**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Number** (*if previously endorsed*)**:** 323

**Measure Title**: Adult Kidney Disease: Hemodialysis Adequacy: Solute

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 2/27/2015

|  |
| --- |
| **Instructions**  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * Respond to all questions as instructed with answers immediately following the question. All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Maximum of 10 pages (*incudes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.*** * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

|  |
| --- |
| **Note: The information provided in this form is intended to aid the Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**   1a. Evidence to Support the Measure Focus The measure focus is evidence-based, demonstrated as follows:   * Health outcome: [**3**](#Note3) a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm) and [methods](http://www.uspreventiveservicestaskforce.org/methods.htm), or Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org/publications/index.htm).  **5.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**: (*should be consistent with type of measure entered in De.1*)

Outcome

Health outcome:

Patient-reported outcome (PRO): Click here to name the PRO

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors*

Intermediate clinical outcome (*e.g., lab value*): Adequate dialysis dose

Process: Click here to name the process

Structure: Click here to name the structure

Other: Click here to name what is being measured

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**HEALTH OUTCOME/PRO PERFORMANCE MEASURE**  *If not a health outcome or PRO, skip to* [*1a.3*](#Section1a3)

**1a.2.** **Briefly state or diagram the path between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.**

This measure captures the number of calendar months during which patients have a spKt/V > or= 1.2, which is a measurement of the adequacy of hemodialysis, an intermediate clinical outcome. Adequate dialysis dose is linked to improved health outcomes such as attaining highest quality and quantity of life after onset of illness, decreasing morbidity and mortality, and increasing treatment effectiveness.

**1a.2.1.** **State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (*i.e., influence on outcome/PRO*).**

The guideline recommendation focuses on the same patient population as the measure, patients receiving hemodialysis three times per week. The guideline states that the minimally adequate dose of HD given to this patient population should be an spKt/v (excluding [Residual Kidney Function] RKF) of 1.2 per dialysis. Therefore, the measure is written to capture the calendar months during which patients have a spKt/v > or = 1.2, consistent with the guideline recommendations.

*Note: For health outcome/PRO performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measure**

**1a.3.****Briefly state or diagram the path between structure, process, intermediate outcome, and health outcomes**. Include all the steps between the measure focus and the health outcome.

**1a.3.1.** **What is the source of the systematic review of the body of evidence that supports the performance measure?**

Clinical Practice Guideline recommendation – ***complete sections*** [***1a.4***](#Section1a4)***, and*** [***1a.7***](#Section1a7)

US Preventive Services Task Force Recommendation – ***complete sections*** [***1a.5***](#Section1a5) ***and*** [***1a.7***](#Section1a7)

Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)

Other – ***complete section*** [***1a.8***](#Section1a8)

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** **Guideline citation** (*including date*) and **URL for guideline** (*if available online*):

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)

<http://www.ajkd.org/article/S0272-6386%2806%2900554-3/fulltext#sec10> or

<http://www.kidney.org/sites/default/files/docs/12-50-0210_jag_dcp_guidelines-hd_oct06_sectiona_ofc.pdf>

**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

Recommendation 4.1:

The minimally adequate dose of HD given 3 times per week to patients with Kr less than 2 mL/min/1.73m2 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 URR of 65% (A).

**1a.4.3.** **Grade assigned to the quoted recommendation with definition of the grade:**

Grade: A

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.

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

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.

**1a.4.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.4.1*)**:**

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

Yes **→ *complete section*** [***1a.7***](#Section1a7)

No **→ *report on another systematic review of the evidence in sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)***; if another review does not exist, provide what is known from the guideline review of evidence in*** [***1a.7***](#Section1a7)

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**1a.5.** **UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1.** **Recommendation citation** (*including date*) and **URL for recommendation** (*if available online*):

**1a.5.2.** **Identify recommendation number and/or page number** and **quote verbatim, the specific recommendation**.

**1a.5.3.** **Grade assigned to the quoted recommendation with definition of the grade**:

**1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: the* *grading system for the evidence should be reported in section 1a.7.*)

**1a.5.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.5.1*)**:**

***Complete section*** [***1a.7***](#Section1a7)

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** **Citation** (*including date*) and **URL** (*if available online*):

**1a.6.2.** **Citation and** **URL for methodology for evidence review and grading** (*if different from 1a.6.1*)**:**

***Complete section*** [***1a.7***](#Section1a7)

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE supporting the measure**

*If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.*

**1a.7.1.** **What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?**

A total of 2,526 citations were screened, of which 319 were review articles and 14 were added by [NKF] 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 [NKF] Work Group. Articles in adults were randomly assigned to individual [NKF] Work Group members for data extraction. Of these, 23 studies answered questions pertinent to topics chosen for systematic listing in Summary Tables [within the guideline].

**1a.7.2.** **Grade assigned for the quality of the quoted evidence with definition of the grade**:

Grade A

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.**

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.

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: 1999-2005

**QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5.****How many and what type of study designs are included in the body of evidence**? (*e.g., 3 randomized controlled trials and 1 observational study*)

A total of 2,526 citations were screened, of which 319 were review articles and 14 were added by [NKF] 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 [NKF] Work Group. Articles in adults were randomly assigned to individual [NKF] Work Group members for data extraction. Of these, 23 studies answered questions pertinent to topics chosen for systematic listing in Summary Tables [within the guideline].

**1a.7.6.** **What is the overall quality of evidence across studies in the body of evidence**? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

The present adequacy guideline for a minimally adequate dose remains unchanged from the previous (2000) guidelines. In deciding whether this guideline needed to be changed, the committee considered 3 lines of evidence. The first was results of the primary analysis of the NIH HEMO Study, published in 2002. The committee also had access to as-treated results of the HEMO Study, which were published at the time the draft guidelines were released in November 2005.98 This report was judged to be of some importance because it identified a dose-targeting bias in the analysis of delivered therapy versus mortality in cross-sectional data sets, which potentially impacts on the weight of evidence derived from such data sets. The second was a series of articles suggesting that dosing of dialysis should not be based on URR or its derivative, Kt/V (which essentially is volume of blood cleared divided by the modeled urea volume, V), but on the volume of blood cleared (Kt) only. The third was a series of analyses of delivered dose (ie, [Urea Reduction Ratio] URR) versus mortality based on either the USRDS-Medicare data set or the Fresenius Medical Care subset of these data.

HEMO Clinical Study: Primary (Randomized) Results

Primary results of the HEMO Study, which randomized patients to a delivered eKt/V of 1.16 versus 1.53, equivalent to URR values of about 63% versus 75% or spKt/V values of about 1.3 versus 1.7, revealed little evidence to support increasing the dose of dialysis beyond the current (2000) KDOQI recommendations, respectively. The lack of benefit, without even a trend that was close to statistical significance, appeared not only in the primary outcome of mortality, but also in a variety of main secondary composite outcomes relating to various causes of hospitalization combined with mortality. Furthermore, analysis of minor secondary composite outcomes dealing with nutritional measures—including changes in weight and serum albumin levels, as well as QOL measures—also failed to support a beneficial effect of increasing the dose of dialysis. Of all trials evaluated, the HEMO Study was by far the largest, and its randomized design and measurement of hard outcomes were given an enormous weight in determining whether the 2000 KDOQI HD Adequacy Guidelines needed to be changed. The Work Group realized that the recently published European guidelines recommended substantially higher minimal doses of HD based on an eKt/V measure, corresponding to spKt/V minimum targets of about 1.4 to 1.5.12

HEMO Clinical Study: As-Treated Results

The HEMO dose-versus-mortality question also was assessed within each treatment arm, measuring the effects of actual delivered dose over time versus mortality. This study identified a dose-targeting bias and suggested that patients in a cross-sectional analysis receiving less dialysis are also at greater risk for death. This increased death risk was of a high magnitude and was incompatible with a biological effect of dose. Although conditions of the 2 HEMO Study arms were not representative of how dialysis is prescribed in the field, documentation of such a strong potential dose-targeting bias (which may be operative in cross-sectional studies, albeit to a lesser degree) convinced the Work Group members to place less weight on dose-versus-mortality relationships derived from observational studies despite the large numbers of patients included in such studies.

Studies Advocating Alternate Measures of Urea-Based Adequacy

These studies are discussed in more detail in CPG 2, Methods for Measuring and Expressing the HD Dose. Since the 2000 KDOQI HD Adequacy Guidelines were published, 1 group of investigators in particular, using data derived from Fresenius Medical Care North America patients in the United States, argued that dose of dialysis should not be factored by modeled V [volume]. The arguments against using [Urea Reduction Ratio] URR or its derivative Kt/V fall into 2 general categories: (1) doing so may result in relative underdialysis of women and small patients of both sexes, and (2) because modeled V is itself a predictor of mortality, use of dialysis dose factored by V may confound dialysis dose-versus-mortality relationships found in cross-sectional studies in complex and not always predictable ways. A secondary analysis of the intent-to-treat results of the HEMO Study suggested that the higher dose of dialysis may result in better survival in women, who also tended to be smaller than the men in that particular trial. The Work Group decided, based on suggestive evidence, that more dialysis (beyond 2000 KDOQI levels) may be better for women and, perhaps, smaller patients, but that the level of evidence did not reach a point at which the existing guideline should be changed. Hence, 2 CPRs were derived suggesting that more dialysis in women and/or in smaller patients might be beneficial. Despite the theoretical arguments, as well as attempts to address confounding effects of V in cross-sectional data sets, the committee believed that, at present, the data are not compelling enough to depart from the 2000 recommendation to follow small-molecule clearance using Kt/V.

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)

**ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7.** **What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence**? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

The [NKF] Work Group focused more intently on the target dose and its relationship with the minimum dose which, in light of HEMO Study findings, remains 1.2 Kt/V units per dialysis for patients dialyzed 3 times per week. Data from the HEMO Study also revealed a coefficient of variation within patients of approximately 0.1 Kt/V units; therefore, the previous target of 1.3 was considered too low. To grant 95% confidence that the dose will not decrease to less than 1.2 per dialysis, the target dose was increased to 1.4 per dialysis. This is in keeping with current practice and is consistent with the target spKt/V of approximately 1.4 set by the European Standards Group.12 The Work Group favored high-flux membranes. The HEMO Study did not provide definitive answers, but data suggested that dialysis vintage and flux are related and CVD might be affected favorably by the use of high-flux dialysis. The issue of sex also was addressed by the [NKF] Work Group, which believed that dialysis doses and targets should remain the same in women compared with men. However, in light of suggestive findings from the HEMO Study and observational studies, clinicians should be aware of a possible increased responsiveness to dialysis in females compared with males.

**1a.7.8.** **What harms were studied and how do they affect the net benefit (benefits over harms)?**

Concern was raised by the Work Group about malnourished patients with respect to both the initiation and adequacy of HD. Initiation is confounded by errors in calculation of glomerular filtration rate (GFR) for patients with diminishing muscle mass, and adequacy is confounded by the effect of malnutrition on patients´ water volume (V), the denominator of the integrated urea clearance expression (Kt/V). Estimation equations for calculating GFR before starting dialysis therapy are based on serum creatinine level, but are adjusted for sex, size, race, and other factors that tend to alter the relationship between concentration and clearance. Most of these factors either increase or decrease the generation of creatinine, but the patient´s state of nutrition—which is well known to affect creatinine generation—is not a variable in this equation. The consequent error in malnourished patients would tend to underestimate GFR and thus endanger the patient from the ill consequences of the delayed initiation of dialysis therapy. In addition, if the patient is malnourished, dialysis probably is better started early.

After a patient starts dialysis therapy, loss of weight because of malnutrition will decrease V, increasing the Kt/V, potentially to values higher than the desired target range. Reducing the dialysis dose (Kt/V) in such patients may lead to potential harm from inadequate dialysis. The Work Group addressed this problem in Clinical Practice Recommendation (CPR) 4.6, which calls for an increase in Kt/V when signs of malnutrition are present. The magnitude of the increase is left to the clinician, who might take into consideration the absolute level of Kt/V and cause of the malnutrition. If Kt/V is already much greater than the minimum, an additional increase probably would not benefit the patient. Similarly, if malnutrition is caused by a condition other than uremia, increasing the dose may have no effect. This issue will require revisiting in the future, hopefully with more available hard data.

**UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9.** **If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review**.

**N/a**

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**1a.8 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

**1a.8.1** **What process was used to identify the evidence?**

**1a.8.2.** **Provide the citation and summary for each piece of evidence.**