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

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

**Measure Title**: Anemia of chronic kidney disease: Dialysis facility standardized transfusion ratio (STrR)

**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: Transfusions

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*): Click here to name the intermediate outcome

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.**

In the ESRD population, blood transfusion has been linked to survival indirectly via patient access to transplantation. Studies have shown superior patient survival with kidney transplantation compared to chronic dialysis (Wolfe, et al NEJM).

Blood transfusion has been shown to increase anti-HLA antibodies in chronic dialysis patients, decreasing access to kidney transplantation. (Chapter 4, KDIGO Anemia Management Guidelines) Furthermore, Ibrahim, et al studied 43,025 patients added to the kidney transplant waitlist from 1999-2004, using USRDS data. They evaluated the impact of receiving one or more blood transfusion after kidney transplant listing on panel reactive antibody% (PRA). Over the years 1999-2004, 26-30% of patients listed for kidney transplant received one or more blood transfusion after listing. Ibrahim, et al calculated the one year and three year cumulative incidence of transfusions while on the waiting list at 10.8% and 27.7% respectively. Receiving pre-transplant transfusion was associated with higher odds of PRA% elevation. For men, post-listing transfusion was associated with an odds ratio of 1.77 and 1.67 for having a PRA > 20% and > 80% at time of transplantation, respectively. For parous women, odds ratios were 1.62 and 1.89 for PRA > 20% and > 80% at time of transplantation, respectively.

In addition, unnecessary use of blood products in this population will likely have a negative impact on the health outcomes of other patient populations by reducing a rate-limiting health resource needed for treatment of other life-threatening conditions.

KDIGO Anemia Guidelines 2012: Guideline 4.1.1: When managing chronic anemia, we recommend avoiding, when possible, red cell transfusions to minimize the general risks related to their use. (1B)

References:

Wolfe, Robert, Ashby, Valarie, Milford, Edgar et al. Comparison of Mortality in all Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant. The New England Journal of Medicine (1999) 341:1725-30.

Ibrahim HN, Skeans MA, Li Q, Ishani A, Snyder JJ. Blood transfusions in kidney transplant candidates are common and associated with adverse outcomes. Clin Transplant (2011) 25;653-659.

**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 risks associated with aggressive treatment of anemia of CKD with ESAs have been well documented in KDIGO Anemia Management Guidelines as well as in updated FDA package insert information for ESAs. In contrast, the effect of anemia management paradigms that target to lower hemoglobin levels, and generally use less ESA, on transfusion risk is less well defined. Several clinical interventional trials comparing higher vs. lower hemoglobin targets have shown higher transfusion rates in those patients randomized to lower hemoglobin targets. The importance of these observations is limited by lack of predefined criteria for use of blood transfusion in most studies.

It has been postulated that a national trend toward increased use of transfusions in dialysis patients would adversely affect the supply of blood available for acute injuries and surgical procedures. Lastly, greater exposure to human leukocyte antigens, present in transfused blood, may increase anti-HLA antibodies in kidney transplant candidates, resulting in reduced access to kidney transplantation.

The inverse relationship between achieved hemoglobin and transfusion events has been reported previously for Medicare dialysis patients ( Ma 1999) and for non-dialysis CKD patients treated in the Veterans Administration system (Lawler 2010)

Lawler EV, Bradbury BD, Fonda JR, et al. "Transfusion burden among patients with chronic kidney disease and anemia." Clinical journal of the American Society of Nephrology : CJASN (2010) 5:667-72. PMID: 20299366

Ma JZ, Ebben J, Xia H, et al. "Hematocrit level and associated mortality in hemodialysis patients." Journal of the American Society of Nephrology : JASN (1999) 10:610-9. PMID: 10073612

*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*):

Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335. <http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO-Anemia%20GL.pdf>

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

KDIGO Anemia Guidelines 2012: Guideline 3.2: In initiating and maintaining ESA therapy, we recommend balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension). (1B).

• KDIGO Anemia Guidelines 2012: Guideline 4.1.1: When managing chronic anemia, we recommend avoiding, when possible, red cell transfusions to minimize the general risks related to their use. (1B)

• KDIGO Anemia Guidelines 2012: Guideline 4.1.3: When managing chronic anemia, we suggest that the benefits of red cell transfusions may outweigh the risks in patients in whom (2C): o ESA therapy is ineffective (e.g., hemoglobinopathies, bone marrow failure, ESA resistance)

o The risks of ESA therapy may outweigh its benefits (e.g., previous or current malignancy, previous stroke)

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

The KDIGO Guidelines used the GRADE system; the grades given are listed above with the relevant guidelines.

**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.*)

Nomenclature and Description for Rating Guideline Recommendations

Within each recommendation, the strength of the recommendation is indicated as Level 1, Level 2, or Not Graded, and the quality of the supporting evidence is shown as A, B, C, or D.

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| Grade | Patients | Clinicians | Policy |
| Level 1  “We recommend” | Most people in your situation would want the recommended course of action and only a small proportion would not. | Most patients should receive the recommended course of action | The recommendation can be evaluated as a candidate for developing a policy or performance measure |
| Level 2 “We suggest” | The majority of people in your situation would want the recommended course of action, but many would not. | Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences. | The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined. |

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| Grade | Quality of Evidence | Meaning |
| A | High | We are confident that the true effect lies close to the estimate of that effect. |
| B | Moderate | The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| C | Low | The true effect may be substantially different from the estimate of the effect. |
| D | Very Low | The estimate of the effect is very uncertain, and often will be far from the truth. |

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

GRADE Working Group. Systems for grading the quality of evidence and the strength of recommendations II: a pilot study of a new system for grading the quality of evidence and the strength of recommendations. BMC Health Serv Res 2005 2005; 5: 25.

Uhlig K, Macleod A, Craig J et al. Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease Improving Global outcomes (KDIGO). Kidney Int 2006;70:2058-2065

**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*):

N/A

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

N/A

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

N/A

**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.*)

N/A

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

N/A

***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*):

N/A

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

N/A

***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?**

N/A

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

N/A

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

N/A

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

N/A

**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*)

N/A

**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*)

N/A

**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*)

N/A

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

N/A

**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

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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?**

The 2013 Clinical TEP reviewed a suite of articles related to transfusions in ESRD patients.

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

1. Hollenbeak et. al. The Impact of End-Stage Renal Disease Transfusion Demand on Blood Utilization and Blood Supply in the United States Health Outcomes Research in Medicine Volume 3, Issue 2, May 2012, Pages e67–e77
2. Liu et. al. Development of a Facility-Level Transfusion Quality of Care Metric, 2012 American Society of Nephrology Annual Kidney Week
3. Ibrahim HN, et. al. Temporal Trends in red blood transfusion among US dialysis patients, 1992-2005. Am J Kidney Dis 2008: 52: 1115
4. U.S. Renal Data System, USRDS 2013 Annual Data Report: Atlas of End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2013.
5. FDA Drug Safety Communication: Modified dosing recommendations to improve the safe use of Erythropoiesis-Stimulating Agents (ESAs) in chronic kidney disease. http://www.fda.gov/Drugs/DrugSafety/ucm259639.htm
6. Highlights of prescribing information: Epogen (epoetin alfa) http://www.accessdata.fda.gov/drugsatfda\_docs/label/2011/103234Orig1s5166\_103234Orig1s5266lbl.pdf
7. Highlights of prescribing information: Aranesp (darbepoetin alfa) http://www.accessdata.fda.gov/drugsatfda\_docs/label/2011/103951Orig1s5173\_103951Orig1s5258lbl.pdf
8. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney inter., Suppl. 2012; 2: 279–335.
9. Besarab A, Bolton WK, Browne JK, et al. "The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin." The New England journal of medicine (1998) 339:584-90. PMID: 9718377
10. Drüeke TB, Locatelli F, Clyne N, et al. "Normalization of hemoglobin level in patients with chronic kidney disease and anemia." The New England journal of medicine (2006) 355:2071-84. PMID: 17108342
11. Foley RN, Curtis BM, Parfrey PS. "Hemoglobin targets and blood transfusions in hemodialysis patients without symptomatic cardiac disease receiving erythropoietin therapy." Clinical journal of the American Society of Nephrology : CJASN (2008) 3:1669-75. PMID: 18922988
12. Lawler EV, Bradbury BD, Fonda JR, et al. "Transfusion burden among patients with chronic kidney disease and anemia." Clinical journal of the American Society of Nephrology : CJASN (2010) 5:667-72. PMID: 20299366
13. Ma JZ, Ebben J, Xia H, et al. "Hematocrit level and associated mortality in hemodialysis patients." Journal of the American Society of Nephrology : JASN (1999) 10:610-9. PMID: 10073612
14. Pfeffer MA, Burdmann EA, Chen CY, et al. "A trial of darbepoetin alfa in type 2 diabetes and chronic kidney disease." The New England journal of medicine (2009) 361:2019-32. PMID: 19880844
15. Association between recombinant human erythropoietin and quality of life and exercise capacity of patients receiving haemodialysis. Canadian Erythropoietin Study Group." BMJ (Clinical research ed.) (1990) 300:573-8. PMID: 2108751
16. Wolfe, Robert, Ashby, Valarie, Milford, Edgar et al. Comparison of Mortality in all Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant. The New England Journal of Medicine (1999) 341:1725-30.
17. Ibrahim HN, Skeans MA, Li Q, Ishani A, Snyder JJ. Blood transfusions in kidney transplant candidates are common and associated with adverse outcomes. Clin Transplant (2011) 25;653-659.