

IN THE LITERATURE

Dialysis Facility Ownership and Epoetin Dosing in Patients Receiving Hemodialysis: The Authors Respond

The following is a commentary on the In the Literature editorials that appeared in the September issue of AJKD (volume 50, pages 349-370)

First, we want to thank the *American Journal of Kidney Diseases* for organizing a discussion of an important issue for dialysis patients and their providers. We address the editorialists' comments on our paper and highlight the areas of controversy and some goals for future research.

Weiner and Levey¹ provide an excellent summary of the history of epoetin utilization and reimbursement in the United States, and of the key findings of our study. They, like Lazarus and Hakim,² would have preferred our using the median doses, as opposed to the mean doses, to compare epoetin use between for-profit and not-for-profit dialysis facilities. Table 1 provides the median doses by provider type by hematocrit level. Although the use of the median might be misleading (eg, it would detect no differences between two doctors that prescribe the same doses to half of their patients but extremely different doses to the other half), the conclusions from our study remain unchanged whether we use means or medians.

In our article³ we suggested several reasons for the use of higher doses in for-profit facilities. These include quality of care considerations, as encouraged by Medicare requirements for reporting the percentage of patients at a facility with hemoglobin greater than 11 g/dL (110 g/L) with a goal of 80% or greater compliance, and a reimbursement policy consistent with the prescription of higher epoetin doses. Most of the editorialists acknowledge the importance of financial incentives and the editorial by Coyne⁴ accompanying our publication strongly suggests that economic considerations might assume greater im-

portance in epoetin dosing decisions in for-profit facilities. Lazarus and Hakim do not question our main finding—epoetin doses are higher in for-profit than not-for-profit facilities—but they strongly dismiss the possibility that financial incentives might affect epoetin dosing. According to Lazarus and Hakim, “physicians, not nurses or managers . . . prescribe treatment and determine appropriate outcomes, whether in for-profit or not-for-profit facilities.” Because physicians' decisions are not influenced by their employers, they claim “it is a gross distortion to suggest that dialysis providers . . . determine hemoglobin levels or the dose of erythropoietin for any patient.” We did not suggest that dialysis providers directly determine hemoglobin levels or the dose of epoetin, but that providers might influence these decisions. Lazarus and Hakim acknowledge the use of dosing algorithms and we recognize that these are important tools for quality improvement. If these algorithms are furnished by the dialysis provider, as we believe they are in many cases, the dialysis provider will have a strong role in influencing treatment decisions. Furthermore, Lazarus and Hakim acknowledge that at the chain they represent “physicians are encouraged to meet the target of 80% of patients achieving a hemoglobin value of 11 g/dL (110 g/L),” and the chain “identifies facilities with a high or atypical percentage of patients above 12.5 g/dL (125 g/L) and encourages physicians in those facilities to modify their prescriptions.” Even if one shares Lazarus and Hakim's conviction that physicians are free to make decisions regarding epoetin dosing in both for-profit and not-for-profit chains, the question remains: Why do physicians prescribe higher doses in for-profit than in not-for-profit chains?

Another possibility is that patients attending for-profit facilities might require, on average, a greater epoetin dose. As an example, Lazarus and Hakim point out that blacks require higher epoetin doses than whites and our study reported

Address correspondence to Dennis Cotter, MSE, Medical Technology and Practice Patterns Institute, 4733 Bethesda Avenue, Suite 510, Bethesda, Maryland 20814. E-mail: dcott@mtpi.org

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Table 1. Median Epoetin Dose by Hematocrit Level

Type of Facility	Overall	Hematocrit Level (%)*				
		<30	30-<33	33-<36	36-<39	>=39
Median Epoetin Dose, U/wk in December 2004						
For-profit	13,928	40,133	25,583	15,788	11,455	8,129
Not-for-profit	11,742	30,710	18,828	12,069	9,414	7,724
Chain						
1	13,548	38,621	24,138	14,226	11,247	8,593
2	15,540	67,429	43,405	21,781	12,100	6,698
3	14,121	41,766	28,903	17,026	12,552	9,333
4	14,023	37,864	23,484	14,452	11,381	7,748
5	11,923	32,974	19,623	11,828	8,468	5,413
6	12,520	39,103	20,865	13,802	8,834	5,721
Nonchain	12,698	31,613	20,571	13,210	10,313	7,933
Hospital-based	10,705	27,180	16,258	10,983	9,100	8,129

*Hematocrit level was taken in November 2004.

that for-profit facilities had a 6% higher prevalence of blacks compared to not-for-profit facilities. However, they fail to point out that we also provided race-adjusted estimates (which show that race imbalances are insufficient to explain the dosage differences) and that the nation's largest not-for-profit chain (Chain 5) has the greatest proportion of black patients, and yet used the lowest epoetin doses among the free-standing facilities.

An additional possibility is that doctors working at for-profit and not-for-profit facilities make independent decisions that are, somehow, fundamentally different. As a result of these decisions, large for-profit chains would have a consistently higher epoetin use across all hematocrit groups than not-for-profit facilities or smaller chains. This explanation begs the question: what makes doctors working at for-profit facilities so different from others working elsewhere—training, experience, clinical objectives, access to medical literature, marketing campaigns? Lazarus and Hakim offer no specific response to this question. They do mention potential differences in how physicians at for-profit facilities treat iron deficiency or choose the route of erythropoietin administration, but again the question is: Why should clinical practice vary by profit status if physicians make their own decisions?

Returning to the possibility that employers might affect physicians' prescription behavior, Lazarus and Hakim speculate that for-profit chains fear "being identified in the Centers for

Medicare and Medicaid Services (CMS) Dialysis Facility Compare website as having facilities that fail to achieve the goal of 80% of patients with a hemoglobin value above 11 g/dL (110 g/L)," which makes them encourage the use of higher epoetin doses. However, the nation's largest not-for-profit chain (Chain 5) also met the 80% goal and yet used significantly smaller doses of epoetin than any of the large for-profit chains. Lazarus and Hakim correctly point out that Chain 5 also has 6% more patients below 11 g/dL (110 g/L) than the for-profit chains, but their assertion that lower hemoglobin levels are associated with worse outcomes must be viewed with extreme caution because the available evidence comes from observational studies in which there was inappropriate adjustment of measured confounding by indication,⁵⁻⁷ and which have been contradicted by numerous randomized controlled trials.⁸⁻¹³ In fact, no study has shown a benefit on clinical outcomes using a lower limit for target hemoglobin of greater than 10 g/dL (100 g/L).¹⁴ Although some observers have suggested improved quality of life at hemoglobins greater than 11 g/dL (110 g/L), as Kasiske points out in his editorial, such conclusions remain controversial. Finally, Lazarus and Hakim express concern that Chain 2, which treated 14% of the patients in our study, used even higher epoetin doses than doctors in other for-profit chains. Again, the question is why could this happen.

We concur with Macdougall's¹⁵ suggestion that it is short-sighted to examine hemoglobin

without knowledge or consideration of the epoetin doses used to achieve this result. Although, as Macdougall states, “it is still too soon to suggest that the higher epoetin dosages used in the for-profit dialysis facilities . . . may increase the risk of death,” we hope that studies comparing the effects of various anemia management strategies on hemoglobin, mortality and cardiovascular morbidity will soon be undertaken. Macdougall also highlights the different economic considerations in Europe and how they influence route of administration and dosing, providing additional support for our suggestion that financial incentives might affect treatment decisions.

Cohen and Neumann, two health care economists,¹⁶ cite additional evidence for the influence of financial incentives on medical treatment. We agree with the authors that it “is not the profit motive per se,” but rather that “existing incentives for treating ESRD patients are not optimally structured.” We echo their call for more research to develop and optimize epoetin dosing algorithms, to examine the reasons for the heterogeneity in the dose response relationships, and to structure reimbursement policy to optimize treatment and to examine the impact of any change in policy.

The editorialists closed with their recommendations for providers and CMS. It is interesting to note the diversity of opinions regarding physicians’ dosing decisions. Kasiske,¹⁷ a nephrologist in a university-based practice in the United States, advocates a target hemoglobin of 10 to 12 g/dL (100 to 120 g/L) and careful attention to other factors that might affect epoetin responsiveness such as iron deficiency. Macdougall, a UK nephrologist, does not provide specific suggestions for US nephrologists but notes that, unlike in the US, authorities in other countries have not revised their anemia treatment guidelines and many nephrologists continue to allow hemoglobins to reach levels no greater than 13 g/dL (130 g/L). Lazarus and Hakim, representing the views of the largest US dialysis chain, emphasize the need for prescribers to achieve a hemoglobin of 11 g/dL (110 g/L) or greater in 80% of their patients and to target an upper bound for hemoglobin of 12.5 g/dL (125 g/L), and advocate the use of treatment algorithms that allow for appropriate modification by physicians. Regarding recommendations for CMS, Cohen and Neumann,

Kasiske, and Macdougall acknowledge the role of financial incentives in influencing anemia management decisions and Cohen and Neumann, and Kasiske suggest that current CMS policy might not be optimizing the cost-efficient use of epoetin. Kasiske specifically calls for research on how to achieve the best outcomes in the most cost-effective manner. Lazarus and Hakim do not suggest any changes in CMS policy, but we infer that they believe that current reimbursement policy is consistent with their anemia management goals.

We believe this diversity of opinion reflects the continuing controversy about appropriate hemoglobin targets. Although all editorialists recognize that targeting hemoglobins greater than 13 g/dL (130 g/L) have not been shown to have benefit and might cause harm, it seems that the optimal hemoglobin target below this upper boundary has not been convincingly established. As recognized by the editorialists, more research is needed to optimize anemia management and improve reimbursement policy. We need to test different dosing algorithms and hemoglobin targets using recognized clinical outcomes such as mortality and cardiovascular morbidity, as well as validated quality of life measures. Research to date has not examined the role of treatment algorithms as determinants of outcomes, but the results of recent randomized studies, such as CHOIR¹² and CREATE,¹³ raise the possibility that high doses of epoetin might, in themselves, result in adverse health outcomes. Further, the variability in epoetin responsiveness, as highlighted by lower dosing requirements outside the United States, needs to be understood. It is likely that a single dosing algorithm that disregards epoetin responsiveness might not be optimal. As we address these research objectives, we need to consider how clinical objectives can be supported by an appropriate reimbursement policy.

Mae Thamer, PhD

Medical Technology and Practice Patterns
Institute
Bethesda, Maryland

Yi Zhang, MS

Medical Technology and Practice Patterns
Institute
Bethesda, Maryland

James Kaufman, MD

Veterans Affairs Boston Healthcare Systems and
Boston University School of Medicine
Boston, Massachusetts

Dennis Cotter, MSE

Medical Technology and Practice Patterns
Institute
Bethesda, Maryland

Miguel A. Hernán, MD

Department of Epidemiology
Harvard School of Public Health
Boston, Massachusetts

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REFERENCES

- Weiner DE, Levey AS: Dialysis facility ownership and epoetin dosing in hemodialysis patients: An overview. *Am J Kidney Dis* 50:349-353, 2007
- Lazarus JM, Hakim RM: Dialysis facility ownership and epoetin dosing in hemodialysis patients: A dialysis provider's perspective. *Am J Kidney Dis* 50:366-370, 2007
- Thamer M, Zhang Y, Kaufman J, Cotter D, Dong F, Hernan MA: Dialysis facility ownership and epoetin dosing in patients receiving hemodialysis. *JAMA* 297:1667-1674, 2007
- Coyne DW: Use of epoetin in chronic renal failure. *JAMA* 297:1713-1716, 2007
- Li S, Collins AJ: Association of hematocrit value with cardiovascular morbidity and mortality in incident hemodialysis patients. *Kidney Int* 65:626-633, 2004
- Collins AJ, Li S, St. Peter W, et al: Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. *J Am Soc Nephrol* 12:2465-2473, 2001
- Ofsthun N, LaBrecque J, Lacson E, Keen M, Lazarus JM: The effects of higher hematocrit levels on mortality and hospitalization in hemodialysis patients. *Kidney Int* 63:1908-1914, 2003
- Besarab A, Bolton WK, Browne JK, et al: The effects of normal as compared with low hematocrit values in patients with cardiac disease who are receiving hemodialysis and epoetin. *N Engl J Med* 339:584-590, 1998
- Parfrey PS, Foley RN, Wittreich BH, Sullivan DJ, Zagari MJ, Frei D: Double-blind comparison of full and partial anemia correction in incident hemodialysis patients without symptomatic heart disease. *J Am Soc Nephrol* 16:2180-2189, 2005
- Foley RN, Parfrey PS, Morgan J, et al: Effect of hemoglobin levels in hemodialysis patients with asymptomatic cardiomyopathy. *Kidney Int* 58:325-335, 2000
- Laupacis A: A randomized double-blind study of recombinant human erythropoietin in anaemic hemodialysis patients. Canadian Erythropoietin Study Group. *Transplant Proc* 23:1825-1826, 1991
- Singh AK, Szczech L, Tang KL, et al, for the CHOIR Investigators: Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med* 355:2085-2098, 2006
- Drueke TB, Locatelli F, Clyne N, et al, for the CREATE Investigators: Normalization of hemoglobin level in patients with chronic kidney disease and anemia. *N Engl J Med* 355:2071-2084, 2006
- Cotter D, Thamer M, Narasimhan K, Zhang Y, Bullock K: Translating epoetin research into practice: Role of the government and use of scientific evidence. *Health Affairs* 25:1249-1259, 2006
- Macdougall IC: Dialysis facility ownership and epoetin dosing in hemodialysis patients: A view from Europe. *Am J Kidney Dis* 50:358-361, 2007
- Cohen JT, Neumann PJ: Dialysis facility ownership and epoetin dosing in hemodialysis patients: A medical economic perspective. *Am J Kidney Dis* 50:362-365, 2007
- Kasiske BL: Dialysis facility ownership and epoetin dosing in hemodialysis patients: A US physician perspective. *Am J Kidney Dis* 50:354-357, 2007