Report for the Standardized Transfusion Ratio

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Introduction

As mandated by the Affordable Care Act (ACA), assuring delivery of high quality and affordable care requires reliable and meaningful quality measures that focus on important outcomes and processes, including patient experience, across the breadth of the healthcare system (CMS, 2013). This view has reinforced CMS' stated goal of providing the highest quality of evidence-based care, which is personalized, prevention-oriented and patient-centered. Achieving this goal requires development of measures that incorporate heterogeneities at both population and individual levels, across traditional institutional or provider domains to address coordination and continuity of care, and focus on outcomes most important to patients. In addition, measures ought to address the efficiency of care delivery at the individual and population levels in order to support value-based purchasing initiatives, and to foster a delivery system that works efficiently for providers by reducing their administrative burdens, while facilitating coordinated care. Most importantly, measures should incorporate the evidence-based results of the latest high quality research and scientific advances in health outcomes research, clinical medicine, public health, and health care delivery. Anemia management in chronic dialysis patients is a complex clinical issue of importance to patients, providers and healthcare administrators. Development of quality measures for this clinical topic reflecting the aforementioned principles is necessary and appropriate in this time of rapidly evolving understanding of the risks and potential benefits of anemia treatments in this population.

Anemia is a complication of end stage renal disease (ESRD), affecting most patients with this condition. Management of anemia in ESRD patients is the responsibility of the patient's dialysis facility as specified in CMS' ESRD Conditions for Coverage and paid for as part of the Medicare ESRD Prospective Payment System. According to FDA Prescribing Information, goals of successful treatment should include minimization of blood transfusion risk. According to some, additional potential benefits of anemia treatment may include improvement of the quality of life and health of dialysis patients.

Several recent scientific findings and Medicare ESRD Program policy changes likely impacted anemia management in dialysis facilities. These include identification of safety concerns associated with aggressive erythropoiesis-stimulating agent (ESA) use, expansion of the ESRD prospective payment System bundled payment to include payment for ESAs, and the development of the ESRD Quality Incentive Program. Potential unintended consequences of these events include possible underutilization of ESAs by dialysis facilities and, consequently, increasing frequency of red blood cell transfusion in the US chronic dialysis population.

The inverse relationship between achieved hemoglobin and transfusion events has been reported previously for Medicare dialysis patients (Ma, 1999; Collins, 2014) 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 rise 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 have recently 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. (Hirth, 2014).

The national trend toward increased use of transfusion in dialysis patients has raised several concerns. First, blood transfusion carries a defined risk of transmitted blood borne infections and development of transfusion reactions. In addition, use of transfusions to treat anemia of CKD is wasteful of precious healthcare resources, including our finite blood supply used for emergent medical indications. 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.

At the patient level, blood transfusion may be an indicator for underutilization of treatments that increase endogenous red blood cell production (e.g. ESA, iron). Monitoring the risk-adjusted transfusion rate at the dialysis facility level, relative to a national standard, is of particular importance for the following reasons. First, it will identify facilities with extraordinary transfusion rates. As providers use fewer ESAs in an effort to minimize the risks associated with aggressive anemia treatment, it becomes more important to monitor anemia management practices that may demonstrate an overreliance on transfusions. Second, implementation of the transfusion measure at the facility level will provide valuable feedback to dialysis facilities and nephrologists and bring increased transparency to anemia management care processes. This is especially vital for small and independent facilities as they continue to provide anemia management care to dialysis patients, working to prevent unnecessary transfusions.

Methods

Overview

In April 2012, a CMS Technical Expert Panel (TEP) on anemia management recommended development of a risk-adjusted, facility-level standardized transfusion measure. We subsequently developed the STrR, a measure of transfusion at the facility level for the purpose of dialysis patient anemia management in the U.S. We identify Medicare-covered transfusions and exclude ineligible cases associated with each patient's comorbidity and transplant hospitalization history, using Medicare administrative data, which we derived from inpatient, outpatient institutional, home health, hospice and skilled nursing facility claims. After initial development, including a public comment period, the STrR was reviewed by the NQF Measure Application Partnership, which supported the overall direction of the measure.

The Standardized Transfusion Ratio (STrR) for all adult dialysis patients is designed to reflect the number of eligible red blood cell transfusion events occurring in patients dialyzing at a facility, relative to the number of eligible transfusions that would be expected under a national norm, after accounting for the patient characteristics within each facility. Specifically, the STrR is calculated as the ratio of two

numbers: the numerator ("observed") is the actual number of transfusion events over a year period, and the denominator ("expected") is the number of transfusion events that would be expected if patients at that facility experienced transfusion events at the national average rate for patients with similar characteristics.

Data Sources

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

Outcome Definition

The outcome for this measure is the risk adjusted facility level transfusion event count among adult Medicare eligible dialysis patients.

Identification of Transfusion Events

Our method for counting transfusion events relies on a conservative counting algorithm and, because of the way transfusion information is reported in Medicare claims, we use different rules for counting transfusion events, depending on whether or not the event occurs in the inpatient setting, or an outpatient setting. The most common way events are reported on claims is by reporting a revenue center or value code (inpatient claims) or for outpatient claims, reporting HCPCS codes for a revenue center date.

One "transfusion event" is counted per inpatient claim if one or more transfusion-related revenue center or value codes are present. This is the way most inpatient transfusion events are reported on claims (i.e., using revenue center or value codes, not procedure codes). We only count a single transfusion event for an inpatient claim regardless of the number of transfusion revenue center and value codes reported so that the number of discrete events counted is the same whether the claim indicates 1 unit of blood or multiple units of blood. This results in a very conservative estimate of blood transfusions from inpatient claims. A small fraction of inpatient transfusion events are identified using specific procedure codes. For these cases, we are able to identify multiple transfusion events for some hospitalizations and count a unique "transfusion events" for each transfusion procedure code listed on an inpatient claim. CMS allows the transfusion procedure to be billed only once per day per visit.

Transfusion events are not common in outpatient settings, but similar rules apply. 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. In other words, 3 pints of blood reported with the same revenue center date would be counted as a single transfusion event.

The detailed procedures to determine unique transfusion events at the claim level are included in Appendix II.

Cohort Definition

Assignment of Patients to Facilities

As patients can receive dialysis treatment at more than one facility in a given year, we assign each patient day to a facility (or no facility, in some cases) based on a set of conventions below, which largely align with those for the Standardized Mortality Ratio (SMR) and Standardized Hospitalization Ratio (SHR). We detail patient inclusion criteria, facility assignment and how to count days at risk, all of which are required for the risk adjustment model.

General Inclusion Criteria for Dialysis Patients

Though a patient's follow-up in the database can be incomplete during the first 90 days of ESRD therapy, we only include a patient's follow-up into the tabulations after that patient has received chronic renal replacement therapy for at least 90 days. Thus, hospitalizations, mortality and survival during the first 90 days of ESRD do not enter into the calculations. This minimum 90-day period also assures that most patients are eligible for Medicare, either as their primary or secondary insurer. It also excludes from analysis patients who die or recover during the first 90 days of ESRD.

In order to exclude patients who only received temporary dialysis therapy, we assigned patients to a facility only after they had been on dialysis there for at least 60 days. This 60 day period is used both for patients who started ESRD for the first time and for those who returned to dialysis after a transplant. That is, transfusion events during the first 60 days of dialysis at a facility do not affect the STrR of that facility.

Identifying Facility Treatment Histories for Each Patient

For each patient, we identify the dialysis provider at each point in time. Starting with day 91 after onset of ESRD, we attribute patients to facilities according to the following rules. A patient is attributed to a facility once the patient has been treated there for 60 days. When a patient transfers from one facility to another, the patient continues to be attributed to the original facility for 60 days and then is attributed to the destination facility. In particular, a patient is attributed to their current facility on day 91 of ESRD if that facility had treated him or her for at least 60 days. If on day 91, the facility had treated a patient for fewer than 60 days, we wait until the patient reaches day 60 of treatment at that facility before attributing the patient to that facility. When a patient is not treated in a single facility for a span of 60 days (for instance, if there were two switches within 60 days of each other), we do not attribute that patient to any facility. Patients are removed from facilities three days prior to transplant in order to

exclude the transplant hospitalization. Patients who withdrew from dialysis or recovered renal function remain assigned to their treatment facility for 60 days after withdrawal or recovery.

If a period of one year passes with neither paid dialysis claims nor SIMS information to indicate that a patient was receiving dialysis treatment, we consider the patient lost to follow-up and do not include that patient in the analysis. If dialysis claims or other evidence of dialysis reappears, the patient is entered into analysis after 60 days of continuous therapy at a single facility.

Days at Risk for Medicare Dialysis Patients

After patient treatment histories are defined as described above, periods of follow-up in time since ESRD onset are created for each patient. In order to adjust for duration of ESRD appropriately, we define 6 time intervals with cut points at 6 months, 1 year, 2 years, 3 years and 5 years. A new time period begins each time the patient is determined to be at a different facility, or at the start of each calendar year or when crossing any of the above cut points.

Transfusion rates are similar to hospitalization rates in that patients can be transfused more than once during a year and transfusion data are not always as complete as mortality data. As with the hospitalization statistics, this measure should ideally include only patients whose Medicare billing records include all transfusions for the period. To achieve this goal, we apply the same rules as for the hospitalization measure and require that patients reach a certain level of Medicare-paid dialysis bills to be included in transfusion statistics, or patients have a Medicare-paid inpatient claim during the period. For the purpose of analysis, each patient's follow-up time is broken into periods defined by time since dialysis initiation. For each patient, months within a given period are included if that month in the period is considered 'eligible'; a month is deemed eligible if it is within two month of a month having at least $900 of Medicare–paid dialysis claims or at least one Medicare-paid inpatient claim. In setting this criterion, our aim is to achieve completeness of information on transfusions for all patients included in the analysis.

The number of days at risk in each of these patient-ESRD-year-facility time periods is used to calculate the expected number of transfusions for the patient during that period. The STrR for a facility is the ratio of the total number of observed transfusions to the total number of expected transfusions during all time periods at the facility.

Risk Adjustment

Choosing Adjustment Factors

Some general considerations played an important role in the selection of risk factors for which adjustment was to be made. For example, the literature suggests that transfusions are more common in patients with higher overall comorbidity burden, and occur most often during hospitalizations. From this perspective, it is appropriate to risk adjust the model for characteristics that are generally associated with comorbidity burden. Adjustment factors included in the calculation of the STrR are those included in the model for CMS' NQF-endorsed Standardized Hospitalization Ratio (SHR) for admissions, (http://www.dialysisreports.org/pdf/esrd/public/shrmodel.xls ; NQF #1463

http://www.qualityforum.org/QPS/1463), with one exception: sex is adjusted for in the SHR but not included in the STrR model. The STrR adjustments include age, years on dialysis, patient comorbidity index at incidence, patient BMI at incidence, and nursing home status of patient.

We developed the model to align with CMS' existing dialysis facility measures of hospitalization and mortality (SHR and SMR). STrR includes the following adjustors:

- patient age
- diabetes mellitus as the primary cause of ESRD
- at incidence of ESRD, comorbidity status
- at incidence of ESRD, BMI
- time on dialysis
- an indicator for whether a patient was in a nursing home in the previous calendar year
- categorical indicators for missing values for cause of ESRD, comorbidity index, and BMI and a categorical indicator for comorbidity index is 0
- calendar year
- two way interaction terms
  - diabetes as cause of ESRD * time on ESRD
  - age * diabetes as cause of ESRD

Analyses of the STrR by race, sex and ethnicity indicate relatively little variation and no substantial disparities among these groups. Although females are somewhat more likely to receive transfusions than males, analyses showed that a model with race and sex included and a model without these variables yielded very similar results for the facility STrR measure as well as for the parameter estimates for other variables. Table 1 below shows the parameter estimates for the race, sex and ethnicity variables based on a model that included these variables along with other covariates.

Table 1: Estimates for race, sex, and ethnicity when added to the STrR model.

Parameter	Estimate	Standard Error	P value
Females	0.08126	0.00672	<.0001
Native American*	-0.15707	0.01795	<.0001
Asian-American*	-0.23275	0.01065	<.0001
African-American*	-0.0816	0.00464	<.0001
Other Race*	-0.05411	0.01843	0.0033
Hispanic #	-0.1919	0.00662	<.0001

*Caucasian as reference

Non-Hispanic as reference

Adjustment in STrR

The regression model used to compute a facility's "expected" number of transfusions for the STrR measure contains many factors associated with frequency of hospitalization and thought to be associated with transfusion event rates. Specifically, the model adjusts for patient age, diabetes, duration of ESRD, nursing home status, BMI at incidence, comorbidity index at incidence, and calendar year. This model allows the baseline transfusion rates to vary between strata (facilities), but assumes that the regression coefficients are the same across all strata; this approach is robust to possible differences between facilities in the patient mix being treated.
The patient characteristics included in the stage 1 model as covariates are

- Age: We determine each patient's age for the birth date provided the SIMS and REMIS databases and categorize as 18-24 years old, 25-44 years old, 45-59 years old, 60-74 years old, or 75+ years old.
- Diabetes as cause of ESRD (diabetes or other): We determine each patient's primary cause of ESRD from his/her CMS 2728.
- Nursing home status is identified as in or not in a nursing home in the previous calendar 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.
- Comorbidity index at incidence is calculated as a weighted linear combination of comorbidities reported on the Medical Evidence Form (CMS-2728) namely alcohol dependence, atherosclerotic heart disease, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, diabetes, diabetes (currently on insulin), drug dependence, inability to ambulate, inability to transfer, malignant neoplasm, cancer, other cardiac disease, peripheral vascular disease, tobacco use (current smoker) using the same weights as used for Standardized Hospitalization Ratio (http://www.dialysisreports.org/pdf/esrd/public/shrmodel.xls; NQF #1463).
- Years on ESRD: We determine each patient's length of time on dialysis using the first service date from 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.
- Calendar year
- Categorical indicator variables are included as covariates in the stage 1 model to flag records with missing values for cause of ESRD, comorbidity index, and BMI. These variables have a value of 1 if the patient is missing the corresponding piece of information and a value of 0 otherwise.
- Categorical indicator variable included as a covariate to flag records with value of 1 if the patient has a comorbidity index of 0 and a value of 0 otherwise.
- Beside main effects, some two way interaction terms are also included in the model based on their clinical and statistical significance.
    - Diabetes as cause of ESRD * Time on ESRD
    - Age* Diabetes as cause of ESRD

Comorbidity Exclusions and Method of Testing Exclusions

In addition to the aforementioned general risk-adjustments, the STrR risk adjustment paradigm utilizes several patient exclusions described here. Transfusions associated with a 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

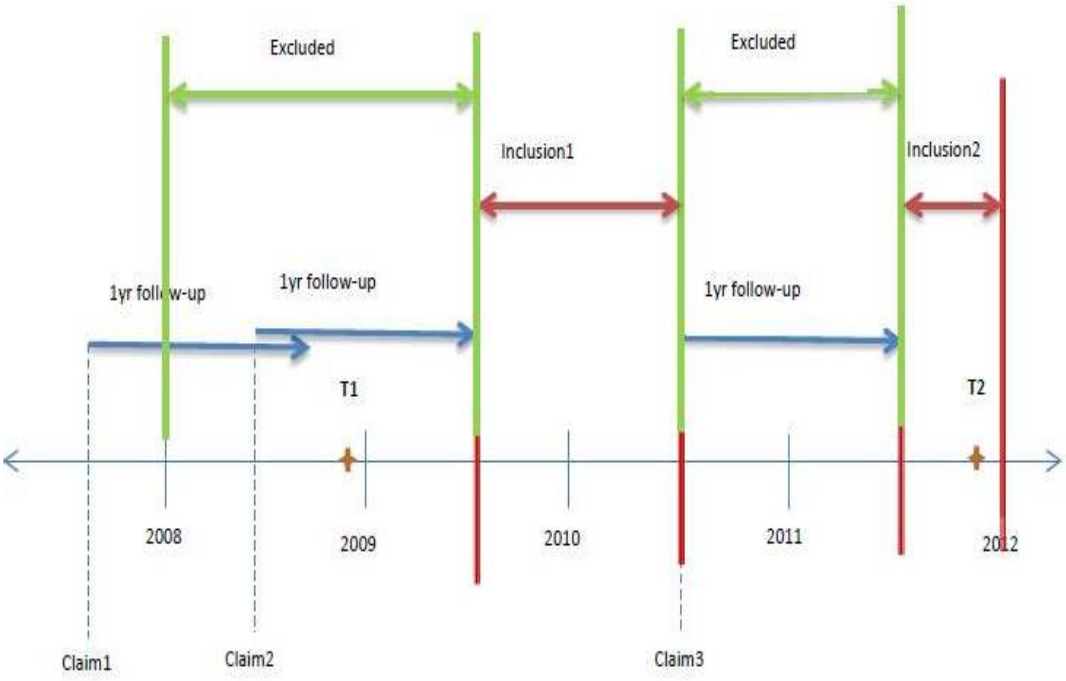
#1463 http://www.qualityforum.org/QPS/1463) and SMR NQF #0369 http://www.qualityforum.org/QPS/0369).

Patients are also excluded if they have a Medicare claim (Part A inpatient, home health, hospice, and skilled and nursing facility claims; Part B outpatient and physician supplier) 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, or sickle cell anemia within one year of their patient at risk time. The 2012 Anemia TEP felt that development of a risk-adjustment strategy encompassing these specific comorbidity categories for use in the facility-level transfusion metric was critically important. These prevalent comorbidities define a sub-population of patients who are at increased risk of blood transfusions, and in addition, are less likely to respond to recommended doses of exogenous ESAs. Furthermore, they are likely at increased risk for ESA-related complications. Lastly, the TEP members agreed that the aforementioned comorbidities were outside the sphere of influence of the dialysis facilities. The TEP considered additional comorbidities but recommended against their use in the risk-adjustment paradigm if the comorbidity could potentially be the result of care provided by the dialysis facility.

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 the exclusion list. We assessed 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 by performing multivariate logistic regression with transfusion count as the dependent variable. Results showed that 1-year look back period for each of the above mentioned comorbidities was the most predictive of one or more RBC transfusions.

Figure 1 describes the inclusion and exclusion period of a hypothetical patient.

Figure 1: Algorithm for exclusion of periods of time within 1 year of an exclusion comorbidity



In the figure, 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 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.

Calculating Expected Number of Transfusions

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

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

where $\boldsymbol{X}_{ik}$ is the vector of covariates for the (i,k)th patient and $\boldsymbol{\beta}$ 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 facility effects.

The patient characteristics $\boldsymbol{X}_{ik}$ 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, comorbidity index at incidence, 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. The comorbidity index is included as a linear variable. 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, comorbidity index, and BMI. These variables have a value of 1 if the patient is missing the corresponding piece of information and a value of 0 otherwise. Another categorical indicator variable is included as a covariate in the stage 1 model to flag records where the comorbidity index is 0. This variable has a value of 1 if the patient has a comorbidity index of 0 (indicating no comorbidities are recorded as present) 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, $r_0(t)$, across all facilities by considering the model

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

where $R_{ik} = \exp(\boldsymbol{\beta}'\boldsymbol{X}_{ik})$ 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

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

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

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

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

$$\mathbf{STrR = Obs/Exp} \; .$$

Missing Data

Patients with missing data are not excluded from the model. For the purposes of calculation, missing values for the comorbidity index and BMI are replaced with mean values for patients of similar age and identical race, sex, and cause of ESRD. Missing values for cause of ESRD are replaced with the other/unknown category. No patients were missing age, sex, or date of first ESRD treatment. Indicator variables identifying patients with missing values for cause of ESRD, comorbidity index, and BMI are also included as covariates in the model.

Calculation of STrR P-Values and Confidence Intervals

To overcome the possible over-dispersion of the data, we compute the p-value for our estimates using the empirical null distribution, an approach that possesses more robustness (Efron, 2004; Kalbfleisch and Wolfe, 2013). Our algorithm consists of the following concrete steps. First, we fit an over-dispersed Poisson model (e.g., SAS PROC GENMOD with link=log, dist=poisson and scale=dscale) for the number of transfusions

$$\log(E[\mathbf{n_{ik}}]) = \log(\mathbf{E_{ik}}) + \boldsymbol{\theta_k},$$

where $\mathbf{n_{ik}}$ is the observed number of event for patient *i* in facility *k*, $\mathbf{E_{ik}}$ is the expected number of events for patient *i* in facility *k* and $\boldsymbol{\theta_k}$ is the facility-specific intercept. Here, i ranges over the number of patients $\mathbf{n_{ik}}$ who are treated in the kth facility. The natural log of the STrR for the kth facility is then given by the corresponding estimate of $\boldsymbol{\theta_k}$. The standard error of $\boldsymbol{\theta_k}$ is obtained from the robust estimate of variance arising from the overdispersed Poisson model.

Second, we obtain a z-score for each facility by dividing the natural log of its STrR by the standard error from the general linear model described above. These z-scores are then grouped into quartiles based on the number of patient years at risk for Medicare patients in each facility. Finally, using robust estimates

of location and scale based on the normal curve fitted to the center of the z-scores for the STrR, we derive the mean and variance of a normal empirical null distribution for each quartile. This empirical null distribution is then used to calculate the p-value for a facility's STrR.

Example

The uncertainty or confidence intervals are obtained by applying the following steps:

- From the general linear model we obtain the natural log of the STrR (ln STrR) as well as its standard error, (SE). From the empirical null, we obtain a mean (μ) and a standard deviation (σ). The 95% uncertainty interval for the 'true' log standardized transfusion ratio for this facility is

  $$\ln \text{STrR} - \mu * \text{SE} \pm 1.96 * \sigma * \text{SE}.$$

  Note that 1.96 is the critical point from the standard normal distribution for a 95% interval.

- Exponentiating the endpoints of this interval gives the uncertainty interval for the true STrR.

For example, consider a hypothetical facility whose STrR is 0.927 for which ln STrR = -0.076 with corresponding standard error, SE = 0.118. This facility falls in a quartile where the empirical null has μ = -0.143 and σ = 1.479. The corresponding uncertainty interval for the log STrR is

$$-0.076 - (-0.143)*0.118 \pm 1.96 *0.118*1.479 = (-0.401, 0.283).$$

The 95% interval for the true STrR is then 0.67 to 1.33.

Results

Population Characteristics*, Data Years 2009–2012

Characteristic	2009	2010	2011	2012
Patients	370,133	387,213	396,577	417,351
Facilities	4,797	4,985	5,117	5,278
Transfusions	209,296	210,282	233,929	247,109

*Among facilities receiving a STrR (a facility is required to have a total of at least 10 patient-years at risk during the year in order to receive a STrR)

Risk Factor Frequency (%) in Data Samples*, Data Years 2009–2012

Risk Factor	2009	2010	2011	2012
Incident comorbidity index				
0	24.5	24.0	23.7	23.6
0.001 - 0.135	16.5	15.9	15.2	15.0
0.136 - 0.271	21.1	21.9	22.7	23.6
0.272 - 0.437	19.2	19.2	19.2	19.1
0.438 -	18.7	19.0	19.1	18.8
Cause of ESRD: Diabetes	46.7	46.9	47.1	47
Age				
18-24	1.1	1.0	1	0.9
25-44	13.1	13.0	12.8	12.7
45-59	28.1	28	28	28.1
60-74	22.7	24.2	25.2	27.9
75+	21.7	21.7	21.5	21.1
Incident BMI				
Underweight	3.1	2.96	2.88	2.81
Normal weight	28.38	27.56	26.64	25.88
Overweight	30.27	29.85	29.58	29.57
Obese	38.25	39.63	40.89	41.74
Time on ESRD				
91 days-6 months	11.9	11.5	10.9	10.1
6 months-1 year	13.8	13.6	13.1	12.5
1-2 years	17.5	17.4	17.3	16.8
2-3 years	15.4	15.1	15.2	15.3
3-5 years	18.4	18.6	18.7	19.4
5+ years	23.1	23.8	24.7	26
In nursing home the previous year	7	7	6.5	4.5

*The table reports the percentage of patient-treatment records with the risk factor

Model Coefficients, Data Years 2009–2012

Covariate	Coefficient	P-value
Incident comorbidity index		
0	-0.127	<.0001
Incident comorbidity index (continuous)	0.375	<.0001
Missing	-0.068	0.012
Cause of ESRD		
Diabetes	-0.075	<.0001
Missing	-0.038	0.063
Age		
18-24	0.087	0.312
25-44	-0.234	<.0001
45-59	-0.169	<.0001
60-74	Reference	
75+	0.008	0.213
BMI		
Log BMI	-0.193	<.0001
BMI missing	0.108	<.0001
Calendar year		
2009	Reference	
2010	-0.033	<.0001
2011	-0.040	<.0001
2012	-0.067	<.0001
In nursing home the previous year	0.542	<.0001
Diabetes as cause of ESRD & time on ESRD interaction term		
91 days-6 months	Reference	
6 months-1 year	0.072	<.0001
1-2 years	0.102	<.0001
2-3 years	0.127	<.0001
3-5 years	0.078	<.0001
5+ years	0.058	<.0001
Age & diabetes as cause of ESRD interaction term		
0-14		
15-24	0.26	0.002
25-44	0.272	<.0001
45-59	0.126	<.0001
60-74	Reference	
75+	0.012	0.176

Reliability Testing

The reliability of the STrR was assessed using data among ESRD dialysis patients during 2009-2012. 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.

Here we describe our approach to calculating IUR. Let $T_1,\ldots,T_N$ be the STrR for these facilities. Within each facility, select at random and with replacement B = 100 bootstrap samples. That is, if the ith facility has n_i subjects, randomly draw with replacement n_i subjects from those in the same facility, find their corresponding STrR$_i$ and repeat the process 100 times. Thus, for the ith facility, we have bootstrapped STrRs of $T^*_{i1}\ldots, T^*_{i100}$. Let S^*_i be the sample variance of this bootstrap sample. From this it can be seen that

$$s^2_{t,w} = \frac{\sum_{i=1}^{N}[(n_i - 1)S^{*2}_i]}{\sum_{i=1}^{N}(n_i - 1)}$$

is a bootstrap estimate of the within-facility variance in the STrR, namely $\sigma^2_{t,w}$. Calling on formulas from the one way analysis of variance, an estimate of the overall variance of T_i is

$$s^2_t = \frac{1}{n'(N-1)}\sum_{i=1}^{N} n_i(T_i - \bar{T})^2$$

where

$$\bar{T} = \sum n_i T_i / \sum n_i$$

is the weighted mean of the observed STrR and

$$n' = \frac{1}{N-1}\left(\sum n_i - \sum n_i^2 \Big/ \sum n_i\right)$$

is approximately the average facility size (number of patients per facility). Note that s_t^2 is an estimate of $\sigma_b^2 + \sigma_{t,w}^2$ where σ_b^2 is the between-facility variance, the true signal reflecting the differences across facilities. Thus, the IUR, which is defined by

$$IUR = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_{t,w}^2}$$

can be estimated with $(s_t^2 - s_{t,w}^2)/s_t^2$

The STrR calculation only included facilities with at least 10 patient years at risk. Overall, we found that IURs for the STrR have a range of 0.49-0.55 across the years 2009, 2010, 2011 and 2012, which indicates that around half of the variation in the STrR can be attributed to the between-facility differences and half 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 2: IUR for STrR, Overall and by Facility Size, 2009-2012

	2009		2010		2011		2012	
Facility Size (Number of patients)	**IUR**	**N**	**IUR**	**N**	**IUR**	**N**	**IUR**	**N**
All	**0.49**	4797	**0.53**	4985	**0.55**	5117	**0.54**	5278
Small (<=46)	**0.36**	1513	**0.44**	1576	**0.38**	1706	**0.36**	1743
Medium (47–78)	**0.46**	1637	**0.49**	1682	**0.52**	1687	**0.54**	1817
Large (>=79)	**0.59**	1647	**0.6**	1727	**0.66**	1724	**0.65**	1718

Validity Testing

We examined STrR's correlations with the other measures of quality among ESRD population and reported significant correlation estimates. We assessed the validity of the measure through various comparisons of this measure with other quality measures in use, and in May 2012 there was an assessment of face validity based on polling of a CMS Technical Expert Panel (TEP).

6/6 voting members of CMS' 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 such as hereditary anemia, chronic bone marrow failure conditions and active cancer.

The validity of the STrR measure is supported by its association with other known quality measures, which include both dialysis facility outcomes and practices. Spearman's rho is reported for all measures. For year 2012, we find that the measure is positively correlated with two health outcome measures: the one-year Standardized Hospitalization Ratio for Admissions (rho = 0.40, $p < .0001$), the one-year Standardized Mortality Ratio (rho = 0.23, $p < .0001$), and the one-year Standardized Readmission Ratio (rho = 0.17, $p < .0001$). We also checked the correlation with average hemoglobin value of all ESA-treated dialysis patients and (rho = -0.16, $p < .0001$) a negative correlation indicates that lower values of hemoglobin are associated with higher values of STrR. Similarly, a positive correlation with the percent of patients with Hgb < 10 (rho = 0.20, $p < .0001$) indicates that higher % of patients with Hgb < 10 is associated with higher STrR.

Furthermore, the STrR is correlated with catheter use (rho =0.22, $p < .0001$), indicating that higher values of STrR are associated with increased use of catheters. The STrR is negatively correlated with the percentage of patients with Kt/V>=1.2 (rho = -0.09, $p < .0001$) and using a fistula (rho = -0.08, $p < .0001$). That is, higher values of STrR are associated with lower rates of Kt/V>=1.2 and fistula use.

The overall measure demonstrates both strong face and 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 mortality and more hospital admissions than would be expected based on national rates.

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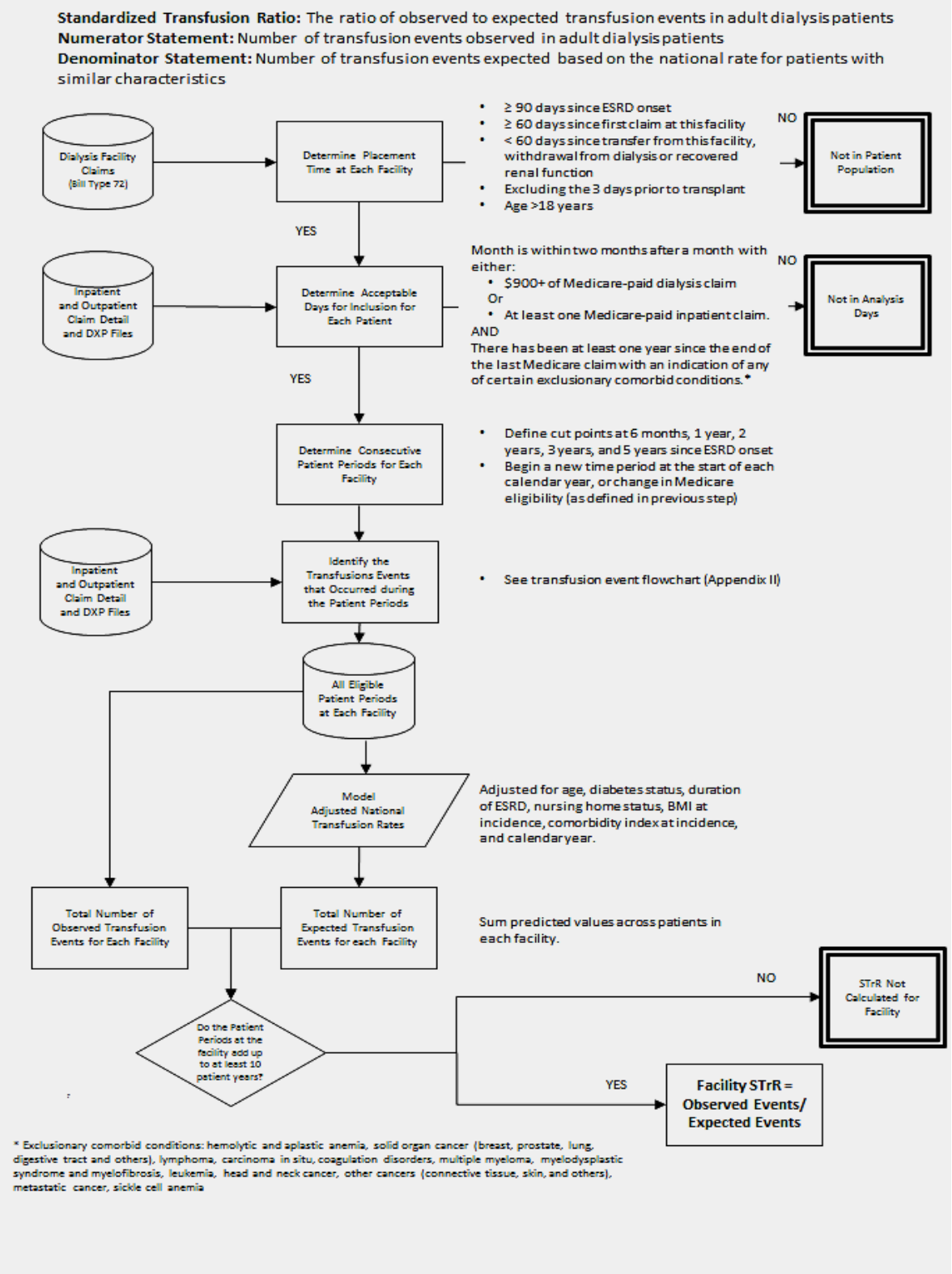
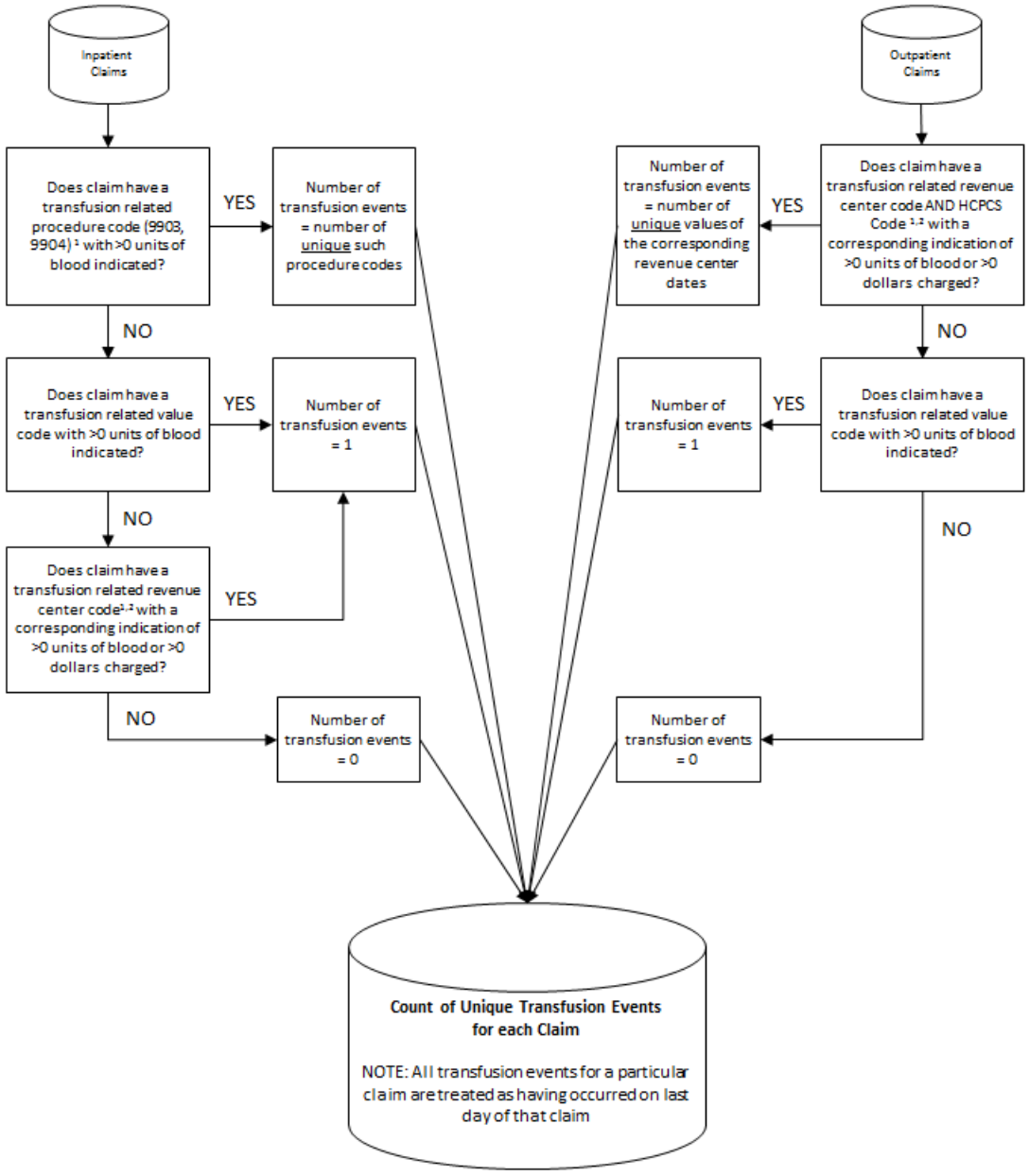
Appendix

Appendix I. Measure Calculation Flow Chart



Appendix II. Determining Transfusion Events Flow Chart

Determination of the Number of Unique Transfusion Events for each Claim



[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

Appendix III.

Description of Relevant Revenue Center Codes, Procedure Codes, Value Codes and HCPCS Codes.

Field	Value	Meaning
Revenue Center Codes	0380	Blood - General Classification
	0381	Blood - Packed Red Cells
	0382	Blood - Whole Blood
	0389	Blood - Other Blood
	0390	Blood Storage and Processing - General Classification
	0391	Blood Storage and Processing - Administration
	0392	Blood Storage and Processing - Blood Processing and Storage
	0399	Blood Storage and Processing - Other Storage & Processing
Procedure Codes	9903	Other Transfusion Of Whole Blood
	9904	Transfusion Of Packed Cells
Value Code	37	Pints of blood furnished
HCPCS 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