

DRAFT

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

3a Measure Information Form (MIF)

Data Source

- ◆ Electronic administrative data/ Claims

Data Source or Collection Instrument:

Data for the measure are derived from an extensive national ESRD patient database, which is derived from Program Medical Management and Information System (PMMIS/REMIS), Medicare claims, the Standard Information Management System (SIMS) database maintained by the 18 ESRD Networks, the CMS Annual Facility Survey (Form CMS-2744), Medicare dialysis and hospital payment records, the CMS Medical Evidence Form (Form CMS-2728), transplant data from the Organ Procurement and Transplant Network (OPTN), the Death Notification Form (Form CMS-2746), the Nursing Home Minimum Dataset, and the Social Security Death Master File. The database is comprehensive for Medicare patients. Information on transfusions is obtained from Medicare Inpatient and Outpatient Claims Standard Analysis Files (SAFs).

Data Source or Collection Instrument Reference:

<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs-Items/CMS018912.html>

Data Dictionary or Code Table:

<http://www.resdac.org/sites/resdac.org/files/RIF%20Inpatient%20SNF%20SAF%20Version%20J%20CMS.pdf>

Measure Set ID

- ◆ N/A

Version Number and effective date

- ◆ V. 1.4, 6/21/2013

CMS approval date

- ◆ Pending

NQF ID

- ◆ N/A

Date Endorsed

- ◆ N/A

Care Setting

- ◆ Dialysis Facility

Unit of Measurement

- ◆ Facility-level measure

Measurement Duration

- ◆ 1 year

Measurement Period

- ◆ 1 year

Measure Type

- ◆ Outcome

Measure Scoring

- ◆ Ratio/proportion

Payer source

- ◆ Medicare

Improvement notation

- ◆ Better quality = lower score

Measure steward

- ◆ CMS

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- ◆ N/A

Measure description

- ◆ Risk adjusted facility level transfusion ratio “STrR” for dialysis patients. It is a ratio of observed number of red blood cell transfusion events for each facility over the measurement period to expected number based on national experience and adjusted for patient mix.

Rationale

- ◆ Several changes in the ESRD system are likely to impact anemia management. These include identification of safety concerns associated with aggressive erythropoiesis-stimulating agent (ESA) use, expansion of the ESRD Prospective Payment System bundled payment, and the development of the ESRD Quality Incentive Program. There are concerns that these changes could result in underutilization of ESAs, with lower achieved hemoglobin values that may increase the frequency of red blood cell transfusion in the US chronic dialysis population.
- ◆ Blood transfusion may be an indicator for underutilization of treatments to increase endogenous red blood cell production (e.g. ESA, iron). In addition, dialysis patients who are eligible for kidney transplant and are transfused risk the development of becoming sensitized to the donor pool thereby making transplant more difficult to accomplish. Blood transfusions carry a small risk of transmitting blood borne infections, development of a

transfusion reaction, and using infusion centers or hospitals to transfuse patients is expensive, inconvenient, and could compromise future vascular access.

- ◆ Monitoring the risk-adjusted transfusion rate at the dialysis facility level, relative to a national standard, allows for detection of treatment patterns in dialysis-related anemia management. This is of particular importance due to recent FDA guidance regarding minimizing the use of ESAs and new economic incentives to minimize ESA use introduced by Medicare bundling payment for ESAs. As providers use less ESAs in an effort to minimize the risks associated with aggressive anemia treatment it becomes more important to monitor for an overreliance on transfusions.

Clinical Recommendation Statement

- ◆ Erythropoiesis-stimulating agents are indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion. The FDA recommends that therapy of ESAs should be individualized to the patient and the lowest possible ESA dose given to reduce the need for transfusions.
- ◆ From the package insert for Epogen (epoetin alfa), for patients with CKD on dialysis: “Use the lowest Epogen dose sufficient to reduce the need for red blood cell (RBC) transfusions.”
- ◆ From the package insert for Aranesp (darbepoetin alfa). For patients with CKD on dialysis: “Use the lowest Aranesp dose sufficient to reduce the need for red blood cell (RBC) transfusions.”
- ◆ 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). The notation reflects the grading of the underlying evidence as explained in the table below.
- ◆ 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). The notation reflects the grading of the underlying evidence as explained in the table below.
- ◆
- ◆ 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):
 - ESA therapy is ineffective (e.g., hemoglobinopathies, bone marrow failure, ESA resistance)
 - The risks of ESA therapy may outweigh its benefits (e.g., previous or current malignancy, previous stroke)

The notation reflects the grading of the underlying evidence as explained in the table below.

— NOMENCLATURE AND DESCRIPTION FOR RATING GUIDELINE RECOMMENDATIONS

Within each recommendation, the strength of 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**.

Grade*	Implications		
	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 a 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.

*The additional category 'Not Graded' was used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding monitoring intervals, counseling, and referral to other clinical specialists. The ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect lies close to that of the estimate of the 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 effect is very uncertain, and often will be far from the truth.

References

- ◆ 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>
- ◆ Highlights of prescribing information: Epogen (epoetin alfa) http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/103234Orig1s5166_103234Orig1s5266lbl.pdf
- ◆ Highlights of prescribing information: Aranesp (darbepoetin alfa) http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/103951Orig1s5173_103951Orig1s5258lbl.pdf
- ◆ 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.

Release Notes / Summary of Changes

- ◆ Updates were made to clarify the target population, denominator exclusions and details, numerator, and risk-adjustment sections.

Technical Specifications

- ◆ Target Population

All (both in-center and home dialysis) adult dialysis patients (>=18 years old) on dialysis for 90+ days; exclusion of patients with comorbid conditions that may lead to transfusions unrelated to dialysis facility anemia management practice.

Denominator

- ◆ Denominator Statement

Number of red blood cell transfusion events (as defined in the numerator statement) that would be expected among eligible patients at a facility during the reporting period, given the patient mix at the facility.

◆ Denominator Details

Starting with day 91 after onset of ESRD, a patient is attributed to a facility once the patient has been treated there for 60 days and for 60 days after transfer to another dialysis facility.

Based on a risk adjustment model for the overall national transfusion rates, we compute the expected number of red blood cell transfusion events for each patient attributed to a given facility. The sum of all such expectations over patients in a facility yields the overall expected number of transfusions for a given facility given the specific patient mix and this forms the denominator of the measure.

This measure is based on Medicare administrative claims and databases. . Thus, the measure is relevant to patients covered by Medicare.

◆ Denominator Exceptions and Exclusions

All transfusions associated with transplant hospitalization are excluded. Patients are excluded if they have a Medicare claim for hemolytic and aplastic anemia, solid organ cancer (breast, prostate, lung, digestive tract and others),lymphoma, carcinoma in situ, coagulation disorders, multiple myeloma, myelodysplastic syndrome and myelofibrosis, leukemia, head and neck cancer, other cancers (connective tissue, skin, and others),metastatic cancer, sickle cell anemia within one year of their patient at risk time. Since these comorbidities are associated with higher risk of transfusion and require different anemia management practices that the measure is not intended to address, every patient’s risk window is modified to have at least 1 year of claim free period.

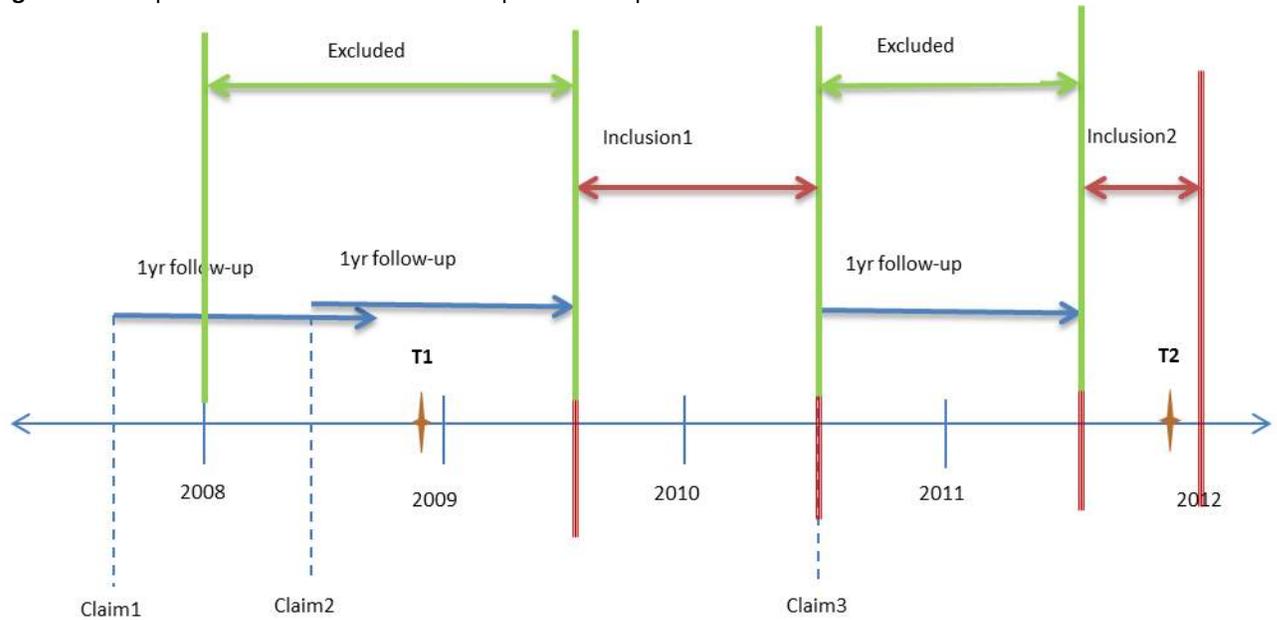
◆ Details

Relevant exclusion with International Classification of Diseases, Ninth Edition, Clinical Modification codes are listed in Appendix A.

Details: Definitions and instructions as needed.

We performed multivariate logistic regression and it showed that 1-year look back period for each of the above mentioned comorbidities was the most predictive of one or more RBC transfusions. The following figure describes the inclusion and exclusion period of a hypothetical patient.

Figure1: Description of Inclusion and Exclusion periods of a patient



In the figure above, a hypothetical patient has patient years at risk at a facility from 1/1/2008 to 12/31/2011. Review of Medicare claims identified presence of one or more exclusion comorbidities (see above and Appendix) in 2007 (Claim1), 2008 (Claim2) and 2010 (Claim3). Each claim is followed by a one year exclusion period. The revised inclusion periods are defined as risk windows with at least 1 year of claim-free period (Inclusion1 and Inclusion2 in Figure1). The patient has two transfusion events, marked as T1 and T2 in late 2008 and late 2011 respectively. However, since T1 falls in the exclusion period, it will not be counted towards the facility's transfusion count as presence of exclusion comorbidity claims within a year might have increased the risk of transfusion unrelated to dialysis facility anemia management practice. However, T2, which occurs in late 2011 and in Inclusion2 period, will be counted since there is at least a year gap between this transfusion event and the last claim observed.

Numerator

◆ Numerator Statement

Number of observed red blood cell transfusion events (defined as transfer of one or more units of blood or blood products as described in the following code set into recipient's blood stream) among eligible patients at the facility during the inclusion episodes of the reporting period.

◆ Numerator Details

Red blood cell transfusions are identified by in-patient records with revenue center codes in (0380, 0381, 0382, 0389, 0390, 0391, 0392, 0399) or value code = 37 or procedure code in (9903, 9904) and with out-patient records with revenue center codes in (0380, 0381, 0382, 0389, 0390, 0391, 0392, 0399) and HCPCS code in (P9010, P9011, P9016, P9021, P9022, P9038, P9039, P9040, P9051, P9054, P9056, P9058, 36430).

Table of Code Meanings

Field	Value	Meaning
Revenue Center Code	0380	Blood - General Classification
	0381	Blood - Packed Red Cells
	0382	Blood - Whole Blood
	0389	Blood - Other Blood
	0390	Blood Storage and Processing - General Classification
	0391	Blood Storage and Processing - Administration
	0392	Blood Storage and Processing - Blood Processing and Storage
	0399	Blood Storage and Processing - Other Storage & Processing
Procedure Codes	9903	Other Transfusion Of Whole Blood
	9904	Transfusion Of Packed Cells
Value Code	37	Pints of blood furnished
HCPCS Code	P9010	Whole blood for transfusion
	P9011	Blood split unit
	P9016	RBC leukocytes reduced
	P9021	Red blood cells unit
	P9022	Washed red blood cells unit
	P9038	RBC irradiated
	P9039	RBC deglycerolized
	P9040	RBC leukoreduced irradiated
	P9051	Blood, l/r, cmv-neg
	P9054	Blood, l/r, froz/degly/wash
	P9056	Blood, l/r, irradiated
	P9057	RBC, frz/deg/wsh, l/r, irradiated
	P9058	RBC, l/r, cmv-neg, irradiated
	36430*	Transfusion, blood or blood component

*36430 is CPT code, but is found in the HCPCS code field

Details: Definitions and instructions as needed.

The numerator is calculated using Medicare Claims data. Transfusion event is identified by using the above mentioned codes and then the patient is identified and attributed to a dialysis facility using the rules discussed in the denominator details. The numerator is the count of all such transfusion events over the inclusion periods (which are at least 1 year claim free risk windows) as defined above, for a given facility.

Stratification or Risk Adjustment

The denominator of the “STrR” uses expected transfusions calculated from a Cox model (Cox, 1972) as extended to handle repeated events (Lawless and Nadeau, 1995; Lin et al., 2000; Kalbfleisch and Prentice, 2002). For computational purposes, we adopt a model with piecewise constant baseline rates (e.g. Cook and Lawless, 2007) and computational methodology as developed in Liu, Schaubel and Kalbfleisch (2010). A stage 1 model is first fitted to the national data with piecewise-constant baseline rates stratified by facility; transfusion rates are adjusted for patient age, diabetes, duration of ESRD, nursing home status, BMI at incidence, comorbidity index at incidence, and calendar year. This model allows the baseline transfusion rates to vary between strata (facilities), but assumes that the regression coefficients are the same across all strata; this approach is robust to possible differences between facilities in the patient mix being treated. The linear predictor for each patient based on the regression coefficients in the stage 1 model is used to compute a risk adjustment factor that is then used as an offset in the stage 2 model.

The patient characteristics included in the stage 1 model as covariates are age (18-24 years old, 25-44 years old, 45-59 years old, 60-74 years old, or 75+ years old), cause of ESRD (diabetes or other), nursing home status, BMI at incidence, comorbidity index at incidence, duration of ESRD (91 days-6 months, 6 months-1 year, 1-2 years, 2-3 years, 3-5 years, or 5+ years as of the period start date) and calendar year. Nursing home status is identified as in or not in a nursing home in the previous calendar year. The comorbidity index is calculated as a weighted linear combination of comorbidities reported on the Medical Evidence Form (CMS-2728) namely alcohol dependence, atherosclerotic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, diabetes, diabetes (currently on insulin), drug dependence, inability to ambulate, inability to transfer, malignant neoplasm, cancer, other cardiac disease, peripheral vascular disease, tobacco use (current smoker) using the same weights as used for Standardized Hospitalization Ratio (<http://www.dialysisreports.org/pdf/esrd/public/shrmodel.xls>; NQF #1463 <http://www.qualityforum.org/QPS/1463>). BMI is included as a log-linear term. Categorical indicator variables are included as covariates in the stage 1 model to flag records with missing values for cause of ESRD, comorbidity index, and BMI. These variables have a value of 1 if the patient is missing the corresponding piece of information and a value of 0 otherwise. Another categorical indicator variable included as a covariate to flag records where the comorbidity index is 0 has a value of 1 if the patient has a comorbidity index of 0 and a value of 0 otherwise. Beside main effects, some two way interaction terms are also included in the model based on their clinical and statistical significance.

The parameter estimates as well as the corresponding standard error and a p-value indicating if the coefficient is significantly different from 0, resulting from the Cox Model are shown below:

Table of Parameter Estimates of Transfusion Events for Medicare-Covered Dialysis Patients

Parameter	Level	Type	Estimate	Standard Error	p value
Age					
15-24 years old		Categorical (60-74 is ref)	0.00449	0.01868	0.8099
25-44 years old		Categorical (60-74 is ref)	-0.22946	0.00766	<.0001
45-59 years old		Categorical (60-74 is ref)	-0.15471	0.00628	<.0001
75 or older		Categorical (60-74 is ref)	-0.01219	0.00632	0.0539
Diabetes		Categorical (0 versus 1)	-0.06332	0.01431	<.0001
Cause of ESRD Missing		Categorical (0 versus 1)	-0.01637	0.02115	0.439
Patient in Nursing Home		Categorical (0 versus 1)	0.57879	0.00527	<.0001
Log of BMI		Continuous	-0.1859	0.00686	<.0001
BMI Missing		Categorical (0 versus 1)	0.10727	0.0097	<.0001
Comorbidity Index		Continuous	0.36235	0.0075	<.0001
Comorbidity Index of 0		Categorical (0 versus 1)	-0.12799	0.00569	<.0001
Comorbidity Index Missing		Categorical (0 versus 1)	-0.10521	0.02735	0.0001
Year	2009	Categorical	-0.01961	0.00475	<.0001
Year	2010	Categorical	-0.05124	0.00478	<.0001
Year	2011	Categorical	0.01687	0.00475	0.0004

Parameter	Level	Type	Estimate	Standard Error	p value
Duration_of_ESRD*Diabetes	6 months-1 year	Interaction (Duration of ESRD in Diabetes)	0.05305	0.01729	0.0021
Duration_of_ESRD*Diabetes	1-2 years	Interaction (Duration of ESRD in Diabetes)	0.07938	0.01593	<.0001
Duration_of_ESRD*Diabetes	2-3 years	Interaction (Duration of ESRD in Diabetes)	0.09658	0.01634	<.0001
Duration_of_ESRD*Diabetes	3-5 years	Interaction (Duration of ESRD in Diabetes)	0.0526	0.01551	0.0007
Duration_of_ESRD*Diabetes	5+ years	Interaction (Duration of ESRD in Diabetes)	0.03218	0.01502	0.0322
Age*Diabetes	15-24 years old	Interaction (Age in Diabetes)	0.34143	0.08241	<.0001
Age*Diabetes	25-44 years old	Interaction (Age in Diabetes)	0.27137	0.01189	<.0001
Age*Diabetes	45-59 years old	Interaction (Age in Diabetes)	0.1303	0.00846	<.0001
Age*Diabetes	75 or older	Interaction (Age in Diabetes)	0.02373	0.009	0.0084

References:

- ◆ Cox, D.R. (1972) Regression Models and Life Tables (with Discussion). J. Royal statistical Society, Series B, 34, 187-220.
- ◆ Cook, R. and Lawless, J. The Statistical Analysis of Recurrent Events. New York: Springer. 2007.
- ◆ Cook, R. and Lawless, J. Marginal analysis of recurrent events and a terminal event. Statistics in Medicine 1997; 16: 911-924.
- ◆ Kalbfleisch, J.D. and Prentice, R. L. The Statistical Analysis of Failure Time Data. Wiley, New York, 2002.
- ◆ Lawless, J. F. and Nadeau, C. Some simple and robust methods for the analysis of recurrent events, Technometrics, 37 1995, 355-364.
- ◆ Lin, D.Y., Wei, L.J., Yang, I. and Ying, Z. Semi parametric regression for the mean and rate functions of recurrent events, Journal of the Royal Statistical Society Series B, 62, 2000, 771-730
- ◆ Liu, D., Schaubel, D.E. and Kalbfleisch, J.D. Computationally efficient marginal models for clustered recurrent event data, University of Michigan Department of Biostatistics Technical Reports, 2010.
- ◆ <http://www.dialysisreports.org/pdf/esrd/public/SHRdocumentation.pdf>

Sampling

2a1.24. If measure is based on a sample (or survey), provide instructions for obtaining the sample and conducting the survey, and guidance on minimum sample size (response rate).

N/A

Calculation Algorithm

Calculation Algorithm/Measure logic: 2a1.20, 2a1.21. Describe the calculation of the measure as a flow chart or series of steps.

Numerator is the observed number of transfusion events for a facility and denominator for the same facility is the expected number of transfusion events adjusted for patient mix. The measure for a given facility is calculated by dividing the numerator by the denominator.