

**MTPPI Epoetin Research Activities
1991-2009**

Background

Since 1991, MTPPI (www.mtppi.org) has engaged in a multi-year project that has amassed CMS data on over one million ESRD patients to examine epoetin therapy; *a service intended to treat blood transfusion dependent dialysis patients (~10-30% of the ESRD patient pool) is provided to virtually all dialysis patients, costing Medicare in excess of \$20 billion and ESRD patients over \$4 billion since 1989.* This research has produced 14 publications and numerous presentations to public agencies and professional groups (listed below). The long-term study, entitled "Human Recombinant Erythropoietin Utilization in the Medicare Patient Populations," provided an ongoing opportunity, originally using HCFA REBUS and now USRDS Medicare claims data. In conducting this research, we have worked closely with MTPPI's Technical Advisory Committee (TAC, see Attachment B), first convened June 1992, and commissioned to examine access, utilization and costs of epoetin therapy among the U.S. ESRD population. The eighteenth gathering of this group, was comprised of nationally recognized nephrologists, Federal agency representatives (CMS, FDA, NCI, NHLBI, NIDDK, VA, & others) and private sectors groups (ESRD Network, RPA, and others). Currently there is no outside sponsorship of the TAC. Between 1991-98 Ortho Biotech sponsored the research effort and 2004-06 the research was partially funded by an NIDDK grant.

Publications related to our long-term study:

10. Thamer M, Ray NF, Richard C, Greer JW, Pearson BC, Cotter DJ. Excluded from universal coverage: ESRD patients not covered by Medicare. *Health Care Financ Rev.* 1995 Winter;17(2):123-46.
11. Thamer, Mae; Richard, C., Ray, N.F., Greer J., Cotter, D.J., Pearson, B: "The Effect of Insurance Status on Recombinant Erythropoietin Therapy in Three States." *American Journal of Kidney Diseases* 1996;28:235-49.
12. Cotter, D.J., Thamer, M, Kimmel, PL, Sadler, JH: "Secular Trends in Recombinant Erythropoietin Therapy Among the U.S. Hemodialysis Population: 1990 - 1996." *Kidney International* 1998;54:2129-39.
13. Thamer M, Richard CM, Klinkmann J, Ivanovich P, Lang G, Cotter DJ. Use of clinical guidelines for treatment of anemia among hemodialysis patients. *Artif Organs.* 2000 Feb;24(2):91-4.
15. Cotter, D.J., Stefanik K, Zhang Y, Thamer M. Improved survival with higher hematocrits: where is the evidence? *Semin Dial.* 2004 May-Jun;17(3):181-3.
16. Cotter, D.J., Stefanik K, Zhang Y, Thamer M, Scharfstein D, Kaufman J, Evaluation of Hematocrit as a Surrogate Endpoint for Survival Among Epoetin-Treated Hemodialysis Patients. *J Clin Epidemiol, J Clin Epidemiol.* 2004 Oct;57(10):1086-95.
17. Cotter, D.J. Challenges in Establishing a Clinically and Scientifically Robust Epoetin Policy, *Clin Nephrol* 2004 Jul;62(1):69-70.

18. Zhang Y, Thamer M, Stefanik K, Kaufman J, Cotter DJ. Epoetin requirements predict mortality in hemodialysis patients. *Am J Kidney Dis.* 2004 Nov;44(5):866-76.
19. Zhang Y, Thamer M, Stefanik K, Cotter DJ. Does dose matter? *Nephrol Dial Transplant.* 2004 Jun;19(6):1658;
20. Yi Zhang, Mae Thamer, Firas Marayati, Dennis J. Cotter, James Kaufman, Factors Influencing Route of Administration for Epoetin Treatment Among Hemodialysis Patients in the United States, *Am J Kidney Dis.* 2006 Jul;48(1):77-87
21. Cotter D, Thamer M, Narasimhan K, Zhang Y, Bullock K. Translating epoetin research into practice: the role of government and the use of scientific evidence. *Health Aff (Millwood).* 2006 Sep-Oct;25(5):1249-59.
22. Thamer M, Zhang Y, Kaufman J, Dong F, Cotter D, Hernan MA Dialysis Facility Ownership and Epoetin Dosing in Patients Receiving Hemodialysis *JAMA,* 2007 Apr 18;297(15):1667-74.
23. Cotter D, Thamer M, Zhang Y, Kaufman J, Hernan MA The Effect of Epoetin Dose on Hematocrit, *Kidney Int.* 2007 Oct;72(8):1247.
24. Zhang Y, Thamer M, **Cotter D**, Kaufman J, Hernan MA "The Estimated Effect of Epoetin Dose on Survival among Elderly Hemodialysis Patients in the United States " *Clin J Am Soc Nephrol.* March 1 2009, Volume 4, Issue 3

Letters To-the-editor:

1. Cotter DJ. Is the evidence for high hematocrit targets valid? *Am J Kidney Dis.* 2003 Feb;41(2):520.
2. Cotter D. Does the evidence for anemia treatment support a survival benefit? *Arch Intern Med.* 2003 Oct 27;163(19):2395-6; author reply 2396-7.
3. Zhang Y, Thamer M, Stefanik K, Cotter DJ. Does dose matter? *Nephrol Dial Transplant.* 2004 Jun;19(6):1658; author reply 1658-9.
4. Cotter D, To the editor: The December 2006 issue of *NN&I* contained a letter to the editor and excerpts from a position paper attacking our policy paper published in *Health Affairs.* *Nephrology News & Issues,* February 2007, pgs 12 & 17.
5. Mae Thamer; Yi Zhang; Dennis J. Cotter; James Kaufman; Miguel A. Hernán Epoetin Dosing and Dialysis Facility Ownership—Reply *JAMA,* August 22/29, 2007; 298: 862.
6. Thamer M, Zhang Y, Kaufman J, Dong F, Cotter D, Hernan MA In the literature: Dialysis facility ownership and epoetin dosing in patients receiving hemodialysis – the authors respond, *Am J Kid Dis,* 50(4) October 2007 538-541.
7. Cotter D, Thamer, M Zhang, Y To the editor: Exploring Relative Mortality and Epoetin Alfa

Dose Among Hemodialysis Patients: A Researcher's Perspective, The Challenge of Analyzing the Effect of Epoetin Dose Levels Am J Kid Dis, 2008 accepted.

8. Cotter D, Zhang Y, Thamer M, Kaufman J, Hernan MA Response to "The Effect of Epoetin Dose on Hematocrit " Kidney Int. 2008 Sep;74(6):827-8.

MTPPI EPO Presentations to Federal Agencies:

FDA - Presentation to Drs. Richard Pazdur, Karen Weiss, Dwaine Rieves and staff: Preliminary Epoetin Research Findings, March 07, 2007; Presentation to Cardiovascular and Renal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, September 11, 2007. *accessible at:*

http://www.fda.gov/ohrms/dockets/ac/07/slides/2007-4315s1-03-MTPPI-Cotter_files/frame.htm

CDER Seminar on Epoetin Safety and Product Labeling, February 27, 2009

NIH/NIDDK Seminar Epoetin therapy: Steps to the future, March 12, 2009

CMS - Presentation to Drs. Straube and Phurrough and staff: Preliminary Epoetin Research Findings, April 03, 2007

Congress/GAO - Presentation to Bruce Steinwald and staff, Preliminary Epoetin Research Findings, March 2007; Beneficiary Differences in Medicare Treatment and Payment for Beneficiaries with End-Stage Renal Disease (ESRD) Interview Questions December 16, 2008; Bundling of Epoetin into the ESRD Composite Rate Payment, March 3, 2009

Congress/MedPAC - Presentation to Mark E. Miller, Nancy Ray and staff: Achieving Equity Should Epoetin Become a Component of the ESRD Composite Rate, February 01, 2007; Bundling of Epoetin into the ESRD Composite Rate Payment, March 3, 2009

Congress - The Committee on Ways and Means, Hearing on Patient Safety and Quality Issues in End Stage Renal Disease Treatment, December 6, 2006 *accessible at:*

<http://waysandmeans.house.gov/hearings.asp?formmode=view&id=5371> - Staffs of: House The Energy and Commerce Committee and Committee on Ways and Means and Senate Committee on Finance presentation on Seminar on Epoetin Safety and Bundling of Epoetin into the ESRD Composite Rate Payment, March 3, 2009

