symptoms or history of aluminum exposure (see Guideline 11).

2.3 Bone radiographs are not indicated for the assessment of bone disease of CKD, but they are useful in detecting severe peripheral vascular calcification and bone disease resulting from β_2 microglobulin amyloidosis (see Guideline 10).

2.4 Bone mineral density (BMD) should be measured by DXA in people with fractures and in those with known risk factors for osteoporosis.

GUIDELINE 3: EVALUATION OF SERUM PHOSPHORUS LEVEL

3.1 In people wih CKD (stages 3 and 4), the serum level of phosphorus should be maintained at or above 2.7 mg/dL (0.87 mmol/L) and no higher than 4.6 mg/dL (1.49 mmol/L).

3.2 In people with CKD with kidney failure (stage 5) and those treated with HD or PD, the serum levels of phosphorus should be maintained between 3.5 and 5.5 mg/dL (1.13–1.78 mmol/L).

GUIDELINE 4. RESTRICTION OF DIETARY PHOSPHORUS IN PEOPLE WITH CKD

4.1 Dietary phosphorus should be restricted to 800 to 1,000 mg/day (adjusted for dietary protein needs) when the serum phosphorus levels are elevated >4.6 mg/dL (1.49 mmol/L) at stages 3 and 4 of CKD, and >5.5 mg/dL (1.78 mmol/L) in those with kidney failure (stage 5).

4.2 Dietary phosphorus should be restricted to 800 to 1,000 mg/day (adjusted to dietary protein needs) when the plasma levels of intact PTH are elevated above target range of the CKD stage (see Table 15).

4.3 The serum phosphorus levels should be monitored every month following the initiation of dietary phosphorus restriction.

GUIDELINE 5: USE OF PHOSPHATE BINDERS IN CKD

In people with CKD (stages 3 and 4):

5.1 If phosphorus or intact PTH levels cannot be controlled within the target range (see Guidelines 1, 3), despite dietary phosphorus restriction (see Guideline 4), phosphate binders should be prescribed.

5.2 Calcium-based phosphate binders are effective in lowering serum phosphorus levels and may be used as the initial binder therapy.

In people with CKD with kidney failure (stage 5):

5.3 Both calcium-based phosphate binders and other noncalcium-, nonaluminum-, and nonmagnesium-containing phosphate-binding agents (such as sevelamer HCl) are effective in lowering serum phosphorus levels and either may be used as the primary therapy.

5.4 In people on dialysis who remain hyperphosphatemic (serum phosphorus >5.5 mg/dL [1.78 mmol/L]) despite the use of either of calcium-based phosphate binders or other noncalcium-, nonaluminum-, nonmagnesium-containing phosphate-binding agents, a combination of both should be used.

5.5 The total dose of elemental calcium provided by the calcium-based phosphate binders should not exceed 1,500 mg/day, and the total intake of elemental calcium (including dietary calcium) should not exceed 2,000 mg/day.

5.6 Calcium-based phosphate binders should not be used in people on dialysis who are hypercalcemic (corrected serum calcium of >10.2 mg/dL [2.54 mmol/L]), or whose plasma PTH levels are <150 pg/mL (16.5 pmol/L) on two consecutive measurements.

5.7 Noncalcium-containing phosphate binders are preferred in people on dialysis with severe vascular and/or other soft-tissue calcifications.

5.8 In people with serum phosphorus levels >7.0 mg/dL (2.26 mmol/L), aluminum-based phosphate binders may be used as a short-term therapy (four weeks), and for one course only, to be replaced thereafter by other phosphate binders. In such people, more frequent dialysis should also be considered.

GUIDELINE 6: SERUM CALCIUM AND CALCIUM-PHOSPHORUS PRODUCT

In people with CKD (stages 3 and 4):

6.1 The serum levels of corrected total calcium should be maintained within the "normal" range for the laboratory used.

In people with CKD with kidney failure (stage 5):

6.2 Serum levels of corrected total calcium should be maintained within the normal range for the laboratory used, preferably toward the lower end (8.4–9.5 mg/dL [2.10–2.37 mmol/L]).

6.3 In the event corrected total serum calcium level exceeds 10.2 mg/dL (2.54 mmol/L), therapies that cause serum calcium to rise should be adjusted as follows:

6.3a In people taking calcium-based phosphate binders, the dose should be reduced or therapy switched to a noncalcium-, nonaluminum-, nonmagnesium-containing phosphate binder (see Guideline 5).

6.3b In people taking active vitamin D sterols, the dose should be reduced or therapy discontinued until the serum levels of corrected total calcium return to the target range (8.4–9.5 mg/dL [2.10–2.37 mmol/L]; see Guideline 8B).

6.3c If hypercalcemia (serum levels of corrected total calcium >10.2 mg/dL [2.54 mmol/L]) persists despite modification of therapy with vitamin D and/or discontinuation of calcium-based phosphate binders, dialysis using low-dialysate calcium (1.5–2.0 mEq/L) may be used for three to four weeks (see Guideline 9).

In people with CKD (stages 3–5):

6.4 Total elemental calcium intake (including both dietary calcium intake and calcium-based phosphate binders) should not exceed 2,000 mg/day (see Guideline 5).

6.5 The serum calcium-phosphorus product should be maintained at <55 mg^2/dL^2. This is best achieved by controlling serum levels of phosphorus within the target range (see Guidelines 3–5).

6.6 People whose serum levels of corrected total calcium are below the lower limit for the laboratory used (<8.4 mg/dL [2.10 mmol/L]) should receive therapy to increase serum calcium levels if:

6.6a There are clinical symptoms of hypocalcemia such as paresthesia, Chvostek's and Trousseau's signs, bronchospasm, laryngospasm, tetany and/or seizures *or*

6.6b The plasma intact PTH level is above the target range for the CKD stage (see Table 15).

6.7 Therapy for hypocalcemia should include calcium salts such as calcium carbonate and/or oral vitamin D sterols (see Guideline 8B).

GUIDELINE 7: PREVENTION AND TREATMENT OF VITAMIN D INSUFFICIENCY AND VITAMIN D DEFICIENCY IN PEOPLE WITH CKD (ALGORITHM 1)

In people with CKD (stages 3 and 4):

7.1 If plasma intact PTH is above the target range for the stage of CKD (Table 15), serum 25-hydroxyvitamin D should be measured at first encounter. If it is normal, repeat annually.

7.2 If the serum level of 25-hydroxyvitamin D is <30 ng/mL (75 nmol/L), supplementation with vitamin D_2 (ergocalciferol) should be initiated (Table 26).

7.3 Following initiation of vitamin D therapy:

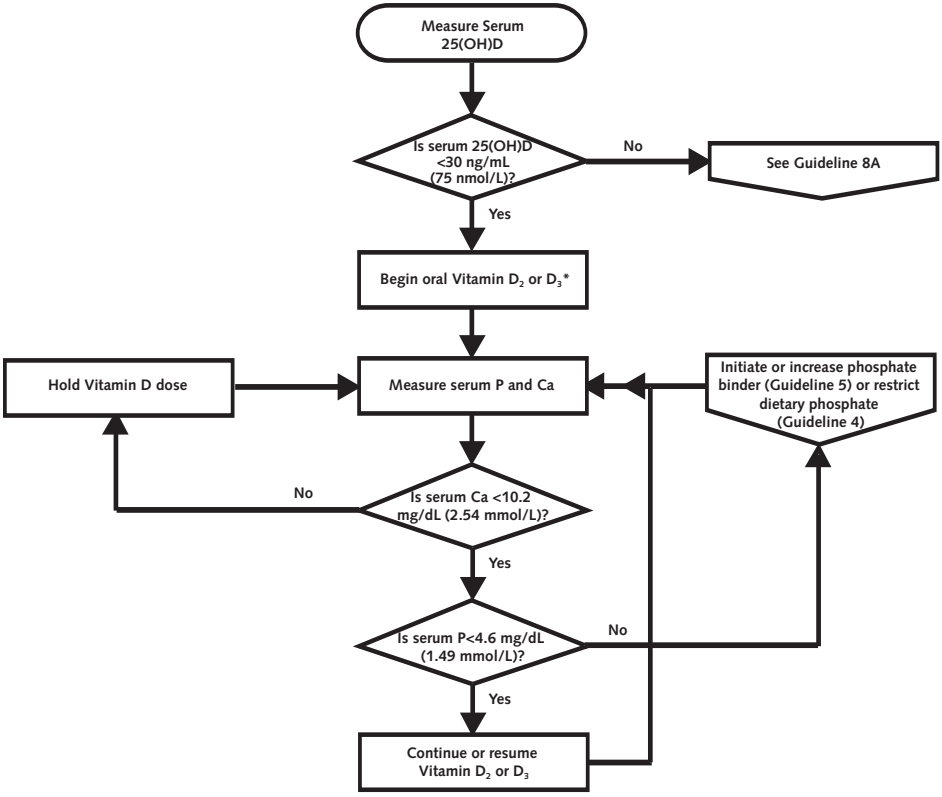
7.3a The use of ergocalciferol therapy should be integrated with the serum calcium and phosphorus (Algorithm 1).

7.3b The serum levels of corrected total calcium and phosphorus should be measured at least every three months.

7.3c If the serum levels of corrected total calcium exceed 10.2 mg/dL (2.54 mmol/L), discontinue ergocalciferol therapy and all forms of vitamin D therapy.

Algorithm 1. Vitamin D supplementation in CKD (Stages 3 and 4).

In CKD patients with serum P <4.6 mg/dL (1.49 mmol/L), serum Ca <9.5 mg/dL (2.37 mmol/L), and serum PTH in the higher level of the target range for CKD stage (Stage 3: 35-70 pg/mL [3.85-7.7 pmol/L]; Stage 4: 70-110 pg/mL [7.7-12.1 pmol/L])



* Vitamin D_2 (ergocalciferol) may be safer than D_3 (cholecalciferol). When the 25 (OH)D level is <15 ng/mL (37 nmol/L), 50,000 IU weekly for 4 doses followed by monthly for 4 doses is effective. With 25 (OH)D levels of 20-30 ng/mL (50-75 nmol/L), 50,000 IU monthly for 6 months is recommended.

7.3d If the serum phosphorus exceeds 4.6 mg/dL (1.49 mmol/L), add or increase the dose of phosphate binder (see Guidelines 4 and 5). If hyperphosphatemia persists, discontinue vitamin D therapy.

7.3e Once patients are replete with vitamin D, continued supplementation with a vitamin D-containing multi-vitamin preparation should be used with annual reassessment of serum levels of 25-hydroxyvitamin D, and the continued assessment of corrected total calcium and phosphorus every three months.

In people with CKD with kidney failure (stage 5):

7.4 Therapy with an active vitamin D sterol (calcitriol, alfacalcidol, paricalcitol or doxercalciferol) should be provided if the plasma levels of intact PTH are >300 pg/mL (33.0 pmol/L) (see Guideline 8B).

Table 26. Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Patients with CKD Stages 3 and 4

Serum 25(OH)D (ng/mL) [nmol/L]	Definition	Ergocalciferol Dose (Vitamin D_2)	Duration (months)	Comment
<5 [12]	Severe vitamin D deficiency	50,000 IU/wk orally x 12 wks; then monthly	6 months	Measure 25(OH)D levels after 6 months
		500,000 IU as single I.M. dose		Assure patient adherence; measure 25(OH)D at 6 months
5-15 [12-37]	Mild vitamin D deficiency	50,000 IU/wk x 4 weeks, then 50,000 IU/month orally	6 months	Measure 25(OH)D levels after 6 months
16-30 [40-75]	Vitamin D insufficiency	50,000 IU/month orally	6 months	

GUIDELINE 8: VITAMIN D THERAPY IN PEOPLE WITH CKD

This guideline encompasses two parts: Guideline 8A, which deals with active vitamin D sterol therapy in CKD stages 3 and 4, and Guideline 8B, which deals with CKD stage 5.

GUIDELINE 8A: ACTIVE VITAMIN D THERAPY IN STAGES 3 AND 4 CKD (ALGORITHM 2)

8A.1 In people with CKD stages 3 and 4, therapy with an active oral vitamin D sterol (calcitriol, alfacalcidol or doxercalciferol) is indicated when serum levels of 25(OH)-vitamin D are >30 ng/mL (75 nmol/L) and plasma levels of intact PTH are above the target range for the CKD stage (see Table 15). The initial doses are provided in Table 27.

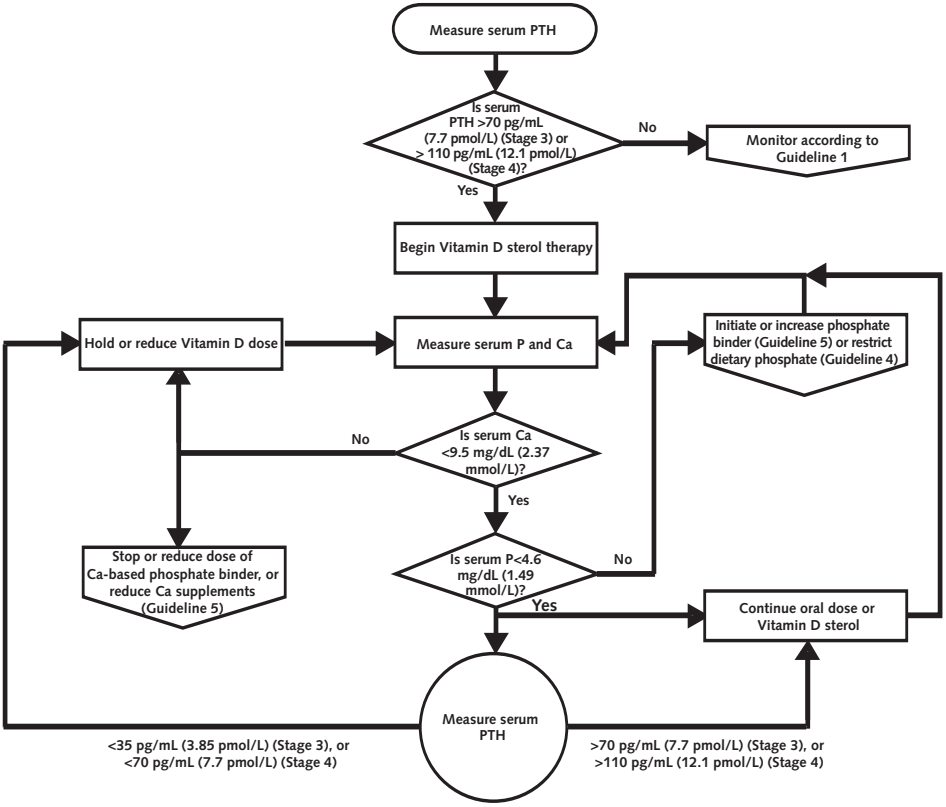
8A.1a Treatment with an active vitamin D sterol should be undertaken only in patients with serum levels of corrected total calcium <9.5 mg/dL (2.37 mmol/L) and serum phosphorus <4.6 mg/dL (1.49 mmol/L).

8A.1b Vitamin D sterols should not be prescribed for people with rapidly worsening kidney function or those who are noncompliant with medications or follow-up.

8A.2 During therapy with vitamin D sterols, serum levels of calcium and phosphorus should be monitored at least every month after initiation

Algorithm 2. Management of People with CKD (Stages 3 and 4) with Active Vitamin D Sterols.

In CKD patients, Stages 3 and 4, with stable renal function, compliant with visits and medications with serum phosphorus levels <4.6 mg/dL (1.49 mmol/L), calcium <9.5 mg/dL (2.37 mmol/L), and 25(OH)D ≥30 ng/mL (75 nmol/L)



Oral active vitamin D sterols available include calcitriol, alfacalcidol, and doxercalciferol; calcitriol (USA, Canada) and alfacalcidol (Canada and Europe) are approved for use in CKD, Stages 3 and 4. Initial doses should be low (calcitriol 0.25 µg/day or alfacalcidol, 0.25 µg/day). The dose of calcitriol should rarely exceed 0.5 µg/day and then only if the corrected levels of calcium increase by less than 0.2-0.3 mg/dL.

of therapy for the first three months, then every three months thereafter. Plasma PTH levels should be measured at least every three months for six months, and every three months thereafter.

8A.3 Dosage adjustments for patients receiving active vitamin D sterol therapy should be made as follows:

Table 27. Serum Levels of PTH, Calcium and Phosphate Required for Initiation of Oral Vitamin D Sterol Therapy, and Recommended Initial Doses in Patients with Stages 3 and 4 CKD

Plasma PTH pg/mL or [pmol/L]	Serum Ca mg/dL [mmol/L]	Serum P mg/dL [mmol/L]	Dose Oral Calcitriol	Dose Oral Alfacalcidol	Dose Oral Doxercalciferol
>70 [7.7] (CKD Stage 3) Or >110 [12.1] (CKD Stage 4)	<9.5 [2.37]	<4.6 [1.49]	0.25 μg/day	0.25 μg/day	2.5 μg 3x/week

8A.3a If plasma levels of intact PTH fall below the target range for the CKD stage (Table 15), hold active vitamin D sterol therapy until plasma levels of intact PTH rise to above the target range, then resume treatment with the dose of active vitamin D sterol reduced by half. If the lowest daily dose of the active vitamin D sterol is being used, reduce to alternate-day dosing.

8A.3b If serum levels of corrected total calcium exceed 9.5 mg/dL (2.37 mmol/L), hold active vitamin D sterol therapy until serum calcium returns to <9.5 mg/dL (2.37 mmol/L), then resume treatment at half the previous dose. If the lowest daily dose of the active vitamin D sterol is being used, reduce to alternate-day dosing.

8A.3c If serum levels of phosphorus rise to >4.6 mg/dL (1.49 mmol/L), hold active vitamin D therapy, initiate or increase dose of phosphate binder until the levels of serum phosphorus fall to ≤4.6 mg/dL (1.49 mmol/L); then resume the prior dose of active vitamin D sterol.

GUIDELINE 8B: VITAMIN D THERAPY IN PEOPLE ON DIALYSIS (CKD STAGE 5)

8B.1 People treated with HD or PD with serum levels of intact PTH levels >300 pg/mL (33.0 pmol/L) should receive an active vitamin D sterol (such as calcitriol, alfacalcidol, paricalcitol or doxercalciferol; see Table 28) to reduce the serum levels of PTH to a target range of 150 to 300 pg/mL.

8B.1a The intermittent, IV administration of calcitriol is more effective than daily oral calcitriol in lowering serum PTH levels.

8B.1b In people with corrected serum calcium and/or phosphorus levels above the target range (see Guidelines 3 and 6, respectively), a trial of alternative vitamin D analogs, such as paricalcitol or doxercalciferol, may be warranted.

8B.2 When therapy with vitamin D sterols is initiated or the dose is increased, serum levels of calcium and phosphorus should be monitored

at least every two weeks for one month and then monthly thereafter. The plasma PTH should be measured monthly for at least three months and then every three months once target levels of PTH are achieved.

8B.3 For people treated with PD, oral doses of calcitriol (0.5 to 1.0 μg) or doxercalciferol (2.5 to 5.0 μg) can be given two or three times weekly. Alternatively, a lower dose of calcitriol (0.25 μg) can be administered daily.

8B.4 When people on HD or PD are treated with active vitamin D sterols, management should integrate the changes in serum calcium, serum phosphorus and plasma PTH. Each of these three variables is considered separately with suggested interventions based on the various values obtained in Algorithms 3–5.

Table 28. Recommended Initial Dosing for Vitamin D Sterols by Serum Levels of Intact PTH, Calcium, Phosphorus, and Ca-P Product

Plasma PTH pg/mL or [pmol/L]	Serum Ca mg/dL [mmol/L]	Serum P mg/dL [mmol/L]	Ca-P Product	Dose per HD Calcitriol†	Dose per HD Paricalcitol*	Dose per HD Doxercalciferol†
300-600 [33-66]	<9.5 [2.37]	<5.5 [1.78]	<55	IV: 0.5-1.5 μg Oral: 0.5-1.5 μg	2.5-5.0 μg	Oral: 5 μg IV: 2 μg
600-1000 [66-110]	<9.5 [2.37]	<5.5 [1.78]	<55	IV: 1.0-3.0 μg Oral: 1-4 μg	6.0-10 μg	Oral: 5-10 μg IV: 2-4 μg
>1000 [110]	<10.0 [2.50]	<5.5 [1.78]	<55	IV: 3.0-5.0 μg Oral: 3-7 μg	10-15 μg	Oral: 10-20 μg IV: 4-8 μg

*Intravenous; † Oral

GUIDELINE 9: DIALYSATE CALCIUM CONCENTRATIONS

9.1 The dialysate calcium concentration in HD or PD should be 2.5 mEq/L (1.25 mmol/L).

9.2 Higher or lower dialysate calcium levels are indicated in selected people.

GUIDELINE 10: β_2 MICROGLOBULIN AMYLOIDOSIS

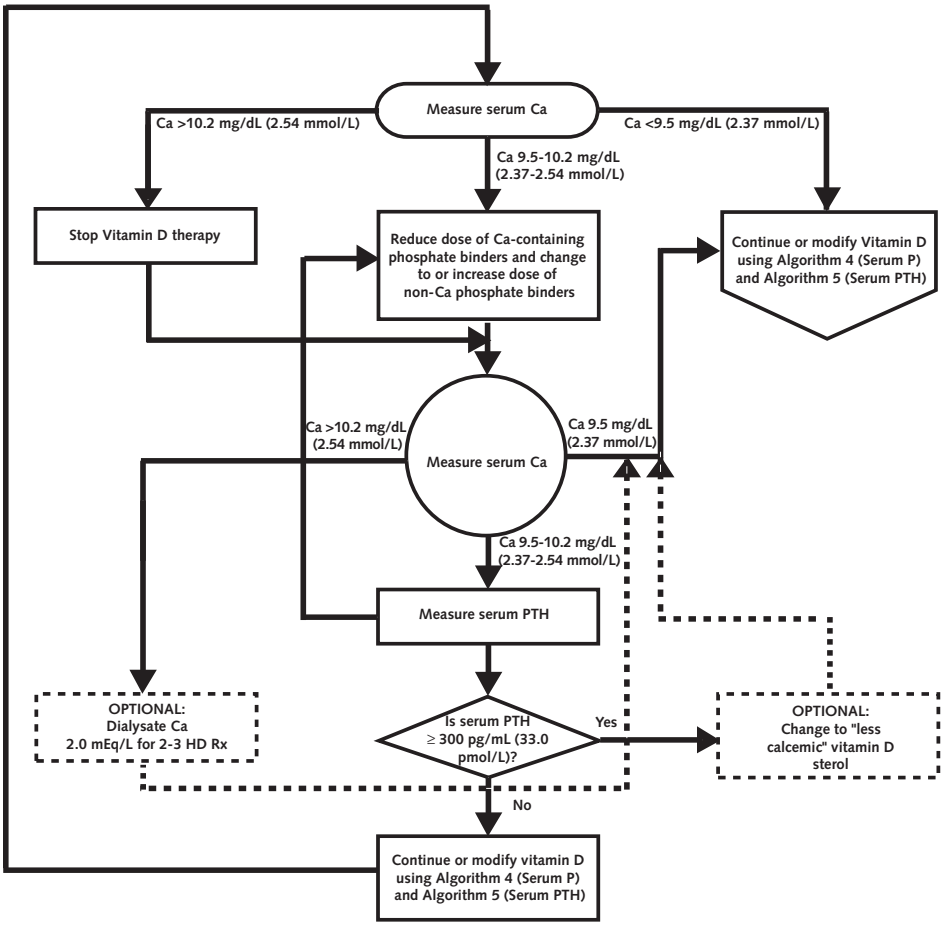
10.1 Screening for β_2 microglobulin amyloidosis, including measurement of serum levels of β2M, is not recommended.

10.1a No currently available therapy (except kidney transplantation) can stop disease progression of β2M amyloidosis or provide symptomatic relief.

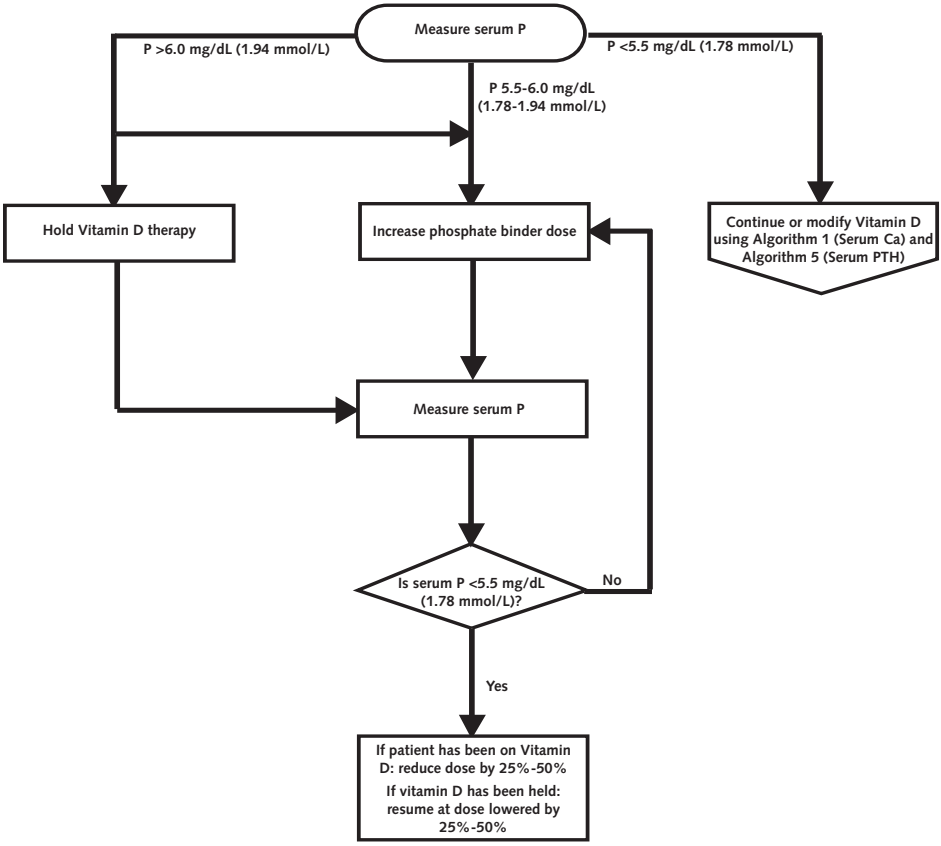
10.1b Kidney transplant should be considered to stop disease progression or provide symptomatic relief in people with β2M amyloidosis.

10.1c In people with evidence of, or at risk for, β2M amyloidosis noncuprophane, high-flux dialyzers should be used.

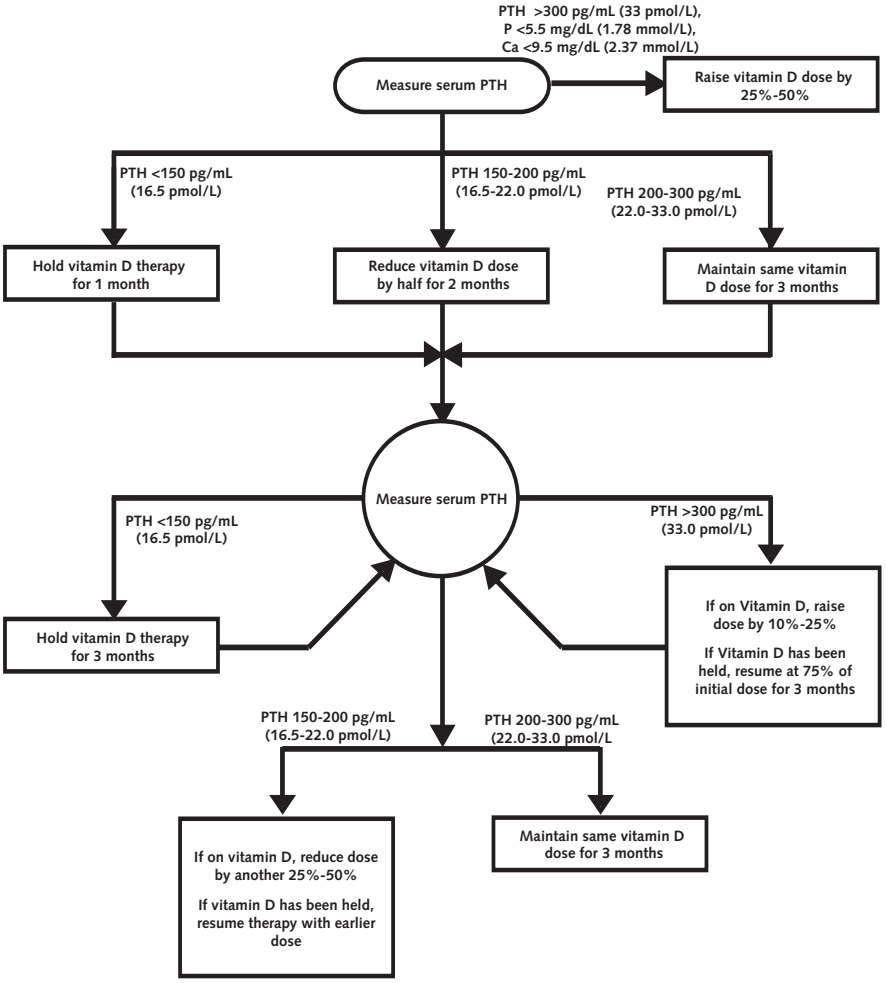
Algorithm 3. Managing Vitamin D Sterols Based on Serum Calcium Levels.



Algorithm 4. Managing Vitamin D Sterols Based on Serum Phosphorus Levels.



Algorithm 5. Managing Vitamin D Sterols Based on intact PTH Levels.



When intact serum PTH is between 300-500 pg/mL (33.0-55.0 pmol/L) and changes on two successive determinations are small (<25%), there is no need to modify vitamin D dose as long as P and Ca are within the desired limits (see Algorithms 3 and 4).

When intact PTH is persistently >500-800 pg/mL (55.0-88.0 pmol/L) and P is 5.5-6.5 mg/dL (1.78-1.94 mmol/L) and/or Ca is 10.2-10.5 mg/dL (2.54-2.62 mmol/L), a trial with a "less calcemic" analog may be warranted for 3-5 months; if such a patient fails to respond, parathyroidectomy may be required.

GUIDELINE 11: ALUMINUM OVERLOAD AND TOXICITY IN CKD

11.1 To prevent aluminum toxicity, the regular administration of aluminum should be avoided and the dialysate concentration of aluminum should be maintained at <10 μg/L.

11.1a People with CKD ingesting aluminum should not receive citrate salts simultaneously.

11.2 To assess aluminum exposure and the risk of aluminum toxicity, serum aluminum levels should be measured at least yearly and every three months in those receiving aluminum-containing medications.

11.2a Baseline levels of serum aluminum should be <20 μg/L.

11.3 A deferoxamine (DFO) test should be performed if there are elevated serum aluminum levels (60–200 μg/L), clinical signs and symptoms of aluminum toxicity or if the patient has had aluminum exposure prior to parathyroid surgery (see Algorithms 6 and 7).

11.3a The test is done by infusing 5 mg/kg of DFO during the last hour of the dialysis session with serum aluminum measured before DFO infusion and two days later, before the next dialysis session.

11.3b The test is considered positive if the increment of serum aluminum is ≥50 μg/L.

11.3c A DFO test should not be performed if the serum levels of aluminum are >200 μg/L to avoid DFO-induced neurotoxicity.

11.4 The presence of aluminum bone disease can be predicted by a rise in serum aluminum of ≥50 μg/L following DFO challenge combined with plasma levels of intact PTH of <150 pg/mL (16.5 pmol/L). However, the gold standard for the diagnosis of aluminum bone disease is a bone biopsy showing increased aluminum staining of the bone surface (≥15–25%) using aluminum stain and often adynamic bone or osteomalacia.

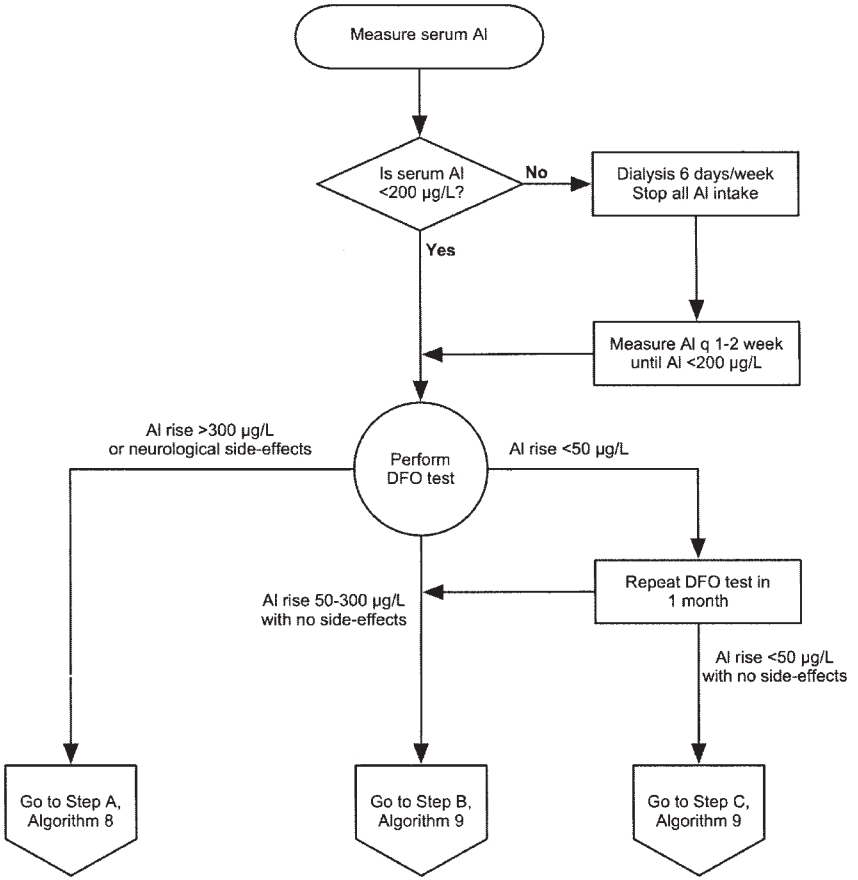
GUIDELINE 12: TREATMENT OF ALUMINUM TOXICITY (ALGORITHMS 8 AND 9)

12.1 In all people with baseline serum aluminum levels >60 μg/L, a positive DFO test or clinical symptoms consistent with aluminum toxicity (for more information, please see Table 31 on p. S109 in *K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease*) the source of aluminum should be identified and eliminated.

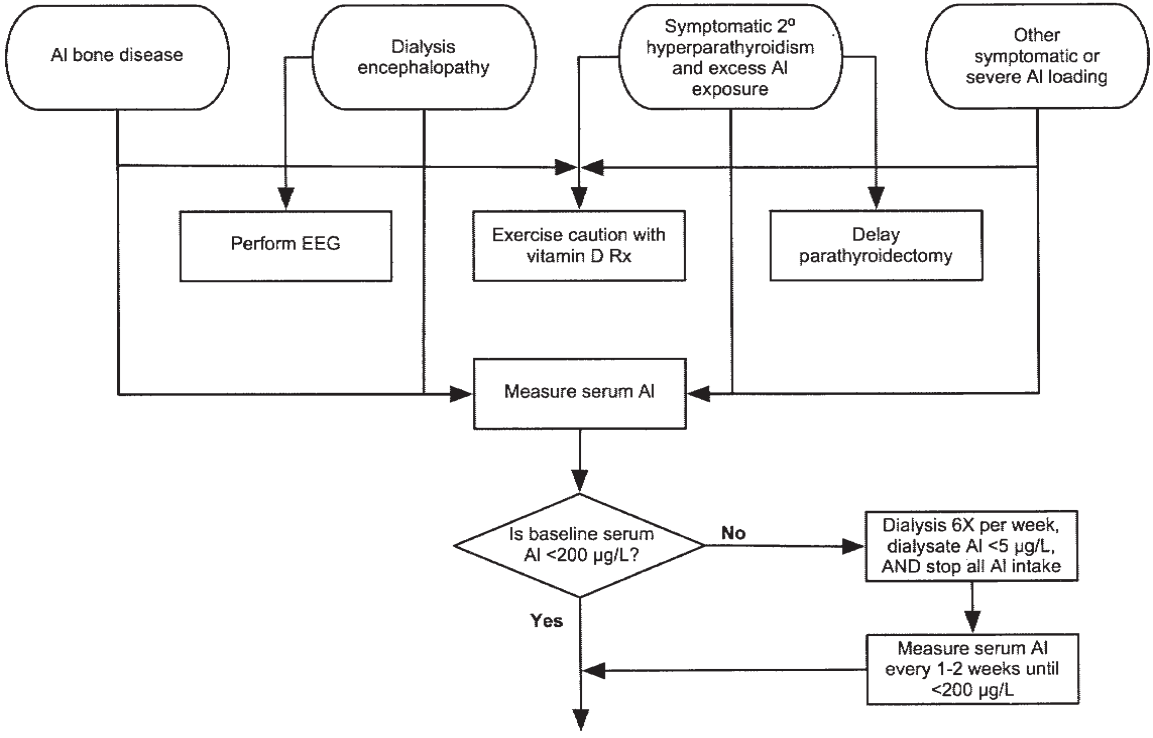
12.2 In symptomatic people with serum aluminum levels >60 μg/L but <200 μg/L or a rise in aluminum after DFO >50 μg/L, DFO should be given to treat the aluminum overload (see Algorithms 8 and 9).

12.3 To avoid DFO-induced neurotoxicity in people with serum aluminum >200 μg/L, DFO should not be given until intensive dialysis (six days per week) with high-flux dialysis membrane and a dialysate aluminum level of <5 μg/L and until the predialysis serum aluminum level has been reduced to <200 μg/L.

Algorithm 6. Evaluation of Aluminum Neurotoxicity.

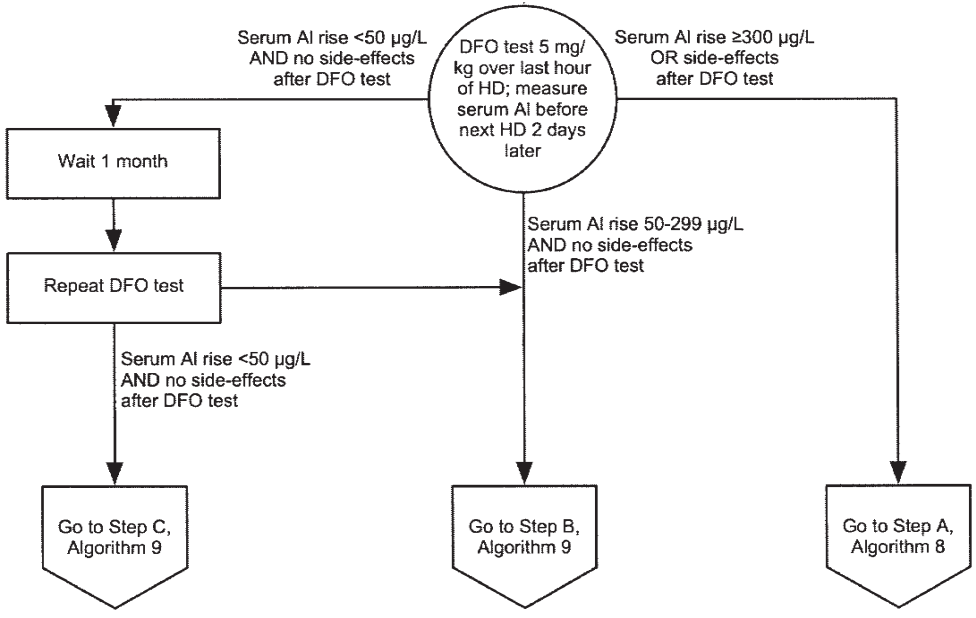


Algorithm 7. Evaluation of Aluminum-related Disorders: Considerations for DFO Test and Subsequent DFO Ttreatment.



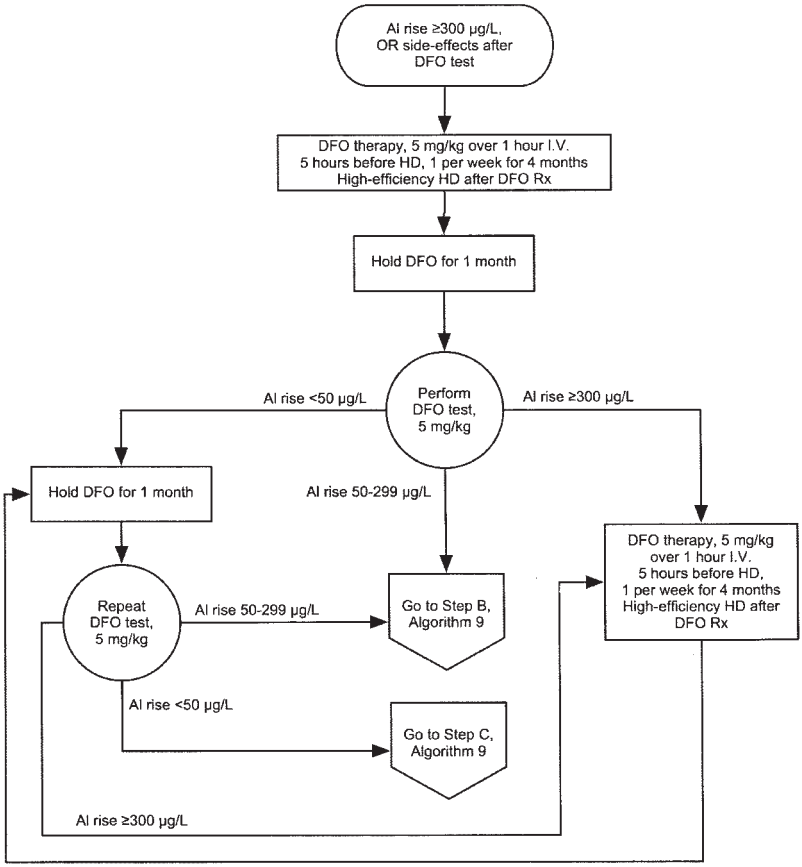
Algorithm continued on next page

Algorithm 7. Evaluation of Aluminum-related Disorders: Considerations for DFO Test and Subsequent DFO Ttreatment.

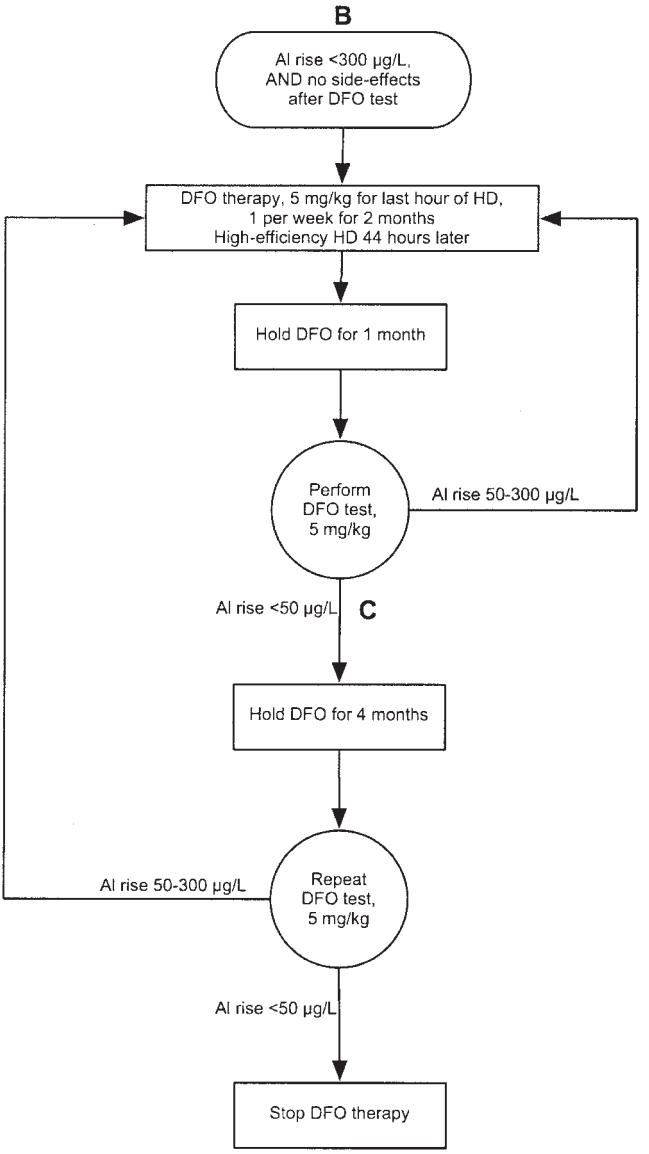


This algorithm is exclusive of acute Al neurotoxicity

Algorithm 8. DFO Treatment after Plasma Aluminum Level Rise $300 mg/L.



Algorithm 9. DFO Treatment after Plasma Aluminum Level Rise Between 50 and 300 mg/L.



GUIDELINE 13: TREATMENT OF BONE DISEASE IN CKD

The therapeutic approach to bone disease in CKD is based on its specific type. As such, this guideline encompasses three parts: Guideline 13A deals with high-turnover and mixed bone disease, Guideline 13B with osteomalacia and Guideline 13C with adynamic bone disease.

GUIDELINE 13A: HYPERPARATHYROID (HIGH TURNOVER) AND MIXED (HIGH-TURNOVER WITH MINERALIZATION DEFECT) BONE DISEASE

13A.1 In people with CKD (stages 3 and 4) who have plasma levels of intact PTH >70 pg/mL (7.7 pmol/L; stage 3) or >110 pg/mL (12.1 pmol/L; stage 4) on more than two consecutive measurements, dietary phosphate intake should be restricted. If this is ineffective in lowering plasma PTH levels, calcitriol or one of its analogs (alfacalcidol or doxercalciferol) should be given to prevent or ameliorate bone disease (see Guideline 8A). Refer to addendum regarding oral vitamin D.

13A.2 In people with CKD (stage 5) who have elevated plasma levels of intact PTH (>300 pg/mL [33.0 pmol/L]), calcitriol or one of its analogs (doxercalciferol, alfacalcidol or paricalcitol) should be used to reverse the bone features of PTH overactivity (i.e., high-turnover bone disease) and to treat defective mineralization (see Guideline 8B).

GUIDELINE 13B: OSTEOMALACIA

13B.1 Osteomalacia due to aluminum toxicity should be prevented in people on dialysis by maintaining aluminum concentration in dialysate fluid at <10 μg/L and avoiding the use of aluminum-containing compounds (including sucralfate).

13B.2 Aluminum overload leading to aluminum bone disease should be treated with DFO (see Guidelines 11 and 12).

13B.3 Osteomalacia due to vitamin D2 or D3 deficiency or phosphate depletion, though uncommon, should be treated with vitamin D2 or D3 supplementation (see Guideline 7) and/or phosphate administration, respectively.

13B.3a If osteomalacia due to vitamin D deficiency fails to respond to ergocalciferol or cholecalciferol, particularly in people with kidney failure (stage 5), treatment with an active vitamin D sterol may be given (see Guideline 8B).

13B.3b Doses of phosphate supplementation should be adjusted upward until normal serum levels of phosphorus are achieved.

GUIDELINE 13C: ADYNAMIC BONE DISEASE

13C.1 Adynamic bone disease in stage 5 CKD (as determined either by bone biopsy or intact PTH <100 pg/mL [11.0 pmol/L]) should be treated by

allowing plasma levels of intact PTH to rise in order to increase bone turnover.

13C.1a This can be accomplished by decreasing doses of calcium-based phosphate binders and vitamin D or eliminating such therapy.

GUIDELINE 14: PARATHYROIDECTOMY IN PEOPLE WITH CKD

14.1 Parathyroidectomy should be recommended in people with severe hyperparathyroidism (persistent serum levels of intact PTH >800 pg/mL [88.0 pmol/L]), associated with hypercalcemia and/or hyperphosphatemia that are refractory to medical therapy.

14.2 Effective surgical therapy of severe hyperparathyroidism can be accomplished by subtotal parathyroidectomy or total parathyroidectomy with parathyroid tissue autotransplantation.

14.3 In people who undergo parathyroidectomy the following should be done:

14.3a The blood level of ionized calcium should be measured every four to six hours for the first 48 to 72 hours after surgery, and then twice daily until stable.

14.3b If the blood levels of ionized or corrected total calcium fall below normal (<0.9 mmol/L or <3.6 mg/dL corresponding to corrected total calcium of 7.2 mg/dL [1.80 mmol/L]), a calcium gluconate infusion should be initiated at a rate of 1 to 2 mg elemental calcium/kg body weight/h and adjusted to maintain an ionized calcium in the normal range (4.6–5.4 mg/dL or 1.15–1.36 mmol/L). *A 10-mL ampoule of 10% calcium gluconate contains 90 mg of elemental calcium.*

14.3c The calcium infusion should be gradually reduced when the level of ionized calcium attains the normal range and remains stable.

14.3d When oral intake is possible, the patient should receive 1 to 2 g calcium carbonate three times a day, as well as calcitriol of up to 2 μg/day, and these therapies should be adjusted as necessary to maintain the level of ionized calcium in the normal range.

14.3e If the patient was receiving phosphate binders prior to surgery, this therapy may need to be discontinued or reduced as dictated by the levels of serum phosphorus.

14.4 Imaging of parathyroid glands with 99Tc-Sestamibi scan, ultrasound, CT scan or MRI should be done prior to re-exploration parathyroid surgery.

GUIDELINE 15: METABOLIC ACIDOSIS

15.1 In CKD stages 3–5, the serum level of total CO_2 should be measured.

15.1a The frequency of these measurements should be based on the stage of CKD as shown in Table 32.

15.2 In these patients, serum levels of total CO_2 should be maintained at ≥22 mEq/L (22 mmol/L). If necessary, supplemental alkali salts should be given to achieve this goal.

Table 32. Frequency for Measurement of Serum Levels of Total CO_2

CKD Stage	GFR Range (mL/min/1.73 m^2)	Frequency of Measurement
3	30-59	At least every 12 months
4	15-29	At least every 3 months
5	<15	At least every 3 months
	Dialysis	At least every month

GUIDELINE 16: BONE DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

16.1 Serum levels of calcium, phosphorus, total CO_2 and plasma intact PTH should be monitored following kidney transplantation.

16.1a The frequency of these measurements should be based on the time following transplantation, as shown in Table 33.

16.2 During the first week after kidney transplantation, serum levels of phosphorus should be measured daily. Kidney transplant recipients who develop persistently low levels of serum phosphate (<2.5 mg/dL [0.81 mmol/L]) should be treated with phosphate supplementation.

16.3 To minimize bone mass loss and osteonecrosis, the immunosuppressive regimen should be adjusted to the lowest effective dose of glucocorticoids.

Table 33. Frequency for Measurement of Calcium, Phosphorus, PTH and Total CO_2 after Kidney Transplantation

Parameter	First 3 Months	3 Months to 1 year
Calcium	Every 2 weeks	Monthly
Phosphorus	Every 2 weeks	Monthly
PTH	Monthly	Every 3 months
Total CO_2	Every 2 weeks	Monthly

One year after transplantation, the frequency of measurements should follow the recommendations of Table 14, 15 and Guideline 1, depending on the level of kidney function.

16.4 Kidney transplant recipients should have BMD measured by DXA to assess the presence or development of osteoporosis.

16.4a DXA scans should be obtained at time of transplant and one and two years post-transplant.

16.4b If BMD *t*-score is equal to or less than −2 at the time of the transplant, or at subsequent evaluations, therapy with parenteral amino-bisphosphonates should be considered.

16.5 Treatment of disturbances in bone and mineral metabolism is determined by the level of kidney function in the transplant recipient as provided in Guidelines 1–15 for people with CKD.

ADDENDUM

Since these guidelines were published, some new considerations are:

- Cinacalcet (Sensipar®, Amgen) was added to the U.S. market. Cinacalcet lowers intact PTH through an interaction with the calcium-sensing receptor on the parathyroid gland.
- Paricalcitol (Zemplar®) was approved by the Food and Drug Administration as an oral dosage form.

SECTION 6

DYSLIPIDEMIAS

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines for Managing Dyslipidemias in Chronic Kidney Disease*. Am J Kidney Dis 41:S1–S92, 2003 (Suppl 4). Available at: http://www.kidney.org/professionals/kdoqi/guidelines_lipids/index.htm

The original document is divided into five sections containing five guidelines. The guidelines cover people with CKD stages 1 to 5, including kidney transplant recipients. They cover adolescents (defined by the onset of puberty to age 18) and adults (≥18 years). Guidelines, tables, and figures are numbered according to the original document for easy cross-referencing.

ASSESSMENT OF DYSLIPIDEMIAS

GUIDELINE 1

1.1 All adults and adolescents with CKD should be evaluated for dyslipidemias.

1.2 For adults and adolescents with CKD, the assessment of dyslipidemias should include a complete fasting lipid profile with total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides.
Note: (B) *The Friedewald formula is recommended for routine determination of LDL (LDL = [total cholesterol − HDL] − [triglycerides/5] in mg/dL).*

1.3 For adults and adolescents with stage 5 CKD, dyslipidemias should be evaluated upon presentation (when the patient is stable), at two to three months after a change in treatment or other conditions known to cause dyslipidemias, and at least annually thereafter.

GUIDELINE 2

2.1 For adults and adolescents with stage 5 CKD, a complete lipid profile should be measured after an overnight fast whenever possible.

2.2 People on HD should have lipid profiles measured either before dialysis, or on days not receiving dialysis.

GUIDELINE 3

People with stage 5 CKD with dyslipidemias should be evaluated for remediable, secondary causes.

TREATMENT OF ADULTS WITH DYSLIPIDEMIAS (SEE TABLE 25)

GUIDELINE 4

4.1 For adults with stage 5 CKD and fasting triglycerides ≥500 mg/dL (≥5.65 mmol/L) that cannot be corrected by removing an underlying

cause, treatment with therapeutic lifestyle changes (TLCs) and a triglyceride-lowering agent should be considered.

4.2 For adults with stage 5 CKD and LDL ≥100 mg/dL (≥2.59 mmol/L), treatment should be considered to reduce LDL to <100 mg/dL (<2.59 mmol/L).

4.3 For adults with stage 5 CKD and LDL <100 mg/dL (<2.59 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) ≥130 mg/dL (≥3.36 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <130 mg/dL (<3.36 mmol/L).

Table 25. The Management of Dyslipidemias in Adults with Chronic Kidney Disease.

Dyslipidemia	Goal	Initiate	Increase	Alternative
TG ≥500 mg/dL	TG <500 mg/dL	TLC	TLC + Fibrate or Niacin	Fibrate or Niacin
LDL 100-129 mg/dL	LDL <100 mg/dL	TLC	TLC + low dose Statin	Bile acid seq. or Niacin
LDL ≥130 mg/dL	LDL <100 mg/dL	TLC + low dose Statin	TLC + max. dose Statin	Bile acid seq. or Niacin
TG ≥200 mg/dL and non-HDL ≥130 mg/dL	Non-HDL <130 mg/dL	TLC + low dose Statin	TLC + max. dose Statin	Fibrate or Niacin

To convert mg/dL to mmol/L, multiply triglycerides by 0.01129, and cholesterol by 0.02586.
Abbreviations: TG, triglycerides; LDL, low-density lipoprotein cholesterol; TLC, therapeutic lifestyle changes.

Recommendations are provided for dosage adjustment for some medications where there is reduced kidney function (Table 30).

TREATMENT OF ADOLESCENTS WITH DYSLIPIDEMIAS

GUIDELINE 5

5.1 For adolescents with stage 5 CKD and fasting triglycerides ≥500 mg/dL (≥5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with TLCs should be considered.

5.2 For adolescents with stage 5 CKD and LDL ≥130 mg/dL (≥3.36 mmol/L), treatment should be considered to reduce LDL to <130 mg/dL (<3.36 mmol/L).

5.3 For adolescents with stage 5 CKD and LDL <130 mg/dL (<3.36 mmol/L), fasting triglycerides ≥200 mg/dL (≥2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) ≥160 mg/dL (≥4.14 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <160 mg/dL (<4.14 mmol/L).

Table 30. Lipid-Lowering Medication Dose Adjustments for Reduced Kidney Function.

	Adjust for Reduced GFR (mL/min/1.73 m²)			
Agent	**60-90**	**15-59**	**<15**	**Notes**
Atorvastatin[326]	No	No	No	
Cerivastatin[330]	No	↓ to 50%	↓ to 50%	Withdrawn
Fluvastatin	?	?	?	
Lovastatin[329]	No	↓ to 50%	↓ to 50%	
Pravastatin[327,328]	No	No	No	
Simvastatin	?	?	?	
Nicotinic acid[331]	No	No	↓ to 50%	34% kidney excretion
Cholestipol	No	No	No	Not absorbed
Cholestyramine	No	No	No	Not absorbed
Colesevelam	No	No	No	Not absorbed
Bezafibrate[332-334]	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Clofibrate[335-337]	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Ciprofibrate	?	?	?	May ↑ serum creatinine
Fenofibrate[338]	↓ to 50%	↓ to 25%	Avoid	May ↑ serum creatinine
Gemfibrozil[339,340]	No	No	No	May ↑ serum creatinine

Abbreviations: GFR, glomerular filtration rate; USFDA, United States Food and Drug Administration.

ADDENDUM

There is ongoing controversy about the exact goal for LDL, total cholesterol and triglycerides in people with CKD. These issues are briefly addressed in the *NKF K/DOQI Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients* (2005) and by a report from the National Cholesterol Education Program to update the Adult Treatment Panel III guidelines (2004). Further, there have been more recent related findings from studies such as 4D (Wanner C, Krane V, März W, et al. *Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis.* N Engl J Med 353:238–248, 2005).

SECTION 7

USE OF ANTIHYPERTENSIVE AGENTS AND TREATMENT OF HYPERTENSION IN CKD

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease*. Am J Kidney Dis 43:S1–S290, 2004 (Suppl 1). Available at: **http://www.kidney.org/professionals/kdoqi/guidelines_bp/index.htm**

The original document includes several sections incorporating 13 guidelines, and covers the topics listed in Table 8. Guidelines, tables and figures are numbered according to the original document for easy cross-referencing.

Table 8. Topics and Guidelines

Topics	Guidelines
Goals	1. Goals
Evaluation	2. Evaluation of CKD and hypertension 3. Measurement of blood pressure 4. Evaluation for renal artery disease
General principles of antihypertensive therapy	5. Self-management 6. Lifestyle modification 7. Pharmacological therapy for CVD
Pharmacological therapy for CKD	8. Diabetic kidney disease 9. Nondiabetic kidney disease 10. Kidney disease in kidney transplant recipients
Use of selected antihypertensive agents in CKD	11. Use of ACE inhibitors and ARBs 12. Use of diuretics
Special populations	13. Guidelines in children

The document contains a wealth of information on drug dosing, interactions, adverse events and related material. The following text summarizes some of the guidelines.

GUIDELINE 1: GOALS OF ANTIHYPERTENSIVE THERAPY IN CKD

1.1 Antihypertensive therapy should be used in CKD to:

1.1.a Lower blood pressure.

1.1.b Reduce the risk of CVD, in patients with or without hypertension.

1.1.c Slow progression of kidney disease, in patients with or without hypertension.

1.2 Modifications to antihypertensive therapy should be considered based on the level of proteinuria during treatment.

1.3 Antihypertensive therapy should be coordinated with other therapies for CKD as part of a multi-intervention strategy.

1.4 If there is a discrepancy between the treatment recommended to slow progression of CKD and to reduce the risk of CVD, individual decision making should be based on risk stratification.

GUIDELINE 2: EVALUATION OF PEOPLE WITH CKD OR HYPERTENSION

2.1 Blood pressure should be measured at each health encounter.

2.2 Initial evaluation should include the following elements:

- **2.2.a Description of CKD:**
  - **2.2.a.i Type (diagnosis), level of GFR and level of proteinuria (Table 49).**
  - **2.2.a.ii Complications of decreased GFR.**
  - **2.2.a.iii Risk for progression of kidney disease.**
- **2.2.b Presence of clinical CVD and CVD risk factors.**
- **2.2.c Comorbid conditions.**
- **2.2.d Barriers to self-management, adherence to diet and other lifestyle modifications and adherence to pharmacological therapy.**
- **2.2.e Complications of pharmacological therapy.**

2.3 A clinical action plan should be developed for each patient, based on the stage of CKD (see Table 51).

2.4 Recommended intervals for follow-up evaluation for monitoring antihypertensive therapy should be guided by clinical conditions (Table 52).

2.5 People with resistant hypertension should undergo additional evaluation to ascertain the cause (Table 71).

2.6 Patients should be referred to specialists, when possible. (see Table 53)

Table 49. Laboratory Measurements for Ascertainment of CKD

For all patients at increased risk for CKD: • Serum creatinine to estimate GFR; • Albumin-to-creatinine or protein-to-creatinine ratio in a first-morning or random untimed "spot" urine specimen; • Examination of the urine sediment or dipstick for red blood cells and white blood cells.
For patients found to have CKD: • Imaging of the kidneys, usually by ultrasound; • Serum electrolytes (sodium, potassium, chloride and bicarbonate).

Table 51. Clinical Action Plans for Various Stages of CKD

Stage	Description	GFR (mL/min/1.73 m^2)	Action*
1	Kidney damage with normal or ↑ GFR	≥90	Diagnosis and treatment, Treatment of comorbid conditions, Slowing progression, CVD risk reduction
2	Kidney damage with mild ↓ GFR	60–89	Estimating progression
3	Moderate ↓ GFR	30–59	Evaluating and treating complications
4	Severe ↓ GFR	15–29	Preparation for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	Replacement (if uremia present)

CKD is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.
* Includes actions from preceding stages.
Reprinted with permission.[1]

Table 52. Recommended Interval for Follow-Up Evaluation in CKD

Clinical Condition	After Initiation or Increase in Dose of Antihypertensive Therapy	
	4-12 weeks	<4 weeks
SBP (mm Hg)	120-139*	≥140 or <120
GFR (mL/min/1.73 m^2)	≥60	<60
Early GFR decline (70)	<15	≥15
Serum potassium (meq/L)	>4.5[a] or ≤4.5[b]	≤4.5[a] or >4.5[b]
	After Blood Pressure is at Goal and Dose is Stable	
	6-12 months	1-6 months
GFR (mL/min/1.73 m^2)	≥60	<60
GFR decline (mL/min/1.73 m^2 per year) (Table 67)	<4 (slow)	≥4 (fast)
Risk factors for faster progression of CKD (Table 68)	No	Yes
Risk factors for acute GFR decline (Table 69)	No	Yes
Comorbid conditions (Table 71)	No	Yes

Clinicians are advised to evaluate each parameter and select the follow-up interval for the parameter that requires the earliest follow-up
[a]for thiazide or loop diuretic therapy, [b]for ACE inhibitor or ARB therapy
* 120-129 mmHg, to monitor for hypertension; 130-139 mmHg, to reach blood pressure goal

Table 71. Causes of Resistant Hypertension

Worsening CKD
Volume overload • Excessive sodium intake • Fluid retention from hypotension • Inadequate diuretic therapy
Pseudoresistance • "White-coat hypertension" (WCH) or office elevation in blood pressure • Pseudohypertension in older patients • Use of regular size blood pressure cuff on very large arm
Re-Assessment for barriers to adherence
Consideration for testing for secondary causes of hypertension
Drug-related causes • Doses too low • Wrong type of diuretic • Inappropriate combinations • Rapid inactivation (e.g. hydralazine) • Drugs that can raise blood pressure • Drug actions and interactions
Associated conditions • Smoking • Increasing obesity • Sleep apnea • Insulin resistance/hyperinsulinemia • Ethanol intake >1 oz (30 mL) per day • Anxiety-induced hyperventilation or panic attacks • Chronic pain • Intense vasoconstriction (arteritis) • Organic brain syndrome (e.g. memory deficit)

Table 53. Recommendations for Referral to Specialists for Consultation and Co-Management of CKD*

Indication	Specialist
Evaluation and management of CKD, as described in K/DOQI CKD Clinical Action Plan	Kidney disease specialist (C); Other specialists as appropriate (C)
GFR <30 mL/min/1.73 m^2	Kidney disease specialist (B)
Spot urine total protein-to-creatinine ratio >500-1000 mg/g	Kidney disease specialist (C)
Increased risk for progression of kidney disease	Kidney disease specialist (C)
GFR decline >30% within 4 months without explanation**	Kidney disease specialist (C)
Hyperkalemia (serum potassium concentration >5.5 mEq/L) despite treatment	Kidney disease specialist (C)
Resistant hypertension	Kidney disease or hypertension specialist (C)
Difficult-to-manage drug complications	Kidney disease or hypertension specialist (C)
Acute presentations of CVD	Cardiovascular disease specialist (C)
Complex or severe chronic CVD conditions	Cardiovascular disease specialist (C)
Age <18 years	Pediatric kidney disease specialist (C)

*Availability of specialists may vary, depending on location.
**Defined as "fast" GFR decline (>4 mL/min/1.73 m^2 per year) or risk factors for fast GFR decline. Short-term decline in GFR up to 30% may be seen after initiation of ACE inhibitor or ARB and does not require referral to specialists in the absence of other indications.
Letters in parenthesis denotes strength of recommendations

GUIDELINE 3: MEASUREMENT OF BLOOD PRESSURE IN ADULTS

3.2 Patients should be taught to measure and record their blood pressure, whenever possible.

3.3 Ambulatory blood pressure monitoring should be considered for people with CKD for the following indications:

- **3.3.a Suspected white coat hypertension.**
- **3.3.b Resistant hypertension.**
- **3.3.c Hypotensive symptoms while taking antihypertensive medications.**
- **3.3.d Episodic hypertension.**
- **3.3.e Autonomic dysfunction.**

GUIDELINE 4: EVALUATION FOR RENAL ARTERY DISEASE (RAD)

4.1 For people in whom there is a clinical suspicion of RAD (see Table 77), the clinician should do one or more of the following:

- **4.1.a Estimate the probability of RAD using a predictive index derived from clinical characteristics.**
- **4.1.b Obtain a noninvasive screening test for RAD.**
- **4.1.c Refer to a kidney disease specialist or hypertension specialist for evaluation.**

4.2 Patients found to have hemodynamically significant RAD should be referred to a kidney disease specialist or hypertension specialist for management.

Table 77. Clinical Clues Suggesting the Presence of Renal Artery Disease as the Cause of Hypertension and CKD

• Age at onset of hypertension <30 yr or >55 yr
• Abrupt onset of hypertension
• Acceleration of previously well-controlled hypertension
• Hypertension refractory to an appropriate three-drug regimen
• Accelerated hypertensive retinopathy
• Malignant hypertension
• History of Tobacco Use
• Systolic-diastolic abdominal bruit
• Flash pulmonary edema
• Evidence of generalized atherosclerosis obliterans
• Asymmetry in kidney size on imaging studies
• Acute kidney failure with treatment with an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker

GUIDELINE 5: EDUCATION ON SELF-MANAGEMENT BEHAVIOR

5.1 Self-management principles should be incorporated into the treatment plan.

5.3 All patients should be assessed for barriers to adherence and self-management, and referred for further counseling as needed (to a nurse practitioner, registered nurse, registered dietitian, masters prepared social worker, pharmacist, physician assistant or other professional).

GUIDELINE 6: DIETARY AND OTHER THERAPEUTIC LIFESTYLE CHANGES IN ADULTS

6.1 Dietary sodium intake of <2.4 g/d (<100 mmol/d) should be recommended in most adults with CKD and hypertension.

6.2 Other dietary recommendations for adults should be modified according to the stage of CKD (Table 83).

6.3 Lifestyle modifications recommended for CVD risk reduction should be recommended as part of the treatment regimen (Table 84).

Table 83. Macronutrient Composition and Mineral Content of the Dietary Approaches to Stop Hypertension (DASH) Diet Recommended by JNC 7, with Modification for Stages 3–4 of CKD

Nutrient	Stage of CKD	
	Stages 1-4	
Sodium (g/d)*	<2.4	
Total Fat (% of calories)	<30	
Saturated Fat (% of calories)	<10	
Cholesterol (mg/d)	<200	
Carbohydrate (% of calories)**	50-60	
	Stages 1-2	Stages 3-4
Protein (g/kg/d, % of calories)	1.4 (~18)	0.6-0.8 (~10)
Phosphorus (g/d)	1.7	0.8-1.0
Potassium (g/d)	>4	2-4

*Not recommended for patients with "salt-wasting."
**Adjust so total calories from protein, fat and carbohydrate is 100%.

Table 84. Other Lifestyle Modifications Recommended by JNC 7

Lifestyle Component	Recommendation
Weight maintenance if BMI <25 kg/m^2	Balanced diet to maintain desirable body weight
Weight loss if overweight or obese (BMI ≥25 kg/m^2)	Calorie restricted, balanced diet
Exercise and physical activity	Moderate intensity for 30 minutes/day, most days of the week
Moderation of alcohol intake	≤2 drinks/day (men) ≤1 drink/day (women)
Smoking cessation	Counseling, nicotine supplementation

GUIDELINE 7: PHARMACOLOGICAL THERAPY: USE OF ANTIHYPERTENSIVE AGENTS IN CKD

All antihypertensive agents can be used to lower blood pressure in CKD. Multidrug regimens will be necessary in most people with CKD to achieve therapeutic goals. People with specific causes of kidney disease and CVD will benefit from specific classes of agents.

7.1 People with CKD should be considered in the "highest-risk" group for CVD for implementing recommendations for pharmacological therapy, irrespective of cause of CKD.

7.2 Target blood pressure for CVD risk reduction in CKD should be <130/80 mm Hg.

7.3 Antihypertensive agents should be prescribed as follows, when possible:

7.3.a Preferred agents should be used first (see Guidelines 8–11).

7.3.b Diuretics should be included in the antihypertensive regimen in most patients.

7.3.c Choose additional agents based on CVD-specific indications to achieve therapeutic and preventive targets (Table 86) and to avoid side effects and interactions.

7.4 The antihypertensive regimen should be simplified as much as possible.

7.4.1 Long-acting (once-daily agents) should be used when possible.

7.4.2 Two agents, either as separate prescriptions or as a fixed-dose combination containing preferred agents, may be considered as initial therapy for systolic blood pressure >20 mm Hg above goal according to the stage of CKD and CVD risk.

7.4.3 Fixed-dose combinations may be used for maintenance therapy after the antihypertensive regimen has been established.

Table 86. Preferred Antihypertensive Agents for CVD

Types of CVD	Thiazide or Loop Diuretics	ACE Inhibitors or ARBs	Beta-Blockers	Calcium-Channel Blockers	Aldosterone Antagonists
Heart Failure with Systolic Dysfunction	X	X	X[a]		X
Post MI with Systolic Dysfunction		X	X		X
Post MI			X		
Chronic Stable Angina			X	X	
High-Risk for Coronary Artery Disease	X	X	X	X	
Recurrent Stroke Prevention	X	X			
Supraventricular Tachycardias			X	X[b]	

[a] Only some beta-blockers (carvedilol, bisoprolol, metoprolol succinate)
[b] Nondihydropyridine calcium-channel blockers.

GUIDELINE 8: PHARMACOLOGICAL THERAPY: DIABETIC KIDNEY DISEASE

8.1 Target blood pressure in diabetic kidney disease should be <130/80 mm Hg (Table 104).

8.2 People with diabetic kidney disease with or without hypertension should be treated with an ACE inhibitor or an ARB (Table 104).

Table 104. Hypertension and Antihypertension Agents in Diabetic Kidney Disease

Clinical Assessment	Target Blood Pressure		Preferred Agents for CKD		Other Agents to Reduce CVD Risk and Reach Target Blood Pressure	
Blood pressure ≥130/80 mm Hg	<130/80 mm Hg	B	ACE inhibitor or ARB	A	Diuretic preferred, then beta-blocker or calcium-channel blocker	A
Blood pressure <130/80 mm Hg			ACE inhibitor or ARB	A		

Letters in shaded areas denote strength of recommendations

GUIDELINE 9: PHARMACOLOGICAL THERAPY: NONDIABETIC KIDNEY DISEASE

9.1 Target blood pressure in nondiabetic kidney disease should be <130/80 mm Hg (Table 111).

9.2 People with nondiabetic kidney disease and spot urine total protein-to-creatinine ratio ≥200 mg/g, with or without hypertension, should be treated with an ACE inhibitor or ARB (Table 111).

Table 111. Hypertension and Antihypertension Agents in Nondiabetic Kidney Disease

Clinical Assessment	Target Blood Pressure		Preferred Agents for CKD		Additional Agents to Reduce CVD Risk and Reach Target Blood Pressure	
Blood pressure ≥130/80 mm Hg and spot urine total protein-to-creatinine ratio ≥200 mg/g	<130/80 mm Hg	A	ACE inhibitor or ARB	A	Diuretic preferred, then beta-blocker or calcium-channel blocker	A
Blood pressure ≥130/80 mm Hg and spot urine total protein-to-creatinine ratio <200 mg/g	<130/80 mm Hg	B	None preferred		Diuretic preferred, then ACE inhibitor, ARB, beta-blocker or calcium-channel blocker	A
Blood pressure <130/80 mm Hg and spot urine total protein-to-creatinine ratio ≥200 mg/g			ACE inhibitor or ARB	C	Diuretic preferred, then beta-blocker or calcium-channel blocker	A
Blood pressure <130/80 mm Hg and spot urine total protein-to-creatinine ratio <200 mg/g			None preferred			

Letters in shaded areas represent strength of recommendations.

GUIDELINE 10: PHARMACOLOGICAL THERAPY: KIDNEY DISEASE IN THE KIDNEY TRANSPLANT RECIPIENT

10.1 The target blood pressure in kidney transplant recipients should be <130/80 mm Hg (Table 119).

10.2 People with CKD in the kidney transplant should be treated with any of the following to reach the target blood pressure: calcium channel blockers (CCBs), diuretics, ACE inhibitors, ARBs or β-blockers.

Table 119. Hypertension and Antihypertension Agents in Kidney Disease in the Transplant Recipient

Clinical Assessment	Target Blood Pressure		Preferred Agents for CKD	Additional Agents to Reduce CVD Risk and Reach Target Blood Pressure	
Blood pressure ≥130/80 mm Hg	<130/80 mm Hg	B	None preferred	CCB, diuretics, ACE inhibitor, ARB, beta-blocker	B
Blood pressure <130/80 mm Hg			None preferred		

Letters in shaded areas denote strength of recommendations

GUIDELINE 11: USE OF ACE INHIBITORS AND ARBs IN CKD

ACE inhibitors and ARBs can be used safely in most people with CKD.

11.1 ACE inhibitors and ARBs should be used at moderate to high doses.

11.2 ACE inhibitors and ARBs should b used as alternatives to each other, if the preferred class cannot be used.

11.3 ACE inhibitors and ARBs can be used in combination to lower blood pressure or reduce proteinuria.

11.4 Patients treated with ACE inhibitors or ARBs should be monitored for hypotension, decreased GFR and hyperkalemia.

11.5 The interval for monitoring blood pressure, GFR and serum potassium depends on baseline levels (Table 123).

11.6 In most patients, the ACE inhibitor or ARB can be continued if:

11.6.1 GFR decline over four months is <30% from baseline value.

11.6.2 Serum potassium is ≤5.5 mEq/L.

11.7 ACE inhibitors and ARBs should not be used or used with caution in the circumstances noted in Table 124.

Table 123. Recommended Intervals for Monitoring Blood Pressure, GFR and Serum Potassium for side effects of ACE Inhibitors or ARBs in CKD

Baseline Value	SBP (mm Hg)	≥120*	<120
	GFR (mL/min/1.73 m²)	≥60	<60
	Early GFR Decline (%)	<15	≥15
	Serum Potassium (mEq/L)	≤4.5	>4.5
Interval	After Initiation or Increase in Dose of ACE Inhibitor or ARB	4-12 weeks	≤4 weeks
	After Blood Pressure is at Goal and Dose is Stable	6-12 months	1-6 months

*See Guideline 7, Table 90, for recommended intervals to reach blood pressure goal.

Table 124. Circumstances in which ACE Inhibitors and ARBs Should Not Be Used

	Do Not Use	Use with Caution
ACE Inhibitor	Pregnancy (A) History of angioedema (A) Cough due to ACE inhibitors (A) Allergy to ACE or ARB (A)	Women not practicing contraception (A) Bilateral renal artery stenosis* (A) Drugs causing hyperkalemia (A)
ARB	Allergy to ACE inhibitor or ARB (A) Pregnancy (C) Cough due to ARB (C)	Bilateral renal artery stenosis* (A) Drugs causing hyperkalemia (A) Women not practicing contraception (C) Angioedema due to ACE inhibitors (C)

*Including renal artery stenosis in the kidney transplant or in a solitary kidney.
Letters in parentheses denote strength of recommendations.

GUIDELINE 12: USE OF DIURETICS IN CKD

Choice of diuretic agents depends on the level of GFR and need for reduction in extracellular fluid (ECF) volume.

12.1 Most people with CKD should be treated with a diuretic.

12.1.a Thiazide diuretics given once daily are recommended in people with GFR ≥30 mL/min/1.73 m² (CKD stages 1–3).

12.1.b Loop diuretics given once or twice daily are recommended in people with GFR <30 mL/min/1.73 m² (CKD stages 4–5).

12.1.c Loop diuretics given once or twice daily, in combination with thiazide diuretics, can be used for patients with ECF volume expansion and edema.

12.1.d Potassium-sparing diuretics should be used with caution:

12.1.d.i In people with GFR <30 mL/min/1.73 m² (CKD stages 4–5).

12.1.d.ii In people receiving concomitant therapy with ACE inhibitors or ARBs.

12.1.d.iii In people with additional risk factors for hyperkalemia.

12.2 People treated with diuretics should be monitored for:

12.2.a Volume depletion, manifest by hypotension or decreased GFR.

12.2.b Hypokalemia and other electrolyte abnormalities.

12.2.c The interval for monitoring depends on baseline values for blood pressure, GFR and serum potassium concentration (Table 145).

12.3 Long-acting diuretics and combinations of diuretics with other antihypertensive agents should be considered to increase patient adherence.

Table 145. Recommended Intervals for Monitoring Blood Pressure, GFR, and Serum Potassium for Side Effects of Diuretics in CKD

Baseline Value	Baseline SBP (mm Hg)	≥120*	<120
	Baseline GFR (mL/min/1.73 m²)	≥60	<60
	Early GFR Decline (%)	<15	≥15
	Baseline Serum Potassium (mEq/L) for Thiazide and Loop Diuretics	>4.5	≤4.5
	Baseline Serum Potassium (mEq/L) for Potassium-Sparing Diuretics	≤4.0	>4.0
Interval	After Initiation or Increase in Dose	4-12 weeks	≤4 weeks
	After Blood Pressure is at Goal and Dose is Stable	6-12 months	1-6 months

*See Guideline 7, Table 90, for recommended intervals to reach blood pressure goal.

GUIDELINE 13: SPECIAL CONSIDERATIONS IN CHILDREN

13.2 The cause of CKD and age of the child should be considered in selecting the class of antihypertensive agent.

13.3 Target blood pressure in children should be lower than the 90th percentile for normal values adjusted for age, gender and height or 130/80 mm Hg, whichever is lower.

ADDENDUM

- New data have confirmed the usefulness of combination therapy with ACE inhibitors plus ARBs.
- There is a possibility that target blood pressures and glycosylated hemoglobin A_1C values in diabetic patients may be lowered.

SECTION 8

CARDIOVASCULAR DISEASE IN DIALYSIS PATIENTS

Source: National Kidney Foundation. *K/DOQI Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients*. Am J Kidney Dis 45:S1–S154, 2005 (Suppl 3). Available at: http://www.kidney.org/professionals/kdoqi/guidelines_cvd/index.htm

The original document is subdivided into three sections containing 16 CPGs. Selected guidelines in adult and pediatric dialysis patients are included here. Guidelines, tables and figures are numbered according to the original document for easy cross-referencing.

GUIDELINES ON EVALUATION AND MANAGEMENT OF CVD

GUIDELINE 1: EVALUATION OF CVD IN ADULT AND PEDIATRIC PATIENTS

CVD is prevalent in people receiving dialysis therapies, and it affects long-term outcomes as well as the ability to deliver dialysis in some situations. Thus, it is important to evaluate the extent of all aspects of CVD in people on dialysis. In those inidividuals with limited life expectancy due to severe noncardiac comorbidity, evaluation and therapy should be individualized.

1.1 At the initiation of dialysis, all people — regardless of symptoms — require assessment for CVD (coronary artery disease [CAD], cardiomyopathy, valvular heart disease [VHD], cerebrovascular disease [CBVD], and peripheral vascular disease [PVD]), as well as screening for both traditional and nontraditional cardiovascular risk factors.

1.1.1 Echocardiograms should be performed in all people at the initiation of dialysis, once they have achieved dry weight (ideally within one to three months of dialysis initiation), and at three-year intervals thereafter (see Guideline 6).

1.2 Children commencing dialysis should be evaluated for the presence of cardiac disease (cardiomyopathy and valvular disease) using echocardiography once they have achieved dry weight (ideally within three months of the initiation of dialysis therapy). Children commencing dialysis should be screened for traditional cardiovascular risk factors such as dyslipidemia and hypertension.

GUIDELINE 2: CORONARY ARTERY DISEASE

Ischemic heart disease (IHD) due to atherosclerotic CAD is common in people on dialysis. Although its evaluation and treatment are important components of the ongoing care of people on dialysis, there are special considerations for both the evaluation and treatment in people on dialysis due to the issues of preservation of kidney function, vascular access and bleeding tendencies.

2.1 The evaluation of CAD in people on dialysis depends on individual patient status.

2.1.a If the individual is on the kidney transplant waitlist and has diabetes (and initial evaluation is negative for CAD), then evaluation for CAD every 12 months is recommended.

2.1.b If the individual is on the transplant waitlist but does not have diabetes and is classified as "high risk," then evaluation for CAD every 24 months is recommended.*

2.1.c If the individual is on the transplant waitlist and is not classified as high risk, then evaluation for CAD every 36 months is recommended.*

2.1.d If the individual is on the transplant waitlist with known CAD (and not revascularized), evaluation for CAD should be performed every 12 months.

2.1.e If the individual is on the transplant waitlist and has a history of percutaneous transluminal coronary angioplasty or coronary stent, evaluation for CAD should be performed every 12 months.

2.1.f If the individual has "complete" coronary revascularization (i.e., all ischemic coronary vascular beds are bypassed), the first re-evaluation for CAD should be performed three years after coronary artery bypass (CAB) surgery, then every 12 months thereafter.

2.1.g If the individual has "incomplete" coronary revascularization after CAB surgery (i.e., not all ischemic coronary beds are revascularized), then evaluation for CAD should be performed annually.

2.1.h If there is a change in symptoms related to IHD or clinical status (e.g., recurrent hypotension, CHF unresponsive to dry weight changes or inability to achieve dry weight because of hypotension), evaluation for CAD is recommended.

2.1.i People on dialysis with significant reduction in LV systolic function (ejection fraction [EF] <40%) should be evaluated for CAD.

2.1.j Evaluation for heart disease should occur at initiation of dialysis and include a baseline electrocardiogram (ECG) and echocardiogram (see Guideline 6.1.3. for echocardiography after dialysis initiation). Both of these tests provide information pertinent to, but not restricted to, CAD evaluation. Annual ECGs are recommended after dialysis initiation.

*High-risk (>20% per 10 years cardiovascular event rate risk) according to Framingham data includes those with two or more "traditional" risk factors, a known history of coronary disease, LV ejection fraction ≤40%, or PVD.

2.2 In people fulfilling 2.1.a–2.1.i, CAD evaluation should also include exercise or pharmacological stress echocardiographic or nuclear imaging tests. "Automatic" CAD evaluation with stress imaging is currently not recommended for all people on dialysis (i.e., patients not fulfilling 2.1.a–2.1.i). Stress imaging is appropriate (at the discretion of the patient's physician) in selected high-risk dialysis patients for risk stratification even in people who are not renal transplant candidates.

2.3 Patients who are candidates for coronary interventions and have stress tests that are positive for ischemia should be referred for consideration of angiographic assessment.

2.4 Special considerations in people on dialysis regarding CAD evaluation include the following:

2.4.a To minimize the risk of potential volume overload from the performance of angiographic studies, iso-osmolar radiocontrast media (e.g., iodixanol) should be used.

2.4.b Some people on dialysis have residual renal function; there are no data on the value of "nephroprotective" strategies to reduce the potential risk of contrast nephropathy in these patients. The use of *N*-acetylcysteine (and iodixanol) is appropriate in people on dialysis with residual renal function, as both may offer benefit without known harm. Sodium bicarbonate and hydration are not routinely recommended, as intravascular volume expansion may pose risk to dialysis patients with increased cardiac filling pressures.

2.5 In patients undergoing invasive coronary procedures, it is important to avoid internal jugular sites and to preserve brachial and radial arteries for future dialysis catheter and arteriovenous fistula creation, respectively.

2.6 Patients undergoing planned invasive procedures for evaluation or treatment of CAD should be assessed for hemorrhagic risk and presence of anemia, as anticoagulants and/or antiplatelet agents may be administered adjunctively for percutaneous coronary intervention (PCI).

GUIDELINE 3: ACUTE CORONARY SYNDROME

The diagnosis of acute coronary syndrome (ACS) in people on dialysis and in the general population is usually based on the triad of symptoms, ECG findings, and cardiac biomarkers. The outcomes of people on dialysis with ACS are often poor, which may be related to the lack of a consistent and standard approach to the treatment of ACS.

3.1 All people on dialysis presenting with ACS should be treated as in the non-dialysis population, with the exception of specific attention to drugs that have altered clearances in kidney failure (e.g., low-molecular-weight

heparin). These therapies include PCI, CABG, antiplatelet agents, β-blockers, thrombolytic therapy and lipid-lowering agents.

3.1.2 People on dialysis with ST-segment elevation myocardial infarction should receive acute reperfusion therapy (as do people in the nondialysis population). With the potential for increased hemorrhagic risk associated with thrombolytic therapy, emergent PCI is the preferred treatment if it is available.

GUIDELINE 4: CHRONIC CAD

4.1 The medical management of chronic CAD in dialysis patients should follow that of the general population. In particular, patients should receive acetylsalicylic acid (ASA), beta-blockers, nitroglycerin, ACE inhibitors or ARBs, statins, and/or calcium channel blockers (CCB) as indicated. Dose adjustments are required for medications that are renally excreted or dialyzed.

4.2 Unique aspects of management in the dialysis population include:

4.2.a Maintenance of hemodynamic dry weight.

4.2.b Maintenance of Hb levels in accordance with KDOQI guidelines.

4.2.c Modification of dosing regimens so that cardiovascular medications do not adversely impact the delivery of dialysis and ultrafiltration. Nocturnal dosing of medications should be considered.

4.2.d Loop diuretics to increase urine output may be helpful for those patients with substantial residual renal function.

4.3 In patients with obstructive CAD lesions, PCI and CAB grafting (CABG) are appropriate revascularization techniques.

4.3.a Drug-eluting or conventional stents should be implemented according to local practice. The incidence of restenosis after PCI with drug-eluting stents is reduced in the nondialysis population. Because the risk of restenosis is higher in people on dialysis, the use of drug-eluting stents is favored.

4.3.b Patients with three-vessel and/or left main disease should undergo CABG as preferred therapy.

GUIDELINE 5: VALVULAR HEART DISEASE

The presence of VHD impacts long-term outcomes, as in the general population. In addition, VHD in people on dialysis may impair the ability to adequately deliver dialysis, which, in turn, may limit ultrafiltration and toxin removal, resulting in exacerbation of CVD.

5.1 Evaluation of VHD in dialysis patients:

5.1.a Patients should be evaluated for the presence of VHD and for follow-up of VHD in the same manner as the general population except for frequency of follow-up for aortic stenosis.

5.1.b Special considerations for echocardiographic evaluation in people on dialysis:

5.1.b.i Dry weight optimization should be achieved prior to testing to enhance the interpretation of results.

5.1.b.ii The interpretation of repeat echocardiographic evaluations should be done with consideration of the relationship between the echo exam and either the HD treatment or the presence or absence of PD fluid in the peritoneal cavity.

5.2 Management of VHD in people on dialysis:

5.2.a Published recommendations for the management of VHD in the general population should be followed.

5.2.b Both mechanical and tissue valves can be used for replacement, with similar outcomes, in people on dialysis.

5.2.c People on dialysis who are asymptomatic and on the transplant waitlist with moderate or more severe aortic stenosis (aortic valve area $\leq$1.0 cm^2) should have annual Doppler echocardiograms (because aortic stenosis progresses faster in dialysis patients than general population). The same frequency of follow-up is appropriate in other people on dialysis who would be suitable candidates for aortic valve replacement based on overall clinical status.

5.2.d People with VHD who are newly or increasingly symptomatic (e.g., displaying dyspnea, angina, fatigue and unstable intradialytic hemodynamics) should be (re)-evaluated for VHD severity by echocardiography (and referred to a cardiologist for further evaluation if the patient is deemed suitable for intervention on clinical grounds).

5.3 Children with VHD should be evaluated by echocardiography. Management of valvular disease should follow recommendations provided by the American College of Cardiology/American Heart Association (AHA) Guidelines for the Management of Patients with Valvular Heart Disease VI.

GUIDELINE 6: CARDIOMYOPATHY (SYSTOLIC OR DIASTOLIC DYSFUNCTION)

The prevalence of systolic or diastolic dysfunction, or overt LVH, is estimated to be at least 75% at dialysis initiation. De novo and recurrent heart failure occurs in a substantial proportion of people on dialysis, and affects morbidity and mortality, as well as the ability to deliver adequate dialysis.

6.1 Evaluation of cardiomyopathy (systolic or diastolic dysfunction) in people on dialysis:

6.1.a People on dialysis should be evaluated for the presence of cardiomyopathy (systolic or diastolic dysfunction) in the same manner as the general population, using echocardiographic testing.

6.1.b Patients should be re-evaluated if there is change in clinical status (e.g., symptoms of CHF, recurrent hypotension on dialysis, post-cardiac events) or considered for kidney transplant.

6.1.c Echocardiograms should be performed in all people at the initiation of dialysis, once they have achieved dry weight (ideally within one to three months of dialysis initiation), and at three-year intervals thereafter.

6.1.d As in the general population, people on dialysis identified with significant reduction in LV systolic function (EF <40%) should be evaluated for CAD (if not done previously). This evaluation may include both noninvasive testing (stress imaging) and invasive testing (coronary angiography). In patients at high risk for CAD (e.g., those with diabetic CKD), coronary angiography may be appropriate, even in those with negative stress imaging test, because of the lower diagnostic accuracy of noninvasive stress imaging test in people with CKD.

6.2 The treatment of cardiomyopathy in the dialysis population is similar to that in the nondialysis population, with the important exception of potential effects of therapeutic agents (e.g., ACE inhibitors or β-blockers) on intrahemodialytic hemodynamics.

6.2.a Congestive heart failure unresponsive to changes in target dry weight may also be a complication of unsuspected VHD or IHD; clinical re-evaluation should be considered in these patients.

6.2.b Dosing of therapeutic agents may need to be empirically individualized to hemodialysis schedules (in hypotensive patients).

6.2.c The consistent maintenance of euvolemia is a cornerstone of treatment of CHF in dialysis patients.

6.3 Target "hemodynamic dry weight" may need to be adjusted to compensate for hemodynamic effects of therapeutic agents.

6.4 Children should be evaluated for the presence of cardiomyopathy (systolic and diastolic dysfunction) using echocardiographic testing.

GUIDELINE 7: DYSRHYTHMIA

Patients on MD are at increased risk for dysrhythmias, cardiac arrest and sudden cardiac death (SCD). The risk of SCD or cardiac arrest increases with age and dialysis duration.

7.1 Evaluation of people on dialysis:

7.1.a All people on dialysis, regardless of age, should undergo a routine 12-lead ECG at the initiation of dialysis.

7.1.b People with dysrhythmias should be treated in the same manner as the general population with regard to antiarrhythmic agents (including β-blockers) and pacing devices (including internal defibrillators). Refer to Table 5 for dosage adjustments and drugs to be avoided.

Table 5. Dosage Adjustments and Drugs To Be Avoided

Antiarrhythmic Class	Name of the Drug	What To Do in Patients with Renal Failure?
Class Ia agents	Procainamide: Normally 50% of procainamide is excreted unchanged by kidneys. Procainamide is metabolized to NAPA in different proportions based on the acetylator status, e.g., 16%-22% in slow acetylators and 24%-30% in rapid acetylators is converted to NAPA. Two-thirds of NAPA is eliminated by the kidneys.	Procainamide should be avoided in dialysis patients. NAPA levels should be monitored every 6-8 hours. Procainamide-induced lupus anticoagulants may increase the risk of thrombosis, including the thrombosis of the dialysis access.
	Disopyramide: The elimination half-life is 6-9 hours and renal excretion accounts for 40%-60% of elimination of the unchanged drug; an additional 30% is excreted as metabolites. Protein binding is highly variable, ranging from 40%-90%, and with higher doses and higher plasma concentration, greater concentration of the drug remains unbound resulting in an increased risk for toxicity.	The pharmacokinetics of disopyramide on dialysis is not known. The dose modification is required if used in dialysis-dependent patients. Great caution should be exercised in patients with pre-existing heart failure, as the use of disopyramide is associated with worsening of CHF. There may be an increased risk of developing torsades de pointes with the use of disopyramide in dialysis patients.
Class Ib agents	Tocainide: It is an amine analogue of lidocaine, thus allowing oral administration. Bioavailability is almost 100% following oral administration. Some 40% is excreted unchanged in urine and between 10%-50% is bound to plasma proteins.	The dose of tocainide should be reduced in dialysis patients with an aim to maintain the trough levels of tocainide between 4-10 µg/mL.
Class Ic agents	Flecainide: It is a derivative of procainamide. The fraction of flecainide excreted unchanged in the urine is 30% (range 10%-50%) and the rest of the drug is metabolized in liver. The relationship between flecainide elimination and creatinine clearance is poorly understood.	Dose reductions are necessary in patients with renal failure but the magnitude of the clearance by dialysis is not known. However, it is prudent to decrease the dose by 50% of the normal recommended dose (100 mg every 12 hours) in patients with renal and liver failure and to maintain the trough level of 0.2-1.0 µg/mL. Also, flecainide should be used with caution in patients with CHF.
Class II agents	Acebutolol: After an oral dose, 40% of the drug is converted to the major metabolite (diacetolol) that is equally active but more cardioselective than the parent compound. Another 40% of the parent drug is eliminated by the kidneys and almost all of the diacetolol is cleared by the kidneys. Both acebutolol and diacetolol are hydrophilic and hence cleared by dialysis therapy.	Patients with advanced renal failure and not on dialysis will need dose reduction to avoid the accumulation of diacetolol. On the contrary, patients on dialysis should be advised to take acebutolol at the end of dialysis therapy and patients on daily dialysis will need a supplemental dose at the end of dialysis.
Class III agents	Sotalol: After oral administration, bioavailability varies from 60%-100%. It is not protein bound and 75% of the administered dose is excreted unchanged; hence it accumulates in patient with renal failure. No active or inactive metabolites have been found.	Dosage reduction is necessary in patients with impaired renal function. Its use should be avoided in dialysis patients.
	Dofetilide: Bioavailability is >90% after an oral dose. Eighty percent of the drug is excreted in urine unchanged and the remaining is excreted in the form of various metabolites. Dofetilide use is associated with prolongation of the Q-T interval, and the prolongation of Q-T interval is directly related to the plasma concentration of dofetilide.	Dofetilide is contraindicated in patients with creatinine clearance of <20 mL/min. The dose is reduced to 125 µg twice a day, 250 µg twice a day, and 500 µg twice a day in patients with estimated creatinine clearance of 20-40 mL/min, 40-60 mL/min and >60 mL/min, respectively. Its use should be avoided in dialysis-dependent patients.
	Tedisamil: About 60% of the drug is absorbed after oral administration, 90% of the drug is protein bound and is excreted by the kidney as an active drug. Plasma concentration and half-life are increased in patients with renal disease.	Dose modifications are necessary if Tedisamil is used in patients with renal impairment. Due to lack of PK data in dialysis patients, it may be prudent to monitor QTc interval and the drug use should be stopped if QTc increases more than 550 ms.
Miscellaneous group	Magnesium: Only 1% of total magnesium is found in the serum and the kidney is the principal organ responsible for the maintenance of magnesium homeostasis. Progressive increase in magnesium concentration results in hypotension, prolongation of PR, QRS intervals and peaked T waves. At a level of 5 mmol/L, areflexia, respiratory paralysis, and cardiac arrest may occur.	Dialysis patients if treated with intravenous magnesium should have continuous electrocardiographic monitoring and frequent estimation of serum magnesium levels to avoid the development of hypermagnesemia.

GUIDELINE 8: EXTERNAL DEFIBRILLATION

The capability for effective, rapid defibrillation (with negligible risk of inappropriate treatment) is widely available with the development of automatic external defibrillators (AEDs). Given the high prevalence of dysrhythmias (see Guideline 7), the availability of AEDs in dialysis facilities may impact the outcomes of people who experience cardiac events during dialysis therapy.

8.1 All dialysis units should have on-site capability for external cardiac defibrillation. Automatic external defibrillators are the simplest, most cost-effective means to achieving this guideline, because they do not require advanced life support training by staff for operation, require minimal maintenance and are designed for use by nonmedical personnel.

8.1.a All dialysis units caring for pediatric patients need to have on-site external automatic defibrillators and/or appropriate pediatric equipment available. Automated external defibrillators may be used for children 1–8 years of age, and should ideally deliver pediatric doses and have an arrhythmia detection algorithm.

GUIDELINE 9: CEREBROVASCULAR DISEASE

Stroke is the third leading cause of death in the general population in the United States and many other countries, with large economic and human burdens as a consequence. People with CKD are at increased risk for stroke relative to the general population.

9.1 All people on dialysis should follow the AHA guidelines for the prevention, screening, evaluation and treatment of stroke.

9.2 Special considerations in people on dialysis include:

9.2.a Anticoagulation in nonvalvular atrial fibrillation: People on dialysis are at increased risk for bleeding and careful monitoring should accompany intervention.

9.2.b Acute stroke in people on dialysis: Given that acute stroke syndromes can result from either thrombotic or bleeding events in people on dialysis, the immediate goal of localization and cause is particularly important because of increased risk of bleeding associated with anticoagulants in this population. Therefore, imaging with established methods should be undertaken.

9.3 Treatment of stroke and transient ischemic attack (TIA):

9.3.a Treatment of TIAs and strokes should follow the same principles used in the general population for both medical management and surgical management, with the exception of thrombolytics in people on HD.

9.3.a.i Assessment of the risk of bleeding in people recently receiving heparin on dialysis should be conducted when considering the use of thrombolytics.

GUIDELINE 10: PERIPHERAL VASCULAR DISEASE

People on dialysis with and without diabetes are at risk for PVD, with approximately 15% of incident patients having a clinical diagnosis of PVD.

10.1 Diagnosis of PVD:

10.1.a At the time of dialysis initiation, all people should be evaluated for the presence of PVD.

10.1.b Evaluation should include physical examination including assessment of arterial pulse and skin integrity.

10.1.c Further specialized studies, such as duplex studies or invasive testing, should be undertaken if abnormalities are detected on physical examination and interventions should be considered.

10.2 Approach to therapy of PVD:

10.2.a People with PVD should be treated in the same manner as the general population in regard to smoking cessation, lipid-lowering therapy, glycemic control, blood pressure control and the use of ACE inhibitors and antiplatelet agents. In addition, supervised exercise regimens and medications to increase vasodilation should be considered in people with claudication and without critical leg ischemia. Established national guidelines, similar to those for stroke, are not available for PVD in the general population.

GUIDELINE 11: DIABETES

11.1 All people on dialysis who have diabetes should follow the American Diabetes Association guidelines.

There are some oral hypoglycemic agents that either should be used with caution, or not used at all, in people on dialysis (see Table 8).

Table 8. Oral Hypoglycemic Agents Contraindicated or To Be Used with Caution in Dialysis Patients

Medication		Rationale
Metformin	Contraindicated	Decreased clearance; possibility of lactic acidosis
Glyburide, glipizide, glimepride, tolazamide, chlorpropamide	Use with Caution	High risk of persistent hypoglycemia due to low clearance of sulfonylurea class drugs and their metabolites

GUIDELINE 12: BLOOD PRESSURE

The management of blood pressure is an important component of CVD risk management for all aspects of CVD: CAD, cardiomyopathy, VHD, CBVD and PVD. There are unique challenges in both the measurement and management of blood pressure in people on dialysis.

12.1 Measurement of blood pressure:

12.1.a In people who have undergone multiple surgical procedures for vascular accesses in both arms, blood pressure should be measured in the thighs or legs. However, health care professionals should use the appropriate cuff size and measure blood pressure only in the supine position.

12.2 Predialysis and postdialysis blood pressure goals should be <140/90 mm Hg and <130/80 mm Hg, respectively.

12.3 Management of blood pressure by adjustment of dry weight:

12.3.a Management of hypertension in people on dialysis requires attention to both management of fluid status and adjustment of antihypertensive medications. This requires close collaboration among health care providers.

Excessive fluid accumulation between dialysis sessions should be managed with:

- **Education and regular counseling by dietitians.**
- **Low sodium intake (2–3 g/day sodium intake).**
- **Increased ultrafiltration.**
- **Longer dialysis.**
- **More than three dialysis treatments per week.**
- **Drugs that reduce salt appetite.**

12.4 Management of hypertension with drugs in people on dialysis (see Table 12):

12.4.a Drugs that inhibit the renin-angiotensin system, such as ACE inhibitors or angiotensin II-receptor blockers should be preferred because they cause greater regression of LVH, reduce sympathetic nerve activity, reduce pulse wave velocity, may improve endothelial function and may reduce oxidative stress.

12.4.b Antihypertensive drugs should be given preferentially at night because they may reduce the nocturnal surge of blood pressure and minimize intradialytic hypotension, which may occur when drugs are taken the morning before a dialysis session.

12.4.c In people with hypertension that is difficult to control, the dialyzability of antihypertensive medications should be considered (see Table 10).

Algorithm 4. Hypertension Treatment Algorithm in Dialysis Patients.

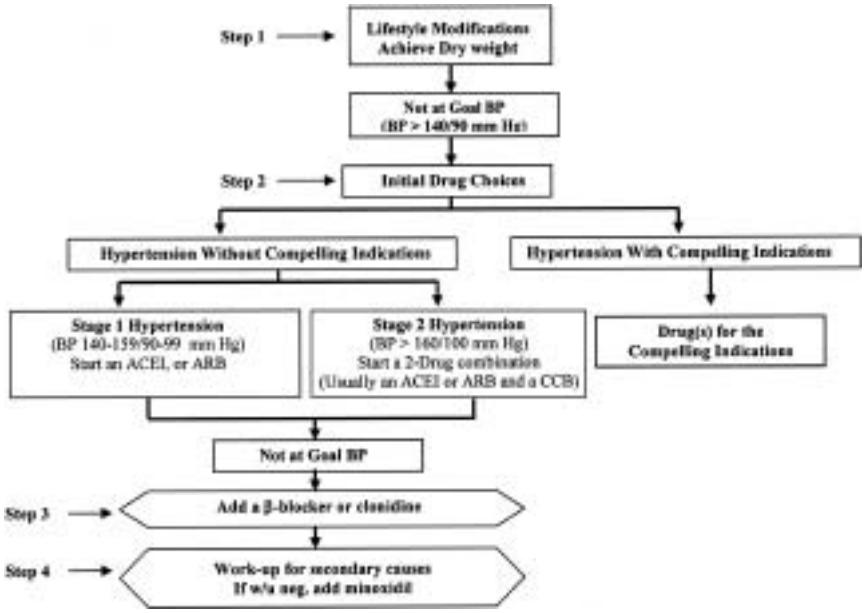


Table 12. Antihypertensive Drug Therapy in Dialysis: Guidelines for Selection

Clinical Situation	Preferred	Relatively or Absolutely Contraindicated
Angina pectoris	β-Blockers, CCBs	Direct vasodilators
Post-MI	Non-ISA β-blockers	Direct vasodilators
Hypertrophic cardiomyopathy with diastolic dysfunction	β-Blockers, diltiazem, verapamil	Direct vasodilators, α_1-blockers
Bradycardia, heart block, sick sinus syndrome		β-blockers, labetalol, verapamil, diltiazem
Heart failure (decreased LV ejection fraction)	ACE inhibitors, ARBs, β-blockers	CCBs
Peripheral vascular disease		β-blockers
Diabetes mellitus	ACE inhibitors, ARBs	
Asthma/COPD		β-blockers
Cyclosporine-induced hypertension	CCBs, labetalol	Nicardipine,[a] verapamil,[a] diltiazem[a]
Liver disease		Labetalol, methyldopa
Erythropoietin-induced hypertension	Calcium antagonists	ACE inhibitors[b]

a. May increase serum levels of cyclosporine
b. May increase erythropoietin requirement

Table 10. Removal of Antihypertensive Drugs with Dialysis

	Percent Removal with Dialysis	
	HD	PD
ACE Inhibitors		
Benazepril	Yes	?
Enalapril	35	?
Fosinopril	2	?
Lisinopril	50	?
Ramipril	Yes	?
Calcium Channel Blockers		
Amlodipine	?	?
Diltiazem	?	?
Nifedipine	Low	Low
Nicardipine	?	?
Felodipine	?	?
Verapamil	Low	Yes
β-Blockers		
Atenolol	75	53
Acebutolol	70	50
Carvedilol	None	None
Labetalol	<1	<1
Metoprolol	High	?
Antiadrenergic Drugs		
Clonidine	5	?
Guanabenz	None	None
Methyldopa	60	30-40
Vasodilators		
Hydralazine	None	None
Minoxidil	Yes	Yes
Angiotensin Receptor Blockers		
Losartan	None	None
Candesartan	None	?
Eprosartan	None	None
Telmisartan	None	?
Valsartan	None	None
Irbesartan	None	None

12.5 Determination and management of blood pressure in children should follow recommendations by *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*.*

12.5.a Optimal systolic and diastolic blood pressure should be <95% for age, gender and height.

12.5.b Management of hypertension on dialysis requires attention to fluid status and antihypertensive medications, minimizing intradialytic fluid accumulation by:

- **Education by dietitians every three months.**

*National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. *The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents.* Pediatrics 114:555–576, 2004 (2 Suppl 4th Report).

- **Low salt intake (2 g/day sodium intake).**
- **Increased ultrafiltration.**
- **Longer dialysis duration.**
- **Intradialytic sodium modeling to minimize intradialytic hypotension.**
- **More than three dialysis treatments per week.**
- **Antihypertensives: consider if medications are cleared on dialysis.**

GUIDELINE 13: DYSLIPIDEMIA

The reader is referred to NKF-KDOQI CPGs for Managing Dyslipidemia (see Section 6) along with seven key trials that have been published since the guidelines were published.

1. Liu Y, Coresh J, Eustace JA, et al. *Association between cholesterol level and mortality in dialysis patients: role of inflammation and malnutrition*. JAMA 291:451–459, 2004.
2. Holdaas H, Fellstrom B, Jardine AG, et al. *Effect of fluvastatin on cardiac outcomes in renal transplant patients recipients: a multicentre, randomised, placebo-controlled trial*. Lancet 361:2024–2031, 2003.
3. Sever PS, Dahlof B, Poulter NR, et al. *Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre, randomised, controlled trial*. Lancet 361:1149–1158, 2003.
4. Tonelli M, Moye L, Sacks FM, et al. *Pravastatin for secondary prevention of cardiovascular events in persons with mild chronic renal insufficiency*. Ann Intern Med 138:98–104, 2003.
5. Heart Protection Study Collaborative Group. *MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial*. Lancet 360:7–22, 2002.
6. Colhoun HM, Betteridge DJ, Durrington PN, et al. *Primary prevention of CVD with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial*. Lancet 364:685–696 2004.
7. Wanner C, Krane V, März W, et al. *Atorvastatin with type 2 diabetes mellitus undergoing hemodialysis*. N Engl J Med 353:238–248, 2005.

GUIDELINE 14: SMOKING, PHYSICAL ACTIVITY AND PSYCHOLOGICAL FACTORS

14.1 All people on dialysis should be counseled and regularly encouraged to stop smoking. Referral to smoking cessation specialists is recommended.

14.2 All people on dialysis should be counseled and regularly encouraged by nephrology and dialysis staff to increase their level of physical activity.

14.3 Measurement of physical functioning:

14.3.a Evaluation of physical functioning and re-evaluation of the physical activity program should be done at least every six months.

14.3.b Physical functioning can be measured using physical performance testing or questionnaires (e.g., SF-36 [a multipurpose health survey]).

14.4 Physical activity recommendations:

14.4.a Many people on dialysis are severely deconditioned and therefore may need a referral for physical therapy to increase strength and endurance to the point where they are able to adopt the recommended levels of physical activity.

14.4.a.i People who qualify for cardiac rehabilitation should be referred to a specialist.

14.4.a.ii The goal for activity should be for cardiovascular exercise at a moderate intensity for 30 minutes most, if not all, days per week. Patients who are not currently physically active should start at very low levels and durations, and gradually progress to this recommended level.

14.5 Depression, anxiety and hostility should be identified and treated in people on dialysis.

14.5.a Every person on dialysis should be seen by the dialysis social worker at initiation of dialysis, and at least biannually thereafter, to assess the individual's psychological state, with specific focus on the presence of depression, anxiety and hostility.

14.5.b People on dialysis should be treated for depression, anxiety and hostility if they are experiencing these psychological states.

GUIDELINE 15: ANEMIA

The reader is referred to NKF KDOQI CPGs for Treatment of Anemia (see Section 1).

GUIDELINE 16: ARTERIAL STIFFNESS, VASCULAR AND VALVULAR CALCIFICATION, CALCIUM, PHOSPHORUS AND PTH

16.1 All people on dialysis should have pulse pressure (PP) determined monthly before dialysis.

16.1.a For PP >60 mm Hg and systolic blood pressure >135 mm Hg, it is recommended that PP be reduced by achieving ideal body weight and the use of antihypertensive medication with the target PP being 40 mm Hg.

16.2 Identification and treatment of calcification:

16.2.a If arterial calcification is identified by plain radiography in any of the following sites (abdominal aorta, carotid arteries, ileo-femoral axis or femoro-popliteal axis), identification of calcification at another site should be sought.

16.2.b If vascular calcification is present in two or more sites, consideration should be given to prescription of a non-calcium-containing phosphate binder.

16.3 All people on dialysis should follow current KDOQI guidelines (see Section 5) for treatment of calcium, phosphate and PTH.