

Decreased Population Hb Levels and Increased Transfusion Rates Under New ESA Guidelines in Patients With ESRD at an LDO

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Introduction

- Patients with chronic kidney disease require iron and erythropoiesis-stimulating agents (ESAs) such as Epogen® (epoetin alfa) to treat anemia that is commonly associated with this disease.
- In June 2011, 6 months after the Center for Medicare and Medicaid Services (CMS) added injectable medications (eg, ESAs, vitamin D, and intravenous iron) to the bundled payment for dialysis service, the United States Food and Drug Administration (FDA) revised label language for ESAs in patients with chronic kidney disease.
- Dosing to a target range of hemoglobin (Hb) 10 g/dL to 12 g/dL is no longer suggested. The FDA-approved ESA labels now include black box language stating that patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a Hb concentration > 11 g/dL.²
- The ESA labels still recommend using the lowest ESA dose sufficient to reduce the need for red blood cell transfusions in patients.²

Objective

The objective of the current analysis was to assess the potential effects of ESA label changes (released 24 June 2011) on Hb concentrations and transfusion rates in end-stage renal disease (ESRD) patients receiving hemodialysis in a large dialysis organization (LDO).

Methods

Hb Concentrations

• Based on electronic medical records of dialysis patients (1 June 2010-1 April 2012), 146,439 individuals met the initial study eligibility criteria (≥ 18 years old, > 6 months of data) and were analyzed to determine the mean monthly Hb concentration over the study period.

Transfusions During Patient Hospitalizations

 As transfusion events occur primarily outside of chronic dialysis facilities, the medical records from a subset of 70,202 patients with identified hospitalization events between 1 January 2011 and 31 October 2011 were analyzed. Controls were hospitalized patients without a transfusion during the same month. Patient data were used to estimate the monthly proportion of patients transfused during hospitalizations using Generalized Estimating Equation models.

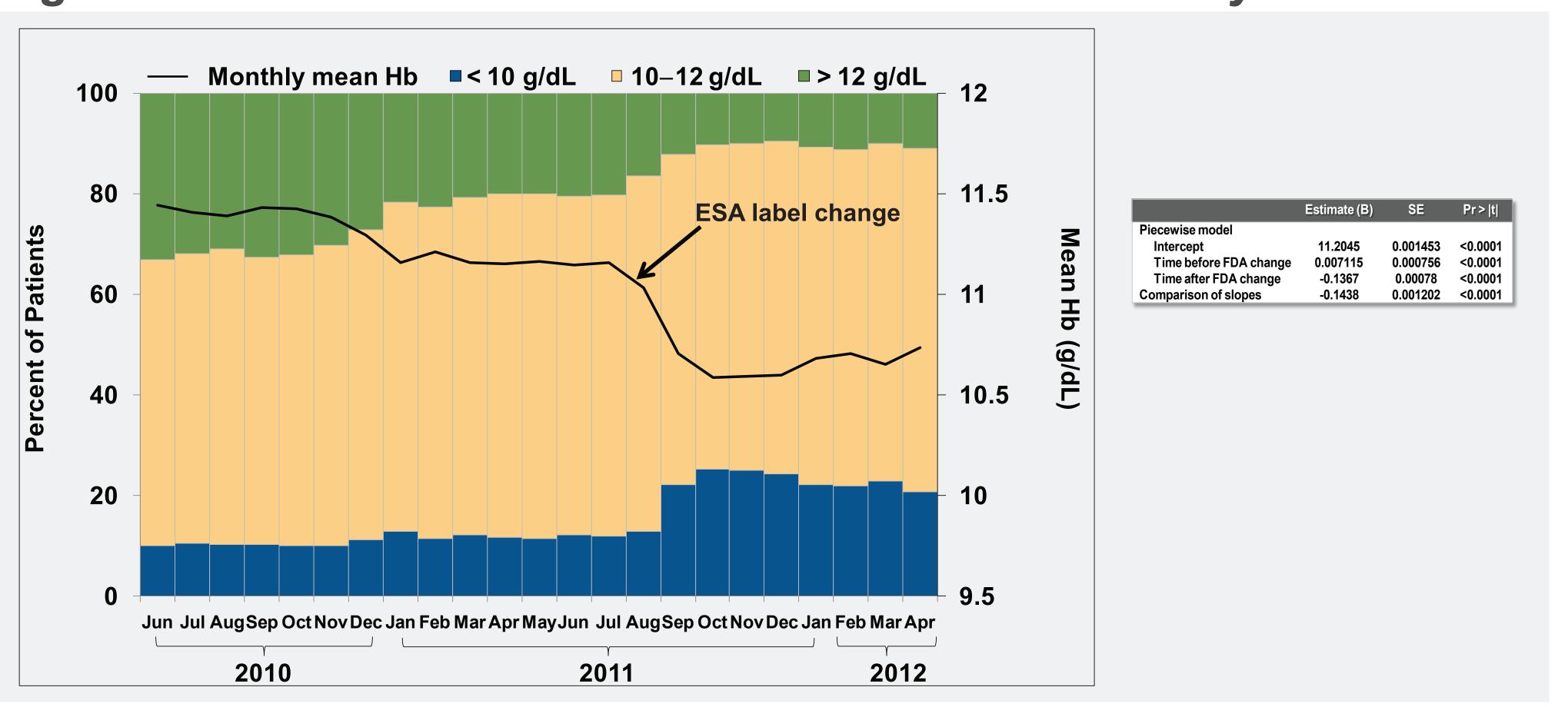
Multivariate Modeling

 Logistic regression models were used to evaluate risk factors for transfusion among the subset of hospitalized patients

Results

• Mean Hb in this LDO population decreased after the June 2011 label revision (Figure 1). Mean levels were 11.4 g/dL in June 2010 and 10.7 g/dL in April 2012. The proportion of patients with Hb levels < 10 g/dL increased, likely due to the mean population Hb level shifting lower. The percentage of patients with Hb < 10 g/dL was 9.64% in October 2010 (the low) and 24.25% in October 2011 (the high).

Figure 1: Mean Hb and Hb Distribution Over the Study Period



tient Ns varied: June 2010, n = 129,744; Dec 2010, n = 133,241; June 2011, n = 144,845, Dec 2011, n = 148,901, April 2012, n = 153,106.

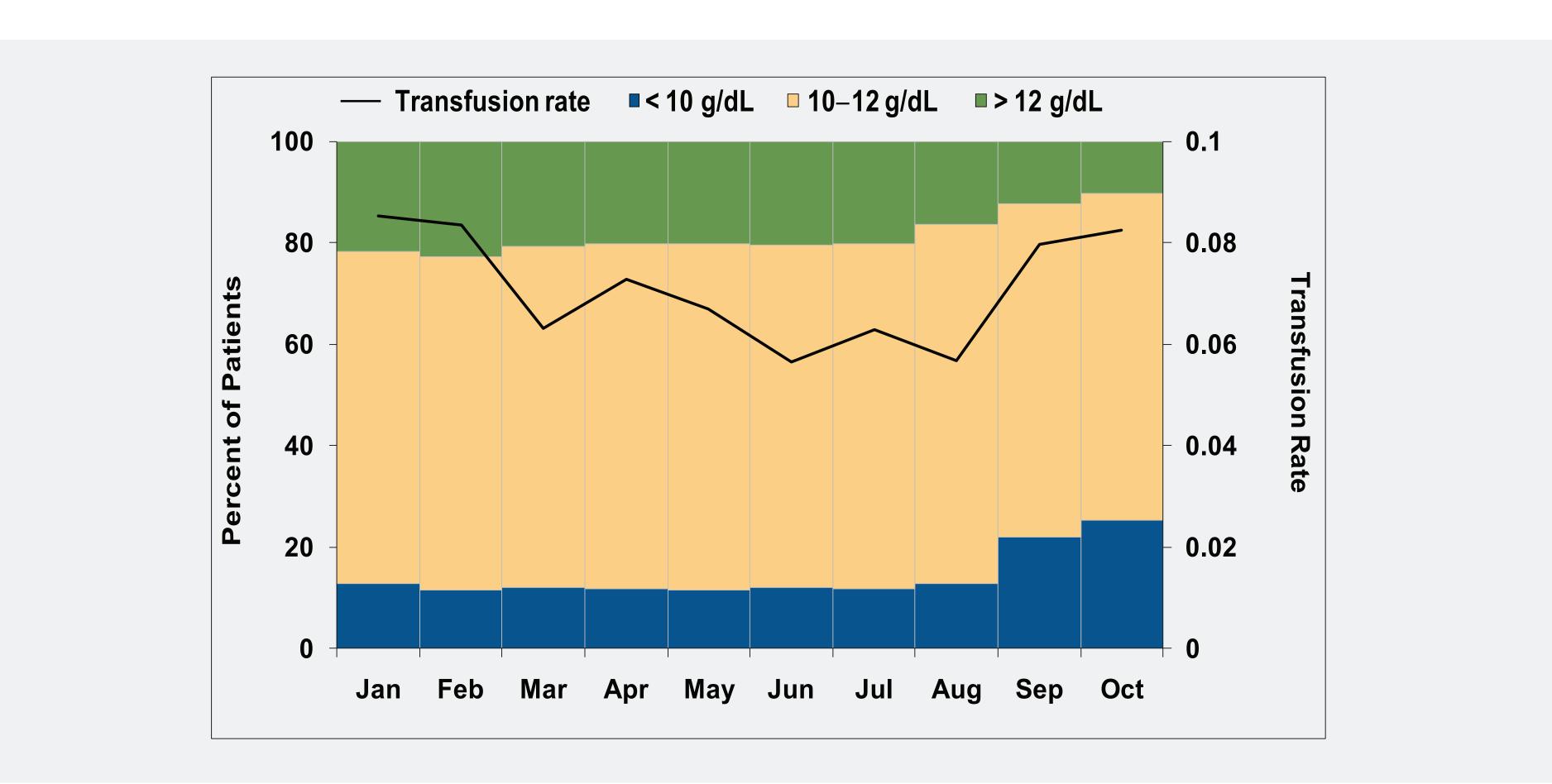
• The characteristics of dialysis patients who were hospitalized are shown in Table 1, differentiated by those individuals receiving transfusions during hospitalization events.

Table 1: Hospitalized Patient Characteristics

	Controls	Transfused	P value
Patients (N)	62,991	7,211	
Female gender (%)	49.93	51.1	0.0545
Hemoglobin (%) in g/dL			
< 81.83	10.66		
≥ 8 - < 10	21.34	31.75	
≥ 10 - < 12	60.34	44.07	< 0.0001
≥ 12	12.18	7.04	
Missing	4.30	6.48	
Race/Ethnicity (%)			
White	43.00	44.62	
Black	35.91	37.14	
Hispanic	13.92	11.32	< 0.0001
Asian	2.32	2.51	
American Native	2.48	1.61	
Comorbidity (%)			
Diabetic Kidney Disease	64.33	58.98	< 0.0001
Hypertensive Kidney Disease	39.61	38.97	0.283
Acute CMA*	8.57	12.31	< 0.0001
Chronic CMA*	1.96	5.08	< 0.0001
Body Mass Index (%) in kg/m2			
< 25	40.94	45.4	
≥ 25 - 30	26.08	24.46	< 0.0001
> 30	30.12	26.49	

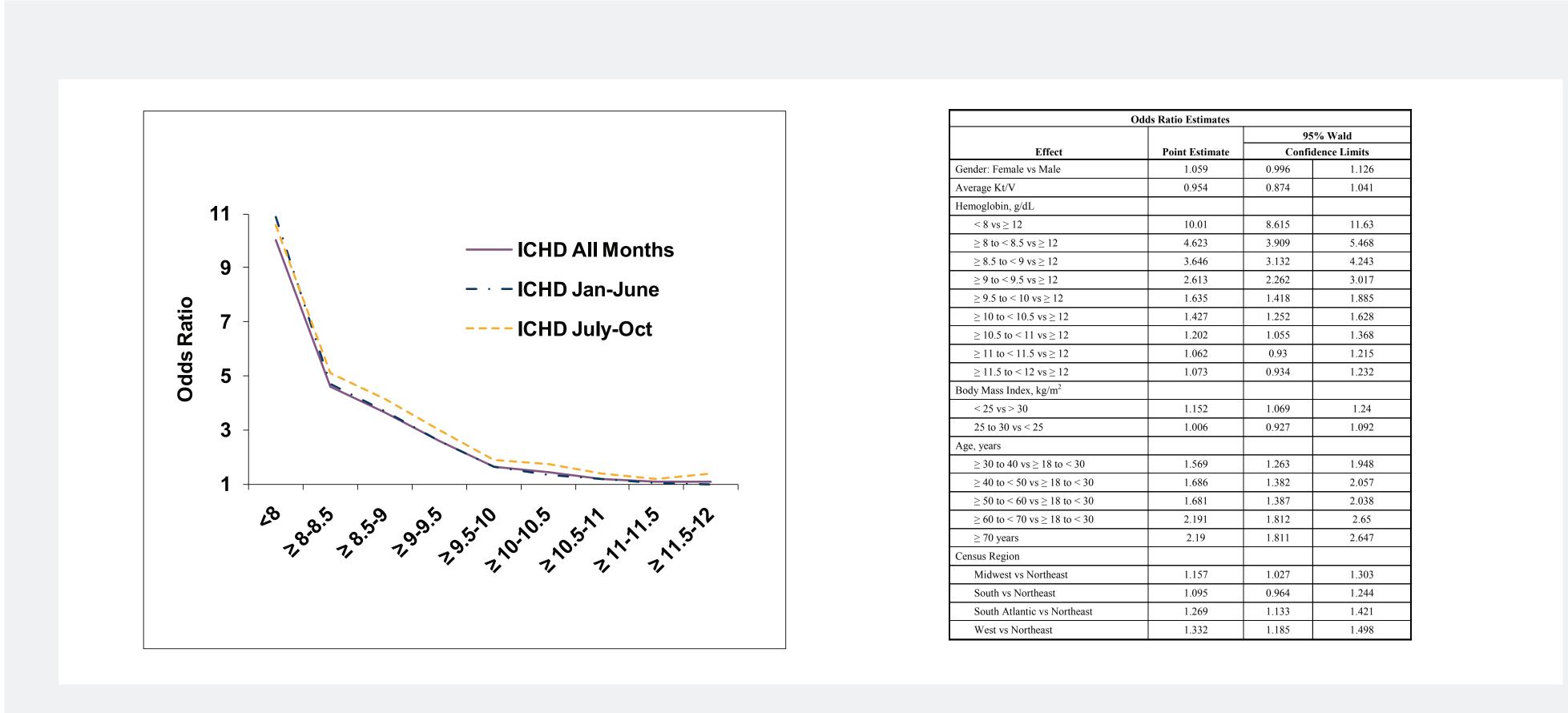
*Acute case-mix adjuster (CMA) refers to pericarditis or gastrointestinal bleed; chronic CMA refers to sickle cell, monoclonal gammopathy, myelodysplastic syndrome.

Figure 2: Mean Hb by Strata and Proportion of Hospitalized Patients With Transfusion for 9 Months in 2011*



*Monthly Hb trends are shown for the LDO population; monthly transfusion rates are indicated for the total patients hospitalized, which varied over the study. Jan 2011, n = 10,732; Oct 2011, n = 7,882. The least number of hospitalizations were recorded in April 2011, n = 4,240. The study time frame was limited by the availability of data for the hospitalized dialysis patients identified for this analysis.

Figure 3: Odds Ratio of Transfusion by Hb Concentration



*Abbreviations: ICHD, in-center hemodialysis.

Modeling: Hospitalized Patients Receiving Transfusion

- Among many risk factors, Hb was the most notable risk factor for patient transfusion during a
 hospitalization event prior to and after the label change and accounted for most of the
 transfusion risk in multivariate models (inset for Figure 3).
- Adjustment variables included demographic variables, dialysis-related factors, comorbidities/medical history of available conditions, and monthly changing biomarkers. The risk factors examined were hemoglobin, age, acute and chronic case-mix adjusters (CMAs), region, race/ethnicity, body mass index, diabetes, and primary insurer. The CMAs include the following: acute CMAs, pericarditis, bacterial pneumonia, and gastrointestinal bleed with hemorrhage. The chronic CMAs were hereditary hemolytic or sickle-cell anemia, myelodysplastic syndrome, and monoclonal gammopathy.

Conclusions

- The changes to ESA labeling had a notable effect on patient Hb concentrations. The distribution of mean monthly Hb values across the dialysis population was reduced; compared to before 24 June 2011, a greater proportion of dialysis patients had Hb < 10 g/dL.
- In the overall population, transfusion rates increased concurrently as patient Hb concentration decreased.
- For the given Hb strata, transfusion rates were similar before and after the labeling changes, indicating no adjustment in transfusion practices occurred after the ESA label change.
- Revision of the ESA labels resulted in a population mean reduction in Hb and the odds of transfusion at low Hb concentration remained consistently high.

References

- . Centers for Medicare and Medicaid Services. End-stage renal disease prospective payment system: final rule. Federal Register. 2010;75(155):49,029-49,214.
- 2. Epogen (epoetin alfa) package insert. Thousand Oaks, CA: Amgen, Inc; 2011.

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