

# Evaluation of an Anemia Management Protocol in Chronic Dialysis Patients

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## Introduction

- Anemia is a common complication in patients with chronic kidney disease. Approximately 90% of dialysis patients are anemic.
- Appropriate management of anemia is a major focus of care for dialysis patients.
- Treatment options include erythropoietic stimulating agents (ESAs) and iron products. These drug therapies are expensive and efforts to optimize their use are a priority.
- The use of an anemia management protocol standardizes treatment and could result in cost savings.
- At our local health authority, an anemia management protocol for peritoneal dialysis (PD) and hemodialysis (HD) patients was implemented in 2007.
- This study set out to evaluate the impact of the protocol on anemia outcomes in chronic dialysis patients.

## Objectives

### Primary objectives

- To determine if the protocol resulted in a significant difference in:
  - The proportions of patients below, within and above the target hemoglobin (Hgb) range of 110-120 g/L\*
  - Hgb and iron indices

### Secondary objectives

- To determine if the protocol resulted in a significant difference in:
  - The average percentage of time spent within the target Hgb range
  - The use and cost of parenteral iron products and ESAs

\*Although the recommended target Hgb range is 110-120 g/L in current guidelines, the acceptable range of the protocol is 105-125 g/L. This was chosen to prevent ESA dose changes when Hgb values were slightly outside the extremities of the recommended target. For this study, we evaluated a target of 110-120 g/L.

## Methods

### Design

- Retrospective chart review of dialysis patients initiated on the protocol between January 2007 and March 2009.
- Data collected monthly and divided into two periods: pre-protocol (months 1 to 3) and post-protocol (months 7 to 9).

### Inclusion Criteria

- PD or HD patient
- Started and continued on the protocol for  $\geq 6$  months
- $\geq 18$  years old

### Exclusion Criteria

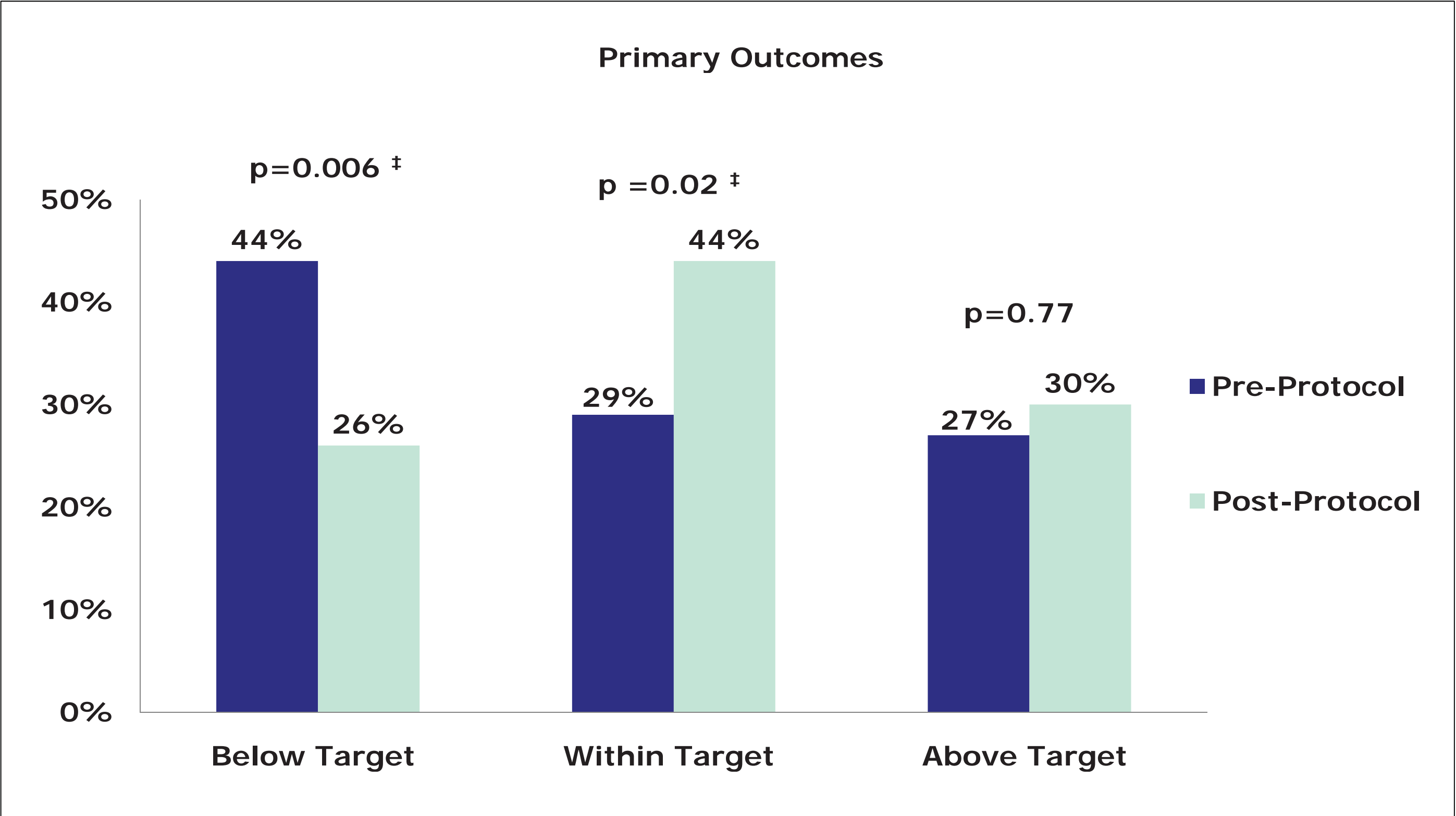
- Kidney transplantation during the study period
- Hospitalization
- Gastrointestinal bleed
- Received blood transfusions

### Data Analysis

- A sample size of 189 was required to detect a 10% difference in patients within the target Hgb range pre- and post-protocol implementation ( $\alpha = 0.05$ ,  $\beta = 0.2$ ).
- Differences in proportions of patients below, within and above the target Hgb range pre- and post-protocol implementation were assessed for statistical significance using Chi-square tests.
- Pre- and post-protocol implementation outcomes were assessed for statistical significance using paired t-tests.

## Results

Figure 1: Proportions of patients below, within and above the target Hgb range pre- and post-protocol implementation (n=118).



Below Target: Hgb < 110 g/L, Within Target: Hgb 110-120 g/L, Above Target: Hgb > 120 g/L

\* Statistically significant. The level of significance was set at  $p < 0.05$ .

Table 1: Comparison of anemia indices pre- and post-protocol implementation (n=118).

Primary Outcomes	Pre-Protocol Mean (SD)	Post-Protocol Mean (SD)	P value
Hgb	106.5 g/L (22.1)	111.0 g/L (20.0)	0.069
TSAT	23.4 % (9.9)	27.6 % (12.0)	<0.001*
Ferritin	165.9 µg/L (138.4)	261.1 µg/L (227.6)	<0.001*

TSAT: Percent Transferrin Saturation, SD: Standard Deviation

\* Statistically significant. The level of significance was set at  $p < 0.05$ .

Table 2: Comparison of secondary outcomes pre- and post-protocol implementation.

Secondary Outcomes	Pre-Protocol Mean (SD)	Post-Protocol Mean (SD)	P value
Sodium ferric gluconate dose (n=56)	189.3 mg (161.4)	279.4 mg (113.9)	0.013*
Iron sucrose dose (n=20)	288.9 mg (246.8)	240.0 mg (144.3)	0.319
Iron dextran dose (n=8)	216.7 mg (144.2)	173.3 mg (95.3)	0.394
Epoetin alfa dose (n=71)	34 323 units (50 723)	41 561 units (49 138)	0.014*
Darbepoietin alfa dose (n=47)	181 mcg (205)	136 mcg (116)	0.039*
Mean % of time spent within the target Hgb range (n=118)	58.0% (37.0)	70.5% (25.6)	0.007*

\* Statistically significant. The level of significance was set at  $p < 0.05$ .

## Results

Table 3: Comparison of parenteral iron products and ESAs costs pre- and post-protocol implementation.

Drug Therapy	Pre-Protocol Mean	Post-Protocol Mean	Mean Difference (95% CI)	Cost Difference per 100 Patients/ Year
Sodium ferric gluconate (n=56)	\$75.97	\$112.11	+\$36.14 (7.97, 64.30)	+\$43 368
Iron sucrose (n=20)	\$116.28	\$96.60	-\$19.67 (-60.55, 21.20)	-\$23 604
Iron dextran (n=8)	\$59.53	\$47.67	-\$11.91 (-42.05, 18.22)	-\$14 292
Epoetin alfa (n=71)	\$523.43	\$633.80	+\$110.37 (23.06, 197.68)	+\$132 444
Darbepoietin alfa (n=47)	\$519.71	\$388.99	-\$130.73 (-254.80, -6.65)	-\$156 870

95% CI: 95% Confidence Interval

## Discussion

- Use of the protocol increases the proportion of patients within the target Hgb range and decreases the proportion of patients below target.
- There was no statistically significant difference in the proportion of patients above the target Hgb range. A possible explanation is that the protocol accepts an upper limit of 125 g/L. Patients with Hgb levels between 121-125 g/L would have remained on their current ESA dose. This demonstrates an upper limit of 125 g/L is not effective at achieving a target Hgb range of 110-120 g/L.
- The protocol increased mean monthly Hgb, TSAT and ferritin levels. However, the increase in Hgb was not statistically significant.
- The mean monthly dose and cost of sodium ferric gluconate increased. This is consistent with published literature and was expected as the protocol provided maintenance iron dosing. Further, the protocol initiated iron loading doses more frequently than standard care. There were no statistically significant differences in the doses and costs of iron sucrose or iron dextran, likely due to small sample sizes.
- The mean monthly dose and cost of epoetin alfa increased while the mean monthly dose and cost of darbepoietin alfa decreased. Previous studies have shown a decrease or no difference in the use of ESAs after protocol implementation. Overall, the combined cost of both agents in this study was similar to the pre-protocol period.

### Limitations

- Retrospective study using surrogate markers of efficacy.
- Target sample size was not reached.
- Adherence to protocol varied on occasion and may have affected protocol performance.
- Equal response to the protocol was assumed in a heterogeneous population (community HD, home HD and PD patients).
- Home HD and PD patients self-administered ESAs - adherence was assumed.
- Quality of life outcomes, impact of workload on nursing staff and nephrologists satisfaction with the protocol were not evaluated.

## Conclusions

- The protocol improves anemia outcomes in chronic dialysis patients.
- Increased costs of parenteral iron products and similar costs of ESAs were observed.
- The acceptable Hgb range should be narrowed to 105-120 g/L to improve performance of the protocol.