

## Individualized Treatment Strategies and Optimal Hematocrit Target for Complex Dialysis Patients

Principal Investigator: Dennis Cotter, MSE  
Institution/Partners: Medical Technology and Practice  
Patterns Institute  
Project Period: 09/30/10 - 09/29/12  
Grant Number: R21 HS19513-01

### Description

Well-being of patients with end-stage renal disease (ESRD) could be improved with better management of anemia, a common complication among dialysis patients. Although epoetin is the standard treatment, its usefulness for patients who also suffer from diabetes and cardiovascular disease is uncertain. This study examined treatment strategies for anemia in ESRD patients given the presence of common comorbidities, such as diabetes and cardiovascular disease, in order to identify the optimal treatment. The findings can help develop clinical guidelines that more accurately reflect an individual patient's comorbidities and might lead to improved product labeling and more cost-effective third-party-payer policies.

### Specific Aims

1. Compare the effects on mortality and cardiovascular disease outcomes of a low (30-<34.5%) versus mid (34.5-<39%) hematocrit target strategies among elderly dialysis patients with diabetes and cardiovascular disease.
2. Given the presence of diabetes or cardiovascular disease, determine the optimal epoetin treatment strategy for anemia in ESRD patients, further disaggregated by patient demographics such as race, gender, and age.

### Findings

- Among both diabetics and non-diabetics, lower epoetin dose levels (<20,000 U/week) were associated with lower risk for both mortality and adverse cardiovascular outcomes (stroke, heart attack, and congestive heart failure).
- No clinical survival or cardiovascular advantage was found for elderly complex dialysis patients targeted to a mid-range vs. the lower hematocrit target recommended by FDA.

### Main Objective

Determine the optimal epoetin treatment strategy for anemia in renal failure patients given the presence of common co-morbidities, such as diabetes and cardiovascular disease.

### Chronic Conditions Considered

End-stage renal disease  
Anemia  
Diabetes  
Cardiovascular disease

### Study Design & Methods

Analytical epidemiologic study  
Inverse probability weighting and marginal structural models.

### Data Sources & Sample Size

Approximately 350,000 patients from the United States Renal Data System Standard Analytic Files, from 2006 to 2008

### Strategies Addressed from the HHS Strategic Framework on Multiple Chronic Conditions

- 3.A. Identify best practices
- 4.C. Increase clinical research
- 4.D. Address health disparities

## Individualized Treatment Strategies and Optimal Hematocrit Target for Complex Dialysis Patients (continued)

- The intention-to-treat hazard ratio (95% confidence interval) for mid versus low hematocrit strategy was 1.05 (0.99, 1.11) for all-cause mortality, and 1.03 (0.98, 1.08) for the composite endpoint. The per-protocol hazard ratio (95% confidence interval) for mid versus low hematocrit strategy was 0.98 (0.78, 1.24) for all-cause mortality and 1.00 (0.81, 1.24) for the composite outcome.

### Implications

Given the high cost and safety concerns associated with the high doses of epoetin required to achieve a higher hematocrit target, these findings support FDA's most recent advisories, which recommend a hematocrit target of less than 33% for treating dialysis patients, including complex patients. Reimbursement policies should reflect the FDA's recommendation.

### Publications (as of September 2013)

Zhang Y, Thamer M, Kaufman J, Cotter D, Hernán MA. Comparative effectiveness of two anemia management strategies for complex elderly dialysis patients. *Medical Care*. In press, 2014.

Zhang Y, Thamer M, Kaufman J, Cotter D, and Hernan M. High doses of epoetin do not lower mortality and cardiovascular risk among elderly hemodialysis patients with diabetes. *Kidney International*. 22 Jun 2011; 80(6):663-669.

### Posters and Presentations

Cotter D, Thamer M, and Zhang Y. Progress toward a rational anemia management strategy for dialysis patients. Teleconference presented to Center for Medicare and Medicaid Services (CMS). April 22, 2013; Bethesda, MD.

Cotter D, Thamer M, and Zhang Y. Progress toward a rational anemia management strategy for dialysis patients. Presented to Center for Outcomes and Evidence, Agency for Healthcare Research and Quality. March 21, 2013; Rockville, MD.

Cotter D. Comparisons of two anemia treatment strategies among elderly dialysis patients with diabetes. Poster presentation at: Moving ahead: Leveraging knowledge and action to improve healthcare quality. 6th Annual Conference of the Agency for Healthcare Research and Quality; 2012 Sept 9-12; Bethesda, MD.

Zhang Y, Thamer M, Kaufman J, Cotter D, and Hernán M. High doses of epoetin do not lower mortality and cardiovascular risk among elderly hemodialysis patients with diabetes. Poster presentation at: 71st Scientific Sessions. American Diabetes Association Annual Meeting; 2011 Jun 24 – 28; San Diego, CA.