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Original Investigation

# Effect of Facility-Level Hemoglobin Concentration on Dialysis Patient Risk of Transfusion

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**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 1 with 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 ($\sim$11%). 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 $\sim$30% 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.

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***INDEX WORDS:*** Anemia; end-stage renal disease; hemodialysis; hemoglobin concentration; red blood cell transfusion.

Since the introduction of erythropoiesis-stimulating agents (ESAs) in 1989, chronic anemia in end-stage renal disease has been reduced; untreated hemoglobin levels of 6-8 g/dL before ESA approval[1] increased to 11-12 g/dL by the late 1990s.[2] Recombinant human erythropoietin (epoetin alfa) received a primary indication of reducing the need for red blood cell (RBC) transfusions in patients receiving dialysis in June 1989.[3] Since then, transfusion requirements have decreased; inpatient and outpatient transfusions reached a nadir of 7.5% per quarter in 2000.[4] In the late 1990s and mid-to-late 2000s, randomized controlled trial evidence showed adverse cardiovascular consequences (stroke, nonfatal myocardial infarction, and death) when hemoglobin levels were targeted to $\geq 13$ g/dL in patients with dialysis-dependent and non–dialysis-dependent chronic kidney disease (relative risks [RRs], 1.3-2.0).[5-8] The accumulation of evidence regarding the risks of treating to higher hemoglobin levels led providers to reduce ESA dosing, resulting in lower achieved hemoglobin levels.[2] In 2011, ESA labels were revised; the hemoglobin target range of 10-12 g/dL was replaced by guidance to "use the lowest dose of ESA to avoid transfusions," initiate with hemoglobin level $< 10$ g/dL, and reduce or interrupt doses when hemoglobin level approaches or exceeds 11 g/dL,[9] effectively lowering the therapeutic range to 10-11 g/dL as implemented by practicing physicians.

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Concerns about the safety of ESAs and potential overuse of injectable medications administered to patients with end-stage renal disease in the fee-for-service setting led Congress to establish a new prospective payment system (PPS) for dialysis, implemented in January 2011. All separately billable medications (including ESAs, intravenous [IV] iron, vitamin D, and others) were included in a per-dialysis-session bundled payment.[10] The new PPS changed provider incentives, possibly resulting in unintended consequences, such as increased transfusion rates, as acknowledged by the Government Accountability Office (GAO) in the original PPS legislation.[11]

In May 2012, monitoring the changes under the PPS, the US Renal Data System (USRDS) reported patient-level changes in medication dosing, declines in hemoglobin levels, and increases in blood transfusions[2,11]; these changes were confirmed by the GAO and the Centers for Medicare & Medicaid Services (CMS).[2,12] However, little is known about dialysis facility–level anemia treatment practices and their potential effect on RBC transfusion use. We aimed to describe trends in patient-level anemia treatment use and outcomes in the first 6 months of each year in 2007-2011 and estimate the effect of facility-level anemia treatment practices on the likelihood of individual patients receiving RBC transfusions, accounting for case-mix differences. Because dialysis facility anemia practices are consistent under defined treatment protocols, we characterized these practices by the prevalence of patients at the facility with hemoglobin levels $< 10$ g/dL over 3 months (reflecting treatment to levels below the lower limit [10 g/dL] of the US Food and Drug Administration label range effective through most of this period).

## METHODS

### Data Sources

Data were from Medicare final action claims for 2007-2011 covering Part A institutional claims (inpatient, outpatient, skilled nursing facility, hospice, or home health agency) and noninstitutional Part B physician/supplier claims. Patient demographic and comorbid condition information and dialysis facility information were obtained from the Medical Evidence Report (form CMS-2728) and provider claims. Patients' facilities were determined from form CMS-2728, the death notification, and facility survey forms, along with revenue files.

### Study Population and Design

This was a retrospective follow-up study. The anemia management trend analysis and transfusion risk analysis each consisted of a common baseline period (July to December of the preceding year) and study period (January to June of the cohort year) for each annual cohort (Fig S1, available as online supplementary material).

#### *Anemia Management Trend Analysis*

Yearly cohorts of point-prevalent in-center hemodialysis patients with Medicare as primary payer were identified for 2007-2011 and defined as of January 1 of each cohort year. Patients were required to contribute 6 months of data in the preceding year (July 1 to December 31; baseline period) and have continuous Medicare coverage (Parts A and B) during the baseline and study (January to June; cohort year) periods, one or more hemoglobin values during the study period, no record of sickle cell disease or trait, and no darbepoetin alfa use during either period. The study period began on January 1 of each year and continued to the earliest date of death, transplantation, loss to follow-up, or end of the study period (June 30; Figs S1 and S2).

#### *Transfusion Risk Analysis*

To evaluate the effect of facility treatment patterns (as assessed by prevalence of patients with hemoglobin levels $< 10$ g/dL) on patient risk of RBC transfusion, we subdivided the study period into exposure (January to March) and follow-up (April to June) periods; to be included, patients also had to survive through April 1 of each year. Each patient's facility was determined at the start of the year or 14 days after hospital discharge, and patients were required to receive care from the same facility during the entire exposure period. During follow-up, patients were censored at change in facility (of $> 14$ days) or for any aforementioned reason. To help ensure stable estimates, we excluded facilities with fewer than 20 patients with hemoglobin records and required facilities to have at least 4 months of hemoglobin data during the study period (Fig S2).

### Exposure, Outcome, and Other Measurements

During the baseline period of each year, we assessed demographic characteristics (age, sex, race, primary cause of end-stage renal disease, and dialysis duration) and comorbid conditions (Table S1) based on form CMS-2728 information completed at dialysis therapy initiation and on claims for services using established methods.[2,13] We also assessed medication use (IV antibiotics, epoetin alfa, and IV iron), hospital admissions and days, and RBC transfusion use.

For the trend analyses, 4 outcomes were assessed monthly during the first 6 months of each year: (1) median IV iron dose (milligrams) and percentage of use, (2) median monthly epoetin alfa dose adjusted for inpatient days (units), (3) percentage of patients with monthly hemoglobin levels $< 10$ g/dL, and (4) transfusion rate (total number of transfusions [inpatient + outpatient] in a month divided by total person-time at risk, expressed as rate per 100 person-months). Transfusion events were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification*, Healthcare Common Procedure Coding System, and *Current Procedure and Terminology* codes (Table S1).

For the risk analysis, we first assigned each dialysis facility a single hemoglobin score (percent of patient-months with hemoglobin levels $< 10$ g/dL), calculated as 100 times the sum of all occurrences of a patient having a month with hemoglobin level $< 10$ g/dL divided by the total number of patient-months with available hemoglobin records, during the exposure period (January to March) of each year. Facilities then were categorized, in each year, into 5 groups based on quintiles defined from the 5-year (2007-2011) distribution of the facility hemoglobin score; selecting a common quintile distribution enabled assessment of distributional shifts across years. We also evaluated epoetin alfa and IV iron use and median monthly dose during this exposure period. We assessed the transfusion event rate (as defined previously) and transfusion event count (used to model the RR of transfusion events) during the 3-month follow-up.

### Statistical Analyses

Patient characteristics across cohort years and facility hemoglobin quintiles were examined using descriptive statistics for