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

**Measure Number** (*if previously endorsed*)**:** Click here to enter NQF number

**Measure Title**: Adult Kidney Disease: ESRD Patients Receiving Dialysis: Hemoglobin Level <9 g/dL

**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

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| **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). |

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| **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: Click here to name the 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*): Decreasing associated illness and improving quality of life. See 1a.2

Process: Click here to name the process

Structure: Click here to name the structure

Other: Click here to name what is being measured

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**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 Hemoglobin level < 9g/dL, which is a measurement of a Hemoglobin level lower than the target range, an intermediate clinical outcome. Identifying patients with a Hemoglobin level lower than the target range is linked to improved health outcomes such as decreasing the incidence of an associated illness and attaining the highest quality and quantity of life after onset of illness.

**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 supporting this measure, focuses on a specific patient population including dialysis and nondialysis patients with CKD receiving ESA therapy. This measure specifically focuses on patients with ESRD who are receiving hemodialysis or peritoneal dialysis. The ESRD population has severe kidney disease and are commonly receiving dialysis. Therefore, the measure development Work Group thought it would be most beneficial to focus on this subset of patients. Although this measure does not address patients receiving ESA therapy, the same target range of 11.0 to 12.0 g/dL is being used for this patient population. The measure focuses on capturing those patients who do not achieve a Hemoglobin level within this specified target range.

*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.*

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**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.*

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**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 Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. Am J Kidney Dis 50, No 3 (September), 2007.

<http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/guide1.htmand> <http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/>

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

Guideline 2.1.2. In dialysis and nondialysis patients with CKD receiving ESA therapy, the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL. (Clinical Practice RECOMMENDATION)

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

A modified version of the GRADE criteria was used to grade the strength of the guideline recommendations. The modified language is below.

• Clinical Practice Recommendation (CPRs) – Based on consensus of the [NKF] Work Group that following the recommendations might improve health outcomes.

**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.*)

Strong – It is strongly recommended that clinicians routinely follow the guideline for eligible patients. There is high-quality evidence that the practice results in net medical benefit to the patient.

• Moderately strong – It is recommended that clinicians routinely follow this guideline for eligible patients. There is at least moderately high-quality evidence that the practice results in net medical benefit to the patient.

• Clinical Practice Recommendation (CPRs) – Based on consensus of the [NKF] Work Group that following the recommendations 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)

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**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)

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**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)

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**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?** For this guideline update, the Evidence Review Team (ERT) at Tufts-New England Medical Center in Boston, MA and the Work Group updated the systematic review of RCTs that compared the effect of targeting different Hb levels with ESA treatment. A detailed description of the methods can be found in the methods chapter of the 2006 Anemia guidelines.[56](http://www2.kidney.org/professionals/KDOQI/guidelines%5FanemiaUP/hd_ref.htm#ref56) The inclusion criteria were: RCTs in patients with CKD stages 1 to 5, with a minimum of 2-month follow-up duration. Outcomes of interest were all-cause mortality; cardiovascular, cerebrovascular, and peripheral vascular disease; left ventricular hypertrophy; quality of life; hospitalizations; progression of kidney disease; dialysis adequacy; hypertension; transfusions; and seizures.

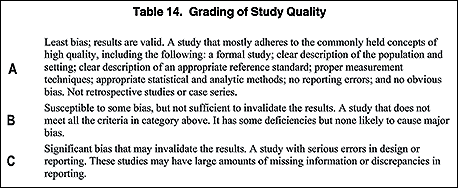
An updated search conducted on December 7, 2006, with the previously used key words of KIDNEY and ANEMIA identified 639 citations of English-language studies indexed in MEDLINE after November 2004. Furthermore, the ERT searched the clinicaltrials.gov registration website to identify additional studies that might be completed. The search update resulted in the addition of 6 RCTs to the systematic review on this topic.[1-6](http://www2.kidney.org/professionals/KDOQI/guidelines%5FanemiaUP/hd_ref.htm#ref1) All were in patients not on dialysis therapy, mostly with CKD stages 3 to 4. The ERT also updated [Table 1](http://www2.kidney.org/professionals/kdoqi/guidelines_anemiaUP/guide1.htm#TBL01) of “ongoing studies” to show what trials will be completed in the future.

The new studies were critically appraised by the ERT. The ERT extracted the data from these studies and added them to the summary tables published in the KDOQI 2006 Anemia in CKD guidelines. Each study was graded with regard to its method quality. The Work Group experts reviewed and confirmed data and quality grades in the summary tables. The ERT and the Work Group members updated the evidence profiles for nondialysis patients following the modified Grades of Recommendation Assessment, Development, and Evaluation (GRADE) approach. [57](http://www2.kidney.org/professionals/KDOQI/guidelines%5FanemiaUP/hd_ref.htm#ref57), [60](http://www2.kidney.org/professionals/KDOQI/guidelines%5FanemiaUP/hd_ref.htm#ref60) The ERT tabulated an evidence matrix that provides an overview of the quality of the reviewed evidence. It tabulates all studies included in the review by type of outcome and quality.

A meeting of the original 2006 KDOQI Anemia guidelines Work Group members, the ERT, and NKF support staff was held in Dallas, TX, on February 2 and 3, 2007. Before the face-to-face meeting in Dallas, all Work Group members and the KDOQI Chair and Vice-Chair completed new financial disclosure statements. Based on these financial disclosure statements, the Work Group chose the KDOQI Vice-Chair to moderate the face-to-face meeting in Dallas. The Work Group reviewed the summary tables; evidence profiles; a FDA-approved prescribing information for ESAs current as of March 2005 (Appendix 1); and the table of ongoing studies (Table 1).

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

A-C (see <http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/guide1.htm#TBL_2>)



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

See above.

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: 1990-2007

**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*)

For systematic review topics, the literature searches yielded 2,756 citations. Of these, 137 articles were reviewed in full. An additional 19 were added by Work Group members. A total of 83 were extracted and of these, 51 studies are included in Summary tables [within the guideline].

Evidence supporting the statement that in dialysis and nondialysis patients with CKD receiving ESA therapy, the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL includes results from 14 RCTs in dialysis patients and 15 RCTs in nondialysis patients.

**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 evidence considered by the [NKF] Work Group to support the statement is confined to results of between-group comparisons generated by intention-to-treat trials that randomly assigned patients to distinct Hb targets, including trials that used ESAs in both treatment arms and trials that used ESAs in 1 treatment arm and either placebo or no treatment in the control arm.

The practitioner approaches the decision to select a Hb treatment goal with the intent to treat the individual patient and should expect that the achieved Hb level will vary considerably from the intended Hb target. To develop these guidelines and recommendations, we therefore appraised only evidence that was generated from intent-to-treat analyses of trials in patients randomly assigned to either higher or lower Hb targets.

In the statement the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL, the word generally emphasizes the need to maintain flexibility in medical decision making given the breadth of variability between patients’ individual needs, values, functional status, disease burden, prognosis, and responsiveness to ESA therapy.

In the statement the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL, the 2 specific values 11.0 g/dL and 12.0 g/dL define inclusively either a single Hb target range (11.0 to 12.0 g/dL) or a range of possible single-point Hb targets between 11.0 and 12.0 g/dL; entail unavoidable subjectivity in selecting Hb cutoff values; explicitly exclude reference to achieved Hb levels; and together reflect the efforts of the Work Group to balance the potential quality-of life benefits and avoidance of transfusion gained by ESA therapy against the potential harm suffered by patients with Hb targets greater than 13 g/dL.

Available RCTs illustrate the distinction between a Hb target range and a discrete Hb target.

The lack of information to support specific Hb cutoff values in defining an optimum Hb target renders [this] a CPR.

**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 evidence base for the statement the selected Hb target should generally be in the range of 11.0 to 12.0 g/dL includes results from trials that examined Hb targets from 6 to 16 g/dL. Early RCTs differ substantially from later RCTs in both size and Hb targets. RCTs conducted before 1998 are characterized by smaller study size, upper Hb targets in the range of 10 to 13 g/dL, and lower Hb targets that reflect assignment to placebo or no-treatment control. Trials published in 1998 and thereafter are characterized by larger study size, higher Hb targets in the range of 12 to 16 g/dL, and lower Hb targets between 9 and 12 g/dL. In more recent trials, by comparison, Hb baseline values are higher than those seen in early trials. Moreover, recent RCTs set lower targets at Hb levels well above those in earlier trials, in which patients in the control arm were assigned to placebo or no-treatment control groups. Both effects combine to render differences between Hb targets smaller in more recent trials.

National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. Am J Kidney Dis 50, No 3 (September), 2007.

Anemia reduces physical capacity, well-being, neurocognitive function, and energy level and worsens quality of life both in predialysis and dialysis patients. Anemia also induces adaptive cardiovascular mechanisms to maintain tissue oxygen supply. This leads to left ventricular hypertrophy, left ventricular dilation, and myocardial ischemia, which are risk factors for cardiovascular disease and death. It is plausible that reversing anemia may reduce this risk.(1)

Aiming for a Hb target within narrow boundaries in ESA-treated patients requires frequent dose adjustments in many patients. More than 60% of patients receiving ESA therapy with Hb targets between 11.0 and 12.0 g/dL require between 6 and 9 dose changes per year.23 No comparative information is available to support evidence-based guidelines for the dosing and administration of ESAtherapy to achieve a target Hb. However, descriptive information from quality improvement interventions and RCT treatment protocols may be helpful to practitioners in weighing options that may best fit patient needs and practice settings.(2)

1. Strippoli GFM, Craig JC, Manno C, Schena FP. Hemoglobin Targets for the Anemia of Chronic Kidney Disease: A Meta-analysis of Randomized, Controlled Trials. J Am Soc Nephrol 15:3154-3165, 2004.

2. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. Am J Kidney Dis 50, No 3 (September), 2007.

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

Limitations:

Most reports provide incomplete information with respect to HRQoL findings. Complete reporting should include point estimates and assessments of dispersion of HRQoL scores for each domain at each interval measured, by Hb target assignment.

Meta-analysis of cardiovascular events in dialysis patients is dominated by the results of the study by Besarab et al14 (1998), and in nondialysis patients with CKD, by the results of the study by Singh et al2 (2006). Although all RCTs have limitations, major limitations of those trials dominating meta-analysis results are of particular importance. In both Besarab et al14 (1998) and Singh et al2 (2006), the decision to prematurely stop the trial was made before the efficacy or futility boundaries were crossed. In Singh et al2 (2006), compared with the group assigned to the lower Hb treatment target, the group assigned to the higher Hb target showed at baseline a statistically greater proportion of patients with a history of hypertension and coronary artery bypass graft. A report posted by the study sponsor (PROCRIT ®: Clinical Study Report PR00-06-014 (CHOIR) SYNOPSIS, 12 September 2006; available at: www.clinicaltrials.gov, last accessed January 12, 2007) indicates that patients assigned to the higher Hb treatment arm also had a significantly greater severity of congestive heart failure (CHF) at baseline. The results of a multivariate analysis, included in this report, indicate that after adjustment for baseline conditions (CHF by National Health and Nutrition Examination Survey CHF score, atrial fibrillation/flutter, serum albumin level, reticulocyte count, and age), the relationship between treatment assignment and primary composite outcome events is no longer statistically significant (hazard ratio, 1.24; 95% CI, 0.95 to 1.62; P = 0.11 compared with the unadjusted hazard ratio of 1.34; 95% CI, 1.03 to 1.74; P = 0.03 reported in the publication2). Thus, although a trend toward greater risk of events in the higher Hb arm remains after adjustment for baseline imbalances, the finding of statistical significance is not robust and the change in the point estimate and CI with adjustment casts doubt on the success of randomization. Quality of the CHOIR study is further limited by censoring at the initiation of dialysis and by lack of information on when HRQoL was measured. One of the limitations of the CREATE trial is that the event rate was much lower than predicted; thus, the power to detect a difference in event rates was decreased.

Several studies are characterized by a failure to achieve the higher Hb target in the majority of patients at any time (Fig 1), and no study provided description of the Hb cycling around the achieved mean for either the higher or lower target treatment. In addition, several studies using subcutaneous (SC) epoetin alfa were prematurely terminated when reports of pure red cell aplasia emerged.

A further limitation of the currently available evidence is that important CKD subgroups have not been specifically studied or are not well represented in the existing studies, including children and young adults and patients with ischemic vascular disease or chronic lung disease.

Finally, trials published to date have not been designed to distinguish between the potential effects of Hb targets, ESA doses, and concomitant anemia therapy, including iron.

In clinical practice, medical decision making in the management of anemia at the level of the individual patient requires selection of the starting Hb level; choice of the initial dose, route, and frequency of ESA therapy; determination of Hb monitoring frequency; the aspiration to reach a threshold Hb or target Hb level; determination of the frequency and size of sequential ESA dose adjustments in relationship to a threshold Hb or target Hb level; and an interpretation of previous therapeutic trends and responsiveness to ESA therapy. Although available RCTs used either a range or a discrete value to represent the aspirational target Hb (Fig 1), published reports include little additional information to assist medical decision making. Specifically, information is lacking about how ESA and iron therapy were actually adjusted based on achieved Hb levels and how closely actual adjustments adhered to study protocol. Comparative information is similarly lacking to determine optimum frequency for monitoring Hb, the number of Hb results needed to reliably measure clinical performance, or the expected day-to-day within-patient variability in Hb levels in different patient populations (nondialysis CKD, hemodialysis CKD, and peritoneal dialysis CKD).

In general, a Hb target range suggests that ESA dose adjustment decisions are made by comparing the patient’s achieved Hb with the selected Hb target. Although performance in managing to a Hb target can be expressed as the proportion of patients with Hb levels within the target range, in practice, only 30% of patients at any 1 time have an actual Hb level in the Hb target range of 11.0 and 12.0 g/dL when targeted to that range. The result of a single sampling in a single patient cannot be expected to lie within a narrow Hb target range (eg, Hb of 11.0 to 12.0 g/dL) or to equal a discrete point Hb target (eg, Hb of either 11.0, 11.5, or 12.0 g/dL). However, mean or median Hb levels of a group of patients or mean Hb levels of a single patient repeated over time would be expected to lie within a Hb target range or to approximate a discrete Hb target. In short, measures of clinical performance, to be clinically useful, must account for a high degree of within-patient and between patient variability.

**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**.

KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease

Kidney International Supplements (2012) 2, 280; doi:10.1038/kisup.2012.38; <http://www.kidney-international.org>

The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Anemia in Chronic Kidney Disease aims to provide guidance on diagnosis, evaluation, management and treatment for all CKD patients (non-dialysis, dialysis, kidney transplant recipients and children) at risk of or with anemia. Guideline development followed an explicit process of evidence review and appraisal. The guideline contains chapters addressing diagnosis

and evaluation of anemia in CKD and the use of various therapeutic agents (iron, ESAs and other agents) and red cell transfusion as means of treatment. Treatment approaches are addressed in each chapter and guideline recommendations are based on systematic reviews of relevant trials. Appraisal of the quality of the evidence and the strength of recommendations followed the GRADE approach. Ongoing areas of controversies and limitations of the evidence are discussed and additional suggestions are also provided for future research.

3.4.2: For adult CKD ND patients with Hb concentration o10.0 g/dl (o100 g/l) we suggest that the decision whether to

initiate ESA therapy be individualized based on the rate of fall of Hb concentration, prior response to iron therapy,

the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to

anemia. (2C)

3.4.3: For adult CKD 5D patients, we suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl (90 g/l) by starting ESA therapy when the hemoglobin is between 9.0–10.0 g/dl (90–100 g/l). (2B)

In adult hemodialysis patients the rate of fall of Hb is faster than in ND patients, and if untreated Hb will frequently fall below 8 g/dl (80 g/l).122 As the risk of transfusions is high in those HD patients whose Hb falls

below 9 g/dl (90 g/l) the KDIGO Work Group suggested that ESA therapy should be used to prevent the Hb concentration from falling below 9.0 g/dl (90 g/l), which in practice means that the Hb concentration at which ESA should be initiated should be between 9.0 and 10.0 g/dl [90 and 100 g/l].

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**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.**