



## Complete Summary

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### GUIDELINE TITLE

NKF-K/DOQI clinical practice guidelines for hemodialysis adequacy: update 2006.

### BIBLIOGRAPHIC SOURCE(S)

Clinical practice guidelines for hemodialysis adequacy. Am J Kidney Dis 2006 Jul;48(1 Suppl 1):S13-97. [364 references]

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: NKF-K/DOQI clinical practice guidelines for hemodialysis adequacy: update 2000. Am J Kidney Dis 2001 Jan;37(1 Suppl 1):S7-S64.

### \*\* REGULATORY ALERT \*\*

### FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse:** This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [July 31, 2008, Erythropoiesis Stimulating Agents \(ESAs\)](#): Amgen and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated.
- [November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents \(ESAs\)](#): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

### COMPLETE SUMMARY CONTENT

\*\* REGULATORY ALERT \*\*

SCOPE

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY  
DISCLAIMER

## SCOPE

### **DISEASE/CONDITION(S)**

End-stage renal disease (ESRD)

### **GUIDELINE CATEGORY**

Treatment

### **CLINICAL SPECIALTY**

Family Practice  
Internal Medicine  
Nephrology  
Pediatrics

### **INTENDED USERS**

Advanced Practice Nurses  
Allied Health Personnel  
Clinical Laboratory Personnel  
Dietitians  
Health Care Providers  
Health Plans  
Nurses  
Patients  
Physician Assistants  
Physicians  
Social Workers

### **GUIDELINE OBJECTIVE(S)**

To update the 2000 Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guidelines on Hemodialysis Adequacy

### **TARGET POPULATION**

Adult and pediatric patients on hemodialysis

## **INTERVENTIONS AND PRACTICES CONSIDERED**

1. Patient education about kidney failure and options for its treatment
2. Estimation of kidney function (glomerular filtration rate)
3. Optimal timing of initiation of dialysis
4. Monitoring of hemodialysis dose (including formal urea kinetic modeling)
5. Assessment of hemodialysis adequacy (including blood urea nitrogen [BUN])
6. Control of fluid volume and blood pressure
7. Preservation of residual kidney function (RKF) (e.g., use of angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers, avoidance of nephrotoxic insults)
8. Quality improvement programs

## **MAJOR OUTCOMES CONSIDERED**

- Morbidity (including cardiovascular and cerebrovascular events) and mortality among end-stage renal disease patients on hemodialysis
- Longevity
- Indicators of hemodialysis adequacy
- Frequency of intradialytic symptoms
- Frequency of hospitalization
- Intermediate outcomes (e.g. clearance and filtration measures)
- Adverse events due to treatment
- Quality of life

## **METHODOLOGY**

### **METHODS USED TO COLLECT/SELECT EVIDENCE**

Hand-searches of Published Literature (Primary Sources)  
Searches of Electronic Databases

### **DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE**

Based on the draft guideline statements, the Work Group members agreed on topics that would be systematically reviewed and formulated questions defining predictors, interventions, comparators, and outcomes of interest. Search strategies were developed based on these questions and topics, in addition to the study designs and years of publications of interest to the Work Group. Articles of interest were identified through MEDLINE searches of English language literature of human studies in May through July 2004. Broad search terms were used to avoid missing potentially pertinent articles. The searches were supplemented by articles identified by Work Group members through June 2005.

Only full journal articles of original data were included. The searches were limited to studies published since January 1997 since earlier publications were reviewed in the previous Dialysis Outcomes Quality Initiatives (DOQI) guidelines. Editorials, letters, abstracts, and unpublished reports were not included. Selected review articles, however, were included for background material. No systematic process was followed to obtain review articles.

Abstracts and titles from the MEDLINE search results were prescreened by members of the Evidence Review Team for general relevance. A second round of screening was performed on the abstracts by Work Group members for relevance using predefined eligibility criteria, described below. Articles were retrieved by the Evidence Review Team and then rescreened by Work Group members and/or the Evidence Review Team. Eligible studies were extracted using standardized extraction forms. Domain experts made the final decisions regarding the eligibility of all articles.

### **Literature Yield**

A total of 2,526 citations were screened, of which 319 were review articles and 14 were added by Work Group members. There were 223 articles (191 studies in adults and 32 in children) that were potentially relevant. These articles were retrieved for full review. Of these, 87 adult articles were accepted for full data extraction by the Work Group members. Eight articles in children were formally data extracted by a pediatric nephrologist on the Work Group. Articles in adults were randomly assigned to individual Work Group members for data extraction. Of these, 23 studies answered questions pertinent to topics chosen for systematic listing in Summary Tables. See Table 4 of Appendix 1 of the original guideline document for further detail on literature yield.

### **Limitations of Approach**

While the literature searches were intended to be comprehensive, they were not exhaustive. MEDLINE was the only database searched, and searches were limited to English language publications. Hand searches of journals were not performed, and review articles and textbook chapters were not systematically searched. However, important studies known to the domain experts that were missed by the literature search were included in the review.

Because of resource limitations and other practical considerations, there were several deviations from the original protocol for several of the update topics. These primarily resulted in nephrologists in the Evidence Review Team, rather than Work Group members, performing the primary article screening and the data extraction for articles included in several Summary Tables. (However, all articles that met criteria for all topics, all completed data extraction forms, and all Summary Tables were distributed to relevant Work Group members for critical review and incorporation into guidelines.)

## **NUMBER OF SOURCE DOCUMENTS**

23

## **METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE**

Weighting According to a Rating Scheme (Scheme Given)

## **RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE**

The quality of evidence was not explicitly graded. It was implicitly assessed according to the criteria outlined in the table below, and considered: i) the methodological quality of the studies; ii) whether or not the studies were carried out in the target population (i.e., patients on dialysis, or in other populations) and iii) whether the studies examined health outcomes directly, or examined surrogate measures for those outcomes (e.g., blood flow instead of access survival).

Outcome	Population	Methodological Quality		
		Well designed and analyzed (little, if any, potential bias)	Some problems in design and/or analysis (some potential bias)	Poorly designed and/or analyzed (large potential bias)
Health outcome(s)	Target population	Strong	Moderately Strong	Weak
Health outcome(s)	Other than the target population	Moderately strong	Moderately strong	Weak
Surrogate measure for health outcome(s)	Target population	Moderately strong	Weak	Weak
Surrogate measure for health outcome(s)	Other than the target population	Weak	Weak	Weak

**Strong:** Evidence includes results from well-designed, well-conducted study/studies in the target population that directly assess effects on health outcomes.

**Moderately Strong:** Evidence is sufficient to determine effects on health outcomes in the target population, but the strength of the evidence is limited by the number, quality, or competency of the individual studies. OR evidence is from a population other than the target population, but from well-designed, well-conducted studies; OR evidence is from studies with some problems in design and/or analysis; OR evidence is from well-designed, well-conducted studies or surrogate endpoints for efficacy and/or safety in the target population.

**Weak:** Evidence is insufficient to assess the effects on net health outcomes because it is from studies with some problems in design and/or analysis on surrogate endpoints for efficacy and/or safety in the target population; OR the evidence is only for surrogate measures in a population other than the target population; OR the evidence is from studies that are poorly designed and/or analyzed.

## METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

### Generation of Data Extraction Forms

Data extraction forms were designed to capture information on various aspects of the primary articles. Forms for all topics included study setting and demographics, eligibility criteria, causes of kidney disease, numbers of subjects, study design, study funding source, dialysis characteristics, comorbid conditions, descriptions of relevant risk factors or interventions, description of outcomes, statistical methods, results, study quality (based on criteria appropriate for each study design (see below), study applicability (see below), and sections for comments and assessment of biases. Training of the Work Group members to extract data from primary articles occurred by emails and teleconferences. Work Group members were assigned the task of data extraction of articles.

### **Generation of Evidence Tables**

The Evidence Review Team condensed the information from the data extraction forms into evidence tables, which summarized individual studies. These tables were created for the Work Group members to assist them with review of the evidence and are not included in the guidelines. All Work Group members received copies of all extracted articles and all evidence tables. During the development of the evidence tables, the Evidence Review Team checked the data extraction for accuracy and re-screened the accepted articles to verify that each of them met the initial screening criteria determined by the Work Group. If the criteria were not met, the article was rejected, in consultation with the Work Group.

### **Format for Summary Tables**

Summary Tables describe the studies according to the following dimensions: study size and follow-up duration, applicability or generalizability, results, and methodological quality. Within each table, the studies are first grouped by outcome type.

Data entered into Summary Tables were derived from the data extraction forms, evidence tables, and/or the articles by the Evidence Review Team. All Summary Tables were reviewed by the Work Group members.

Within each outcome, studies are ordered first by methodological quality (best to worst), then by applicability (most to least), and then by study size (largest to smallest). When relevant, outcome thresholds (e.g., of access flow measurement) are included. Results are presented by using the appropriate metric or summary symbols, as defined in the table footnotes.

### **Systematic Review Topics, Study Eligibility Criteria, and Studies Evaluated**

The topics for each Update were selected by the respective Work Group members for systematic review (see Tables 1 to 3 in Appendix 1 of the original guideline document). The eligibility criteria were defined by the Work Group members of each Update in conjunction with the Evidence Review Team.

### **Grading of Individual Studies**

*Study Size and Duration*

The study (sample) size is used as a measure of the weight of the evidence. In general, large studies provide more precise estimates of prevalence and associations. In addition, large studies are more likely to be generalizable; however, large size alone, does not guarantee applicability. A study that enrolled a large number of selected patients may be less generalizable than several smaller studies that included a broad spectrum of patient populations. Similarly, longer duration studies may be of better quality and more applicable, depending on other factors.

### *Applicability*

Applicability (also known as generalizability or external validity) addresses the issue of whether the study population is sufficiently broad so that the results can be generalized to the population of interest at large. The study population is typically defined primarily by the inclusion and exclusion criteria. The target population was defined to include patients with kidney failure, specifically those on dialysis. A designation for applicability was assigned to each article, according to a three-level scale. In making this assessment, sociodemographic characteristics were considered, as well as comorbid conditions and prior treatments. Applicability is graded in reference to the population of interest as defined in the clinical question. For example for the question of treatment of catheter-related infections the reference population is that of HD patients with infected cuffed tunneled HD catheters (see Appendix 1 of the original guideline document for details).

### *Results*

The type of results available in each study is determined by the study design, the purpose of the study, and the question(s) being asked. The Work Group decided on the eligibility criteria and outcomes of interest (see Tables 1-3 in Appendix 1 of the original guideline document).

### *Diagnostic Test Studies*

For studies of diagnostic tests, sensitivity and specificity data or area under the curve were included when reported. When necessary, sensitivity and specificity data were calculated from the reported data. Diagnostic tests were evaluated according to a hierarchy of diagnostic tests. Each test was assessed according to diagnostic technical capacity, accuracy, diagnostic and therapeutic impact, and patient outcome. This ultimately affected the overall strength of a recommendation regarding a diagnostic test.

### *Methodological Quality*

Methodological quality (or internal validity) refers to the design, conduct, and reporting of the clinical study. Because studies with a variety of types of design were evaluated, a 3-level classification of study quality was devised (see Appendix 1 of the original guideline document for details).

## **Summarizing Reviews and Selected Original Articles**

Work Group members had wide latitude in summarizing reviews and selected original articles for topics that were determined not to require a systemic review of the literature.

## **METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

### **DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

The Work Group sought to update the guidelines using an evidence-based approach. After topics and relevant clinical questions were identified for the updates, the available scientific literature on those topics was systematically searched and summarized.

#### **Creation of Groups**

The Kidney Disease Outcomes Quality Initiative (KDOQI) Advisory Board selected the Work Group Chairs and the Director of the Evidence Review Team then assembled groups to be responsible for the development of the updates. These Work Groups and the Evidence Review Team collaborated closely throughout the project.

The Work Groups consisted of domain experts, including individuals with expertise in nephrology, surgery, radiology, pediatrics, nursing and nutrition. For each guideline update, the first task of the Work Group members was to define the overall topics and goals of the updates. They then further developed and refined each topic, literature search strategies, and data extraction forms. The Work Group members were the principal reviewers of the literature, and from their reviews and detailed data extractions, they summarized the available evidence and took the primary roles of writing the guidelines and rationale statements. Completed data extractions were posted on a National Kidney Foundation (NKF) website for direct access by Work Group members.

The Evidence Review Team consisted of nephrologists (one senior nephrologist and two nephrology fellows), methodologists, and research assistants from Tufts-New England Medical Center with expertise in systematic review of the medical literature. They instructed the Work Group members in all steps of systematic review and critical literature appraisal. The Evidence Review Team also coordinated the methodological and analytical process of the report, defined and standardized the methodology of performing literature searches, of data extraction, and of summarizing the evidence in summary tables. They organized abstract and article screening, created forms to extract relevant data from articles, organized Work Group member data extraction, and tabulated results. Throughout the project the Evidence Review Team led discussions on systematic review, literature searches, data extraction, assessment of quality and applicability of articles, evidence synthesis, and grading of the quality of the body of evidence and the strength of guideline recommendations.

#### **Refinement of Update Topics and Development of Materials**

The Work Group reviewed the 1995 Dialysis Outcomes Quality Initiative (DOQI) Clinical Practice Guidelines and the 2000 KDOQI updates and decided which of the guideline recommendations required updates and which should remain unchanged. These assessments were based primarily on expert opinion regarding the currency of the previous guidelines and the likelihood of availability of new evidence. Preliminary literature searches were made to inform this process. To allow for timely review, it was determined that each set of guidelines would be able to have systematic reviews on only a limited number of topics. After literature review, the experts decided which recommendations would be supported by evidence or by opinion.

The Work Groups and Evidence Review Team developed: a) draft guideline statements; b) draft rationale statements that summarized the expected pertinent evidence; and c) data extraction forms containing the data elements to be retrieved from the primary articles. The topic refinement process began prior to literature retrieval and continued through the process of reviewing individual articles. Recommendations based on adequate evidence were categorized as Guidelines (CPGs), while opinion-based statements were categorized as Clinical Practice Recommendations (CPRs).

### **Rating the Strength of Recommendations**

After literature review, the experts decided which recommendations were supported by evidence and which were supported by consensus of Work Group opinion. Evidence-based guideline recommendations were graded as strong (A) or moderate (B). Recommendations based on weak evidence (C) and/or consensus of expert opinion were labeled as Clinical Practice Recommendations (CPRs). See "Rating Scheme for the Strength of the Recommendations" below.

### **RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

The strength of each guideline recommendation is based on the quality of the supporting evidence as well as additional considerations. Additional considerations, such as cost, feasibility, and incremental benefit were implicitly considered.

**A** It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves health outcomes.

**B** It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderately strong evidence that the practice improves health outcomes.

**CPR** It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence or on the opinions of the Work Group and reviewers that the practice might improve health outcomes.

Health outcomes are health-related events, conditions, or symptoms that can be perceived by individuals to have an important effect on their lives. Improving health outcomes implies that benefits outweigh any adverse effects.

## **COST ANALYSIS**

A formal cost analysis was not performed and published cost analyses were not reviewed.

## **METHOD OF GUIDELINE VALIDATION**

External Peer Review

Internal Peer Review

## **DESCRIPTION OF METHOD OF GUIDELINE VALIDATION**

As was the case with the initial Guidelines, the current guideline updates were subjected to a three-stage review process. They were presented first to the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI) Steering Committee and revised in response to the comments received. In the second stage, the Kidney Disease Outcomes Quality Initiative (K/DOQI) Advisory Board, along with other experts in the field, provided comments. After considering these, the Work Groups produced a third draft of the guidelines. In the final stage, this draft was made available for public review and comment by all interested parties, including End-Stage Renal Disease (ESRD) Networks, professional and patient associations, dialysis providers, government agencies, product manufacturers, managed care groups, and individuals. The comments received were reviewed and, where appropriate, incorporated in the final version of the updated guideline.

# **RECOMMENDATIONS**

## **MAJOR RECOMMENDATIONS**

Definitions for the strength of each guideline (A, B, or CPR), based on the quality of the supporting evidence as well as additional considerations, are provided at the end of the "Major Recommendations" field.

### **Clinical Practice Guidelines (CPGs) for Hemodialysis Adequacy**

#### **Guideline 1. Initiation of Dialysis**

##### **1.1 Preparation for kidney failure:**

Patients who reach chronic kidney disease (CKD) stage 4 (estimated glomerular filtration rate [GFR] < 30 mL/min/1.73 m<sup>2</sup>) should receive timely education about kidney failure and options for its treatment, including kidney transplantation, peritoneal dialysis (PD), hemodialysis (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. **[B]**

### 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 (see Table 1 in the original guideline document) or by measurement of creatinine and urea clearances, not simply by measurement of serum creatinine and urea nitrogen. The tables below summarize special circumstances in which GFR estimates should be interpreted with particular care. **[B]**

#### **Causes of Unusually Low or High Endogenous Creatinine Generation**

<b>Condition</b>	<b>Creatinine Generation</b>
Vegetarian diet	Low
Muscle wasting	Low
Amputation	Low
Spinal cord injury	Low
Advanced liver disease	Low
Muscular habitus	High
Asian race	Low

#### **Causes of Unusually Low or High Kidney Tubular Creatinine Secretion**

<b>Drug or Condition</b>	<b>Kidney Tubular Creatinine Secretion</b>
Trimethoprim	Low
Cimetidine	Low
Fibrates (except gemfibrozil)	Low
Advanced liver disease	High

### 1.3 Timing of therapy:

When patients reach stage 5 CKD (estimated GFR < 15 mL/min/1.73 m<sup>2</sup>), nephrologists should evaluate the benefits, risks, and disadvantages of beginning kidney replacement therapy. Particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5. **[B]**

#### **Guideline 2. Methods for Measuring and Expressing the Hemodialysis 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.

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

2.2 The frequency of treatments should be included in the expression of dose. **[A]**

2.3 The dose of HD should be expressed as  $(K_{\text{urea}} \times T_d)/V_{\text{urea}}$  (abbreviated as  $Kt/V$ ), where  $K_{\text{urea}}$  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  $V_{\text{urea}}$  is the patient's volume of urea distribution in milliliters. **[B]**

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. **[A]**

2.5 Methods described in the appendix of the original guideline document 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). **[B]**

\*By dialysis only, exclusive of residual kidney function (RKF)

### **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. **[A]**

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. **[A]**

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 seconds). **[A]**

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 minutes) before obtaining the postdialysis sample. **[A]**

### **Recommended Predialysis Blood-Drawing Procedure**

#### **A. When using an AV fistula or graft**

1. Obtain the blood specimen from the arterial needle prior to connecting the arterial blood tubing or flushing the needle. Be sure that no saline and/or heparin is in the arterial needle and tubing prior to drawing the sample for BUN measurement.
2. Do not draw a sample for use as a predialysis measure of BUN if HD has been initiated.

#### **B. When using a venous catheter**

1. Using sterile technique, using a 5 mL syringe, withdraw any heparin and saline from the arterial port of the catheter, along with blood, to a total volume of 5 mL. Discard the contents of this syringe.
2. Connect a new syringe or collection device and draw the sample for BUN measurement.
3. Complete initiation of HD per dialysis clinic protocol.

### **Slow-Blood-Flow Method for Obtaining the Postdialysis Sample**

**A. Drawing the sample from the bloodline sampling port**

1. At the completion of HD, turn off the dialysate flow and decrease the UFR to 50 mL/hr, to the lowest TMP/UFR setting, or off. If the dialysis machine does not allow for turning off the dialysate flow, or if doing so violates clinic policy, decrease the dialysis flow to its minimal setting.
2. Decrease the blood flow to 100 mL/min for 15 seconds (longer if the bloodline volume to the sampling port exceeds 15 mL). To prevent pump shut-off as the blood flow rate is reduced, it may be necessary to manually adjust the venous pressure limits downward. At this point, proceed to obtain your sample. You can either shut off the blood pump before sampling, or leave it running at 100 mL/min while the sample is being drawn.
3. After the sample has been obtained, stop the blood pump (if not already stopped) and complete the patient disconnection procedure as per dialysis clinic protocol.

**B. Method that avoids use of an exposed needle: Drawing the sample from the arterial needle tubing using a syringe or vacutainer device.**

1. Proceed with steps (1) and (2) as per A above.
2. After the 15 second slow-flow period (a slow flow period is still required to clear the small volume in the arterial needle tubing of recirculated blood), stop the pump. Clamp the arterial and venous blood lines. Clamp the arterial needle tubing. Disconnect the blood line tubing from the inlet bloodline, and attach either a syringe or a Vacutainer with a Leur-Lok type connection to the arterial needle tubing (or arterial port of the venous catheter). Release the clamp on the arterial needle tubing and obtain the blood sample.
3. Proceed with step (3) as in section A above.

HD: Hemodialysis; UFR: Ultrafiltration rate; TMP: Transmembrane pressure

**Stop-Dialysis-Flow Method of Obtaining the Postdialysis Sample**

1. At the completion of HD, turn off the dialysate flow (or put it into bypass) and decrease the UFR to 50 mL/hr, to the lowest TMP/URF setting, or off.
2. Wait 3 minutes. Do NOT reduce the blood flow rate during this 3-min period.
3. Obtain the blood sample, either from the sample port on the inlet bloodline, or from the arterial needle tubing or from the arterial port of the venous catheter if using the needle-free method as described in the table above, part B. If sampling from the inlet bloodline, it does not matter if you stop or do not stop the blood flow while this sample is being taken. It probably is best to stop the blood pump prior to sampling. In the stop-dialysate-flow method, slowing the blood flow prior to sampling should not be done.
4. After the sample has been obtained, return the patient's blood in the bloodlines and dialyzer per protocol.

HD: Hemodialysis; UFR: Ultrafiltration rate; TMP: Transmembrane pressure

**Guideline 4. Minimally Adequate Hemodialysis**

#### 4.1 Minimally adequate dose:

The minimally adequate dose of HD given 3 times per week to patients with residual native kidney urea clearance ( $K_r$ ) less than 2 mL/min/1.73 m<sup>2</sup> should be an spKt/V (excluding RKF) of 1.2 per dialysis. For treatment times less than 5 hours, an alternative minimum dose is a urea reduction ratio (URR) of 65%. **[A]**

#### 4.2 Target dose:

The target dose for HD given 3 times per week with  $K_r$  less than 2 mL/min/1.73 m<sup>2</sup> should be an spKt/V of 1.4 per dialysis not including RKF, or URR of 70%. **[A]**

4.3 In patients with residual urea clearance ( $K_r$ ) greater than or equal to 2 mL/min/1.73 m<sup>2</sup>, the minimum session spKt/V can be reduced. One method of minimum dose reduction is described in CPR 4.4. In such patients, the target spKt/V should be at least 15% greater than the minimum dose. **[B]**

#### 4.4 Missed and shortened treatments:

Efforts should be made to monitor and minimize the occurrence of missed or shortened treatments. **[B]**

### **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 a patient'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 patients with RKF. **[A]**

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). **[A]**

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

### **Guideline 6. Preservation of Residual Kidney Function**

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 HD patients. **[A]**

6.2 Methods for preserving RKF differ among patients (see CPR 6). **[B]**

### **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 level 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. **[A]**

7.2 Consideration should be given to providing resources and training for expanding the assessment of clinical outcomes beyond mortality to include

hospitalization rates, quality of life (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. **[B]**

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

## **Guideline 8. Pediatric Hemodialysis 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 less than 15 mL/min/1.73 m<sup>2</sup>. **[A]**

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

8.1.3 Dialysis therapy initiation should be considered at higher estimated GFRs when the patient's clinical course is complicated by the presence of the signs and symptoms listed in the table below, Clinical Practice Recommendation (CPR) 1 for adult patients, ("Complications That May Prompt Initiation of Kidney Replacement Therapy"), 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. **[A]**

### 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. **[B]**

8.2.2 Assessment of nutrition status is an essential component of HD adequacy measurement. Normalized protein catabolic rate (nPCR) should be measured monthly by using either formal urea kinetic modeling or algebraic approximation. **[B]**

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

### 8.3 Prescription of adequate HD:

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

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. **[B]**

8.4 Non-dose-related components of adequacy:  
Accurate assessment of patient intravascular volume during the HD treatment should be provided to optimize ultrafiltration. **[B]**

### **Clinical Practice Recommendations (CPRs) for Hemodialysis Adequacy**

#### **Clinical Practice Recommendation for Guideline 1: Initiation of Dialysis**

Certain complications of kidney failure justify initiation of dialysis treatment in patients for whom estimated GFR has not yet decreased to 15 mL/min/1.73 m<sup>2</sup> (see table below).

#### **Complications That May Prompt Initiation of Kidney Replacement Therapy**

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

ECV: Extracellular Volume

#### **Clinical Practice Recommendations for Guideline 2: Methods for Measuring and Expressing the Hemodialysis Dose**

For patients 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 CPG 2).

2.1 Residual kidney urea clearance ( $K_r$ ) is measured best from a timed urine collection.

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

## **Clinical Practice Recommendations for Guideline 4: Minimally Adequate Hemodialysis**

### 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 Beta<sub>2</sub>-microglobulin (Beta<sub>2</sub>M) 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 posttreatment BUN levels, is the same as that for HD.

### 4.3 Minimum spKt/V levels for different dialysis schedules:

4.3.1 Two to 6 treatments per week are appropriate for certain patients.

4.3.2 Twice-weekly HD is not appropriate for patients with  $K_r$  less than 2 mL/min/1.73 m<sup>2</sup>.

4.3.3 Minimum spKt/V targets for 2-, 4-, and 6-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 (stdKt/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 $K_r$ ):

4.4.1 The minimally adequate dose of dialysis can be reduced in patients with  $K_r$  greater than 2 mL/min/1.73 m<sup>2</sup>.

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

4.4.3 When the minimally adequate dose is reduced because of substantial RKF,  $K_r$  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 patients:

An increase in the minimally adequate dose of dialysis should be considered for the following groups of patients:

4.5.1 Women of any body size.

4.5.2 Smaller patients, for example, patients with values for anthropometric or modeled volume (V) of 25 L or lower.

### 4.6 Dialysis adequacy for patients 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 Patients whose weights are 20% less or lower than their peer body weights.

4.6.2 Patients with recent otherwise unexplained and unplanned weight loss.

4.7 Dialysis adequacy for patients 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 Patients with hyperphosphatemia.

4.7.2 Patients 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 Quality of Life (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 patients with  $K_r$  less than 2 mL/min should be at least 3 hours.

#### **Clinical Practice Recommendations 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 (AAMI) *Standards and Recommended Practices* for reuse of hemodialyzers (Association for Advancement of Medical Information [AAMI], 2003).

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.

#### **Clinical Practice Recommendations for Guideline 6: Preservation of Residual Kidney Function**

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 HD patients with significant RKF and who

need antihypertensive medication. Other measures to protect native kidneys are listed in the following table.

### **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; ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blockers

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

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

### **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

COX-2: Cyclooxygenase-2; ECF: Extracellular fluid

### **Definitions:**

## Rating the Strength of Guideline Recommendations

The strength of each guideline recommendation is based on the quality of the supporting evidence as well as additional considerations. Additional considerations, such as cost, feasibility, and incremental benefit were implicitly considered.

**A** It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is strong evidence that the practice improves health outcomes.

**B** It is recommended that clinicians routinely follow the guideline for eligible patients. There is moderately strong evidence that the practice improves health outcomes.

**CPR** It is recommended that clinicians consider following the guideline for eligible patients. This recommendation is based on either weak evidence or on the opinions of the Work Group and reviewers that the practice might improve health outcomes.

Health outcomes are health-related events, conditions, or symptoms that can be perceived by individuals to have an important effect on their lives. Improving health outcomes implies that benefits outweigh any adverse effects.

## Rating the Quality of Evidence

The quality of evidence was not explicitly graded. It was implicitly assessed according to the criteria outlined in the table below, and considered: i) the methodological quality of the studies; ii) whether or not the studies were carried out in the target population (i.e., patients on dialysis, or in other populations); and iii) whether the studies examined health outcomes directly, or examined surrogate measures for those outcomes (e.g., blood flow instead of access survival).

Outcome	Population	Methodological Quality		
		Well designed and analyzed (little, if any, potential bias)	Some problems in design and/or analysis (some potential bias)	Poorly designed and/or analyzed (large potential bias)
Health outcome(s)	Target population	Strong	Moderately Strong	Weak
Health outcome(s)	Other than the target population	Moderately strong	Moderately strong	Weak
Surrogate measure for health outcome(s)	Target population	Moderately strong	Weak	Weak
Surrogate	Other than the	Weak	Weak	Weak

		Methodological Quality		
measure for health outcome(s)	target population			
<p><b>Strong:</b> Evidence includes results from well-designed, well-conducted study/studies in the target population that directly assess effects on health outcomes.</p> <p><b>Moderately Strong:</b> Evidence is sufficient to determine effects on health outcomes in the target population, but the strength of the evidence is limited by the number, quality, or competency of the individual studies. OR evidence is from a population other than the target population, but from well-designed, well-conducted studies; OR evidence is from studies with some problems in design and/or analysis; OR evidence is from well-designed, well-conducted studies or surrogate endpoints for efficacy and/or safety in the target population.</p> <p><b>Weak:</b> Evidence is insufficient to assess the effects on net health outcomes because it is from studies with some problems in design and/or analysis on surrogate endpoints for efficacy and/or safety in the target population; OR the evidence is only for surrogate measures in a population other than the target population; OR the evidence is from studies that are poorly designed and/or analyzed.</p>				

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations")."

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Decreased morbidity and mortality associated with end stage renal disease
- Increased longevity
- Decreased hospitalization
- Improved quality of life (QOL)

### POTENTIAL HARMS

Intradialytic complications include symptomatic hypotension and cramps.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Insults known to be nephrotoxic (e.g., see table in Clinical Practice Recommendation 6 in the "Major Recommendations" section) in patients with normal or impaired kidney function should be assumed, in the absence of direct evidence, to be nephrotoxic for the remnant kidney in hemodialysis patients and therefore should be avoided.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These Clinical Practice Guidelines (CPGs) and Clinical Practice Recommendations (CPRs) are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care, and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.
- Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. (See "Limitations" sections in the original guideline document for more detailed information specific to each guideline.) Every healthcare professional making use of these CPGs and CPRs is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation. The recommendations for research contained within this document are general and do not imply a specific protocol.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation is an integral component of the Kidney Disease Outcomes Quality Initiative process, and accounts for the success of its past guidelines. The Kidney Learning System (KLS) component of the National Kidney Foundation is developing implementation tools that will be essential to the success of these guidelines.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### **BIBLIOGRAPHIC SOURCE(S)**

Clinical practice guidelines for hemodialysis adequacy. Am J Kidney Dis 2006 Jul;48(1 Suppl 1):S13-97. [364 references]

### **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

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### **GUIDELINE DEVELOPER(S)**

National Kidney Foundation - Disease Specific Society

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### **GUIDELINE COMMITTEE**

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## **FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST**

The National Kidney Foundation makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the Work Group.

Specifically, all members of the Work Group are required to complete, sign, and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

- Dr. Daugirdas has received grants from Watson, American Regent, Aksys, Nephros, RRI, HDC Medical, Advanced Renal Technologies, Amgen, Ortho Biotech, Shire, Roche, Astra Zeneca, and Neurochem.
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## **GUIDELINE STATUS**

This is the current release of the guideline.

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## **GUIDELINE AVAILABILITY**

Electronic copies: Available from the [National Kidney Foundation \(NKF\) Web site](#).

Print copies: Available from the National Kidney Foundation (NKF), 30 East 33rd St., New York, NY 10016. These guidelines are also available on CD-ROM from NKF.

## **AVAILABILITY OF COMPANION DOCUMENTS**

None available

## **PATIENT RESOURCES**

None available

## **NGC STATUS**

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