MEASURE INFORMATION FORM

Project Title:

Revisions to the Standardized Transfusion Ratio (STrR)

Project Overview:

The Centers for Medicare & Medicaid Services (CMS) has contracted with the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) develop measures of anemia management in ESRD patients. The contract name is ESRD Quality Measure Development, Maintenance, and Support. The contract number is HHSM-500-2013-13017I.

The specifications for the Standardized Transfusion Ratio have been revised, and we seek comment on these revisions. We developed a more conservative definition of transfusion events. The revised definition excludes inpatient transfusion events for claims that include only 038 or 039 revenue codes without an accompanying procedure or value code. In the revised measure, all inpatient transfusion events include, at a minimum, an appropriate ICD-9 Procedure Code or Value Code. This more conservative definition of transfusion events is used to calculate the restricted STrR. As expected from the information provided above, this more restricted definition of transfusion events results in a reduced total number of events identified as well as the range of total events for dialysis facilities

Date:

Information included is current on April 15, 2016

Measure Name:

Standardized Transfusion Ratio for Dialysis Facilities

Descriptive Information:

Measure Name (Measure Title De.2.)
Standardized Transfusion Ratio for Dialysis Facilities

Measure Type De.1.
Outcome

Brief Description of Measure De.3.
The risk adjusted facility level transfusion ratio "STrR" is specified for all adult dialysis patients. It is a ratio of the number of eligible red blood cell transfusion events observed in patients dialyzing at a facility, to the number of eligible transfusion events that would be expected under a national norm, after accounting for the patient characteristics within each facility. Eligible transfusions are those that do not have any claims pertaining to the comorbidities identified for exclusion, in the one year look back period prior to each observation window. This measure is calculated as a ratio, but can also be expressed as a rate.

If Paired or Grouped De.4.
N/A

Subject/Topic Areas De.5.
Renal, Renal: End Stage Renal Disease (ESRD

Crosscutting Areas De 6.
N/A

Measure Specifications:

Measure-specific Web Page S.1.
N/A

If This Is an eMeasure S.2a.
This is not an eMeasure

Data Dictionary, Code Table, or Value Sets S.2b.
See Data Dictionary Code Table

For Endorsement Maintenance S.3.
N/A

Numerator Statement S.4.
Number of eligible observed red blood cell transfusion events: An event is defined as the transfer of one or more units of blood or blood products into a recipient's blood stream (code set is provided in the numerator details) among patients dialyzing at the facility during the inclusion episodes of the reporting period. Inclusion episodes are those that do not have any claims pertaining to the comorbidities identified for exclusion, in the one year look back period prior to each observation window.

Time Period for Data S.5.
One year

Numerator Details S.6.
Transfusion events in the inpatient setting are counted in the following way. The event is identified by the presence in a Medicare inpatient claim of the appropriate ICD-9 procedure codes (99.03, 99.04), or, value code (37). For inpatient transfusion events that are identified using specific ICD-9 procedure codes (99.03, 99.04), we identify a transfusion event for each transfusion procedure code with a corresponding unique date listed on the inpatient claim, thus allowing determination of multiple transfusion events on inpatient claims with multiple ICD-9 procedure codes present. For inpatient claims with value code (37), we count a single transfusion event regardless of the number of transfusion value codes reported, so that the number of discrete events counted is the same whether the claim value code indicates 1 unit of blood or multiple units of blood. This results in a more conservative estimate of blood transfusion events from inpatient claims with transfusion value codes.

Transfusion events are less common in the outpatient setting. Transfusion events in the outpatient setting are counted in the following way. Events derived from outpatient claims are identified by claims with HCPCS code (P9010, P9011, P9016, P9021, P9022, P9038, P9039, P9040, P9051, P9054, P9056, P9058, 36430); or, value code (37). In outpatient claims we count a transfusion event for each HCPCS and corresponding unique revenue center date to determine the number of unique transfusion events. Therefore, multiple corresponding unique dates for revenue center codes will result in multiple transfusions events, while multiple HCPCS codes reported for the same revenue center date are counted as a single transfusion event, regardless of the number of units of blood recorded. For example, a HCPCS indicating 3 pints of blood reported for two different revenue center dates would equal two transfusion events, while a HCPCS indicating 3 pints of blood reported with the same revenue center date would be counted as a single transfusion event. Finally, outpatient claims with a transfusion related value code (37) is counted as one event.

The detailed procedures to determine unique transfusion events at the claim level are presented in a flow chart in the Appendix (S.19. Calculation Algorithm/Measure Logic Diagram).

Denominator Statement S.7.

Number of eligible red blood cell transfusion events (as defined in the numerator statement) that would be expected among patients at a facility during the reporting period, given the patient mix at the facility. Inclusion episodes are those that do not have any claims pertaining to the comorbidities identified for exclusion, in the one year look back period prior to each observation window.

Target Population Category S.8.

Populations at Risk

Denominator Details S.9.

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

Based on a risk adjustment model for 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 the facility given its specific patient mix. This forms the denominator of the measure. This measure is based on Medicare administrative claims and databases and is applied to patients covered by Medicare.

Denominator Exclusions (NQF Includes “Exceptions” in the “Exclusion” Field) S.10.

All transfusions associated with transplant hospitalization are excluded. Patients are also 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, and sickle cell anemia within one year of their patient time at risk. 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 free of claims that contain these exclusion eligible diagnoses.

Denominator Exclusion Details (NQF Includes "Exceptions" in the "Exclusion" Field) S.11.
We performed multivariate logistic regression demonstrating that a 1-year look back period for the exclusion comorbidities was more predictive of transfusion events compared to longer look back periods. The figure in the appendix describes the inclusion and exclusion period of a hypothetical patient. In the figure included in the Appendix, 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 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 a 1-year claim-free period (Inclusion1 and Inclusion2 in the figure). This 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 total transfusion event count because the presence of the exclusion comorbidity claims within the 1-year look back might have increased the risk of transfusion unrelated to dialysis facility anemia management practices. However, T2, which occurs in late 2011 and in Inclusion2 period, will be counted since there is greater than a 1-year gap between this transfusion event and the last claim observed with the exclusion diagnosis.

Stratification Details/Variables S.12.
N/A

Risk Adjustment Type S.13.
Statistical risk model

Statistical Risk Model and Variables S.14.
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, comorbidities 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 to estimate the population baseline rate without stratifying facilities.
The patient characteristics included in the stage 1 model as covariates are:

- Age: We determine each patient's age for the birth date provided in the SIMS and REMIS databases and group patients into the following categories: 0-14 years old, 15-24 years old, 25-44 years old, 45-59 years old, 60-74 years old, or 75+ years old.
- Diabetes as cause of ESRD: We determine each patient's primary cause of ESRD from his/her CMS-2728, REMIS, SIMS, and CROWNWeb.
- Duration of ESRD: We determine each patient's length of time since start of ESRD treatment using his/her CMS-2728, claims history (all claim types), the SIMS database and the SRTR database and categorize as 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.

- Nursing home status: Using the Nursing Home Minimum Dataset, we determine if a patient was in a nursing home the previous year.
- BMI at incidence: We calculate each patient's BMI as the height and weight provided on his/her CMS 2728. BMI is included as a log-linear term.
- Comorbidities at incidence are determined using a selection of comorbidities reported on the CMS-2728 namely, alcohol dependence, atherosclerotic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, diabetes (includes currently on insulin, on oral medications, without medications, and diabetic retinopathy), drug dependence, inability to ambulate, inability to transfer, malignant neoplasm, cancer, other cardiac disease, peripheral vascular disease, and tobacco use (current smoker). Each comorbidity is included as a separate covariate in the model.
- Calendar year
- Categorical indicator variables are included as covariates in the stage I model to account for records with missing values for cause of ESRD, comorbidities at incidence (missing CMS-2728), and BMI. These variables have a value of 1 if the patient is missing the corresponding variable and a value of 0 otherwise. Another categorical indicator variable is included as a covariate in the stage 1 model to flag records where the patient has at least one of the incident comorbidities listed earlier. This variable has a value of 1 if the patient has at least one of the comorbidities and a value of 0 otherwise.

Beside main effects, two-way interaction terms between age and duration and cause of ESRD are also included:

- Diabetes as cause of ESRD*Duration of ESRD
- Diabetes as cause of ESRD*Age

The same coefficient weights are used as in the Standardized Hospitalization Ratio (see www. dialysisdata.org; NQF #1463 http://www.qualityforum.org/QPS/1463).
Coefficients can be found in the attached excel file.

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.

Detailed Risk Model Specifications S.15.
See Data Dictionary/Code Table

Type of Score S.16.
Ratio

Interpretation of Score S.17.
Better quality = Lower score

Calculation Algorithm/Measure Logic S.18.
The numerator is the observed number of transfusion events for a facility and the 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. See flowchart for further detail (available in attached appendix).

Calculation Algorithm/Measure Logic Diagram URL or Attachment S.19.
Available in attached appendix at A.1

Sampling S.20.
N/A

Survey/Patient-Reported Data S.21.
N/A

Missing Data S.22.
N/A

Data Source S.23.
Administrative claims, Electronic Clinical Data

Data Source or Collection Instrument S.24.
Data are derived from an extensive national ESRD patient database, which is primarily based on the CMS Consolidated Renal Operations in a Web-enabled Network (CROWN) system. The CROWN data include the Renal Management Information System (REMIS), CROWNWeb facility-reported clinical and administrative data (including CMS-2728 Medical Evidence Form, CMS-2746 Death Notification Form, and CMS-2744 Annual Facility Survey Form data), the historical Standard Information Management System (SIMS) database (formerly maintained by the 18 ESRD Networks until replaced by CROWNWeb in May 2012), the National Vascular Access Improvement Initiative's Fistula First Catheter Last project (in CROWNWeb since May 2012), Medicare dialysis and hospital payment records, transplant data from the Organ Procurement and Transplant Network (OPTN), the Nursing Home Minimum Dataset, the Quality Improvement Evaluation System (QIES) Workbench, which includes data from the Certification and Survey Provider Enhanced Report System (CASPER), the Dialysis Facility Compare (DFC) and the Social

Security Death Master File. The database is comprehensive for Medicare patients. Non-Medicare patients are included in all sources except for the Medicare payment records. CROWNWeb provides tracking by dialysis provider and treatment modality for non-Medicare patients. Information on hospitalizations is obtained from Part A Medicare Inpatient Claims Standard Analysis Files (SAFs), and past-year comorbidity is obtained from multiple Part A types (inpatient, home health, hospice, skilled nursing facility claims) and Part B outpatient types of Medicare Claims SAFs.
Information on transfusions is obtained from Medicare Inpatient and Outpatient Claims Standard Analysis Files (SAFs).

Data Source or Collection Instrument (Reference) S.25.
No data collection instrument provided

Level of Analysis S.26.
Facility

Care Setting S.27.
Dialysis Facility

Composite Performance Measure S.28.
N/A

MEASURE JUSTIFICATION FORM

Project Title:
Revisions to the Standardized Transfusion Ratio (STrR)

Project Overview:
The Centers for Medicare & Medicaid Services (CMS) has contracted with the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) develop measures of anemia management in ESRD patients. The contract name is ESRD Quality Measure Development, Maintenance, and Support. The contract number is HHSM-500-2013-13017I.

The specifications for the Standardized Transfusion Ratio have been revised, and we seek comment on these revisions. We developed a more conservative definition of transfusion events. The revised definition excludes inpatient transfusion events for claims that include only 038 or 039 revenue codes without an accompanying procedure or value code. In the revised measure, all inpatient transfusion events include, at a minimum, an appropriate ICD-9 Procedure Code or Value Code. This more conservative definition of transfusion events is used to calculate the restricted STrR. As expected from the information provided above, this more restricted definition of transfusion events results in a reduced total number of events identified as well as the range of total events for dialysis facilities

Date:
Information included is current on April 15, 2016.

Measure Name
Standardized Transfusion Ratio for Dialysis Facilities

Type of Measure
Outcome

Importance
1a—Opportunity for Improvement

1a.1. This is a Measure of
Health outcome: Red Blood Cell Transfusions

1a.2.—Linkage
The indication for blood transfusion is usually severe anemia or moderate anemia with recent, active, or anticipated blood loss. Therefore, risk for blood transfusion is dependent on the current degree of anemia (typically measured by hemoglobin concentration or hematocrit%). Management of underlying anemia in chronic dialysis patients is the responsibility of dialysis providers.

1a.2.1 Rationale

The Medicare ESRD Program requires Medicare certified dialysis facilities to manage the anemia of CKD as one of their responsibilities under the Conditions for Coverage (1). In addition, the Medicare ESRD Program has included payment for ESAs in dialysis facility reimbursement since 1989. It is notable that inclusion of ESAs in dialysis program payment was associated with a dramatic reduction in the use of blood transfusions in the US chronic dialysis population (2-3). Recently, reliance on achieved hemoglobin concentration as an indicator of

successful anemia management in this population has been de-emphasized and use of other clinically meaningful outcomes, such as transfusion avoidance, have been recommended as alternate measures of anemia management (4-7).

Best dialysis provider practice should include effective anemia management algorithms that focus on 1) prevention and treatment of iron deficiency, inflammation and other causes of ESA resistance, 2) use of the lowest dose of ESAs that achieves an appropriate target hemoglobin that is consistent with FDA guidelines and current best practices, and 3) education of patients, their families and medical providers to avoid unnecessary blood transfusion so that risk of allosensitization is minimized, eliminating or reducing one preventable barrier to successful kidney transplantation.

The decision to transfuse blood is intended to improve or correct the pathophysiologic consequences of severe anemia, defined by achieved hemoglobin or hematocrit%, in a specific clinical context for each patient situation (8). Consensus guidelines in the U.S. and other consensus guidelines defining appropriate use of blood transfusions are based, in large part, on the severity of anemia (9-11). Given the role of hemoglobin as a clinical outcome that defines anemia as well as forms a basis for consensus recommendations regarding use of blood transfusion, it is not surprising that the presence of decreased hemoglobin concentration is a strong predictor of subsequent risk for blood transfusion in multiple settings, including chronic dialysis (12-21). For example, Gilbertson, et al found a nearly four-fold higher risk-adjusted transfusion rate in dialysis patients with achieved hemoglobin <10 gm/dl compared to those with >10 gm/dl hemoglobin. (19) In addition to achieved hemoglobin, other factors related to dialysis facility practices, including the facility's response to their patients achieved hemoglobin, may influence blood transfusion risk in the chronic dialysis population (22, 25). In an observational study recently published by Molony, et al (2016) comparing different facility level titration practices, among patients with hemoglobin <10 and those with hemoglobin>11, they found increased transfusion risk in patients with larger ESA dose reductions and smaller dose escalations, and reduced transfusion risk in patients with larger ESA dose increases and smaller dose reductions (25). The authors reported no clinically meaningful differences in all-cause or cause-specific hospitalization events across groups.

The Food and Drug Administration position defining the primary indication of ESA use in the CKD population is for transfusion avoidance, reflecting the assessment of the relative risks and benefits of ESA use versus blood transfusion. Several historical studies, and one recent research study reviewed by Obrador and Macdougall, document the specific risks of allosensitization after blood transfusion and the potential for transfusion-associated allosensitization to interfere with timely kidney transplantation. (23) A recent analysis demonstrated increased odds ratios for allosensitization associated with transfusion, particularly for men and parous women. That study also demonstrated a 28% reduction in likelihood of transplantation in transfused individuals, based on a multivariate risk-adjusted statistical model. (24)

1. ESRD Facility Conditions for Coverage. https://www.cms.gov/Center/Special-Topic/End-Stage-Renal-Disease-ESRD-Center.html

2. Eschbach et al. Recombinant Human Erythropoietin in Anemic Patients with End-Stage Renal Disease. Results of a Phase III Multicenter Clinical Trial. Annals of Internal Medicine. 1989;111:992-1000.
Study Objective: To determine the effectiveness and safety of recombinant human erythropoietin (rHuEpo).
Patients: Hemodialysis patients (333) with uncomplicated anemia (hematocrit < 0.30). All received rHuEpo intravenously, three times per week at 300 or 150 U/kg body weight, which was then reduced to 75 U/kg and adjusted to maintain the hematocrit at 0.35 ± 0.03 (SD).

Results: The baseline hematocrit (0.223 ± 0.002) increased to 0.35, more than 0.06 over baseline within 12

weeks in 97.4% of patients. Erythrocyte transfusions (1030 within the 6 months before rHuEpo therapy) were eliminated in all patients within 2 months of therapy. Sixty-eight patients with iron overload had a 39% reduction in serum ferritin levels after 6 months of therapy. The median maintenance dose of rHuEpo was 75 U/kg, three times per week (range, 12.5 to 525 U/kg). Nonresponders had complicating causes for anemia: myelofibrosis, osteitis fibrosa, osteomyelitis, and acute or chronic blood loss. Adverse effects included myalgias, 5%; iron deficiency, 43%; increased blood pressure, 35%; and seizures, 5.4%. The creatinine, potassium, and phosphate levels increased slightly but significantly. The platelet count increased slightly but there was no increase in clotting of vascular accesses.

Conclusions: The anemia of hemodialysis patients is corrected by rHuEpo resulting in the elimination of transfusions, reduction in iron overload, and improved quality of life. Iron stores and blood pressure must be monitored and treated to maintain the effectiveness of rHuEpo and to minimize the threat of hypertensive encephalopathy.

3. Powe et al. Early dosing practices and effectiveness of recombinant human erythropoietin. Kidney International, Vol. 43 (1993), pp. 1125—1133.

   Early dosing practices and effectiveness of recombinant human erythropoietin. In a national longitudinal-cohort study of 59,462 end-stage renal disease (ESRD) patients, we examined dosing and effectiveness of erythropoietin (EPO) during the first year of its use in clinical practice(July 1989 through June 1990). In unadjusted and multivariate analyses of Medicare claims data, the mean dose of EPO prescribed was: relatively small and similar for initial and maintenance therapy, 2752 (95% confidence interval 2740 to 2764) and 2668 (95% confidence interval 2654 to 2682) units, respectively; lower when initial therapy was started later (591 units lower in September 1989 and 760 units lower in November 1989 vs. July 1989, $P < 0.0001$); tower by 135 units during initial therapy and by 116 units during maintenance therapy for females (who weigh less) compared to males ($P < 0.001$); and lower by 400 units for patients treated in for-profit versus not-for-profit centers. In multivariate analysis: hematocrit response was less and mean maintenance dose was 298 units and 621 units greater for patients whose ESRD was due to multiple myeloma and sickle cell disease, respectively, compared to those with hypertension-related ESRD ($P < 0.01$); and hematocrit response was logarithmically related to dose [hematocrit =0.97 In (dose), $P < 0.0001$]. Forty-four percent of patients had a hematocrit $\geq$ 30 after four months of therapy. The percent of patients transfused during three month periods before and after therapy decreased from 20% to 5%, respectively ($P < 0.0001$). Our results suggest that dosing practices were substantially modified to prescription of smaller and more fixed doses over time, due to the interplay of clinical concerns and economic forces. They also suggest that the effectiveness of EPO in increasing hematocrit levels and reducing transfusion use in routine clinical practice was less than anticipated based on the experience in clinical trials in part as a result of dosing practices.

4. 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

5. 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

6. Kliger et al. KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. Am J Kidney Dis. 62(5):849-859.

   The 2012 KDIGO (Kidney Disease: Improving Global Outcomes) Clinical Practice Guideline for Anemia in

Chronic Kidney Disease provides clinicians with comprehensive evidence-based recommendations to improve patient care. In this commentary, we review these recommendations and the underlying evidence. Most recommendations are well reasoned. For some, the evidence is unclear and recommendations require some qualification. While the KDIGO guideline stresses the potential risks of intravenous iron therapy, withholding iron might have its own risks. The recommendation to avoid hemoglobin levels falling below 9 g/dL sets a lower bound of "acceptability" that may increase blood transfusion. Given the lack of research supporting the optimal transfusion strategy for end-stage renal disease patients, it is difficult to weigh the risks and benefits of red blood cell transfusion. We find a paucity of evidence that hemoglobin concentration targeted between 11 and 11.5 g/dL is associated with a safety risk. Although the evidence that erythropoiesis-stimulating agent use improves patient quality of life is poor, it is possible that the instruments used to measure quality of life may not be well attuned to the needs of chronic kidney disease or dialysis patients. Our last section focuses specifically on the recommendations to treat anemia in children.

7. Berns, Jeffrey S., Moving Away From Hemoglobin-Based Anemia Performance Measures in Dialysis Patients. Am J Kidney Dis. 2014;64(4):486-488.

   Until recently, dialysis facility quality metrics focused on avoiding low hemoglobin (Hb) concentrations, and financial incentives favored use of erythropoiesis-stimulating agents (ESAs). In many dialysis patients, these practices boosted Hb concentrations to levels that are now considered unnecessary and potentially dangerous. Recent clinical trials have demonstrated that there is little to be gained from, and possible risk in, targeting Hb concentrations > 12-13 g/dL rather than ≤10-11 g/dL.1, 2, 3, 4, 5 Whether the risk is a function of higher Hb concentrations, higher ESA doses, both, or neither remains a matter of debate.6

   International clinical practice guideline recommendations7 and, in the United States, product labeling by the Food and Drug Administration (FDA) highlight the need to reduce target Hb concentrations and ESA doses. The primary purpose of ESA therapy now is transfusion avoidance. Including the cost of ESAs in the "bundle" as part of the new Prospective Payment System also created a financial disincentive for ESA use. Thus, the conversation about ESA use and Hb concentrations in maintenance hemodialysis patients has shifted from avoiding concentrations that are "too low" to avoiding those that are "too high." However, as predicted, recent data indicate a decline in ESA use and Hb concentrations and an increase in transfusion rates among maintenance hemodialysis patients.8, 9

   Recognizing that anemia management performance measures in dialysis units that focused solely on achieved Hb concentration did not improve patient outcomes has prompted interest in moving away from quality improvement metrics that are based on laboratory test results. Instead, interest has shifted toward metrics that reflect outcomes important to patients. In this issue of AJKD, Liu et al10 report a proof-of-concept attempt at developing a dialysis facility–specific standardized transfusion ratio (STfR), a more meaningful anemia quality measure than "What was the Hb concentration last month?" (Developing such a risk-adjusted transfusion metric was a principal recommendation of a Technical Expert Panel meeting hosted by the Arbor Research Collaborative for Health in 2012.11)

8. Whitman, Shreay, Gitlin, van Oijen, & Spiegel. Clinical Factors and the Decision to Transfuse Chronic Dialysis Patients. Clin J Am Soc Nephrol 8: ccc–ccc, 2013. doi: 10.2215/CJN.00160113

   Background and objectives: Red blood cell transfusion was previously the principle therapy for anemia in CKD but became less prevalent after the introduction of erythropoiesis-stimulating agents. This study used adaptive choice-based conjoint analysis to identify preferences and predictors of transfusion decision-making in CKD.

Design, setting, participants, & measurements: A computerized adaptive choice-based conjoint survey was administered between June and August of 2012 to nephrologists, internists, and hospitalists listed in the American Medical Association Masterfile. The survey quantified the relative importance of 10 patient attributes, including hemoglobin levels, age, occult blood in stool, severity of illness, eligibility for transplant, iron indices, erythropoiesis-stimulating agents, cardiovascular disease, and functional status. Triggers of transfusions in common dialysis scenarios were studied, and based on adaptive choice-based conjoint-derived preferences, relative importance by performing multivariable regression to identify predictors of transfusion preferences was assessed.

Results: A total of 350 providers completed the survey (n=305 nephrologists; mean age=46 years; 21%women).Of 10 attributes assessed, absolute hemoglobin level was the most important driver of transfusions, accounting for 29% of decision-making, followed by functional status (16%) and cardiovascular comorbidities (12%); 92% of providers transfused when hemoglobin was 7.5 g/dl, independent of other factors. In multivariable regression, Veterans Administration providers were more likely to transfuse at 8.0 g/dl (odds ratio, 5.9; 95% confidence interval, 1.9 to 18.4). Although transplant eligibility explained only 5% of decision-making, nephrologists were five times more likely to value it as important compared with non-nephrologists (odds ratio, 5.2; 95% confidence interval, 2.4 to11.1).
Conclusions: Adaptive choice-based conjoint analysis was useful in predicting influences on transfusion decisions. Hemoglobin level, functional status, and cardiovascular comorbidities most strongly influenced transfusion decision-making, but preference variations were observed among subgroups.

9. Carson et al. Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB. Ann Intern Med. 2012;157:49-58.

   Description: Although approximately 85 million units of red blood cells (RBCs) are transfused annually worldwide, transfusion practices vary widely. The AABB (formerly, the American Association of Blood Banks) developed this guideline to provide clinical recommendations about hemoglobin concentration thresholds and other clinical variables that trigger RBC transfusions in hemodynamically stable adults and children.
   Methods: These guidelines are based on a systematic review of randomized clinical trials evaluating transfusion thresholds. We performed a literature search from 1950 to February 2011 with no language restrictions. We examined the proportion of patients who received any RBC transfusion and the number of RBC units transfused to describe the effect of restrictive transfusion strategies on RBC use. To determine the clinical consequences of restrictive transfusion strategies, we examined overall mortality, nonfatal myocardial infarction, cardiac events, pulmonary edema, stroke, thromboembolism, renal failure, infection, hemorrhage, mental confusion, functional recovery, and length of hospital stay.
   Recommendation 1: The AABB recommends adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients (Grade: strong recommendation; high-quality evidence).
   Recommendation 2: The AABB suggests adhering to a restrictive strategy in hospitalized patients with preexisting cardiovascular disease and considering transfusion for patients with symptoms or a hemoglobin level of 8 g/dL or less (Grade: weak recommendation; moderate-quality evidence).
   Recommendation 3: The AABB cannot recommend for or against a liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with the acute coronary syndrome (Grade: uncertain recommendation; very low-quality evidence).
   Recommendation 4: The AABB suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration (Grade: weak recommendation; low-quality evidence).

10. American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies.

Anesthesiology. 2006;105:198–208.

11. Munoz et al. “Fit to fly”; overcoming barriers to preoperative haemoglobin optimization in surgical patients. Br J Anaesth. 2015 Jul;115(1):15-24.

    In major surgery, the implementation of multidisciplinary, multimodal and individualized strategies, collectively termed Patient Blood Management, aims to identify modifiable risks and optimise patients' own physiology with the ultimate goal of improving outcomes. Among the various strategies utilized in Patient Blood Management, timely detection and management of preoperative anaemia is most important, as it is in itself a risk factor for worse clinical outcome, but also one of the strongest predisposing factors for perioperative allogeneic blood transfusion, which in turn increases postoperative morbidity, mortality and costs. However, preoperative anaemia is still frequently ignored, with indiscriminate allogeneic blood transfusion used as a 'quick fix'. Consistent with reported evidence from other medical specialties, this imprudent practice continues to be endorsed by non-evidence based misconceptions, which constitute serious barriers for a wider implementation of preoperative haemoglobin optimisation. We have reviewed a number of these misconceptions, which we unanimously consider should be promptly abandoned by health care providers and replaced by evidence-based strategies such as detection, diagnosis and proper treatment of preoperative anaemia. We believe that this approach to preoperative anaemia management may be a viable, cost-effective strategy that is beneficial both for patients, with improved clinical outcomes, and for health systems, with more efficient use of finite health care resources.

12. Dunne, Malone, Tracy, Gannon, and Napolitano. Perioperative Anemia: An Independent Risk Factor for Infection, Mortality, and Resource Utilization in Surgery. Journal of Surgical Research 102, 237-244 (2002) Background. Previous studies on patients with hip fractures and in patients with colorectal cancer have documented that perioperative transfusion is associated with a significant increase in postoperative infection rate. Therefore, we sought to investigate the incidence of preoperative and postoperative anemia in noncardiac surgical patients and to determine if transfusion is an independent risk factor for infection and adverse outcome postoperatively.

    Methods. Prospective data from the National Veterans Administration Surgical Quality Improvement Program (NSQIP) was collected on 6301 noncardiac surgical patients at the Veterans Affairs Maryland Healthcare System from 1995 to 2000.

    Results. The mean age of the study cohort was 61 6 13. Descriptive data revealed 95% were male, 44% used tobacco, 19% were diabetic, 9% had COPD, 9% used alcohol, 3% used steroids, 1.7% had a diagnosis of cancer, and 1.2% had ascites. Preoperative anemia (hematocrit less than 36) was found in 33.9% and postoperative anemia was found in 84.1% of the study cohort. In the postoperative period, 32.5% of patients had a hematocrit of 26±30, and 26.5% had a hematocrit of 21±25. Mean units of blood transfused in the perioperative period ranged from 0.1 6 0.9 in patients without anemia to 2.7 6 2.9 in those with anemia. Incidence of pneumonia increased from 2.6 to 5% with increasing degree of anemia. Multiple logistic regression analysis documented that low preoperative hematocrit, low postoperative hematocrit, and increased blood transfusion rates were associated with increased mortality ($P < 0.01$), increased postoperative pneumonia ($P < 0.05$), and increased hospital length of stay ($P < 0.05$).

    Conclusion. There is a high incidence of preoperative and postoperative anemia in surgical patients, with a coincident increase in blood utilization. These factors are associated with increased risk for perioperative infection and adverse outcome (mortality) in surgical patients. Consideration should be given to preoperative diagnosis and correction of anemia with iron, vitamin B12, folate supplementation, or administration of

recombinant human erythropoietin.

13. Covin R, O'Brien M, Grunwald G, Brimhall B, Sethi G, Walczak S, Reiquam W, Rajagopalan C, Shroyer AL Factors affecting transfusion of fresh frozen plasma, platelets, and red blood cells during elective coronary artery bypass graft surgery. Arch Pathol Lab Med. 2003 Apr;127(4):415-23.

    CONTEXT: The ability to predict the use of blood components during surgery will improve the blood bank's ability to provide efficient service. OBJECTIVE: Develop prediction models using preoperative risk factors to assess blood component usage during elective coronary artery bypass graft surgery (CABG). DESIGN: Eighty-three preoperative, multidimensional risk variables were evaluated for patients undergoing elective CABG-only surgery. MAIN OUTCOMES MEASURES: The study endpoints included transfusion of fresh frozen plasma (FFP), platelets, and red blood cells (RBC). Multivariate logistic regression models were built to assess the predictors related to each of these endpoints. SETTING: Department of Veterans Affairs (VA) health care system. PATIENTS: Records for 3034 patients undergoing elective CABG-only procedures; 1033 patients received a blood component transfusion during CABG. RESULTS: Previous heart surgery and decreased ejection fraction were significant predictors of transfusion for all blood components. Platelet count was predictive of platelet transfusion and FFP utilization. Baseline hemoglobin was a predictive factor for more than 2 units of RBC. Some significant hospital variation was noted beyond that predicted by patient risk factors alone. CONCLUSIONS: Prediction models based on preoperative variables may facilitate blood component management for patients undergoing elective CABG. Algorithms are available to predict transfusion resources to assist blood banks in improving responsiveness to clinical needs. Predictors for use of each blood component may be identified prior to elective CABG for VA patients.

14. Jans et al. Role of preoperative anemia for risk of transfusion and postoperative morbidity in fast-track hip and knee arthroplasty. Transfusion. 2014 Mar;54(3):717-26.

    BACKGROUND: Preoperative anemia has been associated with increased risk of allogeneic blood transfusion and postoperative morbidity and mortality. The prevalence of preoperative anemia and its association with postoperative outcomes has not previously been reported in relation to fast-track elective total hip arthroplasty (THA) and total knee arthroplasty (TKA). We aimed to evaluate the prevalence of preoperative anemia in elective fast-track THA and TKA and its association with risk of perioperative transfusion, prolonged length of hospital stay (LOS), and postoperative readmission. STUDY DESIGN AND METHODS: This was a prospective observational database study with data obtained from six high-volume Danish fast-track surgical centers. Preoperative hemoglobin and patient demographics were collected prospectively using questionnaires while outcome and transfusion data were collected using national databases and patient charts. Adjusted risk estimates for transfusion, prolonged LOS, and all-cause readmission according to preoperative anemia status were obtained by multivariate logistic regression. RESULTS: A total of 5.165 THA or TKA procedures were included with a mean patient age of 67 ± 11 years and a median LOS of 2 (interquartile range, 2-3) days. A total of 662 patients (12.8%) had preoperative anemia according to World Health Organization classification. Preoperative anemia was associated with increased risk of receiving transfusion during admission (odds ratio [OR], 4.7; 95% confidence interval [CI], 3.8-5.8), increased risk of readmission within 90 days from surgery (OR, 1.4; 95% CI, 1.1-1.9), and increased risk of LOS of more than 5 days (OR, 2.5; 95% CI, 1.9-3.4) after adjustment for preoperative patient-related risk factors. CONCLUSION: Preoperative anemia in elective fast-track THA and TKA is independently associated with transfusion and increased postoperative morbidity, supporting the need for preoperative evaluation and treatment.

15. Saleh et al. Allogenic Blood Transfusion Following Total Hip Arthroplasty: Results from the Nationwide

Inpatient Sample, 2000 to 2009. J Bone Joint Surg Am. 2014;96:e155(1-10)

Background: The large-scale utilization of allogenic blood transfusion and its associated outcomes have been described in critically ill patients and those undergoing high-risk cardiac surgery but not in patients undergoing elective total hip arthroplasty. The objective of this study was to determine the trends in utilization and outcomes of allogenic blood transfusion in patients undergoing primary total hip arthroplasty in the United States from 2000 to 2009.

Methods: An observational cohort of 2,087,423 patients who underwent primary total hip arthroplasty from 2000 to 2009 was identified in the Nationwide Inpatient Sample. International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes 99.03 and 99.04 were used to identify patients who received allogenic blood products during their hospital stay. Risk factors for allogenic transfusions were identified with use of multivariable logistic regression models. We used propensity score matching to estimate the adjusted association between transfusion and surgical outcomes.

Results: The rate of allogenic blood transfusion increased from 11.8% in 2000 to 19.0% in 2009. Patient-related risk factors for receiving an allogenic blood transfusion include an older age, female sex, black race, and Medicaid insurance. Hospital-related risk factors include rural location, smaller size, and non-academic status. After adjusting for confounders, allogenic blood transfusion was associated with a longer hospital stay (0.58 ± 0.02 day; $p < 0.001$), increased costs ($1731 ± $49 [in 2009 U.S. dollars]; $p < 0.001$), increased rate of discharge to an inpatient facility (odds ratio, 1.28; 95% confidence interval, 1.26 to 1.31), and worse surgical and medical outcomes. In-hospital mortality was not affected by allogenic blood transfusion (odds ratio, 0.97; 95% confidence interval, 0.77 to 1.21).

Conclusions: The increase in allogenic blood transfusion among total hip arthroplasty patients is concerning considering the associated increase in surgical complications and adverse events. The risk factors for transfusion and its impact on costs and inpatient outcomes can potentially be used to enhance patient care through optimizing preoperative discussions and effective utilization of blood-conservation methods.
Level of Evidence: Therapeutic Level IV. See Instructions for Authors for a complete description of levels of evidence.

16. Ejaz, Spolverato, Kim, Frank, and Pawlik. Variations in triggers and use of perioperative blood transfusions in major gastrointestinal surgery. Br. J. Surg. 2014 Oct;101(11):1424-33.

BACKGROUND: The decision to perform intraoperative blood transfusion is subject to a variety of clinical and laboratory factors. This study examined variation in haemoglobin (Hb) triggers and overall utilization of intraoperative blood transfusion, as well the impact of transfusion on perioperative outcomes. METHODS: The study included all patients who underwent pancreatic, hepatic or colorectal resection between 2010 and 2013 at Johns Hopkins Hospital, Baltimore, Maryland. Data on Hb levels that triggered an intraoperative or postoperative transfusion and overall perioperative blood utilization were obtained and analysed.

RESULTS: Intraoperative transfusion was employed in 437 (15·6 per cent) of the 2806 patients identified. Older patients (odds ratio (OR) 1·68), patients with multiple co-morbidities (Charlson co-morbidity score 4 or above; OR 1·66) and those with a lower preoperative Hb level (OR 4·95) were at increased risk of intraoperative blood transfusion (all $P < 0·001$). The Hb level employed to trigger transfusion varied by sex, race and service (all $P < 0·001$). A total of 105 patients (24·0 per cent of patients transfused) had an intraoperative transfusion with a liberal Hb trigger (10 g/dl or more); the majority of these patients (78; 74·3 per cent) did not require any additional postoperative transfusion. Patients who received an intraoperative transfusion were at greater risk of perioperative complications (OR 1·55; $P = 0·002$), although patients

transfused with a restrictive Hb trigger (less than 10 g/dl) showed no increased risk of perioperative morbidity compared with those transfused with a liberal Hb trigger (OR 1·22; P = 0·514).

CONCLUSION: Use of perioperative blood transfusion varies among surgeons and type of operation. Nearly one in four patients received a blood transfusion with a liberal intraoperative transfusion Hb trigger of 10 g/dl or more. Intraoperative blood transfusion was associated with higher risk of perioperative morbidity.

17. Foley, Curtis, & Parfrey. Hemoglobin Targets and Blood Transfusions in Hemodialysis Patients without Symptomatic Cardiac Disease Receiving Erythropoietin Therapy. Clin J Am Soc Nephrol 3: 1669–1675, 2008. doi: 10.2215/CJN.02100508 .

    Background and objectives: Optimal hemoglobin targets for chronic kidney disease patients receiving erythropoiesis-stimulating agents remain controversial. The effects of different hemoglobin targets on blood transfusion requirements have not been well characterized, despite their relevance to clinical decision-making.

    Design, setting, participants, & measurements: Five hundred ninety-six incident hemodialysis patients without symptomatic cardiac disease were randomly assigned to hemoglobin targets of 9.5 to 11.5 g/dl or 13.5 to 14.5 g/dl for 96 wk using epoetin alfa as primary therapy and changes in left ventricular structure as the primary outcome (previously reported). Patients were masked to treatment assignment. Blood transfusion data were prospectively collected at 4-wk intervals.

    Results: The mean age and prior duration of dialysis therapy of the study population were 50.8 and 0.8 yr, respectively. Previously reported mortality was similar in low and high-target subjects, at 4.7 (95% confidence interval 3.0, 7.3) and 3.1 (1.8, 5.4) per hundred patient years, respectively. Transfusion rates were 0.66 (0.59, 0.74) units of blood per year in low and 0.26 (0.22, 0.32) in high-target subjects (P < 0.0001). Hemoglobin level at transfusion (7.7 [7.5, 7.9]) versus 8.1 [7.6, 8.5] g/dl) were similar with both groups. High hemoglobin target was a significant predictor of time to first transfusion independent of baseline associations (hazard ratio 0.42; 95% confidence interval 0.26 – 0.67). Conclusions: In hemodialysis patients with comparatively low mortality risks, normal hemoglobin targets may reduce the need for transfusions.

18. Hirth, Turenne, Wilk et al. Blood transfusion practices in dialysis patients in a dynamic regulatory environment. Am J Kidney Dis. 2014 Oct;64(4):616-21. doi: 10.1053/j.ajkd.2014.01.011. Epub 2014 Feb 19.

    BACKGROUND: In 2011, Medicare implemented a prospective payment system (PPS) covering an expanded bundle of services that excluded blood transfusions. This led to concern about inappropriate substitution of transfusions for other anemia management methods.

    STUDY DESIGN: Medicare claims were used to calculate transfusion rates among dialysis patients pre- and post-PPS. Linear probability regressions adjusted transfusion trends for patient characteristics.
    SETTING & PARTICIPANTS: Dialysis patients for whom Medicare was the primary payer between 2008 and 2012.

    PREDICTOR: Pre-PPS (2008-2010) versus post-PPS (2011-2012).

    OUTCOMES & MEASUREMENTS: Monthly and annual probability of receiving one or more blood transfusions.

    RESULTS: Monthly rates of one or more transfusions varied from 3.8%-4.8% and tended to be lowest in 2010. Annual rates of transfusion events per patient were ~10% higher in relative terms post-PPS, but the absolute

magnitude of the increase was modest (-0.05 events/patient). A larger proportion received 4 or more transfusions (3.3% in 2011 and 2012 vs 2.7%-2.8% in prior years). Controlling for patient characteristics, the monthly probability of receiving a transfusion was significantly higher post-PPS (β = 0.0034; P < 0.001), representing an -7% relative increase. Transfusions were more likely for females and patients with more comorbid conditions and less likely for blacks both pre- and post-PPS.

LIMITATIONS: Possible underidentification of transfusions in the Medicare claims, particularly in the inpatient setting. Also, we do not observe which patients might be appropriate candidates for kidney transplantation.

CONCLUSIONS: Transfusion rates increased post-PPS, but these increases were modest in both absolute and relative terms. The largest increase occurred for patients already receiving several transfusions. Although these findings may reduce concerns regarding the impact of Medicare's PPS on inappropriate transfusions that impair access to kidney transplantation or stress blood bank resources, transfusions should continue to be monitored.

19. Gilbertson, Monda, Bradbury & Collins. RBC Transfusions Among Hemodialysis Patients (1999-2010): Influence of Hemoglobin Concentrations Below 10 g/dL. Am J Kidney Dis. 2013; Volume 62 , Issue 5 , 919 - 928
Background: Changes in anemia management over the past decade have produced downward shifts in hemoglobin concentrations. We aimed to examine the effect on use of red blood cell (RBC) transfusions.
Study Design: Retrospective cohort study.

Setting & Participants: We identified point prevalent Medicare hemodialysis patients as of January 1 of each year (1999-2010) and categorized them based on 3-month (April to June) mean hemoglobin levels (10 or 10 g/dL) in each year.

Predictors: Hemoglobin patterns over time and clinical profiles based on achieved hemoglobin concentrations.

Outcomes: RBC transfusion use. Measurements: We used negative binomial modeling to examine the effect of hemoglobin level 10 g/dL on transfusion use, adjusting for case-mix differences.

Results: Proportions of patients with mean hemoglobin levels10 g/dL decreased from 10% (1999) to4% (2005), but began increasing after 2006 and reached 6% by 2010. Accounting for case-mix differences, transfusion rates remained relatively constant at approximately 7.9 per 100 person-months for patients with hemoglobin levels 10 g/dL and 2 per 100 person-months for patients with hemoglobin levels 10 g/dL.
Patients with average hemoglobin levels 10 g/dL were more likely to receive transfusions (risk ratio, 2.2; 95% CI, 2.1-2.2) even after adjustment; the risk ratio doubled if hemoglobin levels remained 10 g/dL for 6 months (4.4; 95% CI, 3.7-5.2).

Limitations: Limited in generalizability to patients with Medicare as primary payer; residual confounding from factors such as frailty and chronic inflammation cannot be excluded; categorizing patients based on an average of 3 outpatient hemoglobin measurements may introduce some misclassification.

Conclusions: Risk of transfusion increases substantially with hemoglobin concentrations 10 g/dL; risk appears to be independent of other clinical factors. If anemia management patterns shift toward lower hemoglobin concentrations, RBC transfusion use likely will increase in dialysis patients.

20. Collins et al. Effect of Facility-Level Hemoglobin Concentration on Dialysis Patient Risk of Transfusion. Am J Kidney Dis. 2014; 63(6):997-1006.

Background: Changes in anemia management practices due to concerns about erythropoiesis-stimulating agent safety and Medicare payment changes may increase patient risk of transfusion. We examined anemia management trends in hemodialysis patients and risk of red blood cell (RBC) transfusion according to dialysis facility–level hemoglobin concentration.

Study Design: Retrospective follow-up study; 6-month study period (January to June), 3-month exposure/follow-up.

Setting & Participants: For each year in 2007-2011, annual cohorts of point-prevalent Medicare primary payer patients receiving hemodialysis on January 1with one or more hemoglobin measurements during the study period. Annual cohorts averaged 170,000 patients, with 130,000 patients and 3,100 facilities for the risk analysis.

Predictor: Percentage of facility patient-months with hemoglobin level, 10 g/dL.

Outcome: Patient-level RBC transfusion rates.

Measurements: Monthly epoetin alfa and intravenous iron doses, mean hemoglobin levels, and RBC transfusion rates; percentage of facility patient-months with hemoglobin levels, 10 g/dL (exposure) and patient-level RBC transfusion rates (follow-up).

Results: Percentages of patients with hemoglobin levels, 10 g/dL increased every year from 2007 (6%) to 2011 (w11%). Epoetin alfa doses, iron doses, and transfusion rates remained relatively stable through 2010 and changed in 2011. Median monthly epoetin alfa and iron doses decreased 25% and 43.8%, respectively, and monthly transfusion rates increased from 2.8% to 3.2% in 2011, a 14.3% increase. Patients in facilities with the highest prevalence of hemoglobin levels , 10 g/dL over 3 months were at w30% elevated risk of receiving RBC transfusions within the next 3 months (relative risk, 1.28; 95% CI, 1.22-1.34).

Limitations: Possibly incomplete claims data; smaller units excluded; hemoglobin levels reported monthly for patients receiving epoetin alfa; transfusions usually not administered in dialysis units.

Conclusions: Dialysis facility treatment practices, as assessed by percentage of patient-months with hemoglobin levels , 10 g/dL over 3 months, were associated significantly with risk of transfusions in the next 3 months for all patients in the facility, regardless of patient case-mix.

21. Cappell et al. Red blood cell (RBC) transfusion rates among US chronic dialysis patients during changes to Medicare end-stage renal disease (ESRD) reimbursement systems and erythropoiesis stimulating agent (ESA) labels. BMC Nephrology 2014, 15:116.

Background: Several major ESRD-related regulatory and reimbursement changes were introduced in the United States in 2011. In several large, national datasets, these changes have been associated with decreases in erythropoiesis stimulating agent (ESA) utilization and hemoglobin concentrations in the ESRD population, as well as an increase in the use of red blood cell (RBC) transfusions in this population. Our objective was to examine the use of RBC transfusion before and after the regulatory and reimbursement changes implemented in 2011 in a prevalent population of chronic dialysis patients in a large national claims database.

Methods: Patients in the Truven Health MarketScan Commercial and Medicare Databases with evidence of chronic dialysis were selected for the study. The proportion of chronic dialysis patients who received any RBC transfusion and RBC transfusion event rates per 100 patient-months were calculated in each month from

January 1, 2007 to March 31,2012. The results were analyzed overall and stratified by primary health insurance payer (commercial payer or Medicare).

Results: Overall, the percent of chronic dialysis patients with RBC transfusion and RBC transfusion event rates per 100 patient-months increased between January 2007 and March 2012. When stratified by primary health insurance payer, it appears that the increase was driven by the primary Medicare insurance population. While the percent of patients with RBC transfusion and RBC transfusion event rates did not increase in the commercially insured population between 2007 and 2012 they did increase in the primary Medicare insurance population; the majority of the increase occurred in 2011 during the same time frame as the ESRD-related regulatory and reimbursement changes.

Conclusions: The regulatory and reimbursement changes implemented in 2011 may have contributed to an increase in the use of RBC transfusions in chronic dialysis patients in the MarketScan dataset who were covered by Medicare plus Medicare supplemental insurance.

22. House AA, Pham B, Pagé DE. Transfusion and recombinant human erythropoietin requirements differ between dialysis modalities. Nephrol Dial Transplant. 1998 Jul;13(7):1763-9.

BACKGROUND: Before the routine use of recombinant human erythropoietin (rHuEpo), patients dialysed by peritoneal dialysis (PD) received fewer blood transfusions than patients on haemodialysis (HD). We compared transfusion practices in these groups now that the use of rHuEpo has become standard, while controlling for variables known to influence anaemia of end-stage renal disease (ESRD). Maintenance rHuEpo doses were also compared. METHODS: Data were examined for 157 HD and 126 PD patients during a 2-year period. Potential confounders included age, gender, albumin, iron deficiency, parathyroid hormone (PTH), underlying renal disease, comorbid illness, renal transplant, dialysis adequacy and duration. An intent-to-treat analysis was used, with sensitivity analyses to account for change in treatment and transplant.

RESULTS: Mean haemoglobin (Hb) was not different (10.47 g/dl for HD, 10.71 g/dl for PD; P = 0.45). Mean monthly transfusion rate was higher for HD (0.47 units per month vs 0.19; P < 0.01). More HD patients received at least one transfusion (52.9 vs 40.9%; P < 0.01). The maintenance rHuEpo dose was higher for HD (7370 U/week vs 5790 U/week; P = 0.01). The only factors associated with risk of being transfused were dialysis duration and mode of dialysis (less risk for PD, odds-ratio 0.57; 95% confidence interval 0.35-0.92).

CONCLUSIONS: Despite the routine use of rHuEpo, HD patients received more blood and rHuEpo than PD patients to achieve the same Hb. No patient factors were identified to account for this difference. The use of fewer transfusions and less rHuEpo in PD represents an advantage over HD in terms of both cost and safety.

23. Obrador and Macdougall. Effect of Red Cell Transfusions on Future Kidney Transplantation. Clin J Am Soc Nephrol 8: 852–860, 2013.

Red cell transfusions, erythropoiesis-stimulating agents (ESAs), and intravenous iron therapy all have a place in the treatment of anemia associated with CKD. Their relative merits and uses are subject to many clinical and nonclinical factors. New concerns associated with the use of ESA therapy make it likely that the use of blood transfusions will increase, refueling previous debates about their associated risks. Data on whether red cell transfusions increase sensitization to HLA antigens, rendering subsequent transplantation more problematic, are mainly derived from older literature. Older data suggested that women were more at risk of HLA sensitization than men, particularly those with previous multiple pregnancies, although recent U.S. Renal Data System data have challenged this. HLA sensitization prolongs the waiting time for transplantation and reduces graft survival. Leukocyte depletion of red cells does not appear to reduce the risk of HLA sensitization.

This review summarizes much of the data on these issues, as well as highlighting the need for further research on the potential risks for blood transfusion in patients with CKD.

24. Ibrahim, et al. Blood transfusions in kidney transplant candidates are common and associated with adverse outcomes. Clin Transplant 2011: 25: 653–659.

Surprisingly, there are no data regarding transfusion frequency, factors associated with transfusion administration in patients on the kidney transplant waiting list, or transfusion impact on graft and recipient outcomes. We used United States Renal Data System data to identify 43 025 patients added to the waiting list in 1999–2004 and followed through 2006 to assess the relative risk of post-listing transfusions. In 69 991 patients who underwent transplants during the same time period, we assessed the association between pre-transplant transfusions and level of panel-reactive antibody (PRA) at the time of transplant, and associations between PRA and patient outcomes. The three-yr cumulative incidence of transfusions was 26% for patients added to the waiting list in 1999, rising to 30% in 2004. Post-listing transfusions were associated with a 28% decreased likelihood of undergoing transplant, and a more than fourfold increased risk of death. There was a graded association between percent PRA at the time of transplant and adjusted risk of death-censored graft failure, death with function, and the combined event of graft failure and death. These data demonstrate that transfusions remain common and confirm the adverse association between transfusions and PRA, and high PRA and inferior graft and patient outcomes.

25. Molony, et al. Effects of epoetin alfa titration practices, implemented after changes to product labeling, on hemoglobin levels, transfusion use, and hospitalization rates. Am J Kidney Dis 2016: epub before print (published online March 12, 2016).

Background: Little is known about epoetin alfa (EPO) dosing at dialysis centers after implementation of the US Medicare prospective payment system and revision of the EPO label in 2011.

Study Design: Retrospective cohort study.
Setting & Participants: Approximately 412,000 adult hemodialysis patients with Medicare Parts A and B as primary payer in 2009 to 2012 to describe EPO dosing and hemoglobin patterns; of these, about 70,000 patients clustered in about 1,300 dialysis facilities to evaluate facility-level EPO titration practices and patient level outcomes in 2012.

Predictor: Facility EPO titration practices when hemoglobin levels were ,10 and .11 g/dL (grouped treatment variable) determined from monthly EPO dosing and hemoglobin level patterns.

Outcomes: Patient mean hemoglobin levels, red blood cell transfusion rates, and all-cause and cause specific hospitalization rates using a facility-based analysis.
Measurements: Monthly EPO dose and hemoglobin level, red blood cell transfusion rates, and all-cause and cause-specific hospitalization rates.

Results: Monthly EPO doses declined across all hemoglobin levels, with the greatest decline in patients with hemoglobin levels, 10 g/dL (July-October 2011). In 2012, nine distinct facility titration practices were identified. Across groups, mean hemoglobin levels differed slightly (10.5-10.8 g/dL) but within-patient hemoglobin standard deviations were similar (w0.68 g/dL). Patients at facilities implementing greater dose reductions and smaller dose escalations had lower hemoglobin levels and higher transfusion rates. In contrast, patients at facilities that implemented greater dose escalations (and large or small dose reductions) had

higher hemoglobin levels and lower transfusion rates. There were no clinically meaningful differences in all-cause or cause-specific hospitalization events across groups.

Limitations: Possibly incomplete claims data; excluded small facilities and those without consistent titration patterns; hemoglobin levels reported monthly; inferred facility practice from observed dosing.

Conclusions: Following prospective payment system implementation and labeling revisions, EPO doses declined significantly. Under the new label, facility EPO titration practices were associated with mean hemoglobin levels (but not standard deviations) and transfusion use, but not hospitalization rates.

1a.3.— Linkage

1a.3.1. Source of Systematic Review
N/A

1a.4.—Clinical Practice Guideline Recommendation

1a.4.1. Guideline Citation
N/A

1a.4.2. Specific Guideline
N/A

1a.4.3. Grade
N/A

1a.4.4. Grades and Associated Definitions
N/A

1a.4.5. Methodology Citation
N/A

1a.4.6. Quantity, Quality, and Consistency
N/A

1a.5. —United States Preventative Services Task Force Recommendation

1a.5.1. Recommendation Citation
N/A

1a.5.2. Specific Recommendation
N/A

1a.5.3. Grade
N/A

1a.5.4. Grades and Associated Definitions
N/A

1a.5.5. Methodology Citation
N/A

1a.6.—Other Systematic Review of the Body of Evidence
1a.6.1. Review Citation
N/A

1a.6.2. Methodology Citation
N/A

1a.7.—Findings from Systematic Review of Body of the Evidence Supporting the Measure
1a.7.1. Specifics Addressed in Evidence Review
N/A

1a.7.2. Grade
N/A

1a.7.3. Grades and Associated Definitions
N/A

1a.7.4. Time Period
N/A

1a.7.5. Number and Type of Study Designs
N/A

1a.7.6. Overall Quality of Evidence
N/A

1a.7.7. Estimates of Benefit
N/A

1a.7.8. Benefits Over Harms
N/A

1a.7.9. Provide for Each New Study
N/A

1a.8.—Other Source of Evidence
1a.8.1. Process Used
N/A

1a.8.2. Citation
N/A

1b.—Evidence to Support Measure Focus

1b.1. 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 FDA guidance regarding minimizing the use of ESAs, and economic incentives to minimize ESA use introduced by Medicare's bundling of 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.

1b.2. Performance Scores

The STrR is a facility-level measure, comparing the observed number of red blood cell transfusion counts at a facility with the number of transfusions that would be expected under a national norm, after accounting for the patient mix within each facility. Standardized transfusion ratios vary across facilities. The data below show the distribution of STrR using Medicare claims data for 2011-2014.

2011: 5774 facilities, 1.029 mean STrR, 1.348 Standard Error. Facility percentiles: 0.199 (10th), 0.494 (25th), 0.863 (50th), 1.329 (75th), 1.896 (90th).

2012: 5943 facilities, 1.023 mean STrR, 0.972 Standard Error. Facility percentiles: 0.217 (10th), 0.518 (25th), 0.866 (50th), 1.309 (75th), 1.864 (90th).

2013: 6170 facilities, 1.057 mean STrR, 2.883 Standard Error. Facility percentiles: 0.213 (10th), 0.517 (25th), 0.866 (50th), 1.321 (75th), 1.897 (90th)

2014: 6415 facilities, 1.034 mean STrR, 1.408 Standard Error. Facility percentiles: 0.171 (10th), 0.494 (25th), 0.867 (50th), 1.317 (75th), 1.843 (90th)

Data for the measure are derived from an extensive national ESRD patient database, which is largely derived from the CMS Consolidated Renal Operations in a Web-enabled Network (CROWN), which includes Renal Management Information System (REMIS), and the Standard Information Management System (SIMS) database, Medicare claims, 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, the Dialysis Facility Compare (DFC) and the Social Security Death Master File. Information on transfusions is obtained from Medicare Inpatient and Outpatient Claims Standard Analysis Files (SAFs).

The data below show the number of facilities, patients, total count of transfusions and total patient years at risk for each year. Also, we calculate unadjusted or raw transfusion rates per year (defined as total

transfusions divided by total patient years at risk).

2011: 5774 facilities, 387097 patients, 67428 total transfusions, 227935.62 Total Patients Years at risk, 29.58 Raw Transfusion Rate per 100 patient years at risk*.

2012: 5943 facilities, 398769 patients, 74444 total transfusions, 234847.09 Total Patients Years at risk, 31.70 Raw Transfusion Rate per 100 patient years at risk*.

2013: 6170 facilities, 415576 patients, 73122 total transfusions, 241082.06 Total Patients Years at risk, 30.33 Raw Transfusion Rate per 100 patient years at risk*.

2014: 6415 facilities, 429241 patients, 69182 total transfusions, 246710.49 Total Patients Years at risk, 28.04 Raw Transfusion Rate per 100 patient years at risk*.

*This analysis includes all facilities for the given year.

1b.3. Summary of Data Indicating Opportunity
N/A

1b.4. and 1b.5. Disparities
Analyses of the STrR by race, sex and ethnicity indicate relatively little variation and no disparities substantial to the measure among these groups. Although females are somewhat more likely to receive transfusions than males, analyses showed that a model with variables for race and sex included and a model without these variables yielded very similar results for the facility STrR as well as similar parameter estimates for the other covariates. The data below shows the parameter estimates for the race, sex and ethnicity variables included in the model containing the other covariates listed in S.14.

Females: 0.168 estimate, 0.004 standard error, <.0001 p-value.
Native American*: -0.075 estimate, 0.023 standard error, 0.001 p-value.
Asian*: -0.207 estimate, 0.012 standard error, <.0001 p-value.
Black*: -0.046 estimate, 0.005 standard error, <.0001 p-value.
Other Race*: 0.090 estimate, 0.045 standard error, 0.044 p-value.
Hispanic #: -0.181 estimate, 0.007 standard error, <.0001 p-value.

*White as reference
Non-Hispanic as reference

1c.—High Priority

1c.1. Demonstrated High-Priority Aspect of Health Care
High resource use, Patient/societal consequences of poor quality

1c.3. Epidemiologic or Resource Use Data
Safety concerns arising from clinical trials of ESA treatment of anemia of chronic kidney disease (CKD) led to changes in FDA recommendations on ESA use in patients with CKD. In addition, changes in financial incentives for treatment of anemia following the implementation of the revised Medicare ESRD Prospective Payment System (in 2011) have further heightened concerns in the dialysis community that patients with CKD-related anemia may be denied adequate access to ESAs for prevention of red blood cell transfusion. This concern has been further amplified by recently reported trends in anemia management in US chronic dialysis patients,

demonstrating rapid declines in achieved hemoglobin from mid-2010 to the present. 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). Unpublished analyses of Medicare Claims data presented at CMS Technical Expert Panel in May 2012 demonstrate an inverse association between achieved hemoglobin and subsequent transfusion risk using more recent data from 2008-2011. In early 2012, a highly publicized USRDS study presented at the NKF Clinical meeting reported increased dialysis patient transfusion rates in 2011 compared to 2010.

UM-KECC and Arbor Research collaborators presented an analysis of transfusion events in Medicare dialysis patients from 2009-2011, observing increased transfusions in 2011, although the magnitude of change in transfusion rates was much lower than reported by the USRDS.

1c.4. Citations

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

1c.5. Patient-Reported Outcome Performance Measure (PRO-PM)

N/A

Scientific Acceptability:

1.—Data Sample Description

1.1. What Type of Data was Used for Testing?

Measure Specified to Use Data from: administrative claims, clinical database/registry
Measure Tested with Data From: administrative claims, clinical database/registry

1.2. Identify the Specific Dataset

Data are derived from an extensive national ESRD patient database, which is primarily based on the CMS Consolidated Renal Operations in a Web-enabled Network (CROWN) system. The CROWN data include the Renal Management Information System (REMIS), CROWNWeb facility-reported clinical and administrative data (including CMS-2728 Medical Evidence Form, CMS-2746 Death Notification Form, and CMS-2744 Annual Facility Survey Form data), the historical Standard Information Management System (SIMS) database (formerly maintained by the 18 ESRD Networks until replaced by CROWNWeb in May 2012), the National

Vascular Access Improvement Initiative's Fistula First Catheter Last project (in CROWNWeb since May 2012), Medicare dialysis and hospital payment records, transplant data from the Organ Procurement and Transplant Network (OPTN), the Nursing Home Minimum Dataset, the Quality Improvement Evaluation System (QIES) Workbench, which includes data from the Certification and Survey Provider Enhanced Report System (CASPER), Dialysis Facility Compare (DFC), and the Social Security Death Master File. The database is comprehensive for Medicare patients. Non-Medicare patients are included in all sources except for the Medicare payment records. CROWNWeb provides tracking by dialysis provider and treatment modality for non-Medicare patients. Information on hospitalizations is obtained from Part A Medicare Inpatient Claims Standard Analysis Files (SAFs), and past-year comorbidity is obtained from multiple Part A types (inpatient, home health, hospice, skilled nursing facility claims) and Part B outpatient types of Medicare Claims SAFs.

1.3. What are the Dates of the Data Used in Testing?

January 1, 2011 – December 31, 2014

1.4. What Levels of Analysis Were Tested?

Measure Specified to Measure Performance of: hospital/facility/agency
Measure Tested at Level of: hospital/facility/agency

1.5. How Many and Which Measured Entities Were Included in the Testing and Analysis?

For each year, we first included all Medicare certified facilities. The following table (Table 1) shows the count of the facilities each year, before and after exclusions were applied; we also report percent excluded for each year.

Table 1: Count of facilities per year, before and after patient-level comorbidity exclusion.

	Facility Count		
Year	Before Exclusions	After Exclusions	Percent Excluded
2011	5777	5774	0.05%
2012	5955	5943	0.20%
2013	6184	6170	0.23%
2014	6422	6415	0.11%

Table 2. Number of facilities included for testing and analysis for the years 2011-2014.

Year	# of facilities	Mean Facility size (patients)
2011	5774	67.04
2012	5943	67.10
2013	6170	67.35
2014	6415	66.91

1.6. How Many and Which Patients Were Included in the Testing and Analysis?

Table 3. Count of facilities, patients, and total patient years at risk.

Year	# of facilities	# of Patients	Total Patients Years at risk
2011	5774	387097	227935.62
2012	5943	398769	234847.09
2013	6170	415576	241082.06
2014	6415	429241	246710.49

The following table (Table 4) shows the facility level mean number of patients, mean age; mean values for patient years at risk, mean %females , %black, %white, and %Hispanics for each of the four years.

Table 4. Facility level mean values.

Year	# Patients	Age as of end of year	Patient Yrs at Risk	%Female	%Black	%White	%Hisp
2011	67.04	63.32	39.48	45.45	32.17	62.15	14.16
2012	67.10	63.29	39.52	45.55	32.02	62.37	14.37
2013	67.35	63.38	39.07	45.16	31.83	62.46	14.39
2014	66.91	63.50	38.46	44.85	31.71	62.42	14.42

1.7. Sample Differences, if Applicable

All reliability, validity, risk adjustment analyses are done using this data set as explained in Table 1 of Section 1.5 above. For the test of meaningful differences, please refer section 2b.5 for details, facilities with less than 10 patient years at risk are excluded from this analysis.

Table 5. Counts of facilities before and after application of the less than 10 patient years at risk exclusion, 2011-2014.

Year	# Facilities included in the testing and analysis	# Facilities with at least 10 patient years at risk	Percent excluded
2011	5774	5138	11.01%
2012	5943	5318	10.52%
2013	6170	5441	11.82%
2014	6415	5650	11.93%

1.8 What were the patient-level sociodemographic (SDS) variables that were available and analyzed in the data or sample used?

Patient level:

- Employment status 6 months prior to ESRD
- Sex
- Race
- Ethnicity
- Medicare coverage*

**Assessed at a specific time point (e.g., at a transfusion event). The final variable for Medicare coverage in model was recoded*
1. Medicare as primary and Medicaid
2. Medicare as primary and NO Medicaid
3. Medicare Secondary or Medicare HMO
4. Non-Medicare/missing

Data on patient level SDS/SES factors obtained from Medicare claims and administrative data.
ZIP code level – Area Deprivation Index (ADI) elements from Census data:

- Unemployment rate (%)
- Median family income (rescaled as (income-60,000)/10,000)
- Income disparity
- Families below the poverty level (%)
- Single-parent households w/ children <18 (%)
- Home ownership rate (%)
- Median home value (rescaled as (homevalue-200,000)/100,000)
- Median monthly mortgage (rescaled as (mortgage-1,500)/1,000)
- Median gross rent (rescaled as (rent-900)/1,000)
- Population (aged 25+) with <9 years of education (%)
- Population (aged 25+) w/o HS diploma (%)

2a.2—Reliability Testing

2a2.1. Level of Reliability Testing
Performance measure score (e.g., signal-to-noise analysis)

2a2.2. Method of Reliability Testing
The reliability of the STrR was assessed using data among ESRD dialysis patients during 2011-2014. If the measure were a simple average across individuals in the facility, the usual approach for determining measure reliability would be a one-way analysis of variance (ANOVA), in which the between and within facility variation in the measure is determined. The inter-unit reliability (IUR) measures the proportion of the measure variability that is attributable to the between-facility variance. The STrR, however, is not a simple average and we instead estimate the IUR using a bootstrap approach, which uses a resampling scheme to estimate the within facility variation that cannot be directly estimated by ANOVA. A small IUR (near 0) reveals that most of the variation of the measures between facilities is driven by random noise, indicating the measure would not be a good characterization of the differences among facilities, whereas a large IUR (near 1) indicates that most of the variation between facilities is due to the real difference between facilities. Our approach for calculating IUR is presented in the appendix.

2a2.3. Statistical Results from Reliability Testing
The STrR calculation only included facilities with at least 10 patient years at risk. Overall, we found that IURs for the one-year STrR have a range of 0.60-0.66 across the years 2011, 2012, 2013 and 2014, which indicates that around two-thirds of the variation in the one-year STrR can be attributed to the between-facility differences and one-third to within-facility variation. This value of IUR indicates a moderate degree of reliability. When stratified by facility size, we find that, as expected, larger facilities have greater IUR.

Table 6: IUR for One-year STrR, Overall and by Facility Size, 2011-2014.

	2011		**2012**		**2013**		**2014**	
Facility Size	IUR	N	IUR	N	IUR	N	IUR	N
all	0.64	5142	0.66	5319	0.65	5442	0.60	5651
Small (<=46)	0.41	1714	0.41	1828	0.39	1840	0.30	1934
Medium (47–78)	0.55	1699	0.56	1753	0.55	1823	0.50	1941
Large (>=79)	0.78	1729	0.79	1738	0.79	1779	0.78	1776

2a2.4. Interpretation
This value of IUR indicates a moderate degree of reliability. When stratified by facility size, we find that, as expected, larger facilities have greater IUR.

2b2—Validity Testing

2b2.1. Level of Validity Testing
Performance measure score, Empirical validity testing Systematic assessment of face validity of performance measure score as an indicator

2b2.2. Method of Validity Testing
Validity was assessed using Poisson regression models to measure the association between facility level the 2014 Standardized Mortality Ratio (SMR, NQF 0369) and 2014 Standardized Hospitalization Ratio (SHR, NQF 1463) and tertiles of STrR. Facility-level STrR were divided into tertiles (T1 to T3) and the relative risk (RR) of mortality (and hospitalization, separately) was calculated for each tertile, using the T1 as the reference group. Thus, a RR>1.0 would indicate a higher relative risk of mortality or hospitalization, compared to the highest performance tertile (T1) of STrR.

Validity was also assessed using a Poisson regression model to measure the association between facility level STrR and tertiles of % of patients with Hgb < 10. Facility-level % of patients with Hgb < 10 were divided into tertiles (T1 to T3) and relative risk (RR) of transfusions were calculated for each tertile, using the T1 as the reference group. Thus, a RR>1.0 would indicate a higher relative risk of transfusion, compared to the highest performance tertile(T1) of % of patients with Hgb < 10.

In May 2012 there was an assessment of the measure's face validity based on polling of a CMS Technical Expert Panel (TEP).

2b2.3. Statistical Results from Validity Testing
Association of STrR with other facility-level outcomes

Tertiles of STrR were defined as follows:
T1: 0-<0.66
T2: 0.66-<1.15
T3: 1.15-<5.66
*T1 as Reference

Results from the Poisson model indicated that the STrR tertiles were significantly associated with both SMR and SHR.

For the 2014 SMR, the relative risk of mortality increased as the STrR tertiles increased from the reference group (tertile 1). For tertile 2, RR=1.06 (95% CI: 1.04, 1.08; p<0.001), and for tertile 3, RR=1.14 (95% CI: 1.12, 1.16; p<0.001).

Similarly for 2014 SHR, the relative risk of hospitalization increased as the STrR tertiles increased from the reference group (tertile 1) with the lowest risk in tertile 1. For tertile 2, RR=1.11 (95% CI: 1.10, 1.11; p<0.001), and for tertile 3, RR=1.29 (95% CI: 1.29, 1.30; p<0.001).

Association of STrR with facility-level intermediate anemia management outcome

Tertiles of % of patients with Hgb < 10 were defined as follows:
T1: 0-<9.5%
T2: 9.5%-<16.5%
T3: 16.5%-<85.3%

*T1 as Reference
Results from the Poisson model indicated that the % of patients with Hgb < 10 was significantly associated with the risks of transfusion.

The relative risk of transfusions increased as the tertiles of % of patients with Hgb < 10 increased from the reference group (tertile 1). For tertile 2, RR=1.15 (95% CI: 1.13, 1.18; p<0.001), and for tertile 3, RR=1.31 (95% CI: 1.28, 1.33; p<0.001).

Results of TEP Vote Establishing Face Validity of Standardized Transfusion Ratio
Six out of six voting members of CMS's 2012 Technical Expert Panel voted to recommend development of a facility-level Standardized Transfusion Ratio measure. The consensus recommendation of that clinical expert panel included the recommendation to include risk adjustment for conditions that are associated with an increased risk of blood transfusion and in some cases, increased risk of ESA-associated adverse events, such as hereditary anemia, chronic bone marrow failure conditions and active cancer.

2b2.4. Interpretation
The overall measure demonstrates face validity based on the structured 2012 TEP vote.

Furthermore, testing of the measure supports construct validity. The positive correlation between this measure and SMR and SHR respectively indicates that facilities with more transfusions than would be expected based on national rates, also have higher standardized mortality and standardized hospitalization rates.

In addition to the demonstrated association between STrR and other facility outcomes, the above results demonstrate the association between facility-level achieved hemoglobin, an intermediate outcome reflecting facility anemia management processes, and STrR. The results of dialysis facility achieved hemoglobins, grouped into tertiles, demonstrates statistically significant differences across tertiles with reassuring stepwise increments of STrR between tertiles, suggesting "dose effect".

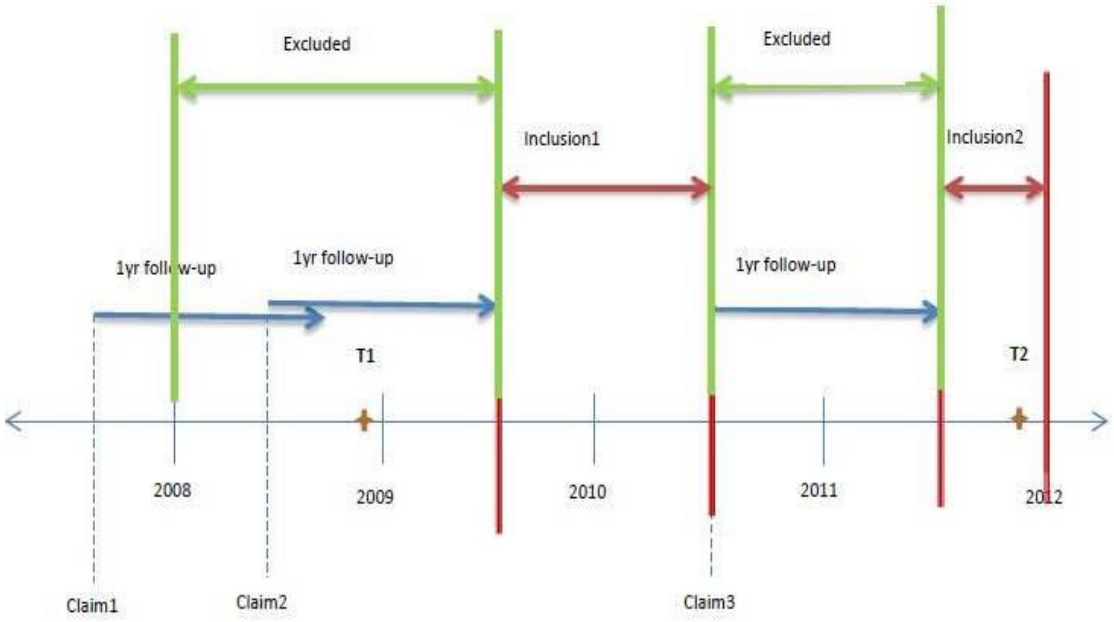
2b3—Exclusion Analysis

2b3.1. Method of Testing Exclusion
Transfusions associated with transplant hospitalization are excluded as they mark a transition of care from the dialysis facility to a transplant team. This convention is used with other dialysis facility measures developed and previously endorsed by NQF (like SHR NQF #1463 http://www.qualityforum.org/QPS/1463) and SMR NQF #0369 http://www.qualityforum.org/QPS/0369)

Patients are also 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 this measure is not intended to address, every patient's risk window is modified to have at least 1 year free of claims that contain diagnoses on this exclusion list. We

assessed the predictive power of these comorbidities on future transfusions, as a function of the time interval between development of the comorbidity and the occurrence of the transfusion by performing multivariate logistic regression with transfusion event as the dependent variable.

The following figure describes the inclusion and exclusion period of a hypothetical 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 the figure). 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 the presence of the 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.

2b3.2. Statistical Results From Testing Exclusion

Multivariate logistic regression with transfusion event as the dependent variable was performed to assess the predictive power of comorbidities on future transfusions, as a function of the time interval between development of the comorbidity and the occurrence of the transfusion. Transfusion event was coded as a binary variable (1 if transfusion). Results using 2011 data showed that a 1-year look back period for each of the exclusion comorbidities was a significant predictor of RBC transfusion events with odds ratio ranging from 1.2 to 3.2.

The following tables show percent of patient years at risk and number of patients excluded as a result of the above mentioned exclusion strategy.

Table 7: Percent of patient years at risk (PYR) excluded each year.

	Patient years at risk	

Year	Before Exclusions	After Exclusions	Percent Excluded
2011	287056.42	227935.62	20.60%
2012	296411.19	234847.09	20.77%
2013	302026.41	241082.06	20.18%
2014	308375.2	246710.49	20.00%

Table 8: Number of patients and percent excluded each year.

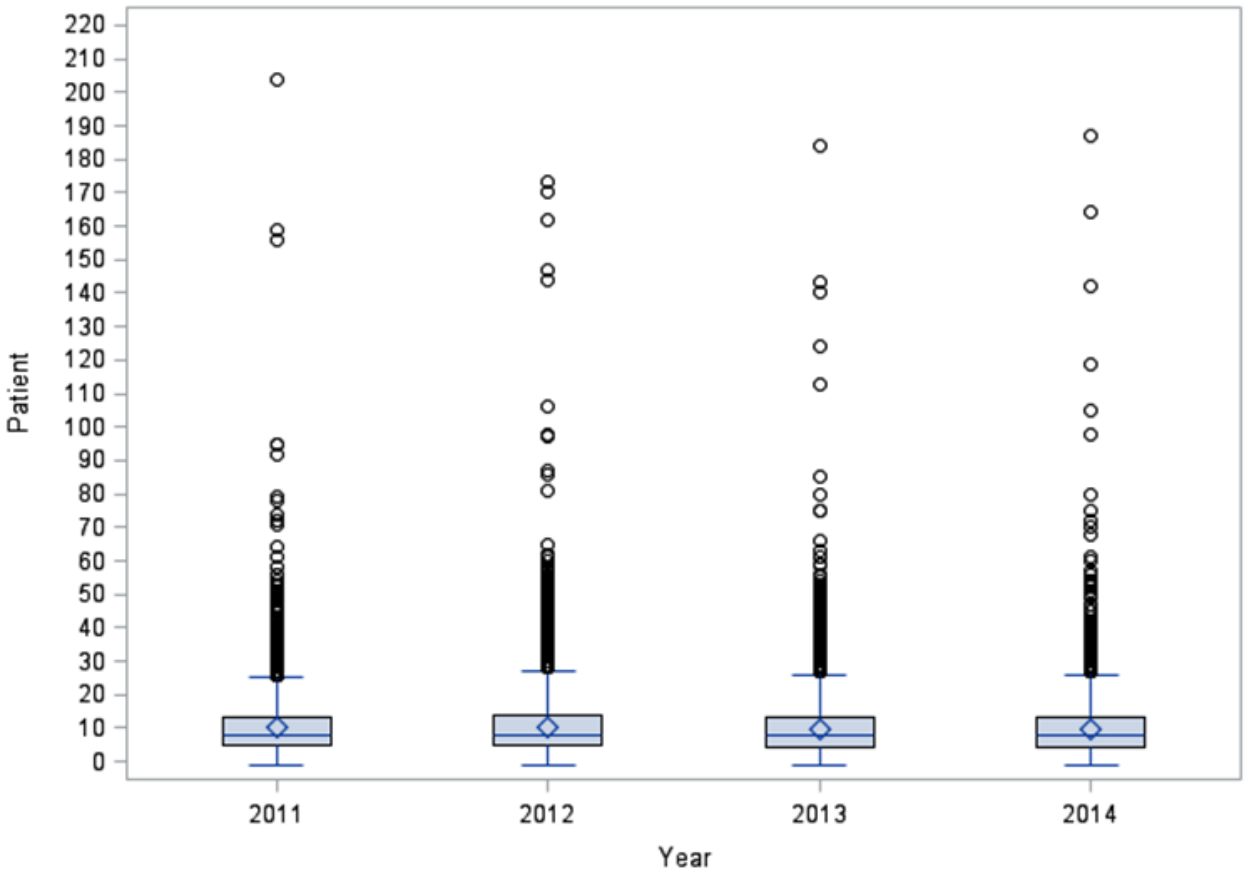
	Number of Patients		
Year	**Before Exclusions**	**After Exclusions**	**Percent Excluded**
2011	452134	387097	14.38%
2012	468592	398769	14.90%
2013	486644	415576	14.60%
2014	503016	429241	14.67%

2b3.3. Interpretation

The list of comorbidities described in section 2b3.1 have been associated with ESA resistance and higher risk of transfusion, as well as increased risk of ESA use. Based on these factors, they require different anemia management practices that this measure is not intended to address; hence the need for the comorbidity exclusions. The Technical Expert Panel had also recommended these exclusions. As described in Section 2b3.2 patients with exclusion comorbidities are at a higher risk to get transfused than patients that do not have these comorbidities.

We also checked the distribution of patients excluded at the facility level and the boxplot shows that there is variability in the number of patients excluded among facilities. The numbers of patients with the exclusion comorbidities are not uniformly distributed across facilities thereby demonstrating the need for an exclusion strategy.

Figure 2: Distribution of Excluded Patients at facility level for 2011-2014



2b4—Risk Adjustment or Stratification
2b4.1. Method of controlling for differences

☒**Statistical risk model with** 40 **risk factors**

2b4.2. Rationale why Risk Adjustment is not Needed
N/A

2b4.3. Conceptual, Clinical, and Statistical Methods
We included all the standard patient characteristics that are included in the facility level modeling for primary outcomes. We sought input from clinicians and epidemiologists and incorporated claims based risk factors and covariate adjustments recommended by the Technical Expert Panel.

The denominator of the "STrR" is an estimate of the expected number of transfusions at the facility; accounting for each patient's follow-up time and risk factors. The expected number of transfusions is based on the recurrent event analog of Cox regression (Cox, 1972), as developed by Lawless and Nadeau (1995) and Lin et al. (2000); see also 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).

The calculation of the STrR is a two-stage approach. At Stage 1, the 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, comorbidities 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 regression parameter estimates from Stage 1 are used to compute the expected number of transfusions for each patient. Stage two involves summing the expected number of transfusions by facility, then computing facility-specific STrRs as the ratio of observed / expected transfusions.

The patient characteristics included in the stage 1 model as covariates are:

- Age: We determine each patient's age for the birth date provided in the SIMS and REMIS databases and group patients into the following categories: 0-14 years old, 15-24 years old, 25-44 years old, 45-59 years old, 60-74 years old, or 75+ years old.
- Diabetes as cause of ESRD: We determine each patient's primary cause of ESRD from his/her CMS-2728, REMIS, SIMS, and CROWNWeb.
- Duration of ESRD: We determine each patient's length of time since start of ESRD treatment using his/her CMS-2728, claims history (all claim types), the SIMS database and the SRTR database and categorize as 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.
- Nursing home status: Using the Nursing Home Minimum Dataset, we determine if a patient was in a nursing home the previous year.
- BMI at incidence: We calculate each patient's BMI as the height and weight provided on his/her CMS 2728. BMI is included as a log-linear term.
- Comorbidities at incidence are determined using a selection of comorbidities reported on the CMS-2728 namely, alcohol dependence, atherosclerotic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, diabetes (includes currently on insulin, on oral medications, without medications, and diabetic retinopathy), drug dependence, inability to ambulate, inability to transfer, malignant neoplasm, cancer, other cardiac disease, peripheral vascular disease, and tobacco use (current smoker). Each comorbidity is included as a separate covariate in the model.
- Calendar year
- Categorical indicator variables are included as covariates in the stage I model to account for records with missing values for cause of ESRD, comorbidities at incidence (missing CMS-2728), and BMI. These variables have a value of 1 if the patient is missing the corresponding variable and a value of 0 otherwise. Another categorical indicator variable is included as a covariate in the stage 1 model to flag records where the patient has at least one of the incident comorbidities listed earlier. This variable has a value of 1 if the patient has at least one of the comorbidities and a value of 0 otherwise.
  Beside main effects, two-way interaction terms between age and duration and cause of ESRD are also included:
- Diabetes as cause of ESRD*Duration of ESRD
- Diabetes as cause of ESRD*Age

In response to the requirements for NQF's Trial Period for the incorporation of sociodemographic factors into quality measures, we investigated several patient and zip code level indicators of SDS/SES (see list in 1.8). Sociodemographic factors included in the analysis were based on conceptual criteria and availability of data for the analyses. We were able to acquire individual area-level variables included in the Area Deprivation Index (ADI) developed by Singh and colleagues at the University of Wisconsin[1]. These testing results and interpretation are presented in the following sections.

2b4.4a. Statistical Results

[1] Singh, GK. Area deprivation and widening inequalities in US mortality, 1969–1998. Am J Public Health. 2003;93(7):1137–1143.

In the table below, we list results from the Stage 1 model described above that includes the selected patient characteristics and other risk adjustors. For a given covariate, the parameter estimate represents the log of the rate ratio (recurrent event version of the relative risk). All covariates have face validity from a clinical perspective. We assume these selected covariates do not reflect the quality of facility care, nor, disparities in care. With the exceptions of BMI=missing and cancer, all main effects are statistically significant at 0.05 level.

Table 9. Parameter estimates for covariates in STrR model.

Covariate	Coefficient	P-value
Cause of ESRD		
Diabetes	-0.118	<.0001
Missing	0.188	<.0001
Age		
18-24	0.084	<.0001
25-44	-0.196	<.0001
45-59	-0.180	<.0001
60-74	Reference	
75+	0.035	<.0001
BMI		
Log BMI	-0.247	<.0001
BMI missing	0.024	0.190
Calendar year		
2011	Reference	
2012	0.068	<.0001
2013	0.027	<.0001
2014	-0.080	<.0001
In nursing home the previous year	0.489	<.0001
Diabetes as cause of ESRD & time on ESRD interaction term		
91 days-6 months	Reference	
6 months-1 year	0.068	0.001
1-2 years	0.128	<.0001
2-3 years	0.135	<.0001
3-5 years	0.090	<.0001
5+ years	0.044	0.014
Age & diabetes as cause of ESRD interaction term		
0-14		
15-24	0.166	0.090
25-44	0.228	<.0001
45-59	0.098	<.0001
60-74	Reference	
75+	0.008	0.445

Covariate	Coefficient	P-value
Incident comorbidities		
atherosclerotic heart disease	0.071	<.0001
other cardiac disease	0.065	<.0001
congestive heart failure	0.049	<.0001
Inability to ambulate	0.108	<.0001
Chronic obstructive pulmonary disease	0.168	<.0001
Inability to transfer	0.097	<.0001
Cancer	0.008	0.541
Diabetes	0.085	<.0001
Peripheral vascular disease	0.134	<.0001
Cerebrovascular disease	0.020	0.005
Tobacco use (current smoker)	0.135	<.0001
Alcohol dependence	0.117	<.0001
Drug dependence	0.097	<.0001
At least one incident comorbidity	0.088	<.0001
Incident comorbidity missing	0.068	0.008

2b4.4b. Statistical Results for SDS factors

The table below shows the parameter estimates for patient and area level SDS/SES variables tested based on a model that included these variables along with the original covariates.

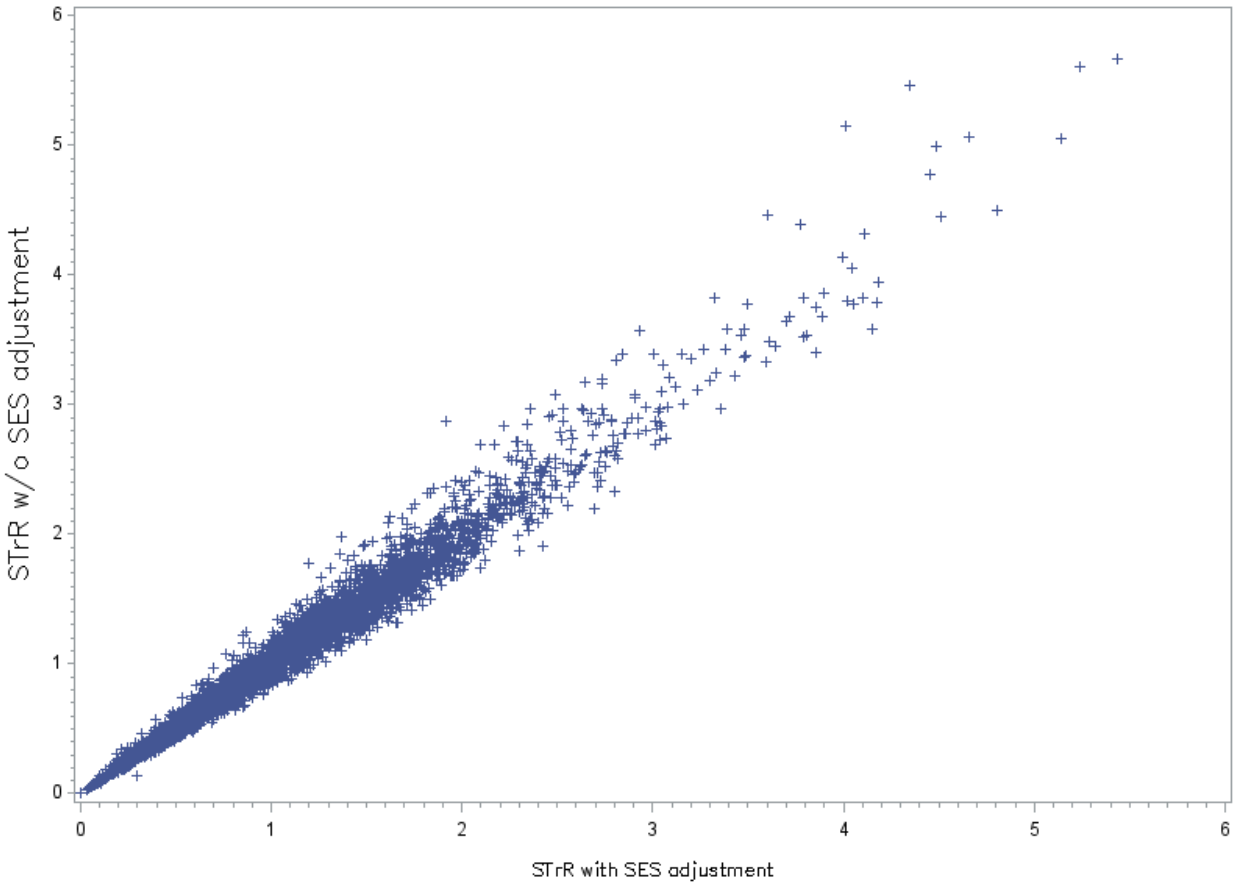
Table 10. Parameter estimates for patient and area level SDS/SES variables

Covariate	Estimates	P-value	Hazard Ratio
Sex: Female	0.163	<.0001	1.177
Race			
White	ref		
Black	-0.048	<.0001	0.953
Asian/Pacific Islander	-0.180	<.0001	0.835
Native American	-0.044	0.058	0.957
Other	-0.031	0.114	0.970
Hispanic	-0.174	<.0001	0.840
Employment status			
Employed	ref		
Unemployed	0.119	<.0001	1.126
Other	0.145	<.0001	1.156
Medicare coverage			
Medicare as primary w/o Medicaid	ref		
Medicare as primary with Medicaid	0.025	<.0001	1.025
Medicare as secondary /Medicare HMO	0.724	<.0001	2.062
Non-Medicare/missing	-0.025	0.585	0.975

Covariate	Estimates	P-value	Hazard Ratio
ADI			
Unemployment rate (%)	0.000	0.829	1.000
Median family income	-0.002	0.502	0.998
Families below the poverty level (%)	0.000	0.868	1.000
Single-parent households w/ children <18 (%)	-0.001	0.176	0.999
Home ownership rate (%)	0.001	0.015	1.001
Median home value	0.011	0.019	1.011
Median monthly mortgage	-0.003	0.826	0.997
Median gross rent	0.007	0.680	1.007
Population (aged 25+) w/o HS diploma (%)	-0.001	0.275	0.999
Income disparity	0.015	0.009	1.016

Patient-level SDS/SES: Compared to males, females were more likely to receive transfusions (HR=1.17; $p<0.01$). Compared to white patients, black patients were less likely to receive transfusions (HR=0.95, $p<0.01$). Hispanics were less likely to have transfusions (HR=0.84; $p<0.01$), compared to non-Hispanics. Compared to Medicare only patients, patients with both Medicare/ Medicaid (HR=1.03, $p<0.01$) and Medicare as secondary /Medicare HMO (HR=2.06, $p<0.01$) were more likely to have transfusions. As for employment status, unemployed and "other" patients were more likely to have transfusions (HR=1.13; $p<0.01$; HR=1.16; $p<0.01$), compared to employed patients. Note that for employment categories, the "Other" category represents diverse patient groups with regards to SES, such as students, homemakers, and those who are retired.
Area-level SDS/SES: Area-level effects were generally all very small and most not statistically significant, with the exception of home ownership rate, median home value, and income disparity.

Correlation between STrRs with and without SDS/SES adjustment in 2014:



*For readability purposes, the graph excludes one extreme outlier facility that was included in the calculation.

The standard and SDS/SES-adjusted STrR were highly correlated at 0.99 (p<.001).

Table 11. Facility performance on STrR, with and without adjustment for SDS/SES factors

	STrR w/o SDS/SES			
STrR with SDS/SES	**Worse than expected**	**As expected**	**Better than expected**	**Total**
Worse than expected	315	31	0	346(6.1%)
As expected	51	5225	6	5282(93.5%)
Better than expected	0	3	19	22(0.4%)
Total	366(6.5%)	5259(93.1%)	25(0.4%)	5650

After adjustment for SDS/SES, 91 facilities (1.6%) changed performance categories. 54 were upgraded (3 from as expected to better; 51 from worse to as expected) and 37 were degraded (6 from better to as expected; 31 from as expected to worse).

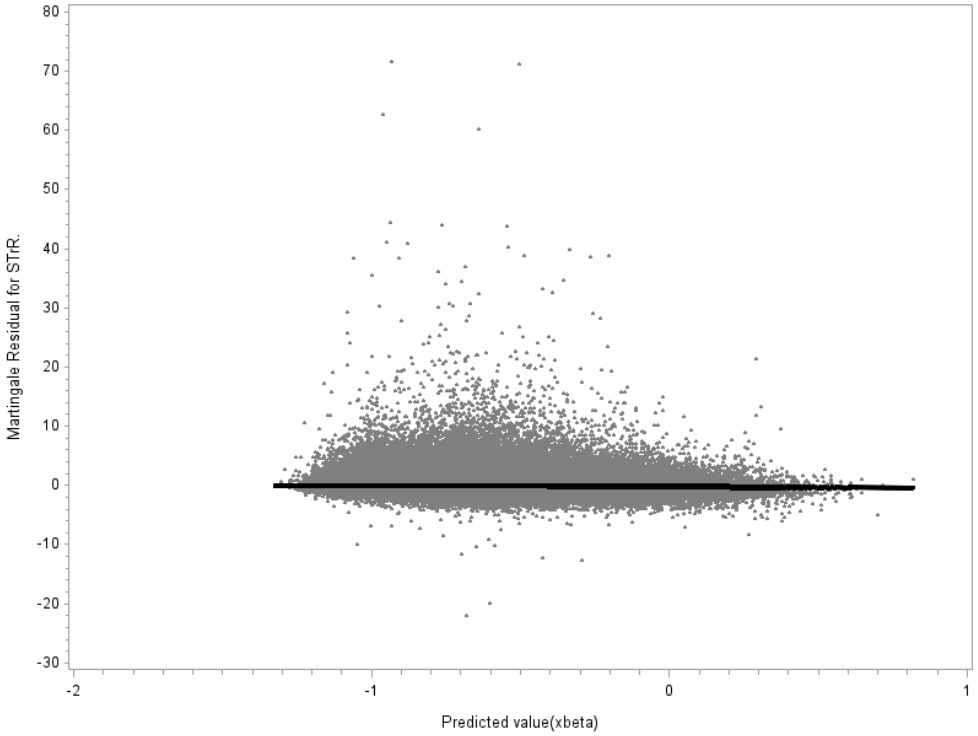
Sex and several SDS/SES factors predict transfusion events in the patient-level model. However, inclusion of the complete set of patient sociodemographic variables, including sex, insurance status and employment status, and the area-level indicators, shifts facility performance ranking for only a small fraction of dialysis facilities. Given the relatively constant distribution of sexes in US dialysis facilities, this demographic variable has little effect on dialysis facility-level transfusion event rates. Regarding employment and insurance status, we believe the association between transfusion events and these factors represent disparities in access to medical care and, therefore we do not believe that they are appropriate risk adjustors for a quality measure. Similarly, among the area-level indicators, all are assumed to reflect levels of economic disadvantage that represent differential access to care. For this reason we decided it was not appropriate to adjust for these differences.

2b4.5. Method Used to Develop the Statistical Model or Stratification Approach

Martingale residuals (Barlow and Prentice, 1988) are an important tool for checking the fit of a Cox regression model or, a model analogous to a Cox model; including the one we fitted at Stage 1. Martingale residual plots are used to investigate the lack of fit of a model. We examined the residual plot and it did not indicate problems with model fit. The LOESS curve of martingale residuals by predicted value (Figure 3) shows that the mean of the residuals is flat indicating no lack of fit.

Reference: Barlow, W. E. and Prentice, R. L. (1988). Residuals for relative risk regression. Biometrika 75, 65{74.

Figure 3: Martingale Residual for STrR



2b4.6. Statistical Risk Model Discrimination Statistics (e.g., c-statistic, R^2)

The C-statistic for a recurrent event model measures the concordance between the observed rate of recurrent events and the model-based rate. The C-statistic for the STrR is 0.65.

2b4.7. Statistical Risk Model Calibration Statistics (e.g., Hosmer-Lemeshow statistic)

We ranked each subject based on their average expected event rate. We then broke the subjects up into deciles and computed decile-specific observed and expected numbers of transfusions. Results are given in the table below; with the relative agreement between the observed and expected counts given in the last column. Overall, the model appears to have good calibration.

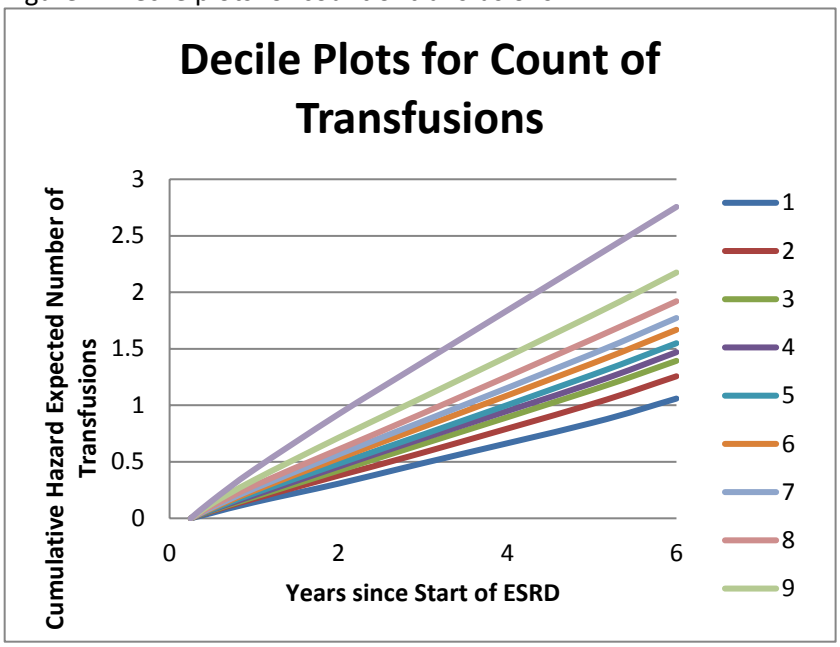
Table 12. Decile-specific observed and expected numbers of transfusions.

Decile	Observed transfusions	Expected transfusions	(Obs- Exp)/Exp
1	22042	22694.68	-0.029
2	24405	24611.55	-0.008
3	24232	24636.46	-0.016
4	24978	25427.46	-0.018
5	25507	26027.7	-0.020
6	26853	26851.19	0.000
7	27689	27377.81	0.011
8	28983	28324.41	0.023
9	31989	30352.24	0.054
10	40683	41057.5	-0.009

2b4.8. Statistical Risk Model Calibration—Risk decile plots or calibration curves

Decile plots (Figure 4) shows piecewise linear estimates of the cumulative rates by years since start of ESRD. The plot demonstrates that the risk factors in the model are discriminating well between patients. There is good separation among all 10 groups and the ordering is as predicted by the model (patients predicted to be at lower risk have lower transfusion rates). The absolute differences between the groups is also large with patients predicted to have the highest transfusion rates (line 10) having almost 3 times higher transfusion rates than those predicted to have the lowest rates (line 1).

Figure 4: Decile plots for count of transfusions.



2b4.9. Results of Risk stratification Analysis
N/A

2b4.10. Interpretation
Covariates used as risk adjusters for STrR all have face and clinical validity and most of them are statistically significant at the 0.05 level. The residual plots show no lack of fit, while goodness-of-fit criteria show that there is added value in risk adjustment. The model appears to adequately discriminate the risk of transfusion among subjects; and, overall, is well-calibrated.

2b4.11. Optional Additional Testing for Risk Adjustment
N/A

2b5—Identification of statistically significant and clinically meaningful differences

2b5.1. Method for determining
The STrR is a ratio of the observed number of red blood cell transfusions to the expected number among patients in a facility over a 1-year. The expectation is obtained based on the overall national average rate of transfusions, adjusted for the particular patient mix at the facility under consideration.
In order to classify facilities as having transfusion rates that are better, no different or worse than the national average, we require a method of obtaining a p-value for classification purposes. A p-value assesses the probability that the facility would experience a number of transfusions more extreme than that observed if the null hypothesis were true; accounting for each facility's patient mix. To do this, a Z-score is first calculated using the estimate and standard error for each facility using the method of generalized estimating equations (GEE; Liang & Zeger, 1986). Specifically, the transfusion rate (or, equivalently: the mean transfusion count, given the exposure) was assumed to follow a multiplicative model and a robust (sandwich) standard error was used. The use of robust standard errors has been advocated for modeling recurrent events (i.e., multiple events per subject), see e.g., Lawless & Nadeau (1995); Lin, Wei, Yang & Ying (2000); Cai & Schaubel (2004). For each facility, the Z-score was computed as the facility's log(STrR), divided by its standard error. Since

log(STrR) is undefined for facilities with 0 transfusions, the Z-score in such cases was computed as (STrR-1), divided by a standard error estimate (sandwich estimator) for STrR.

To account for the over dispersion in the z-scores, as used in Standardized Hospitalization Ratio (NQF #1463 http://www.qualityforum.org/QPS/1463), we use robust estimates of location and scale based on the center of the z-scores (by fitting robust regression on z- scores) and derive normal curves that more closely describe the z-score distribution. This new distribution is referred to as the "empirical null hypothesis" (Efron, 2004) and provide references for assessing the extent to which a given facility's outcomes are extreme in comparison with other facilities. We then use the mean and standard deviation from the empirical null distribution of the STrR z-scores to calculate the p-value for classifying facility performance.

References:

- Lin, D.Y., Wei, L.J., Yang, I. and Ying, Z. (2000). Semiparametric regression for the mean and rate functions of recurrent events. Journal of the Royal Statistical Society Series B, 62, 711–730.
- Cai, J. and Schaubel, D.E.. (2004). Marginal means and rates models for multiple-type recurrent event data. Lifetime Data Analysis, 10, 121-138.
- Liang, K.Y. and Zeger, S.L. (1986). Longitudinal data analysis using generalized linear models. Biometrika, 73, 13-22.
- Lawless, J.F. and Nadeau, C. (1995). Some simple robust methods for the analysis of recurrent events. Technometrics, 37, 158-168.
- Efron, B. (2004). Large scale simultaneous hypothesis testing: the choice of null hypothesis. J. Amer. Statist. Assoc., 99, 96-104.

2b5.2. Statistical Results

The following table shows how the facilities are flagged for the year 2014, based on the method described above.

Table 13: Classification of Efron Empirical Null p-value for year 2014*.

Year 2014	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Better than expected	25	0.44	5284	0.44%
As expected	5259	93.08	5259	93.08%
Worse than Expected	366	6.48	5650	100%

*Only for the facilities with patient years are greater than 10.

2b5.3. Interpretation

The results indicate that the STrR has the ability to classify facilities as being significantly better (or significantly worse) than expected; thereby demonstrating the ability to identify meaningful differences in the performance score across facilities.

2b6—Comparability of performance scores

2b6.1. Method of testing conducted to demonstrate comparability
N/A

2b6.2. Statistical Results
N/A

2b6.3. Interpretation
N/A

Feasibility:

3a.1. How are the data elements needed to compute measure scores generated
Generated or collected by and used by healthcare personnel during the provision of care (e.g., blood pressure, lab value, diagnosis, depression score)

3b.1. Are the data elements needed for the measure as specified available electronically
ALL data elements are in defined fields in a combination of electronic sources

3b.3. If this is an eMeasure, provide a summary of the feasibility assessment
N/A

3c.1. Describe what you have learned or modified as a result of testing
N/A

3c.2. Describe any fees, licensing, or other requirements
N/A

Usability and Use:

4.1—Current and Planned Use
Current Use: Public Reporting
Dialysis Facility Compare
https://www.medicare.gov/dialysisfacilitycompare/

Payment Program
ESRD Quality Incentive Program
https://www.cms.gov/Medicare/Quality-Initiatives-patient-Assessment-Instruments/ESRDQIP/

4a.1. Program, sponsor, purpose, geographic area, accountable entities, patients
DFC:

Purpose: Dialysis Facility Compare helps patients find detailed information about Medicare-certified dialysis facilities. They can compare the services and the quality of care that facilities provide.
Geographic area: United States

Number of accountable entities: All Medicare-certified dialysis facilities eligible for the measure, and have at least 11 patients (due to public reporting requirements). For the most recent DFC report, 5594 facilities were scored on STrR.

Patients included: All patients who meet the requirements to be included in the measure from included facilities.

QIP:
Purpose: The ESRD QIP will reduce payments to ESRD facilities that do not meet or exceed certain performance standards. The measure has been finalized for PY2018.

Geographic area: United States
Number of accountable entities: All Medicare-certified dialysis facilities who are eligible for the measure, and have at least 11 patients (due to public reporting requirements). Number of accountable entities: All Medicare-certified dialysis facilities who are eligible for the measure, and have at least 11 patients (due to public reporting requirements). For the most recent QIP report, 6048 facilities received reports.
Patients included: All patients who meet the requirements to be included in the measure from included facilities.

4a.2. If not publicly reported or used for accountability, reasons
N/A

4a.3. If not, provide a credible plan for implementation
N/A

4b.1. Progress on improvement
N/A

4b.2. If no improvement was demonstrated, what are the reasons
CMS is currently reporting this measure on Dialysis Facility Compare (as of January 2014). This measure has also been finalized for the PY2018 QIP. Given that the measure has only been publically reported for a short time, progress on improvement could not be evaluated. We anticipate that public reporting of this measure would improve patient outcomes, given that blood transfusion has been linked to survival indirectly in that transfusions elevate risk of greater exposure to human leukocyte antigens, present in transfused blood, that may increase anti-HLA antibodies in kidney transplant candidates, resulting in reduced access to kidney transplantation for transfused patients. Studies have shown superior patient survival with kidney transplantation compared to chronic dialysis. See 1a.3 for more information.

Related and Competing Measures:

5—Relation to Other NQF-Endorsed Measures
No

5.1a. The measure titles and NQF numbers are listed here
N/A

5.1b. If the measures are not NQF-endorsed, indicate the measure title
N/A

5a—Harmonization

5a.1. Are the measure specifications completely harmonized
N/A

5a.2. If not completely harmonized, identify the differences rationale, and impact
N/A

5b—Competing measures
N/A

5b.1 Describe why this measure is superior to competing measures
N/A

Additional Information:

Co.1.—Measure Steward Point of Contact

Co.1.1. Organization
Centers for Medicare & Medicaid Services

Co.1.2. First Name
Sophia

Co.1.3. Last Name
Chan

Co.1.4. Email Address
sophia.chan@cms.hhs.gov

Co.1.5. Phone Number
410-786-1158

Co.2.—Developer Point of Contact (indicate if same as Measure Steward Point of Contact

Co.2.1. Organization
University of Michigan Kidney Epidemiology and Cost Center

Co.2.2. First Name
Jennifer

Co.2.3. Last Name
Sardone

Co.2.4. Email Address
jmsto@med.umich.edu

Co.2.5. Phone Number
734-548-3057

Ad.1. Workgroup/Expert Panel Involved in Measure Development

This measure was recommended by a Technical Expert Panel in 2012. In this advisory role, the primary duty of the TEP is to suggest candidate measures and related specifications, review any existing measures, and determine if there is sufficient evidence to support the proposed candidate measures. The following were the members of the 2012 TEP that provided their input on the development of this measure.

1.Jeffrey Berns, MD, Professor of Medicine and Pediatrics, University of Pennsylvania School of Medicine
2.Sheila Doss-McQuitty, BSN RN CNN CRA, Nursing Director of Research, Satellite Healthcare, Inc
3.Diana Hlebovy, RN BSN CHN CNN, Clinical Support Specialist, Fresenius Medical Care
4.Robert C Kane, MD FACP*, Acting Deputy Director for Safety, Office of Hematology Oncology Products, CDER
5.Kathe LeBeau, Director of Patient Services and Public Policy, Northeastern Kidney Foundation
6.Harvey Luksenburg, MD*, Chief, Blood Diseases Branch, Division of Blood Diseases and Resources NHLBI
7.Ruth McDonald, MD, Medical Director of Solid Organ Transplant and Ambulatory Services, Seattle Children's Hospital
8.Klemens Meyer, MD, Director of Dialysis Services, Tufts Medical Center
9.John Stivelman, MD, Senior Medical Director and CMO Emeritus, Northwest Kidney Centers

*non-voting

Ad.2. Year the Measure Was First Released
2016

Ad.3. Month and Year of Most Recent Revision
04, 2016

Ad.4. What is your frequency for review/update of this measure?
Annually

Ad.5. When is your next scheduled review/update for this measure?
04, 2016

Ad.6. Copyright Statement
N/A

Ad.7. Disclaimers
N/A

Ad.8. Additional Information/Comments
N/A

S.15 Detailed risk model specifications

Model Coefficients

Covariate	Coefficient	P-value
Cause of ESRD		
Diabetes	-0.118	<.0001
Missing	0.188	<.0001
Age		
18-24	0.084	<.0001
25-44	-0.196	<.0001
45-59	-0.18	<.0001
60-74	Reference	
75+	0.035	<.0001
BMI		
Log BMI	-0.247	<.0001
BMI missing	0.024	0.19
Calendar year		
2011	Reference	
2012	0.068	<.0001
2013	0.027	<.0001
2014	-0.08	<.0001
In nursing home the previous year	0.489	<.0001
Diabetes as cause of ESRD & time on ESRD interaction term		
91 days-6 months	Reference	
6 months-1 year	0.068	0.001
1-2 years	0.128	<.0001
2-3 years	0.135	<.0001
3-5 years	0.09	<.0001
5+ years	0.044	0.014
Age & diabetes as cause of ESRD interaction term		
0-14		
15-24	0.166	0.09
25-44	0.228	<.0001
45-59	0.098	<.0001
60-74	Reference	
75+	0.008	0.445
Incident comorbidities		
atherosclerotic heart disease	0.071	<.0001
other cardiac disease	0.065	<.0001

congestive heart failure	0.049	<.0001
inability to ambulate	0.108	<.0001
chronic obstructive pulmonary disease	0.168	<.0001
inability to transfer	0.097	<.0001
cancer	0.008	0.541
diabetes	0.085	<.0001
peripheral vascular disease	0.134	<.0001
cerebrovascular disease	0.02	0.005
tobacco use (current smoker)	0.135	<.0001
alcohol dependence	0.117	<.0001
drug dependence	0.097	<.0001
At least one incident comorbidity	0.088	<.0001
Incident comorbidity missing	0.068	0.008

S.15 Detailed risk model specifications

The denominator of the STrR stems from a proportional rates model (Lawless and Nadeau, 1995; Lin et al., 2000; Kalbfleisch and Prentice, 2002). This is the recurrent event analog of the well-known proportional hazards or Cox model (Cox, 1972; Kalbfleisch and Prentice, 2002). To accommodate large-scale data, we adopt a model with piecewise constant baseline rates (e.g. Cook and Lawless, 2007) and the computational methodology developed in Liu, Schaubel and Kalbfleisch (2012). The modeling process has two stages. At stage I, a stratified model is fitted to the national data with piecewise-constant baseline rates and stratification by facility. Specifically, the model is of the following form:

$$Pr(\text{ transfusion on day } t \text{ given covariates } X) = r_{0k}(t)\exp(\beta' X_{ik})$$

where X_{ik} is the vector of covariates for the (i,k)th patient and β is the vector of regression coefficients. The baseline rate function $r_{0k}(t)$ is assumed specific to the k^{th} facility, which is assumed to be a step function with break points at 6 months, 1 year, 2 years, 3 years and 5 years since the onset of dialysis. 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 stratification on facilities is important in this phase to avoid bias due to possible confounding between covariates and facilitv effects.

The patient characteristics X_{ik} included in the stage I model 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), 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), nursing home status, BMI at incidence, individual comorbidities at incidence reported on the Medical Evidence Form (CMS-2728), calendar year, and two-way interaction terms between age and duration and cause of ESRD. Nursing home status is identified as in or not in a nursing home in the previous calendar year. BMI is included as a log-linear term. Categorical indicator variables are included as covariates in the stage I model to flag records missing values for cause of ESRD, 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 two categorical indicator variables are included to flag records with having no comorbidities and having at least one comorbidity at incidence reported on the Medical Evidence Form. These variables have a value of 1 if the patient is having no comorbidities or having at least one comorbidity and a value of 0 otherwise.

At stage II, the relative risk estimates from the first stage are used to create offsets and an unstratified model is fitted to obtain estimates of an overall baseline rate function. That is, we estimate a common baseline rate of transfusions, r0(t), across all facilities by considering the model

$$Pr(\text{transfusion on day } t \text{ given covariates } X) = r_0(t)\, R_{ik},$$

where $R_{ik} = \exp(\beta' X_{ik})$ is the estimated relative risk for patient i in facility k estimated from the stage I. In our computation, we assume the baseline to be a step function with 6 unknown parameters, $\alpha_1, \ldots, \alpha_6$, to estimate. These estimates are used to compute the expected number of transfusions given a patient's characteristics.

Specifically, let t_{iks} represent the number of days that patient i from facility k is under observation in the sth time interval with estimated rate α_s. The corresponding expected number of transfusions in the sth interval for this patient is calculated as:

$$E_{iks} = \alpha_s \; t_{iks} \; R_{ik} \; .$$

It should be noted that tiks and hence E_{iks} can be 0 if patient i from facility k is never at risk during the sth time interval. Summing the E_{iks} over all 6 intervals and all N_k patients in a given facility, k, gives

$$Exp = \sum_{i=1}^{N} \sum_{s=1}^{6} E_{iks} = \sum_{i=1}^{N} \sum_{s=1}^{6} \alpha_s \, t_{iks} \, R_{ik}$$

which is the expected number of transfusions during follow-up at that facility.

Let Obs be the observed total number of transfusions at this facility. The STrR for transfusions is the ratio of the observed total transfusions to this expected value, or

$$STrR = Obs/Exp \; .$$

Field	Value	Meaning
Revenue Center Codes	380	Blood - General Classification
	381	Blood - Packed Red Cells
	382	Blood - Whole Blood
	389	Blood - Other Blood
	390	Blood Storage and Processing - General Classification
	391	Blood Storage and Processing - Administration
	392	Blood Storage and Processing - Blood Processing and Storage
	399	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 Codes	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	Red blood cells, frozen/deglycerolized/washed, leukocytes reduced, irradiated, each unit
	P9058	RBC, l/r, cmv-neg, irrad
	36430	Current Procedural Terminology (CPT) code (transfusion, blood or blood components)

ICD-9 to 10 Mapping: Exclusions

ICD9DX	ICD9::ICD9DX_desc	ICD10CM	ICD10::ICD10CM_desc
1400	Malignant neoplasm of upper lip, vermilion border	C000	C000 Malignant neoplasm of external upper lip
1401	Malignant neoplasm of lower lip, vermilion border	C001	C001 Malignant neoplasm of external lower lip
1403	Malignant neoplasm of upper lip, inner aspect	C003	C003 Malignant neoplasm of upper lip, inner aspect
1404	Malignant neoplasm of lower lip, inner aspect	C004	C004 Malignant neoplasm of lower lip, inner aspect
1405	Malignant neoplasm of lip, unspecified, inner aspect	C005	C005 Malignant neoplasm of lip, unspecified, inner aspect
1406	Malignant neoplasm of commissure of lip	C006	C006 Malignant neoplasm of commissure of lip, unspecified
1408	Malignant neoplasm of other sites of lip	C008	C008 Malignant neoplasm of overlapping sites of lip
1409	Malignant neoplasm of lip, unspecified, vermilion bor	C002	C002 Malignant neoplasm of external lip, unspecified
1410	Malignant neoplasm of base of tongue	C01	C01 Malignant neoplasm of base of tongue
1411	Malignant neoplasm of dorsal surface of tongue	C020	C020 Malignant neoplasm of dorsal surface of tongue
1412	Malignant neoplasm of tip and lateral border of tongu	C021	C021 Malignant neoplasm of border of tongue
1413	Malignant neoplasm of ventral surface of tongue	C022	C022 Malignant neoplasm of ventral surface of tongue
1414	Malignant neoplasm of anterior two-thirds of tongue,	C023	C023 Malignant neoplasm of anterior two-thirds of tongue, part unspecified
1415	Malignant neoplasm of junctional zone of tongue	C028	C028 Malignant neoplasm of overlapping sites of tongue
1416	Malignant neoplasm of lingual tonsil	C024	C024 Malignant neoplasm of lingual tonsil
1418	Malignant neoplasm of other sites of tongue	C028	C028 Malignant neoplasm of overlapping sites of tongue
1419	Malignant neoplasm of tongue, unspecified	C029	C029 Malignant neoplasm of tongue, unspecified
1420	Malignant neoplasm of parotid gland	C07	C07 Malignant neoplasm of parotid gland
1421	Malignant neoplasm of submandibular gland	C080	C080 Malignant neoplasm of submandibular gland
1422	Malignant neoplasm of sublingual gland	C081	C081 Malignant neoplasm of sublingual gland
1428	Malignant neoplasm of other major salivary glands	C089	C089 Malignant neoplasm of major salivary gland, unspecified
1429	Malignant neoplasm of salivary gland, unspecified	C089	C089 Malignant neoplasm of major salivary gland, unspecified
1430	Malignant neoplasm of upper gum	C030	C030 Malignant neoplasm of upper gum
1431	Malignant neoplasm of lower gum	C031	C031 Malignant neoplasm of lower gum
1438	Malignant neoplasm of other sites of gum	C039	C039 Malignant neoplasm of gum, unspecified
1439	Malignant neoplasm of gum, unspecified	C039	C039 Malignant neoplasm of gum, unspecified
1440	Malignant neoplasm of anterior portion of floor of mc	C040	C040 Malignant neoplasm of anterior floor of mouth
1441	Malignant neoplasm of lateral portion of floor of mou	C041	C041 Malignant neoplasm of lateral floor of mouth
1448	Malignant neoplasm of other sites of floor of mouth	C048	C048 Malignant neoplasm of overlapping sites of floor of mouth
1449	Malignant neoplasm of floor of mouth, part unspecifie	C049	C049 Malignant neoplasm of floor of mouth, unspecified
1450	Malignant neoplasm of cheek mucosa	C060	C060 Malignant neoplasm of cheek mucosa
1451	Malignant neoplasm of vestibule of mouth	C061	C061 Malignant neoplasm of vestibule of mouth
1452	Malignant neoplasm of hard palate	C050	C050 Malignant neoplasm of hard palate
1453	Malignant neoplasm of soft palate	C051	C051 Malignant neoplasm of soft palate
1454	Malignant neoplasm of uvula	C052	C052 Malignant neoplasm of uvula
1455	Malignant neoplasm of palate, unspecified	C059	C059 Malignant neoplasm of palate, unspecified
1456	Malignant neoplasm of retromolar area	C062	C062 Malignant neoplasm of retromolar area
1458	Malignant neoplasm of other specified parts of mouth	C0689	C0689 Malignant neoplasm of overlapping sites of other parts of mouth
1459	Malignant neoplasm of mouth, unspecified	C069	C069 Malignant neoplasm of mouth, unspecified
1460	Malignant neoplasm of tonsil	C099	C099 Malignant neoplasm of tonsil, unspecified
1461	Malignant neoplasm of tonsillar fossa	C090	C090 Malignant neoplasm of tonsillar fossa
1462	Malignant neoplasm of tonsillar pillars (anterior) (pos	C091	C091 Malignant neoplasm of tonsillar pillar (anterior) (posterior)
1463	Malignant neoplasm of vallecula epiglottica	C100	C100 Malignant neoplasm of vallecula
1464	Malignant neoplasm of anterior aspect of epiglottis	C101	C101 Malignant neoplasm of anterior surface of epiglottis
1465	Malignant neoplasm of junctional region of oropharyr	C108	C108 Malignant neoplasm of overlapping sites of oropharynx
1466	Malignant neoplasm of lateral wall of oropharynx	C102	C102 Malignant neoplasm of lateral wall of oropharynx
1467	Malignant neoplasm of posterior wall of oropharynx	C103	C103 Malignant neoplasm of posterior wall of oropharynx
1469	Malignant neoplasm of oropharynx, unspecified site	C109	C109 Malignant neoplasm of oropharynx, unspecified
1470	Malignant neoplasm of superior wall of nasopharynx	C110	C110 Malignant neoplasm of superior wall of nasopharynx
1471	Malignant neoplasm of posterior wall of nasopharynx	C111	C111 Malignant neoplasm of posterior wall of nasopharynx
1472	Malignant neoplasm of lateral wall of nasopharynx	C112	C112 Malignant neoplasm of lateral wall of nasopharynx
1473	Malignant neoplasm of anterior wall of nasopharynx	C113	C113 Malignant neoplasm of anterior wall of nasopharynx
1478	Malignant neoplasm of other specified sites of nasopl	C118	C118 Malignant neoplasm of overlapping sites of nasopharynx
1479	Malignant neoplasm of nasopharynx, unspecified site	C119	C119 Malignant neoplasm of nasopharynx, unspecified
1480	Malignant neoplasm of postcricoid region of hypopha	C130	C130 Malignant neoplasm of postcricoid region
1574	Malignant neoplasm of islets of langerhans	C254	C254 Malignant neoplasm of endocrine pancreas
1579	Malignant neoplasm of pancreas, part unspecified	C259	C259 Malignant neoplasm of pancreas, unspecified
1580	Malignant neoplasm of retroperitoneum	C480	C480 Malignant neoplasm of retroperitoneum
1589	Malignant neoplasm of peritoneum, unspecified	C482	C482 Malignant neoplasm of peritoneum, unspecified
1590	Malignant neoplasm of intestinal tract, part unspecifie	C260	C260 Malignant neoplasm of intestinal tract, part unspecified
1591	Malignant neoplasm of spleen, not elsewhere classifie	C261	C261 Malignant neoplasm of spleen
1598	Malignant neoplasm of other sites of digestive system	C269	C269 Malignant neoplasm of ill-defined sites within the digestive system
1599	Malignant neoplasm of ill-defined sites within the dig	C269	C269 Malignant neoplasm of ill-defined sites within the digestive system
1600	Malignant neoplasm of nasal cavities	C300	C300 Malignant neoplasm of nasal cavity
1601	Malignant neoplasm of auditory tube, middle ear, and	C301	C301 Malignant neoplasm of middle ear
1602	Malignant neoplasm of maxillary sinus	C310	C310 Malignant neoplasm of maxillary sinus
1603	Malignant neoplasm of ethmoidal sinus	C311	C311 Malignant neoplasm of ethmoidal sinus
1604	Malignant neoplasm of frontal sinus	C312	C312 Malignant neoplasm of frontal sinus
1605	Malignant neoplasm of sphenoidal sinus	C313	C313 Malignant neoplasm of sphenoid sinus
1608	Malignant neoplasm of other accessory sinuses	C318	C318 Malignant neoplasm of overlapping sites of accessory sinuses
1609	Malignant neoplasm of accessory sinus, unspecified	C319	C319 Malignant neoplasm of accessory sinus, unspecified
1610	Malignant neoplasm of glottis	C320	C320 Malignant neoplasm of glottis
1611	Malignant neoplasm of supraglottis	C321	C321 Malignant neoplasm of supraglottis
1612	Malignant neoplasm of subglottis	C322	C322 Malignant neoplasm of subglottis
1613	Malignant neoplasm of laryngeal cartilages	C323	C323 Malignant neoplasm of laryngeal cartilage
1618	Malignant neoplasm of other specified sites of larynx	C328	C328 Malignant neoplasm of overlapping sites of larynx
1619	Malignant neoplasm of larynx, unspecified	C329	C329 Malignant neoplasm of larynx, unspecified
1620	Malignant neoplasm of trachea	C33	C33 Malignant neoplasm of trachea
1622	Malignant neoplasm of main bronchus	C3400	C3400 Malignant neoplasm of unspecified main bronchus

1623	Malignant neoplasm of upper lobe, bronchus or lung	C3410	C3410 Malignant neoplasm of upper lobe, unspecified bronchus or lung
1624	Malignant neoplasm of middle lobe, bronchus or lung	C342	C342 Malignant neoplasm of middle lobe, bronchus or lung
1625	Malignant neoplasm of lower lobe, bronchus or lung	C3430	C3430 Malignant neoplasm of lower lobe, unspecified bronchus or lung
1628	Malignant neoplasm of other parts of bronchus or lun	C3480	C3480 Malignant neoplasm of overlapping sites of unspecified bronchus and lung
1629	Malignant neoplasm of bronchus and lung, unspecifie	C3490	C3490 Malignant neoplasm of unspecified part of unspecified bronchus or lung
1630	Malignant neoplasm of parietal pleura	C384	C384 Malignant neoplasm of pleura
1631	Malignant neoplasm of visceral pleura	C384	C384 Malignant neoplasm of pleura
1638	Malignant neoplasm of other specified sites of pleura	C384	C384 Malignant neoplasm of pleura
1639	Malignant neoplasm of pleura, unspecified	C384	C384 Malignant neoplasm of pleura
1640	Malignant neoplasm of thymus	C37	C37 Malignant neoplasm of thymus
1641	Malignant neoplasm of heart	C380	C380 Malignant neoplasm of heart
1642	Malignant neoplasm of anterior mediastinum	C381	C381 Malignant neoplasm of anterior mediastinum
1643	Malignant neoplasm of posterior mediastinum	C382	C382 Malignant neoplasm of posterior mediastinum
1648	Malignant neoplasm of other parts of mediastinum	C388	C388 Malignant neoplasm of overlapping sites of heart, mediastinum and pleura
1649	Malignant neoplasm of mediastinum, part unspecifiec	C383	C383 Malignant neoplasm of mediastinum, part unspecified
1650	Malignant neoplasm of upper respiratory tract, part u	C390	C390 Malignant neoplasm of upper respiratory tract, part unspecified
1658	Malignant neoplasm of other sites within the respirat	C399	C399 Malignant neoplasm of lower respiratory tract, part unspecified
1659	Malignant neoplasm of ill-defined sites within the res	C399	C399 Malignant neoplasm of lower respiratory tract, part unspecified
1700	Malignant neoplasm of bones of skull and face, excep	C410	C410 Malignant neoplasm of bones of skull and face
1701	Malignant neoplasm of mandible	C411	C411 Malignant neoplasm of mandible
1702	Malignant neoplasm of vertebral column, excluding sa	C412	C412 Malignant neoplasm of vertebral column
1703	Malignant neoplasm of ribs, sternum, and clavicle	C413	C413 Malignant neoplasm of ribs, sternum and clavicle
1704	Malignant neoplasm of scapula and long bones of upp	C4000	C4000 Malignant neoplasm of scapula and long bones of unspecified upper limb
1705	Malignant neoplasm of short bones of upper limb	C4010	C4010 Malignant neoplasm of short bones of unspecified upper limb
1706	Malignant neoplasm of pelvic bones, sacrum, and coc	C414	C414 Malignant neoplasm of pelvic bones, sacrum and coccyx
1707	Malignant neoplasm of long bones of lower limb	C4020	C4020 Malignant neoplasm of long bones of unspecified lower limb
1708	Malignant neoplasm of short bones of lower limb	C4030	C4030 Malignant neoplasm of short bones of unspecified lower limb
1709	Malignant neoplasm of bone and articular cartilage, si	C419	C419 Malignant neoplasm of bone and articular cartilage, unspecified
1710	Malignant neoplasm of connective and other soft tissu	C490	C490 Malignant neoplasm of connective and soft tissue of head, face and neck
1712	Malignant neoplasm of connective and other soft tissu	C4910	C4910 Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
1713	Malignant neoplasm of connective and other soft tissu	C4920	C4920 Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
1714	Malignant neoplasm of connective and other soft tissu	C493	C493 Malignant neoplasm of connective and soft tissue of thorax
1715	Malignant neoplasm of connective and other soft tissu	C494	C494 Malignant neoplasm of connective and soft tissue of abdomen
1716	Malignant neoplasm of connective and other soft tissu	C495	C495 Malignant neoplasm of connective and soft tissue of pelvis
1717	Malignant neoplasm of connective and other soft tissu	C496	C496 Malignant neoplasm of connective and soft tissue of trunk, unspecified
1719	Malignant neoplasm of connective and other soft tissu	C499	C499 Malignant neoplasm of connective and soft tissue, unspecified
1740	Malignant neoplasm of nipple and areola of female br	C50019	C50019 Malignant neoplasm of nipple and areola, unspecified female breast
1741	Malignant neoplasm of central portion of female brea	C50119	C50119 Malignant neoplasm of central portion of unspecified female breast
1742	Malignant neoplasm of upper-inner quadrant of fema	C50219	C50219 Malignant neoplasm of upper-inner quadrant of unspecified female breast
1743	Malignant neoplasm of lower-inner quadrant of fema	C50319	C50319 Malignant neoplasm of lower-inner quadrant of unspecified female breast
1744	Malignant neoplasm of upper-outer quadrant of fema	C50419	C50419 Malignant neoplasm of upper-outer quadrant of unspecified female breast
1745	Malignant neoplasm of lower-outer quadrant of fema	C50519	C50519 Malignant neoplasm of lower-outer quadrant of unspecified female breast
1746	Malignant neoplasm of axillary tail of female breast	C50619	C50619 Malignant neoplasm of axillary tail of unspecified female breast
1748	Malignant neoplasm of other specified sites of female	C50819	C50819 Malignant neoplasm of overlapping sites of unspecified female breast
1749	Malignant neoplasm of breast (female), unspecified	C50919	C50919 Malignant neoplasm of unspecified site of unspecified female breast
1750	Malignant neoplasm of nipple and areola of male bre	C50029	C50029 Malignant neoplasm of nipple and areola, unspecified male breast
1759	Malignant neoplasm of other and unspecified sites of	C50929	C50929 Malignant neoplasm of unspecified site of unspecified male breast
1760	Kaposi's sarcoma, skin	C460	C460 Kaposi's sarcoma of skin
1761	Kaposi's sarcoma, soft tissue	C461	C461 Kaposi's sarcoma of soft tissue
1762	Kaposi's sarcoma, palate	C462	C462 Kaposi's sarcoma of palate
1763	Kaposi's sarcoma, gastrointestinal sites	C464	C464 Kaposi's sarcoma of gastrointestinal sites
1764	Kaposi's sarcoma, lung	C4650	C4650 Kaposi's sarcoma of unspecified lung
1765	Kaposi's sarcoma, lymph nodes	C463	C463 Kaposi's sarcoma of lymph nodes
1768	Kaposi's sarcoma, other specified sites	C467	C467 Kaposi's sarcoma of other sites
1769	Kaposi's sarcoma, unspecified site	C469	C469 Kaposi's sarcoma, unspecified
179	Malignant neoplasm of uterus, part unspecified	C55	C55 Malignant neoplasm of uterus, part unspecified
1800	Malignant neoplasm of endocervix	C530	C530 Malignant neoplasm of endocervix
1801	Malignant neoplasm of exocervix	C531	C531 Malignant neoplasm of exocervix
1808	Malignant neoplasm of other specified sites of cervix	C538	C538 Malignant neoplasm of overlapping sites of cervix uteri
1809	Malignant neoplasm of cervix uteri, unspecified site	C539	C539 Malignant neoplasm of cervix uteri, unspecified
181	Malignant neoplasm of placenta	C58	C58 Malignant neoplasm of placenta
1821	Malignant neoplasm of isthmus	C540	C540 Malignant neoplasm of isthmus uteri
1828	Malignant neoplasm of other specified sites of body o	C548	C548 Malignant neoplasm of overlapping sites of corpus uteri
1830	Malignant neoplasm of ovary	C569	C569 Malignant neoplasm of unspecified ovary
1832	Malignant neoplasm of fallopian tube	C5700	C5700 Malignant neoplasm of unspecified fallopian tube
1833	Malignant neoplasm of broad ligament of uterus	C5710	C5710 Malignant neoplasm of unspecified broad ligament
1834	Malignant neoplasm of parametrium	C573	C573 Malignant neoplasm of parametrium
1835	Malignant neoplasm of round ligament of uterus	C5720	C5720 Malignant neoplasm of unspecified round ligament
1838	Malignant neoplasm of other specified sites of uterine	C574	C574 Malignant neoplasm of uterine adnexa, unspecified
1839	Malignant neoplasm of uterine adnexa, unspecified si	C574	C574 Malignant neoplasm of uterine adnexa, unspecified
1840	Malignant neoplasm of vagina	C52	C52 Malignant neoplasm of vagina
1841	Malignant neoplasm of labia majora	C510	C510 Malignant neoplasm of labium majus
1842	Malignant neoplasm of labia minora	C511	C511 Malignant neoplasm of labium minus
1843	Malignant neoplasm of clitoris	C512	C512 Malignant neoplasm of clitoris
1844	Malignant neoplasm of vulva, unspecified site	C519	C519 Malignant neoplasm of vulva, unspecified
1849	Malignant neoplasm of female genital organ, site uns	C579	C579 Malignant neoplasm of female genital organ, unspecified
185	Malignant neoplasm of prostate	C61	C61 Malignant neoplasm of prostate
1860	Malignant neoplasm of undescended testis	C6200	C6200 Malignant neoplasm of unspecified undescended testis
1871	Malignant neoplasm of prepuce	C600	C600 Malignant neoplasm of prepuce
1872	Malignant neoplasm of glans penis	C601	C601 Malignant neoplasm of glans penis
1873	Malignant neoplasm of body of penis	C602	C602 Malignant neoplasm of body of penis
1874	Malignant neoplasm of penis, part unspecified	C609	C609 Malignant neoplasm of penis, unspecified

1875	Malignant neoplasm of epididymis	C6300	C6300 Malignant neoplasm of unspecified epididymis
1876	Malignant neoplasm of spermatic cord	C6310	C6310 Malignant neoplasm of unspecified spermatic cord
1877	Malignant neoplasm of scrotum	C632	C632 Malignant neoplasm of scrotum
1879	Malignant neoplasm of male genital organ, site unspe	C639	C639 Malignant neoplasm of male genital organ, unspecified
1880	Malignant neoplasm of trigone of urinary bladder	C670	C670 Malignant neoplasm of trigone of bladder
1881	Malignant neoplasm of dome of urinary bladder	C671	C671 Malignant neoplasm of dome of bladder
1882	Malignant neoplasm of lateral wall of urinary bladder	C672	C672 Malignant neoplasm of lateral wall of bladder
1883	Malignant neoplasm of anterior wall of urinary bladde	C673	C673 Malignant neoplasm of anterior wall of bladder
1884	Malignant neoplasm of posterior wall of urinary bladd	C674	C674 Malignant neoplasm of posterior wall of bladder
1885	Malignant neoplasm of bladder neck	C675	C675 Malignant neoplasm of bladder neck
1886	Malignant neoplasm of ureteric orifice	C676	C676 Malignant neoplasm of ureteric orifice
1887	Malignant neoplasm of urachus	C677	C677 Malignant neoplasm of urachus
1888	Malignant neoplasm of other specified sites of bladde	C678	C678 Malignant neoplasm of overlapping sites of bladder
1889	Malignant neoplasm of bladder, part unspecified	C679	C679 Malignant neoplasm of bladder, unspecified
1890	Malignant neoplasm of kidney, except pelvis	C649	C649 Malignant neoplasm of unspecified kidney, except renal pelvis
1891	Malignant neoplasm of renal pelvis	C659	C659 Malignant neoplasm of unspecified renal pelvis
1892	Malignant neoplasm of ureter	C669	C669 Malignant neoplasm of unspecified ureter
1893	Malignant neoplasm of urethra	C680	C680 Malignant neoplasm of urethra
1894	Malignant neoplasm of paraurethral glands	C681	C681 Malignant neoplasm of paraurethral glands
1898	Malignant neoplasm of other specified sites of urinary	C688	C688 Malignant neoplasm of overlapping sites of urinary organs
1899	Malignant neoplasm of urinary organ, site unspecified	C689	C689 Malignant neoplasm of urinary organ, unspecified
1900	Malignant neoplasm of eyeball, except conjunctiva, cc	C6940	C6940 Malignant neoplasm of unspecified ciliary body
1901	Malignant neoplasm of orbit	C6960	C6960 Malignant neoplasm of unspecified orbit
1902	Malignant neoplasm of lacrimal gland	C6950	C6950 Malignant neoplasm of unspecified lacrimal gland and duct
1903	Malignant neoplasm of conjunctiva	C6900	C6900 Malignant neoplasm of unspecified conjunctiva
1904	Malignant neoplasm of cornea	C6910	C6910 Malignant neoplasm of unspecified cornea
1905	Malignant neoplasm of retina	C6920	C6920 Malignant neoplasm of unspecified retina
1906	Malignant neoplasm of choroid	C6930	C6930 Malignant neoplasm of unspecified choroid
1907	Malignant neoplasm of lacrimal duct	C6950	C6950 Malignant neoplasm of unspecified lacrimal gland and duct
1908	Malignant neoplasm of other specified sites of eye	C6980	C6980 Malignant neoplasm of overlapping sites of unspecified eye and adnexa
1909	Malignant neoplasm of eye, part unspecified	C6990	C6990 Malignant neoplasm of unspecified site of unspecified eye
1910	Malignant neoplasm of cerebrum, except lobes and ve	C710	C710 Malignant neoplasm of cerebrum, except lobes and ventricles
1911	Malignant neoplasm of frontal lobe	C711	C711 Malignant neoplasm of frontal lobe
1912	Malignant neoplasm of temporal lobe	C712	C712 Malignant neoplasm of temporal lobe
1913	Malignant neoplasm of parietal lobe	C713	C713 Malignant neoplasm of parietal lobe
1914	Malignant neoplasm of occipital lobe	C714	C714 Malignant neoplasm of occipital lobe
1915	Malignant neoplasm of ventricles	C715	C715 Malignant neoplasm of cerebral ventricle
1916	Malignant neoplasm of cerebellum nos	C716	C716 Malignant neoplasm of cerebellum
1917	Malignant neoplasm of brain stem	C717	C717 Malignant neoplasm of brain stem
1918	Malignant neoplasm of other parts of brain	C718	C718 Malignant neoplasm of overlapping sites of brain
1919	Malignant neoplasm of brain, unspecified	C719	C719 Malignant neoplasm of brain, unspecified
1920	Malignant neoplasm of cranial nerves	C7250	C7250 Malignant neoplasm of unspecified cranial nerve
1923	Malignant neoplasm of spinal meninges	C701	C701 Malignant neoplasm of spinal meninges
1928	Malignant neoplasm of other specified sites of nervou	C729	C729 Malignant neoplasm of central nervous system, unspecified
1929	Malignant neoplasm of nervous system, part unspecif	C729	C729 Malignant neoplasm of central nervous system, unspecified
193	Malignant neoplasm of thyroid gland	C73	C73 Malignant neoplasm of thyroid gland
1940	Malignant neoplasm of adrenal gland	C7490	C7490 Malignant neoplasm of unspecified part of unspecified adrenal gland
1941	Malignant neoplasm of parathyroid gland	C750	C750 Malignant neoplasm of parathyroid gland
1944	Malignant neoplasm of pineal gland	C753	C753 Malignant neoplasm of pineal gland
1945	Malignant neoplasm of carotid body	C754	C754 Malignant neoplasm of carotid body
1946	Malignant neoplasm of aortic body and other paragar	C755	C755 Malignant neoplasm of aortic body and other paraganglia
1948	Malignant neoplasm of other endocrine glands and re	C758	C758 Malignant neoplasm with pluriglandular involvement, unspecified
1949	Malignant neoplasm of endocrine gland, site unspecif	C759	C759 Malignant neoplasm of endocrine gland, unspecified
1950	Malignant neoplasm of head, face, and neck	C760	C760 Malignant neoplasm of head, face and neck
1951	Malignant neoplasm of thorax	C761	C761 Malignant neoplasm of thorax
1952	Malignant neoplasm of abdomen	C762	C762 Malignant neoplasm of abdomen
1953	Malignant neoplasm of pelvis	C763	C763 Malignant neoplasm of pelvis
1954	Malignant neoplasm of upper limb	C7640	C7640 Malignant neoplasm of unspecified upper limb
1955	Malignant neoplasm of lower limb	C7650	C7650 Malignant neoplasm of unspecified lower limb
1958	Malignant neoplasm of other specified sites	C768	C768 Malignant neoplasm of other specified ill-defined sites
1960	Secondary and unspecified malignant neoplasm of lyn	C770	C770 Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
1961	Secondary and unspecified malignant neoplasm of int	C771	C771 Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
1962	Secondary and unspecified malignant neoplasm of int	C772	C772 Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
1963	Secondary and unspecified malignant neoplasm of lyn	C773	C773 Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
1965	Secondary and unspecified malignant neoplasm of lyn	C774	C774 Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes
1966	Secondary and unspecified malignant neoplasm of int	C775	C775 Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
1968	Secondary and unspecified malignant neoplasm of lyn	C778	C778 Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
1969	Secondary and unspecified malignant neoplasm of lyn	C779	C779 Secondary and unspecified malignant neoplasm of lymph node, unspecified
1970	Secondary malignant neoplasm of lung	C7800	C7800 Secondary malignant neoplasm of unspecified lung
1971	Secondary malignant neoplasm of mediastinum	C781	C781 Secondary malignant neoplasm of mediastinum
1972	Secondary malignant neoplasm of pleura	C782	C782 Secondary malignant neoplasm of pleura
1973	Secondary malignant neoplasm of other respiratory o	C7839	C7839 Secondary malignant neoplasm of other respiratory organs
1974	Secondary malignant neoplasm of small intestine incl	C784	C784 Secondary malignant neoplasm of small intestine
1975	Secondary malignant neoplasm of large intestine and	C785	C785 Secondary malignant neoplasm of large intestine and rectum
1976	Secondary malignant neoplasm of retroperitoneum a	C786	C786 Secondary malignant neoplasm of retroperitoneum and peritoneum
1977	Malignant neoplasm of liver, secondary	C787	C787 Secondary malignant neoplasm of liver and intrahepatic bile duct
1978	Secondary malignant neoplasm of other digestive org	C787	C787 Secondary malignant neoplasm of liver and intrahepatic bile duct
1978	Secondary malignant neoplasm of other digestive org	C7889	C7889 Secondary malignant neoplasm of other digestive organs
1980	Secondary malignant neoplasm of kidney	C7900	C7900 Secondary malignant neoplasm of unspecified kidney and renal pelvis
1982	Secondary malignant neoplasm of skin	C792	C792 Secondary malignant neoplasm of skin
1983	Secondary malignant neoplasm of brain and spinal co	C7931	C7931 Secondary malignant neoplasm of brain
1986	Secondary malignant neoplasm of ovary	C7960	C7960 Secondary malignant neoplasm of unspecified ovary

1987	Secondary malignant neoplasm of adrenal gland	C7970	C7970 Secondary malignant neoplasm of unspecified adrenal gland
19881	Secondary malignant neoplasm of breast	C7981	C7981 Secondary malignant neoplasm of breast
19882	Secondary malignant neoplasm of genital organs	C7982	C7982 Secondary malignant neoplasm of genital organs
19889	Secondary malignant neoplasm of other specified site	C7989	C7989 Secondary malignant neoplasm of other specified sites
1990	Disseminated malignant neoplasm without specificati	C800	C800 Disseminated malignant neoplasm, unspecified
1991	Other malignant neoplasm without specification of sit	C801	C801 Malignant (primary) neoplasm, unspecified
1992	Malignant neoplasm associated with transplant organ	C802	C802 Malignant neoplasm associated with transplanted organ
20001	Reticulosarcoma, lymph nodes of head, face, and nec	C8331	C8331 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
20002	Reticulosarcoma, intrathoracic lymph nodes	C8332	C8332 Diffuse large B-cell lymphoma, intrathoracic lymph nodes
20003	Reticulosarcoma, intra-abdominal lymph nodes	C8333	C8333 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
20004	Reticulosarcoma, lymph nodes of axilla and upper lim	C8334	C8334 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
20005	Reticulosarcoma, lymph nodes of inguinal region and	C8335	C8335 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
20006	Reticulosarcoma, intrapelvic lymph nodes	C8336	C8336 Diffuse large B-cell lymphoma, intrapelvic lymph nodes
20007	Reticulosarcoma, spleen	C8337	C8337 Diffuse large B-cell lymphoma, spleen
20008	Reticulosarcoma, lymph nodes of multiple sites	C8338	C8338 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
20011	Lymphosarcoma, lymph nodes of head, face, and nec	C8351	C8351 Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
20012	Lymphosarcoma, intrathoracic lymph nodes	C8352	C8352 Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
20013	Lymphosarcoma, intra-abdominal lymph nodes	C8353	C8353 Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
20014	Lymphosarcoma, lymph nodes of axilla and upper lim	C8354	C8354 Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
20015	Lymphosarcoma, lymph nodes of inguinal region and	C8355	C8355 Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
20016	Lymphosarcoma, intrapelvic lymph nodes	C8356	C8356 Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
20017	Lymphosarcoma, spleen	C8357	C8357 Lymphoblastic (diffuse) lymphoma, spleen
20018	Lymphosarcoma, lymph nodes of multiple sites	C8358	C8358 Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
20021	Burkitt's tumor or lymphoma, lymph nodes of head, f	C8371	C8371 Burkitt lymphoma, lymph nodes of head, face, and neck
20022	Burkitt's tumor or lymphoma, intrathoracic lymph noc	C8372	C8372 Burkitt lymphoma, intrathoracic lymph nodes
20023	Burkitt's tumor or lymphoma, intra-abdominal lymph	C8373	C8373 Burkitt lymphoma, intra-abdominal lymph nodes
20024	Burkitt's tumor or lymphoma, lymph nodes of axilla a	C8374	C8374 Burkitt lymphoma, lymph nodes of axilla and upper limb
20025	Burkitt's tumor or lymphoma, lymph nodes of inguina	C8375	C8375 Burkitt lymphoma, lymph nodes of inguinal region and lower limb
20026	Burkitt's tumor or lymphoma, intrapelvic lymph node	C8376	C8376 Burkitt lymphoma, intrapelvic lymph nodes
20027	Burkitt's tumor or lymphoma, spleen	C8377	C8377 Burkitt lymphoma, spleen
20028	Burkitt's tumor or lymphoma, lymph nodes of multipl	C8378	C8378 Burkitt lymphoma, lymph nodes of multiple sites
20031	Marginal zone lymphoma, lymph nodes of head, face,	C8381	C8381 Other non-follicular lymphoma, lymph nodes of head, face, and neck
20032	Marginal zone lymphoma, intrathoracic lymph nodes	C8382	C8382 Other non-follicular lymphoma, intrathoracic lymph nodes
20033	Marginal zone lymphoma, intraabdominal lymph nod	C8383	C8383 Other non-follicular lymphoma, intra-abdominal lymph nodes
20034	Marginal zone lymphoma, lymph nodes of axilla and u	C8384	C8384 Other non-follicular lymphoma, lymph nodes of axilla and upper limb
20035	Marginal zone lymphoma, lymph nodes of inguinal re	C8385	C8385 Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
20036	Marginal zone lymphoma, intrapelvic lymph nodes	C8386	C8386 Other non-follicular lymphoma, intrapelvic lymph nodes
20037	Marginal zone lymphoma, spleen	C8387	C8387 Other non-follicular lymphoma, spleen
20038	Marginal zone lymphoma, lymph nodes of multiple sit	C8388	C8388 Other non-follicular lymphoma, lymph nodes of multiple sites
20041	Mantle cell lymphoma, lymph nodes of head, face, an	C8311	C8311 Mantle cell lymphoma, lymph nodes of head, face, and neck
20042	Mantle cell lymphoma, intrathoracic lymph nodes	C8312	C8312 Mantle cell lymphoma, intrathoracic lymph nodes
20043	Mantle cell lymphoma, intra-abdominal lymph nodes	C8313	C8313 Mantle cell lymphoma, intra-abdominal lymph nodes
20044	Mantle cell lymphoma, lymph nodes of axilla and upp	C8314	C8314 Mantle cell lymphoma, lymph nodes of axilla and upper limb
20045	Mantle cell lymphoma, lymph nodes of inguinal regio	C8315	C8315 Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
20046	Mantle cell lymphoma, intrapelvic lymph nodes	C8316	C8316 Mantle cell lymphoma, intrapelvic lymph nodes
20047	Mantle cell lymphoma, spleen	C8317	C8317 Mantle cell lymphoma, spleen
20048	Mantle cell lymphoma, lymph nodes of multiple sites	C8318	C8318 Mantle cell lymphoma, lymph nodes of multiple sites
20070	Large cell lymphoma, unspecified site, extranodal and	C8339	C8339 Diffuse large B-cell lymphoma, extranodal and solid organ sites
20071	Large cell lymphoma, lymph nodes of head, face, and	C8331	C8331 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
20072	Large cell lymphoma, intrathoracic lymph nodes	C8332	C8332 Diffuse large B-cell lymphoma, intrathoracic lymph nodes
20073	Large cell lymphoma, intra-abdominal lymph nodes	C8333	C8333 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
20074	Large cell lymphoma, lymph nodes of axilla and upper	C8334	C8334 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
20075	Large cell lymphoma, lymph nodes of inguinal region	C8335	C8335 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
20076	Large cell lymphoma, intrapelvic lymph nodes	C8336	C8336 Diffuse large B-cell lymphoma, intrapelvic lymph nodes
20077	Large cell lymphoma, spleen	C8337	C8337 Diffuse large B-cell lymphoma, spleen
20078	Large cell lymphoma, lymph nodes of multiple sites	C8338	C8338 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
20081	Other named variants of lymphosarcoma and reticulo	C8381	C8381 Other non-follicular lymphoma, lymph nodes of head, face, and neck
20082	Other named variants of lymphosarcoma and reticulo	C8382	C8382 Other non-follicular lymphoma, intrathoracic lymph nodes
20083	Other named variants of lymphosarcoma and reticulo	C8383	C8383 Other non-follicular lymphoma, intra-abdominal lymph nodes
20084	Other named variants of lymphosarcoma and reticulo	C8384	C8384 Other non-follicular lymphoma, lymph nodes of axilla and upper limb
20085	Other named variants of lymphosarcoma and reticulo	C8385	C8385 Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
20086	Other named variants of lymphosarcoma and reticulo	C8386	C8386 Other non-follicular lymphoma, intrapelvic lymph nodes
20087	Other named variants of lymphosarcoma and reticulo	C8387	C8387 Other non-follicular lymphoma, spleen
20088	Other named variants of lymphosarcoma and reticulo	C8388	C8388 Other non-follicular lymphoma, lymph nodes of multiple sites
20101	Hodgkin's paragranuloma, lymph nodes of head, face,	C8171	C8171 Other classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20102	Hodgkin's paragranuloma, intrathoracic lymph nodes	C8172	C8172 Other classical Hodgkin lymphoma, intrathoracic lymph nodes
20103	Hodgkin's paragranuloma, intra-abdominal lymph noc	C8173	C8173 Other classical Hodgkin lymphoma, intra-abdominal lymph nodes
20104	Hodgkin's paragranuloma, lymph nodes of axilla and u	C8174	C8174 Other classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20105	Hodgkin's paragranuloma, lymph nodes of inguinal re	C8175	C8175 Other classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20106	Hodgkin's paragranuloma, intrapelvic lymph nodes	C8176	C8176 Other classical Hodgkin lymphoma, intrapelvic lymph nodes
20107	Hodgkin's paragranuloma, spleen	C8177	C8177 Other classical Hodgkin lymphoma, spleen
20108	Hodgkin's paragranuloma, lymph nodes of multiple sit	C8178	C8178 Other classical Hodgkin lymphoma, lymph nodes of multiple sites
20110	Hodgkin's granuloma, unspecified site, extranodal and	C8179	C8179 Other classical Hodgkin lymphoma, extranodal and solid organ sites
20111	Hodgkin's granuloma, lymph nodes of head, face, and	C8171	C8171 Other classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20112	Hodgkin's granuloma, intrathoracic lymph nodes	C8172	C8172 Other classical Hodgkin lymphoma, intrathoracic lymph nodes
20113	Hodgkin's granuloma, intra-abdominal lymph nodes	C8173	C8173 Other classical Hodgkin lymphoma, intra-abdominal lymph nodes
20114	Hodgkin's granuloma, lymph nodes of axilla and uppe	C8174	C8174 Other classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20115	Hodgkin's granuloma, lymph nodes of inguinal region	C8175	C8175 Other classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20116	Hodgkin's granuloma, intrapelvic lymph nodes	C8176	C8176 Other classical Hodgkin lymphoma, intrapelvic lymph nodes
20117	Hodgkin's granuloma, spleen	C8177	C8177 Other classical Hodgkin lymphoma, spleen
20118	Hodgkin's granuloma, lymph nodes of multiple sites	C8178	C8178 Other classical Hodgkin lymphoma, lymph nodes of multiple sites
20120	Hodgkin's sarcoma, unspecified site, extranodal and s	C8179	C8179 Other classical Hodgkin lymphoma, extranodal and solid organ sites

20121	Hodgkin's sarcoma, lymph nodes of head, face, and n	C8171	C8171	Other classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20122	Hodgkin's sarcoma, intrathoracic lymph nodes	C8172	C8172	Other classical Hodgkin lymphoma, intrathoracic lymph nodes
20123	Hodgkin's sarcoma, intra-abdominal lymph nodes	C8173	C8173	Other classical Hodgkin lymphoma, intra-abdominal lymph nodes
20124	Hodgkin's sarcoma, lymph nodes of axilla and upper li	C8174	C8174	Other classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20125	Hodgkin's sarcoma, lymph nodes of inguinal region an	C8175	C8175	Other classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20126	Hodgkin's sarcoma, intrapelvic lymph nodes	C8176	C8176	Other classical Hodgkin lymphoma, intrapelvic lymph nodes
20127	Hodgkin's sarcoma, spleen	C8177	C8177	Other classical Hodgkin lymphoma, spleen
20128	Hodgkin's sarcoma, lymph nodes of multiple sites	C8178	C8178	Other classical Hodgkin lymphoma, lymph nodes of multiple sites
20151	Hodgkin's disease, nodular sclerosis, lymph nodes of h	C8111	C8111	Nodular sclerosis classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20152	Hodgkin's disease, nodular sclerosis, intrathoracic lym	C8112	C8112	Nodular sclerosis classical Hodgkin lymphoma, intrathoracic lymph nodes
20153	Hodgkin's disease, nodular sclerosis, intra-abdominal	C8113	C8113	Nodular sclerosis classical Hodgkin lymphoma, intra-abdominal lymph nodes
20154	Hodgkin's disease, nodular sclerosis, lymph nodes of a	C8114	C8114	Nodular sclerosis classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20155	Hodgkin's disease, nodular sclerosis, lymph nodes of i	C8115	C8115	Nodular sclerosis classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20156	Hodgkin's disease, nodular sclerosis, intrapelvic lymph	C8116	C8116	Nodular sclerosis classical Hodgkin lymphoma, intrapelvic lymph nodes
20157	Hodgkin's disease, nodular sclerosis, spleen	C8117	C8117	Nodular sclerosis classical Hodgkin lymphoma, spleen
20158	Hodgkin's disease, nodular sclerosis, lymph nodes of r	C8118	C8118	Nodular sclerosis classical Hodgkin lymphoma, lymph nodes of multiple sites
20161	Hodgkin's disease, mixed cellularity, lymph nodes of h	C8121	C8121	Mixed cellularity classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20162	Hodgkin's disease, mixed cellularity, intrathoracic lym	C8122	C8122	Mixed cellularity classical Hodgkin lymphoma, intrathoracic lymph nodes
20163	Hodgkin's disease, mixed cellularity, intra-abdominal l	C8123	C8123	Mixed cellularity classical Hodgkin lymphoma, intra-abdominal lymph nodes
20164	Hodgkin's disease, mixed cellularity, lymph nodes of a	C8124	C8124	Mixed cellularity classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20165	Hodgkin's disease, mixed cellularity, lymph nodes of i	C8125	C8125	Mixed cellularity classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20166	Hodgkin's disease, mixed cellularity, intrapelvic lymph	C8126	C8126	Mixed cellularity classical Hodgkin lymphoma, intrapelvic lymph nodes
20167	Hodgkin's disease, mixed cellularity, spleen	C8127	C8127	Mixed cellularity classical Hodgkin lymphoma, spleen
20168	Hodgkin's disease, mixed cellularity, lymph nodes of n	C8128	C8128	Mixed cellularity classical Hodgkin lymphoma, lymph nodes of multiple sites
20171	Hodgkin's disease, lymphocytic depletion, lymph node	C8131	C8131	Lymphocyte depleted classical Hodgkin lymphoma, lymph nodes of head, face, and neck
20172	Hodgkin's disease, lymphocytic depletion, intrathorac	C8132	C8132	Lymphocyte depleted classical Hodgkin lymphoma, intrathoracic lymph nodes
20173	Hodgkin's disease, lymphocytic depletion, intra-abdor	C8133	C8133	Lymphocyte depleted classical Hodgkin lymphoma, intra-abdominal lymph nodes
20174	Hodgkin's disease, lymphocytic depletion, lymph node	C8134	C8134	Lymphocyte depleted classical Hodgkin lymphoma, lymph nodes of axilla and upper limb
20175	Hodgkin's disease, lymphocytic depletion, lymph node	C8135	C8135	Lymphocyte depleted classical Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20176	Hodgkin's disease, lymphocytic depletion, intrapelvic l	C8136	C8136	Lymphocyte depleted classical Hodgkin lymphoma, intrapelvic lymph nodes
20177	Hodgkin's disease, lymphocytic depletion, spleen	C8137	C8137	Lymphocyte depleted classical Hodgkin lymphoma, spleen
20178	Hodgkin's disease, lymphocytic depletion, lymph node	C8138	C8138	Lymphocyte depleted classical Hodgkin lymphoma, lymph nodes of multiple sites
20191	Hodgkin's disease, unspecified type, lymph nodes of h	C8191	C8191	Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
20192	Hodgkin's disease, unspecified type, intrathoracic lym	C8192	C8192	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
20193	Hodgkin's disease, unspecified type, intra-abdominal l	C8193	C8193	Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
20194	Hodgkin's disease, unspecified type, lymph nodes of a	C8194	C8194	Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
20195	Hodgkin's disease, unspecified type, lymph nodes of i	C8195	C8195	Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
20196	Hodgkin's disease, unspecified type, intrapelvic lymph	C8196	C8196	Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
20197	Hodgkin's disease, unspecified type, spleen	C8197	C8197	Hodgkin lymphoma, unspecified, spleen
20198	Hodgkin's disease, unspecified type, lymph nodes of n	C8198	C8198	Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
20201	Nodular lymphoma, lymph nodes of head, face, and n	C8291	C8291	Follicular lymphoma, unspecified, lymph nodes of head, face, and neck
20202	Nodular lymphoma, intrathoracic lymph nodes	C8292	C8292	Follicular lymphoma, unspecified, intrathoracic lymph nodes
20203	Nodular lymphoma, intra-abdominal lymph nodes	C8293	C8293	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
20204	Nodular lymphoma, lymph nodes of axilla and upper l	C8294	C8294	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
20205	Nodular lymphoma, lymph nodes of inguinal region a	C8295	C8295	Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb
20206	Nodular lymphoma, intrapelvic lymph nodes	C8296	C8296	Follicular lymphoma, unspecified, intrapelvic lymph nodes
20207	Nodular lymphoma, spleen	C8297	C8297	Follicular lymphoma, unspecified, spleen
20208	Nodular lymphoma, lymph nodes of multiple sites	C8298	C8298	Follicular lymphoma, unspecified, lymph nodes of multiple sites
20211	Mycosis fungoides, lymph nodes of head, face, and ne	C8401	C8401	Mycosis fungoides, lymph nodes of head, face, and neck
20212	Mycosis fungoides, intrathoracic lymph nodes	C8402	C8402	Mycosis fungoides, intrathoracic lymph nodes
20214	Mycosis fungoides, lymph nodes of axilla and upper li	C8404	C8404	Mycosis fungoides, lymph nodes of axilla and upper limb
20215	Mycosis fungoides, lymph nodes of inguinal region an	C8405	C8405	Mycosis fungoides, lymph nodes of inguinal region and lower limb
20216	Mycosis fungoides, intrapelvic lymph nodes	C8406	C8406	Mycosis fungoides, intrapelvic lymph nodes
20217	Mycosis fungoides, spleen	C8407	C8407	Mycosis fungoides, spleen
20218	Mycosis fungoides, lymph nodes of multiple sites	C8408	C8408	Mycosis fungoides, lymph nodes of multiple sites
20221	Sezary's disease, lymph nodes of head, face, and neck	C8411	C8411	Sezary disease, lymph nodes of head, face, and neck
20222	Sezary's disease, intrathoracic lymph nodes	C8412	C8412	Sezary disease, intrathoracic lymph nodes
20223	Sezary's disease, intra-abdominal lymph nodes	C8413	C8413	Sezary disease, intra-abdominal lymph nodes
20224	Sezary's disease, lymph nodes of axilla and upper limb	C8414	C8414	Sezary disease, lymph nodes of axilla and upper limb
20225	Sezary's disease, lymph nodes of inguinal region and l	C8415	C8415	Sezary disease, lymph nodes of inguinal region and lower limb
20226	Sezary's disease, intrapelvic lymph nodes	C8416	C8416	Sezary disease, intrapelvic lymph nodes
20227	Sezary's disease, spleen	C8417	C8417	Sezary disease, spleen
20228	Sezary's disease, lymph nodes of multiple sites	C8418	C8418	Sezary disease, lymph nodes of multiple sites
20230	Malignant histiocytosis, unspecified site, extranodal a	C96A	C96A	Histiocytic sarcoma
20231	Malignant histiocytosis, lymph nodes of head, face, ar	C96A	C96A	Histiocytic sarcoma
20232	Malignant histiocytosis, intrathoracic lymph nodes	C96A	C96A	Histiocytic sarcoma
20233	Malignant histiocytosis, intra-abdominal lymph nodes	C96A	C96A	Histiocytic sarcoma
20234	Malignant histiocytosis, lymph nodes of axilla and upp	C96A	C96A	Histiocytic sarcoma
20235	Malignant histiocytosis, lymph nodes of inguinal regio	C96A	C96A	Histiocytic sarcoma
20236	Malignant histiocytosis, intrapelvic lymph nodes	C96A	C96A	Histiocytic sarcoma
20237	Malignant histiocytosis, spleen	C96A	C96A	Histiocytic sarcoma
20238	Malignant histiocytosis, lymph nodes of multiple sites	C96A	C96A	Histiocytic sarcoma
20241	Leukemic reticuloendotheliosis, lymph nodes of head,	C9140	C9140	Hairy cell leukemia not having achieved remission
20242	Leukemic reticuloendotheliosis, intrathoracic lymph n	C9140	C9140	Hairy cell leukemia not having achieved remission
20243	Leukemic reticuloendotheliosis, intra-abdominal lymp	C9140	C9140	Hairy cell leukemia not having achieved remission
20244	Leukemic reticuloendotheliosis, lymph nodes of axilla	C9140	C9140	Hairy cell leukemia not having achieved remission
20245	Leukemic reticuloendotheliosis, lymph nodes of inguin	C9140	C9140	Hairy cell leukemia not having achieved remission
20246	Leukemic reticuloendotheliosis, intrapelvic lymph noc	C9140	C9140	Hairy cell leukemia not having achieved remission
20247	Leukemic reticuloendotheliosis, spleen	C9140	C9140	Hairy cell leukemia not having achieved remission
20248	Leukemic reticuloendotheliosis, lymph nodes of multi	C9140	C9140	Hairy cell leukemia not having achieved remission
20250	Letterer-siwe disease, unspecified site, extranodal an	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20251	Letterer-siwe disease, lymph nodes of head, face, and	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis

20252	Letterer-siwe disease, intrathoracic lymph nodes	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20253	Letterer-siwe disease, intra-abdominal lymph nodes	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20254	Letterer-siwe disease, lymph nodes of axilla and uppe	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20255	Letterer-siwe disease, lymph nodes of inguinal region	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20256	Letterer-siwe disease, intrapelvic lymph nodes	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20257	Letterer-siwe disease, spleen	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20258	Letterer-siwe disease, lymph nodes of multiple sites	C960	C960	Multifocal and multisystemic (disseminated) Langerhans-cell histiocytosis
20260	Malignant mast cell tumors, unspecified site, extranoc	C962	C962	Malignant mast cell tumor
20261	Malignant mast cell tumors, lymph nodes of head, fac	C962	C962	Malignant mast cell tumor
20262	Malignant mast cell tumors, intrathoracic lymph node	C962	C962	Malignant mast cell tumor
20263	Malignant mast cell tumors, intra-abdominal lymph n	C962	C962	Malignant mast cell tumor
20264	Malignant mast cell tumors, lymph nodes of axilla anc	C962	C962	Malignant mast cell tumor
20265	Malignant mast cell tumors, lymph nodes of inguinal r	C962	C962	Malignant mast cell tumor
20266	Malignant mast cell tumors, intrapelvic lymph nodes	C962	C962	Malignant mast cell tumor
20267	Malignant mast cell tumors, spleen	C962	C962	Malignant mast cell tumor
20268	Malignant mast cell tumors, lymph nodes of multiple	C962	C962	Malignant mast cell tumor
20271	Peripheral T cell lymphoma, lymph nodes of head, fac	C8441	C8441	Peripheral T-cell lymphoma, not classified, lymph nodes of head, face, and neck
20272	Peripheral T cell lymphoma, intrathoracic lymph node	C8442	C8442	Peripheral T-cell lymphoma, not classified, intrathoracic lymph nodes
20273	Peripheral T cell lymphoma, intra-abdominal lymph n	C8443	C8443	Peripheral T-cell lymphoma, not classified, intra-abdominal lymph nodes
20274	Peripheral T cell lymphoma, lymph nodes of axilla anc	C8444	C8444	Peripheral T-cell lymphoma, not classified, lymph nodes of axilla and upper limb
20275	Peripheral T cell lymphoma, lymph nodes of inguinal r	C8445	C8445	Peripheral T-cell lymphoma, not classified, lymph nodes of inguinal region and lower limb
20276	Peripheral T cell lymphoma, intrapelvic lymph nodes	C8446	C8446	Peripheral T-cell lymphoma, not classified, intrapelvic lymph nodes
20277	Peripheral T cell lymphoma, spleen	C8447	C8447	Peripheral T-cell lymphoma, not classified, spleen
20278	Peripheral T cell lymphoma, lymph nodes of multiple	C8448	C8448	Peripheral T-cell lymphoma, not classified, lymph nodes of multiple sites
20281	Other malignant lymphomas, lymph nodes of head, fa	C8581	C8581	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
20282	Other malignant lymphomas, intrathoracic lymph nod	C8582	C8582	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
20283	Other malignant lymphomas, intra-abdominal lymph	C8493	C8493	Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes
20283	Other malignant lymphomas, intra-abdominal lymph	C8583	C8583	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
20284	Other malignant lymphomas, lymph nodes of axilla ar	C8584	C8584	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
20285	Other malignant lymphomas, lymph nodes of inguinal	C8585	C8585	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
20286	Other malignant lymphomas, intrapelvic lymph nodes	C8586	C8586	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
20287	Other malignant lymphomas, spleen	C8587	C8587	Other specified types of non-Hodgkin lymphoma, spleen
20288	Other malignant lymphomas, lymph nodes of multiple	C8588	C8588	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
20300	Multiple myeloma, without mention of having achieve	C9000	C9000	Multiple myeloma not having achieved remission
20301	Multiple myeloma, in remission	C9001	C9001	Multiple myeloma in remission
20302	Multiple myeloma, in relapse	C9002	C9002	Multiple myeloma in relapse
20310	Plasma cell leukemia, without mention of having achi	C9010	C9010	Plasma cell leukemia not having achieved remission
20311	Plasma cell leukemia, in remission	C9011	C9011	Plasma cell leukemia in remission
20312	Plasma cell leukemia, in relapse	C9012	C9012	Plasma cell leukemia in relapse
20400	Acute lymphoid leukemia, without mention of having	C9100	C9100	Acute lymphoblastic leukemia not having achieved remission
20401	Acute lymphoid leukemia, in remission	C9101	C9101	Acute lymphoblastic leukemia, in remission
20402	Acute lymphoid leukemia, in relapse	C9102	C9102	Acute lymphoblastic leukemia, in relapse
20410	Chronic lymphoid leukemia, without mention of havir	C9110	C9110	Chronic lymphocytic leukemia of B-cell type not having achieved remission
20411	Chronic lymphoid leukemia, in remission	C9111	C9111	Chronic lymphocytic leukemia of B-cell type in remission
20412	Chronic lymphoid leukemia, in relapse	C9112	C9112	Chronic lymphocytic leukemia of B-cell type in relapse
20420	Subacute lymphoid leukemia, without mention of hav	C91Z0	C91Z0	Other lymphoid leukemia not having achieved remission
20421	Subacute lymphoid leukemia, in remission	C91Z1	C91Z1	Other lymphoid leukemia, in remission
20422	Subacute lymphoid leukemia, in relapse	C91Z2	C91Z2	Other lymphoid leukemia, in relapse
20480	Other lymphoid leukemia, without mention of having	C91Z0	C91Z0	Other lymphoid leukemia not having achieved remission
20481	Other lymphoid leukemia, in remission	C91Z1	C91Z1	Other lymphoid leukemia, in remission
20482	Other lymphoid leukemia, in relapse	C91Z2	C91Z2	Other lymphoid leukemia, in relapse
20490	Unspecified lymphoid leukemia, without mention of h	C9190	C9190	Lymphoid leukemia, unspecified not having achieved remission
20491	Unspecified lymphoid leukemia, in remission	C9191	C9191	Lymphoid leukemia, unspecified, in remission
20492	Unspecified lymphoid leukemia, in relapse	C9192	C9192	Lymphoid leukemia, unspecified, in relapse
20510	Chronic myeloid leukemia, without mention of having	C9210	C9210	Chronic myeloid leukemia, BCR/ABL-positive, not having achieved remission
20511	Chronic myeloid leukemia, in remission	C9211	C9211	Chronic myeloid leukemia, BCR/ABL-positive, in remission
20512	Chronic myeloid leukemia, in relapse	C9212	C9212	Chronic myeloid leukemia, BCR/ABL-positive, in relapse
20520	Subacute myeloid leukemia, without mention of havir	C9220	C9220	Atypical chronic myeloid leukemia, BCR/ABL-negative, not having achieved remission
20521	Subacute myeloid leukemia,in remission	C9221	C9221	Atypical chronic myeloid leukemia, BCR/ABL-negative, in remission
20522	Subacute myeloid leukemia, in relapse	C9222	C9222	Atypical chronic myeloid leukemia, BCR/ABL-negative, in relapse
20530	Myeloid sarcoma, without mention of having achieve	C9230	C9230	Myeloid sarcoma, not having achieved remission
20531	Myeloid sarcoma, in remission	C9231	C9231	Myeloid sarcoma, in remission
20532	Myeloid sarcoma, in relapse	C9232	C9232	Myeloid sarcoma, in relapse
20580	Other myeloid leukemia, without mention of having a	C92Z0	C92Z0	Other myeloid leukemia not having achieved remission
20581	Other myeloid leukemia, in remission	C92Z1	C92Z1	Other myeloid leukemia, in remission
20582	Other myeloid leukemia, in relapse	C92Z2	C92Z2	Other myeloid leukemia, in relapse
20590	Unspecified myeloid leukemia, without mention of ha	C9290	C9290	Myeloid leukemia, unspecified, not having achieved remission
20591	Unspecified myeloid leukemia, in remission	C9291	C9291	Myeloid leukemia, unspecified in remission
20592	Unspecified myeloid leukemia, in relapse	C9292	C9292	Myeloid leukemia, unspecified in relapse
20600	Acute monocytic leukemia, without mention of havin	C9300	C9300	Acute monoblastic/monocytic leukemia, not having achieved remission
20601	Acute monocytic leukemia,in remission	C9301	C9301	Acute monoblastic/monocytic leukemia, in remission
20602	Acute monocytic leukemia, in relapse	C9302	C9302	Acute monoblastic/monocytic leukemia, in relapse
20610	Chronic monocytic leukemia, without mention of havi	C9310	C9310	Chronic myelomonocytic leukemia not having achieved remission
20611	Chronic monocytic leukemia, in remission	C9311	C9311	Chronic myelomonocytic leukemia, in remission
20612	Chronic monocytic leukemia, in relapse	C9312	C9312	Chronic myelomonocytic leukemia, in relapse
20620	Subacute monocytic leukemia, without mention of ha	C9390	C9390	Monocytic leukemia, unspecified, not having achieved remission
20621	Subacute monocytic leukemia, in remission	C9391	C9391	Monocytic leukemia, unspecified in remission
20622	Subacute monocytic leukemia, in relapse	C9392	C9392	Monocytic leukemia, unspecified in relapse
20680	Other monocytic leukemia, without mention of havin	C93Z0	C93Z0	Other monocytic leukemia, not having achieved remission
20681	Other monocytic leukemia, in remission	C93Z1	C93Z1	Other monocytic leukemia, in remission
20682	Other monocytic leukemia, in relapse	C93Z2	C93Z2	Other monocytic leukemia, in relapse
20690	Unspecified monocytic leukemia, without mention of	C9390	C9390	Monocytic leukemia, unspecified, not having achieved remission

20691	Unspecified monocytic leukemia, in remission	C9391	C9391 Monocytic leukemia, unspecified in remission
20692	Unspecified monocytic leukemia, in relapse	C9392	C9392 Monocytic leukemia, unspecified in relapse
20700	Acute erythremia and erythroleukemia, without ment	C9400	C9400 Acute erythroid leukemia, not having achieved remission
20701	Acute erythremia and erythroleukemia, in remission	C9401	C9401 Acute erythroid leukemia, in remission
20702	Acute erythremia and erythroleukemia, in relapse	C9402	C9402 Acute erythroid leukemia, in relapse
20710	Chronic erythremia, without mention of having achiev	D45	D45 Polycythemia vera
20711	Chronic erythremia, in remission	D45	D45 Polycythemia vera
20712	Chronic erythremia, in relapse	D45	D45 Polycythemia vera
20720	Megakaryocytic leukemia, without mention of having	C9420	C9420 Acute megakaryoblastic leukemia not having achieved remission
20721	Megakaryocytic leukemia, in remission	C9421	C9421 Acute megakaryoblastic leukemia, in remission
20722	Megakaryocytic leukemia, in relapse	C9422	C9422 Acute megakaryoblastic leukemia, in relapse
20800	Acute leukemia of unspecified cell type, without men	C9500	C9500 Acute leukemia of unspecified cell type not having achieved remission
20801	Acute leukemia of unspecified cell type, in remission	C9501	C9501 Acute leukemia of unspecified cell type, in remission
20802	Acute leukemia of unspecified cell type, in relapse	C9502	C9502 Acute leukemia of unspecified cell type, in relapse
20810	Chronic leukemia of unspecified cell type, without me	C9510	C9510 Chronic leukemia of unspecified cell type not having achieved remission
20811	Chronic leukemia of unspecified cell type, in remissio	C9511	C9511 Chronic leukemia of unspecified cell type, in remission
20812	Chronic leukemia of unspecified cell type, in relapse	C9512	C9512 Chronic leukemia of unspecified cell type, in relapse
20820	Subacute leukemia of unspecified cell type, without r	C9590	C9590 Leukemia, unspecified not having achieved remission
20821	Subacute leukemia of unspecified cell type, in remissi	C9591	C9591 Leukemia, unspecified, in remission
20822	Subacute leukemia of unspecified cell type, in relapse	C9592	C9592 Leukemia, unspecified, in relapse
20880	Other leukemia of unspecified cell type, without men	C9590	C9590 Leukemia, unspecified not having achieved remission
20881	Other leukemia of unspecified cell type, in remission	C9591	C9591 Leukemia, unspecified, in remission
20882	Other leukemia of unspecified cell type, in relapse	C9592	C9592 Leukemia, unspecified, in relapse
20890	Unspecified leukemia, without mention of having achi	C9590	C9590 Leukemia, unspecified not having achieved remission
20891	Unspecified leukemia, in remission	C9591	C9591 Leukemia, unspecified, in remission
20892	Unspecified leukemia, in relapse	C9592	C9592 Leukemia, unspecified, in relapse
2301	Carcinoma in situ of esophagus	D001	D001 Carcinoma in situ of esophagus
2302	Carcinoma in situ of stomach	D002	D002 Carcinoma in situ of stomach
2303	Carcinoma in situ of colon	D010	D010 Carcinoma in situ of colon
2305	Carcinoma in situ of anal canal	D013	D013 Carcinoma in situ of anus and anal canal
2306	Carcinoma in situ of anus, unspecified	D013	D013 Carcinoma in situ of anus and anal canal
2308	Carcinoma in situ of liver and biliary system	D015	D015 Carcinoma in situ of liver, gallbladder and bile ducts
2310	Carcinoma in situ of larynx	D020	D020 Carcinoma in situ of larynx
2311	Carcinoma in situ of trachea	D021	D021 Carcinoma in situ of trachea
2312	Carcinoma in situ of bronchus and lung	D0220	D0220 Carcinoma in situ of unspecified bronchus and lung
2318	Carcinoma in situ of other specified parts of respirato	D023	D023 Carcinoma in situ of other parts of respiratory system
2319	Carcinoma in situ of respiratory system, part unspecif	D024	D024 Carcinoma in situ of respiratory system, unspecified
2330	Carcinoma in situ of breast	D0590	D0590 Unspecified type of carcinoma in situ of unspecified breast
2331	Carcinoma in situ of cervix uteri	D069	D069 Carcinoma in situ of cervix, unspecified
2332	Carcinoma in situ of other and unspecified parts of ut	D070	D070 Carcinoma in situ of endometrium
23330	Carcinoma in situ, unspecified female genital organ	D0730	D0730 Carcinoma in situ of unspecified female genital organs
23331	Carcinoma in situ, vagina	D072	D072 Carcinoma in situ of vagina
23332	Carcinoma in situ, vulva	D071	D071 Carcinoma in situ of vulva
23339	Carcinoma in situ, other female genital organ	D0739	D0739 Carcinoma in situ of other female genital organs
2334	Carcinoma in situ of prostate	D075	D075 Carcinoma in situ of prostate
2335	Carcinoma in situ of penis	D074	D074 Carcinoma in situ of penis
2337	Carcinoma in situ of bladder	D090	D090 Carcinoma in situ of bladder
2340	Carcinoma in situ of eye	D0920	D0920 Carcinoma in situ of unspecified eye
2349	Carcinoma in situ, site unspecified	D099	D099 Carcinoma in situ, unspecified
23871	Essential thrombocythemia	D473	D473 Essential (hemorrhagic) thrombocythemia
23874	Myelodysplastic syndrome with 5q deletion	D46C	D46C Myelodysplastic syndrome with isolated del(5q) chromosomal abnormality
23875	Myelodysplastic syndrome, unspecified	D469	D469 Myelodysplastic syndrome, unspecified
23876	Myelofibrosis with myeloid metaplasia	D471	D471 Chronic myeloproliferative disease
23877	Post-transplant lymphoproliferative disorder (PTLD)	D47Z1	D47Z1 Post-transplant lymphoproliferative disorder (PTLD)
2820	Hereditary spherocytosis	D580	D580 Hereditary spherocytosis
2821	Hereditary elliptocytosis	D581	D581 Hereditary elliptocytosis
2823	Other hemolytic anemias due to enzyme deficiency	D558	D558 Other anemias due to enzyme disorders
28240	Thalassemia, unspecified	D569	D569 Thalassemia, unspecified
28241	Sickle-cell thalassemia without crisis	D5740	D5740 Sickle-cell thalassemia without crisis
28242	Sickle-cell thalassemia with crisis	D57419	D57419 Sickle-cell thalassemia with crisis, unspecified
28243	Alpha thalassemia	D560	D560 Alpha thalassemia
28244	Beta thalassemia	D561	D561 Beta thalassemia
28246	Thalassemia minor	D563	D563 Thalassemia minor
28247	Hemoglobin E-beta thalassemia	D565	D565 Hemoglobin E-beta thalassemia
28260	Sickle-cell disease, unspecified	D571	D571 Sickle-cell disease without crisis
28261	Hb-SS disease without crisis	D571	D571 Sickle-cell disease without crisis
28262	Hb-SS disease with crisis	D5700	D5700 Hb-SS disease with crisis, unspecified
28263	Sickle-cell/Hb-C disease without crisis	D5720	D5720 Sickle-cell/Hb-C disease without crisis
28264	Sickle-cell/Hb-C disease with crisis	D57219	D57219 Sickle-cell/Hb-C disease with crisis, unspecified
28268	Other sickle-cell disease without crisis	D5780	D5780 Other sickle-cell disorders without crisis
28269	Other sickle-cell disease with crisis	D57819	D57819 Other sickle-cell disorders with crisis, unspecified
2828	Other specified hereditary hemolytic anemias	D588	D588 Other specified hereditary hemolytic anemias
2829	Hereditary hemolytic anemia, unspecified	D589	D589 Hereditary hemolytic anemia, unspecified
28310	Non-autoimmune hemolytic anemia, unspecified	D594	D594 Other nonautoimmune hemolytic anemias
28311	Hemolytic-uremic syndrome	D593	D593 Hemolytic-uremic syndrome
28319	Other non-autoimmune hemolytic anemias	D594	D594 Other nonautoimmune hemolytic anemias
2839	Acquired hemolytic anemia, unspecified	D599	D599 Acquired hemolytic anemia, unspecified
28401	Constitutional red blood cell aplasia	D6101	D6101 Constitutional (pure) red blood cell aplasia
28409	Other constitutional aplastic anemia	D6109	D6109 Other constitutional aplastic anemia
28411	Antineoplastic chemotherapy induced pancytopenia	D61810	D61810 Antineoplastic chemotherapy induced pancytopenia
28412	Other drug-induced pancytopenia	D61811	D61811 Other drug-induced pancytopenia
28419	Other pancytopenia	D61818	D61818 Other pancytopenia

2842	Myelophthisis	D6182	D6182 Myelophthisis
2849	Aplastic anemia, unspecified	D619	D619 Aplastic anemia, unspecified
2860	Congenital factor VIII disorder	D66	D66 Hereditary factor VIII deficiency
2861	Congenital factor IX disorder	D67	D67 Hereditary factor IX deficiency
2862	Congenital factor XI deficiency	D681	D681 Hereditary factor XI deficiency
2863	Congenital deficiency of other clotting factors	D682	D682 Hereditary deficiency of other clotting factors
2864	Von Willebrand's disease	D680	D680 Von Willebrand's disease
28652	Acquired hemophilia	D68311	D68311 Acquired hemophilia
28653	Antiphospholipid antibody with hemorrhagic disorder	D68312	D68312 Antiphospholipid antibody with hemorrhagic disorder
28659	Other hemorrhagic disorder due to intrinsic circulatin	D68318	D68318 Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
2866	Defibrination syndrome	D65	D65 Disseminated intravascular coagulation [defibrination syndrome]

ICD-9 to 10 Crosswalk: Transfusions

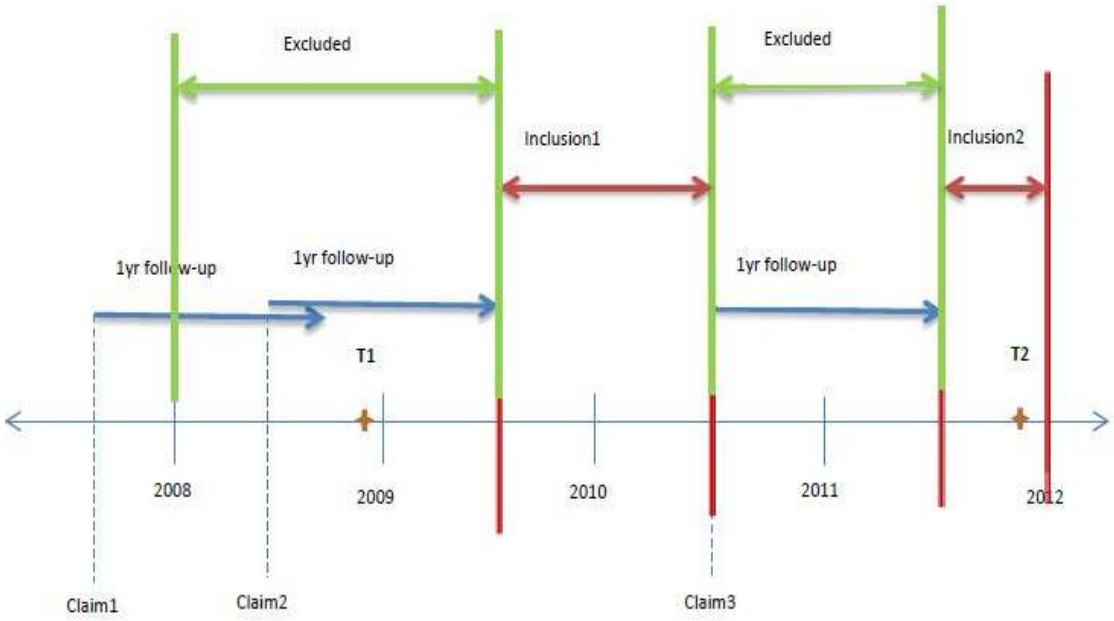
ICD9PCS	ICD9::ICD9PROC_desc	ICD10PCS	I::ICD10PCS_desc
9903	Other transfusion of whole blood	30230H1	30230H1 Transfusion of Nonautologous Whole Blood into Peripheral Vein, Open Approach
9903	Other transfusion of whole blood	30233H1	30233H1 Transfusion of Nonautologous Whole Blood into Peripheral Vein, Percutaneous Approach
9903	Other transfusion of whole blood	30240H1	30240H1 Transfusion of Nonautologous Whole Blood into Central Vein, Open Approach
9903	Other transfusion of whole blood	30243H1	30243H1 Transfusion of Nonautologous Whole Blood into Central Vein, Percutaneous Approach
9903	Other transfusion of whole blood	30250H1	30250H1 Transfusion of Nonautologous Whole Blood into Peripheral Artery, Open Approach
9903	Other transfusion of whole blood	30253H1	30253H1 Transfusion of Nonautologous Whole Blood into Peripheral Artery, Percutaneous Approach
9903	Other transfusion of whole blood	30260H1	30260H1 Transfusion of Nonautologous Whole Blood into Central Artery, Open Approach
9903	Other transfusion of whole blood	30263H1	30263H1 Transfusion of Nonautologous Whole Blood into Central Artery, Percutaneous Approach
9904	Transfusion of packed cells	30230N1	30230N1 Transfusion of Nonautologous Red Blood Cells into Peripheral Vein, Open Approach
9904	Transfusion of packed cells	30230P1	30230P1 Transfusion of Nonautologous Frozen Red Cells into Peripheral Vein, Open Approach
9904	Transfusion of packed cells	30233N1	30233N1 Transfusion of Nonautologous Red Blood Cells into Peripheral Vein, Percutaneous Approach
9904	Transfusion of packed cells	30233P1	30233P1 Transfusion of Nonautologous Frozen Red Cells into Peripheral Vein, Percutaneous Approach
9904	Transfusion of packed cells	30240N1	30240N1 Transfusion of Nonautologous Red Blood Cells into Central Vein, Open Approach
9904	Transfusion of packed cells	30240P1	30240P1 Transfusion of Nonautologous Frozen Red Cells into Central Vein, Open Approach
9904	Transfusion of packed cells	30243N1	30243N1 Transfusion of Nonautologous Red Blood Cells into Central Vein, Percutaneous Approach
9904	Transfusion of packed cells	30243P1	30243P1 Transfusion of Nonautologous Frozen Red Cells into Central Vein, Percutaneous Approach
9904	Transfusion of packed cells	30250N1	30250N1 Transfusion of Nonautologous Red Blood Cells into Peripheral Artery, Open Approach
9904	Transfusion of packed cells	30250P1	30250P1 Transfusion of Nonautologous Frozen Red Cells into Peripheral Artery, Open Approach
9904	Transfusion of packed cells	30253N1	30253N1 Transfusion of Nonautologous Red Blood Cells into Peripheral Artery, Percutaneous Approach
9904	Transfusion of packed cells	30253P1	30253P1 Transfusion of Nonautologous Frozen Red Cells into Peripheral Artery, Percutaneous Approach
9904	Transfusion of packed cells	30260N1	30260N1 Transfusion of Nonautologous Red Blood Cells into Central Artery, Open Approach
9904	Transfusion of packed cells	30260P1	30260P1 Transfusion of Nonautologous Frozen Red Cells into Central Artery, Open Approach
9904	Transfusion of packed cells	30263N1	30263N1 Transfusion of Nonautologous Red Blood Cells into Central Artery, Percutaneous Approach
9904	Transfusion of packed cells	30263P1	30263P1 Transfusion of Nonautologous Frozen Red Cells into Central Artery, Percutaneous Approach

APPENDIX

Standardized Transfusion Ratio for Dialysis Facilities

Denominator Exclusion Details (NQF Includes "Exceptions" in the "Exclusion" Field) S.11.

The following figure describes the inclusion and exclusion period of a hypothetical patient.



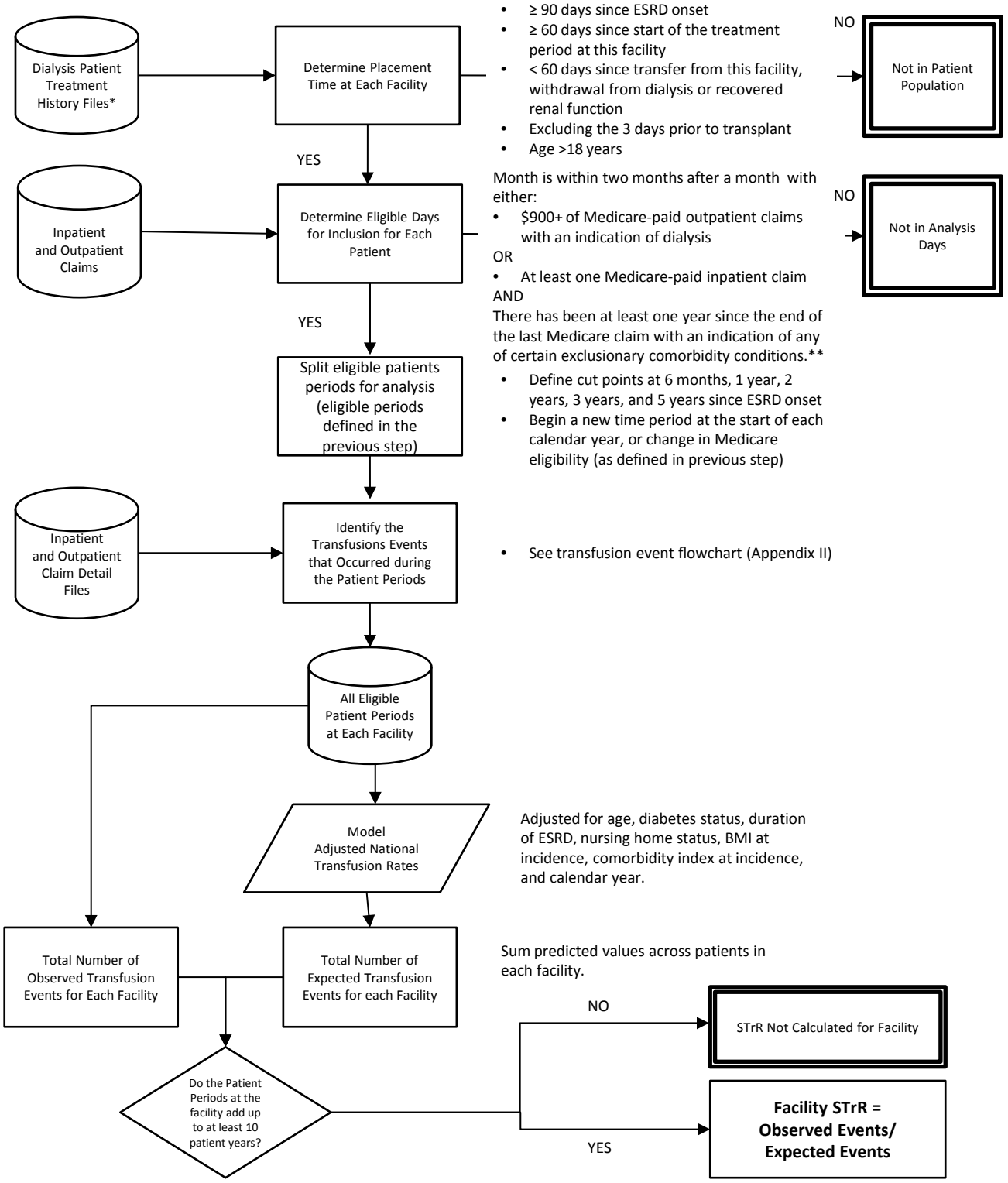
In the figure above, a hypothetical patient has patient years at risk at a facility from 1/1/2008 to 12/31/2011. Review of Medicare claims identified presence of one or more exclusion comorbidities in 2007 (Claim1), 2008 (Claim2) and 2010 (Claim3). Each claim is followed by a one year exclusion period. The revised inclusion periods are defined as risk windows with at least 1 year of claim-free period (Inclusion1 and Inclusion2 in the figure). 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.

Calculation Algorithm/Measure Logic Diagram URL or Attachment S.19.

Standardized Transfusion Ratio: The ratio of observed to expected transfusion events in adult dialysis patients

Numerator Statement: Number of transfusion events observed in adult dialysis patients

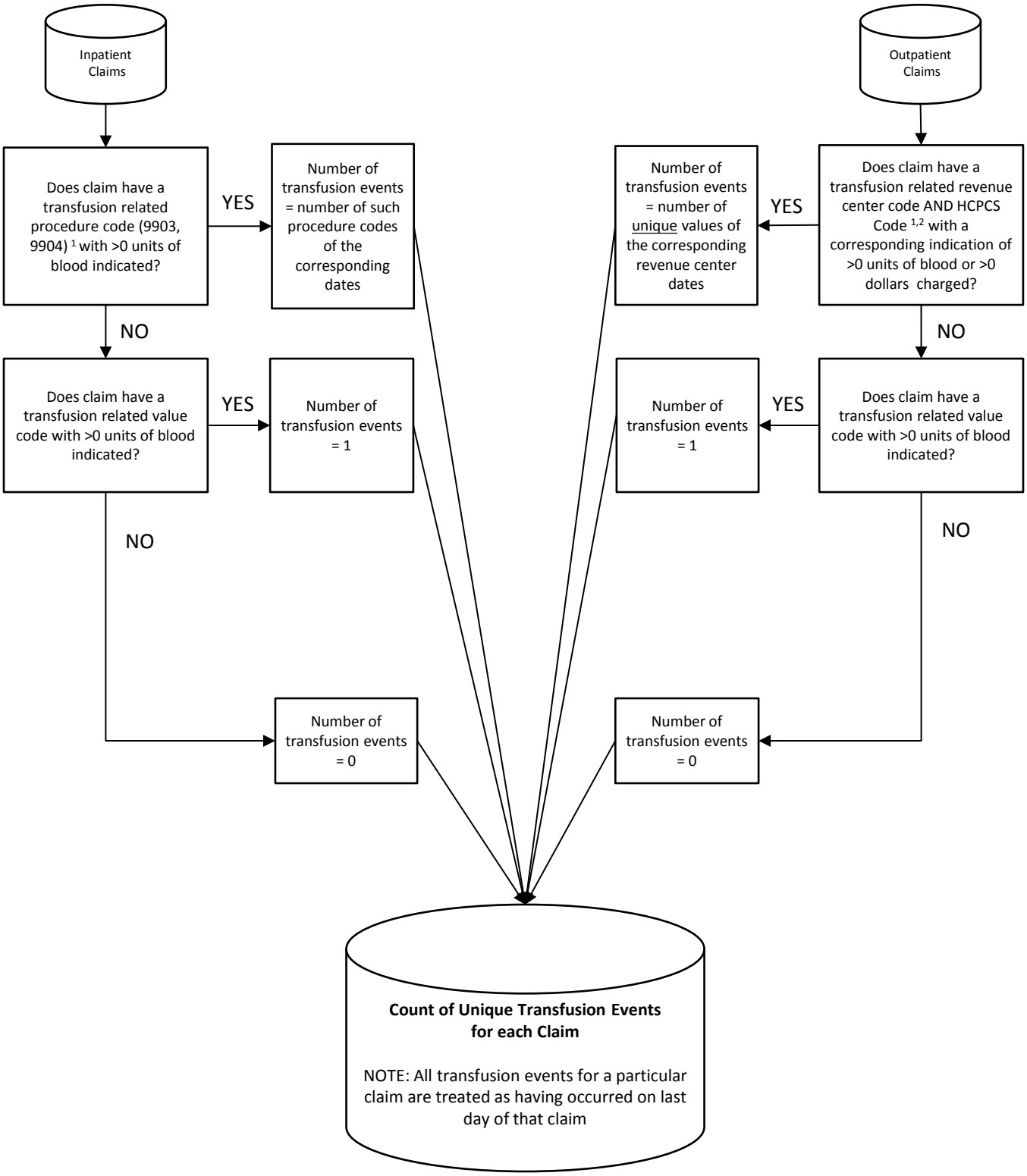
Denominator Statement: Number of transfusion events expected based on the national rate for patients with similar characteristics



*Multiple data sources include CMS Consolidated Renal Operations in a Web-enabled Network (CROWNWeb), 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 Dialysis Facility Compare (DFC) and the Social Security Death Master File.

** Exclusionary comorbidity conditions: 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.

Determination of the Number of Unique Transfusion Events for each Claim
Calculation Algorithm/Measure Logic Diagram URL or Attachment S.19.



[1] See Appendix III for the description of relevant revenue center codes, procedure codes, value codes and HCPCS codes.
[2] Transfusion related revenue center codes: 0380, 0381, 0382, 0389, 0390, 0391, 0392, 0399
Transfusion related HCPCS codes: P9010, P9011, P9016, P9021, P9022, P9038, P9039, P9040, P9051, P9054, P9056, P9057, P9058, 36430