AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

HEARING ON ENSURING KIDNEY PATIENTS RECEIVE SAFE AND APPROPRIATE ANEMIA MANAGEMENT CARE

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

OF THE

COMMITTEE ON WAYS AND MEANS
U.S. HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

FIRST SESSION

JUNE 26, 2007

Serial No. 110–51

Printed for the use of the Committee on Ways and Means

U.S. GOVERNMENT PRINTING OFFICE

49–981 WASHINGTON : 2010

For sale by the Superintendent of Documents, U.S. Government Printing Office
Internet: bookstore.gpo.gov Phone: toll free (866) 512–1800; DC area (202) 512–1800
Fax: (202) 512–2104 Mail: Stop IDCC, Washington, DC 20402–0001

COMMITTEE ON WAYS AND MEANS

CHARLES B. RANGEL, New York, *Chairman*

FORTNEY PETE STARK, California
SANDER M. LEVIN, Michigan
JIM MCDERMOTT, Washington
JOHN LEWIS, Georgia
RICHARD E. NEAL, Massachusetts
MICHAEL R. MCNULTY, New York
JOHN S. TANNER, Tennessee
XAVIER BECERRA, California
LLOYD DOGGETT, Texas
EARL POMEROY, North Dakota
STEPHANIE TUBBS JONES, Ohio
MIKE THOMPSON, California
JOHN B. LARSON, Connecticut
RAHM EMANUEL, Illinois
EARL BLUMENAUER, Oregon
RON KIND, Wisconsin
BILL PASCRELL, JR., New Jersey
SHELLEY BERKLEY, Nevada
JOSEPH CROWLEY, New York
CHRIS VAN HOLLEN, Maryland
KENDRICK MEEK, Florida
ALLYSON Y. SCHWARTZ, Pennsylvania
ARTUR DAVIS, Alabama

JIM MCCRERY, Louisiana
WALLY HERGER, California
DAVE CAMP, Michigan
JIM RAMSTAD, Minnesota
SAM JOHNSON, Texas
PHIL ENGLISH, Pennsylvania
JERRY WELLER, Illinois
KENNY HULSHOF, Missouri
RON LEWIS, Kentucky
KEVIN BRADY, Texas
THOMAS M. REYNOLDS, New York
PAUL RYAN, Wisconsin
ERIC CANTOR, Virginia
JOHN LINDER, Georgia
DEVIN NUNES, California
PAT TIBERI, Ohio
JON PORTER, Nevada

JANICE MAYS, *Chief Counsel and Staff Director*
BRETT LOPER, *Minority Staff Director*

SUBCOMMITTEE ON HEALTH

FORTNEY PETE STARK, California, *Chairman*

LLOYD DOGGETT, Texas
MIKE THOMPSON, California
RAHM EMANUEL, Illinois
XAVIER BECERRA, California
EARL POMEROY, North Dakota
STEPHANIE TUBBS JONES, Ohio
RON KIND, Wisconsin

DAVE CAMP, Michigan
SAM JOHNSON, Texas
JIM RAMSTAD, Minnesota
PHIL ENGLISH, Pennsylvania
KENNY HULSHOF, Missouri

Pursuant to clause 2(e)(4) of Rule XI of the Rules of the House, public hearing records of the Committee on Ways and Means are also published in electronic form. **The printed hearing record remains the official version.** Because electronic submissions are used to prepare both printed and electronic versions of the hearing record, the process of converting between various electronic formats may introduce unintentional errors or omissions. Such occurrences are inherent in the current publication process and should diminish as the process is further refined.

CONTENTS

Page

WITNESSES

Hon. Donna M. Christian-Christensen, M.D., a Delegate to Congress from the United States Virgin Islands 55

Leslie V. Norwalk, Acting Administrator, Centers for Medicare and Medicaid Services 68
Robert A. Vito, Regional Inspector General for the Office of Evaluation and Inspections, U.S. Department of Health and Human Services, Philadelphia, Pennsylvania 85
John K. Jenkins, M.D., Director, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, Maryland 94

Ajay K. Singh, M.D., Clinical Director, Renal Division, Director, Dialysis Services, Associate Professor of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 133
Kris Robinson, Executive Director and CEO, American Association of Kidney Patients, Tampa, Florida 138
Alan S. Kliger, M.D., President, Renal Physicians Association, Rockville, Maryland 143

SUBMISSIONS FOR THE RECORD

Amgen, statement 155
Kidney Care Partners, statement 163
National Renal Administrators Association, statement 166
Renal Support Network, statement 169
Research Utilization Project Proposal, statement 171

HEARING ON ENSURING KIDNEY PATIENTS RECEIVE SAFE AND APPROPRIATE ANEMIA MANAGEMENT CARE

Tuesday, June 26, 2007

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON WAYS AND MEANS,
SUBCOMMITTEE ON HEALTH,
Washington, D.C.

The Subcommittee met, pursuant to call, at 10:05 a.m., in Room 1102, Longworth House Office Building, Hon. Fortney Pete Stark (Chairman of the Subcommittee) presiding.

[The advisory announcing the hearing follows:]

ADVISORY

FROM THE COMMITTEE ON WAYS AND MEANS

SUBCOMMITTEE ON HEALTH

FOR IMMEDIATE RELEASE
June 26, 2007
HL–15

CONTACT: (202) 225 093943

Stark Announces a Hearing on Ensuring Kidney Patients Receive Safe and Appropriate Anemia Management Care

House Ways and Means Health Subcommittee Chairman Pete Stark (D–CA) announced today that the Subcommittee on Health will hold a public hearing on safety concerns regarding the dosing of erythropoiesis stimulating agents (ESAs), variations in utilization of ESAs across providers, and reimbursement issues. **The hearing will take place at 10 a.m. on Tuesday, June 26, 2007, in Room 1100, Longworth House Office Building.**

In view of the limited time available to hear witnesses, oral testimony at this hearing will be from the invited witness only. However, any individual or organization not scheduled for an oral appearance may submit a written statement for consideration by the Committee and for inclusion in the printed record of the hearing.

BACKGROUND:

The Medicare program began covering treatment for patients with End Stage Renal Disease (ESRD) beginning in 1972. According to the U.S. Renal Data System (USRDS), the dialysis population reached nearly 336,000 patients in 2004 at a cost of $20.1 billion. This amounts to a 57 percent increase in Medicare ESRD spending since 1999. In 2004, the average annual cost per Medicare beneficiary was $58,000.

When a patient's kidneys stop working, as is the case with ESRD patients, they often cannot produce enough of the hormone erythropoietin, which helps the body produce red blood cells. As a result, these patients suffer from anemia. Synthetic versions of erythropoietin are collectively referred to as erythropoiesis stimulating agents (ESAs), which are sold in the U.S. under the brand names of Epogen, Procrit, and Aranesp.

Dialysis care has made great strides in treating anemia, and this achievement is directly linked to significant increases in doses of ESAs. Dosing levels increased dramatically in recent years, with average weekly dose of ESAs increasing nearly 4,000 units between 2000 and 2004. Medicare spending for ESAs increased by 17 percent from 2003 to 2004 alone, up to $1.8 billion. Spending on ESAs per person per month is now nearly one-half of the monthly cost for dialysis.

While ESAs are critical to treatment of anemia for ESRD patients, higher doses that raise red blood cells above a certain threshold have been found to pose significant health risks to patients. The Food and Drug Administration (FDA) recently issued a black box label warning of risk of blood clots, strokes, heart failure and heart attacks in kidney patients in such circumstances. Furthermore, as both the Medicare Payment Advisory Commission and the Government Accountability Office point out, there are flaws in the current Medicare reimbursement system. The existing Medicare payment system incentivizes higher doses in certain circumstances, with resulting health risks and higher costs for beneficiaries and taxpayers.

"My priority for Medicare ESRD policy is to ensure patient safety while also protecting taxpayers from unnecessary expenditures," stated Chairman

Stark in announcing the hearing. **"Health risks associated with higher doses and well-documented flaws in a payment system that encourages higher dosing highlights that this issue is ripe for reexamination. We must do better for our ESRD beneficiaries and for the taxpayers."**

FOCUS OF THE HEARING:

The hearing will focus on the safety concerns regarding dosing of ESAs for ESRD, variations in utilization of ESAs across providers, and issues related to reimbursement.

DETAILS FOR SUBMISSION OF WRITTEN COMMENTS:

Please Note: Any person(s) and/or organization(s) wishing to submit for the hearing record must follow the appropriate link on the hearing page of the Committee website and complete the informational forms. From the Committee homepage, *http://waysandmeans.house.gov*, select "110th Congress" from the menu entitled, "Committee Hearings" *(http:*//waysandmeans.house.gov/Hearings.asp?congress=18). Select the hearing for which you would like to submit, and click on the link entitled, "Click here to provide a submission for the record." Once you have followed the online instructions, completing all informational forms and clicking "submit" on the final page, an email will be sent to the address which you supply confirming your interest in providing a submission for the record. You MUST REPLY to the email and ATTACH your submission as a Word or WordPerfect document, in compliance with the formatting requirements listed below, by close of business **Tuesday, July 10, 2007**. Finally, please note that due to the change in House mail policy, the U.S. Capitol Police will refuse sealed-package deliveries to all House Office Buildings. For questions, or if you encounter technical problems, please call (202) 225–1721.

FORMATTING REQUIREMENTS:

The Committee relies on electronic submissions for printing the official hearing record. As always, submissions will be included in the record according to the discretion of the Committee. The Committee will not alter the content of your submission, but we reserve the right to format it according to our guidelines. Any submission provided to the Committee by a witness, any supplementary materials submitted for the printed record, and any written comments in response to a request for written comments must conform to the guidelines listed below. Any submission or supplementary item not in compliance with these guidelines will not be printed, but will be maintained in the Committee files for review and use by the Committee.

1. All submissions and supplementary materials must be provided in Word or WordPerfect format and MUST NOT exceed a total of 10 pages, including attachments. Witnesses and submitters are advised that the Committee relies on electronic submissions for printing the official hearing record.

2. Copies of whole documents submitted as exhibit material will not be accepted for printing. Instead, exhibit material should be referenced and quoted or paraphrased. All exhibit material not meeting these specifications will be maintained in the Committee files for review and use by the Committee.

3. All submissions must include a list of all clients, persons, and/or organizations on whose behalf the witness appears. A supplemental sheet must accompany each submission listing the name, company, address, and telephone and fax numbers of each witness.

Note: All Committee advisories and news releases are available on the World Wide Web at *http://waysandmeans.house.gov*

The Committee seeks to make its facilities accessible to persons with disabilities. If you are in need of special accommodations, please call 202–225–1721 or 202–226–3411 TTD/TTY in advance of the event (four business days notice is requested). Questions with regard to special accommodation needs in general (including availability of Committee materials in alternative formats) may be directed to the Committee as noted above.

Chairman STARK. Good morning. We'll begin our hearing on ensuring that kidney patients receive safe and appropriate anemia management care.

Delegate Christian-Christensen, acting administrator Norwalk, Dr. Jenkins, Mr. Vito and the advocates and researchers on our third panel, I want to thank you for being here today. My hope is that we won't be interrupted by too many votes so that we can proceed and not keep you here all day.

Ms. Norwalk, I believe it will be her last scheduled appearance before the Ways and Means Committee in her current position, and I want to wish her luck in whatever her future endeavors may be and to thank Ms. Norwalk for her service at CMS.

As you know, the issue of Medicare's care for end-stage renal disease, ESRD, patients was one where our former chairman Bill Thomas and I were in agreement. We're here today to advance the discussion of safety issues and the problems with the current reimbursement system that Chairman Thomas raised in our last hearing in December.

In 2005, there were 321,000 Medicare beneficiaries receiving dialysis. We spent 8 billion on their dialysis and drugs including the anti-anemia drug Epogen. From '91 to 2004, Medicare spending on Epogen for ESRD patients grew from $245 million to $2 billion, an increase of over 700 percent.

We fully recognize that Epogen and other drugs like it, known collectively as ESAs, are critical to the treatment of anemia for ESRD patients. No one disputes the underlying benefit of this therapy for people suffering from anemia, however there are two major concerns regarding the use of ESA's.

First, we must put patient safety first. We'll hear from the FDA that when anti-anemia drugs are used to raise red blood cell levels above a certain threshold there's a risk of death, blood clots, strokes, heart failure and heart attacks. We need to keep this in mind as we're dealing with populations that are more vulnerable to these conditions.

Second, we're stewards of taxpayers' dollars. The current Medicare reimbursement system creates incentives for higher dosing of ESAs, which lead not only to the aforementioned health risks, but also come at a higher cost to taxpayers and beneficiaries.

The Office of the Inspector General will present their new report, released today, documenting that large dialysis organizations make a profit on each and every dose of Epogen. Recent research published in JAMA shows that for-profit dialysis centers dose Epogen at higher levels than not-for-profit centers. The payment system leads to perverse incentives that we cannot ignore.

I would say that the opposite is true. If we reduce the payment we might have incentive for providers to cut the level of ESAs and thereby have people's levels dropped to a dangerous level on the minus side.

I did hear this morning that Amgen is releasing some numbers today as a part of an industry public relations stunt. And if Amgen and the rest of the industry are finally admitting that there are health safety concerns and lowering Epogen dosing accordingly, I'm glad to hear it.

This announcement proves however that there are additional efficiencies that can be gained by reducing Epogen doses. Clearly what I've been saying all along is true. The industry only responds when we threaten to do the right thing and remove their incentive to inflate doses as a way to reap profits. Medicare can be a better purchaser of care for dialysis beneficiaries and can do so in a way that ensures more efficient use of ESAs and better health outcomes for beneficiaries.

I'd like to quote from a few letters that I've recently received and will set the stage for what we'll talk about today. Without objection, the letters will be entered into the record in their entirety.

United States Government Accountability Office

GAO

Testimony

Before the Subcommittee on Health, Committee on Ways and Means, House of Representatives

For Release on Delivery
Expected at 10:00 a.m. EDT
Tuesday, June 26, 2007

END-STAGE RENAL DISEASE

Medicare Should Pay a Bundled Rate for All ESRD Items and Services

Statement for the Record of A. Bruce Steinwald
Director, Health Care

GAO-07-1050T

Mr. Chairman and Members of the Subcommittee:

I am pleased to provide, as requested, a statement for the record on Medicare payments for certain drugs provided to patients with end-stage renal disease (ESRD), a condition of permanent kidney failure.[1] Through Medicare's ESRD benefit, patients receive a treatment known as dialysis, which removes excess fluids and toxins from the bloodstream. Patients also receive items and services related to their dialysis treatments, including drugs to treat conditions resulting from the loss of kidney function, such as anemia and low blood calcium. Detailed information on the prudence of bundling payments for all ESRD items and services and a recommendation to establish a bundled payment system as soon as possible are included in our report entitled *End-Stage Renal Disease: Bundling Medicare's Payment for Drugs with Payment for All ESRD Services Would Promote Efficiency and Clinical Flexibility*.[2] This report, along with a testimony statement, was released at a December 6, 2006, hearing of the full Committee on Ways and Means.[3] Today's statement highlights the information in that report and refers to information other witnesses presented at the hearing. The work we performed for the report was conducted in accordance with generally accepted government auditing standards.

[1]These drugs are covered under Medicare Part B, the part of Medicare that covers a broad range of medical services, including physician, laboratory, and hospital outpatient services and durable medical equipment. Part B-covered drugs are typically administered by a physician or other medical professional rather than by patients themselves. In contrast, drugs covered under the new prescription drug benefit, known as Part D, are generally self-administered by patients.

[2]GAO, *End-Stage Renal Disease: Bundling Medicare's Payment for Drugs with Payment for All ESRD Services Would Promote Efficiency and Clinical Flexibility*, GAO-07-77 (Washington, D.C.: Nov. 13, 2006).

[3]GAO, *End-Stage Renal Disease: Medicare Payments for All ESRD Services, Including Injectable Drugs, Should Be Bundled*, GAO-07-208T (Washington, D.C.: Dec. 6, 2006).

Revised Medicare Payment Provisions Do Not Eliminate Incentives to Overuse Certain Drugs Billed for Separately

The way Medicare currently pays for injectable drugs provided to patients during dialysis treatments helps explain the potential for these drugs to be overused. The Centers for Medicare & Medicaid Services (CMS), the agency that administers the Medicare program, divides ESRD items and services into two groups for payment purposes. In the first group are dialysis and associated routine services—such as nursing, supplies, equipment, and certain laboratory tests. These items and services are paid for under a composite rate—that is, one rate for a defined set of services. Paying under a composite rate is a common form of Medicare payment, also known as bundling. In the second group are primarily injectable drugs and certain laboratory tests that were either not routine or not available in 1983 when Medicare implemented the ESRD composite rate. These items and services are paid for separately on a per-service basis and are referred to as "separately billable."

Over time, Medicare's composite rate, which was not automatically adjusted for inflation, covered progressively less of the costs to provide routine dialysis services, while program payments for the separately billable drugs generally exceeded providers' costs to obtain these drugs. As a result, dialysis facilities relied on Medicare's generous payments for separately billable drugs to subsidize the composite rate payments that had remained nearly flat for two decades. In addition, the use of the separately billable drugs by facilities became routine, and program payments for these drugs grew substantially. In 2005, program spending for the separately billable drugs totaled about $2.9 billion.

The effect of several legislative and regulatory changes since the enactment of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA)[9] has been to raise the composite rate for dialysis services while reducing Medicare's generous payments for separately billable ESRD drugs. Under the first legislative change in 2005, Medicare expenditures for certain of these drugs dropped 11.8 percent. Under the current payment method—which for each drug equals the manufacturer's average sales price (ASP) plus 6 percent—Medicare's payment rates have varied from quarter to quarter but have remained relatively consistent with the lower 2005 payment rates.

[9]Pub. L. No. 108-173, 117 Stat. 2066.

The ASP-based rates are an improvement over the pre-MMA method, as ASP is based on actual transactions. However, certain unknowns about the composition of ASP and the ASP-based payment formula make it difficult for CMS to determine whether the ASP-based payment rates are no greater than necessary to achieve appropriate beneficiary access. For one thing, CMS has no procedures for validating the accuracy of a manufacturer's ASP, which is computed by the manufacturer. For another, CMS has no empirical justification for the 6 percent add-on to ASP. Regardless of how payment for these drugs is calculated, as long as facilities receive a separate payment for each administration of each drug and the payment exceeds the cost of acquiring the drug, an incentive remains to use more of these drugs than necessary.

The ASP payment method is of particular concern with respect to Epogen®, which in 2005 accounted for $2 billion in Medicare payments and is Medicare's highest Part B expenditure drug.[4] Most ESRD patients receive injections of Epogen at nearly every dialysis treatment, and whether Epogen is being overused has been called into question by some experts. At the December 2006 hearing of the full Committee, expert witnesses discussed their study results regarding Epogen use. One study found that kidney disease patients who were given high levels of Epogen experienced a higher risk of cardiovascular events and mortality than those who received lower levels of the drug.[5] Another study found that Medicare spent at least a third more on Epogen—amounting to hundreds of millions of dollars—than it would have if the levels of Epogen administered were in line with practice guidelines recommended by the National Kidney Foundation.[6]

[4]Introduced in 1989, Epogen—the brand name for epoetin alpha—was an expensive breakthrough drug used to treat anemia in patients with ESRD. In treating anemia—a condition in which not enough red blood cells carry oxygen throughout the body—Epogen is used to achieve a certain level of hemoglobin, the part of the red blood cell that carries oxygen. The National Kidney Foundation develops guidelines on the optimal hemoglobin range.

[5]See Ajay Singh et al., "Correction of Anemia with Epoetin Alfa in Chronic Kidney Disease," *The New England Journal of Medicine*, vol. 355, no. 20 (Nov. 16, 2006).

[6]See Laura Pizzi et al., "Economic Implications of Non-Adherence to Treatment Recommendations for Hemodialysis Patients with Anemia," *Dialysis and Transplantation*, vol. 35, no. 11 (November 2006).

Our own study found that Epogen use, which grew rapidly in the years before the MMA provisions took effect, continued to grow through the first half of 2006, although at a slower rate than previously. Epogen is the only product available in the domestic ESRD market for anemia management. However, the ASP method relies on market forces to achieve a favorable rate for Medicare. When a product is available through only one manufacturer, Medicare's ASP rate lacks the moderating influence of competition. The lack of price competition may be financially insignificant for noncompetitive products that are rarely used, but for Epogen, which is pervasively and frequently used, the lack of price competition could be having a considerable adverse effect on Medicare spending.

Bundled Payment System for ESRD Services, Including Injectable Drugs, Would Promote Efficiency and Clinical Flexibility

Medicare's approach to paying for most services provided by health care facilities is to pay for a group—or bundle—of services using a prospectively set rate. For example, under prospective payment systems, Medicare makes bundled payments for services provided by acute care hospitals, skilled nursing facilities, home health agencies, and inpatient rehabilitation facilities. In creating one payment bundle for a group of associated items and services provided during an episode of care, Medicare encourages providers to operate efficiently, as providers retain the difference if Medicare's payment exceeds the costs they incur to provide the services. Medicare's composite rate for routine dialysis and related services was introduced in 1983 and was the program's first bundled rate.

Experts contend that a bundled payment for all dialysis-related services would have two principal advantages. First, it would encourage facilities to provide services efficiently; in particular, under a fixed, bundled rate for a defined episode of care,[5] facilities would no longer have an incentive to provide more ESRD drugs than clinically necessary. Second, bundled payments would afford clinicians more flexibility in decision making because incentives to prescribe a particular drug or treatment are reduced. For example, providers might be more willing to explore alternative methods of treatment and modes of drug delivery if there were no financial benefit to providing more drugs and services than necessary.

[5]In the case of the composite rate, one dialysis session constitutes an episode of care. Unlike this method, a newly designed payment bundle could define the episode of care more broadly. For example, the new payment bundle could cover dialysis and related items and services for 1 month.

In response to a congressional mandate that CMS study the feasibility of creating a bundled payment,[9] the agency issued a study in 2003 concluding that developing a bundled ESRD payment rate was feasible and that further study of case-mix adjustment—that is, a mechanism to account for differences in patients' use of resources—was needed. In the MMA, the Congress required CMS to issue a report and conduct a 3-year demonstration of a system that would bundle payment for ESRD services, including drugs that are currently billed separately, under a single rate.[10] Both the CMS report, due in October 2005, and the demonstration, mandated to start in January 2006, are delayed.

Any payment changes based on CMS's report or demonstration would require legislation, because the MMA specified that drugs billed separately in 2003 would continue to be billed separately and not bundled in the composite rate.[11] In light of the uncertain time frame for CMS's test of bundling and the need for explicit legislation, in our report we asked the Congress to consider establishing a bundled payment for all ESRD services as soon as possible. In our view, Medicare could realize greater system efficiency if all ESRD drugs and services were bundled under a single payment. A bundled payment would encourage facilities to use drugs more prudently, as they would have no financial incentive to use more than necessary and could retain the difference between Medicare's payment and their costs. To account for facilities' increased or decreased costs over time, a periodic reexamination of the bundled rate may be necessary. This would ensure that facilities would be paid appropriately and that Medicare could realize the benefit of any cost reductions.

Contacts and Acknowledgments

For more information regarding this statement, please contact A. Bruce Steinwald at (202) 512-7114 or steinwaldab@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. Phyllis Thorburn, Assistant Director; Jessica Farb; and Hannah Fein made key contributions to this statement.

[9]Medicare, Medicaid, and SCHIP Benefits Improvement and Protection Act of 2000, Pub L. No. 106-554, app. F, § 422(b) and (c), 114 Stat. 2763A-463, 2763A-535—2763A-517.

[10]Pub. L. No. 108-173, § 623(e)-(f), 117 Stat. 2066, 2315-17.

[11]MMA § 623(d)(1), § 1881(b)(13)(B), 117 Stat. 2314-15 (to be codified at 42 U.S.C. § 1395rr(b)(13)(B)).

This is a work of the U.S. government and is not subject to copyright protection in the United States. It may be reproduced and distributed in its entirety without further permission from GAO. However, because this work may contain copyrighted images or other material, permission from the copyright holder may be necessary if you wish to reproduce this material separately.

GAO's Mission	The Government Accountability Office, the audit, evaluation and investigative arm of Congress, exists to support Congress in meeting its constitutional responsibilities and to help improve the performance and accountability of the federal government for the American people. GAO examines the use of public funds; evaluates federal programs and policies; and provides analyses, recommendations, and other assistance to help Congress make informed oversight, policy, and funding decisions. GAO's commitment to good government is reflected in its core values of accountability, integrity, and reliability.
Obtaining Copies of GAO Reports and Testimony	The fastest and easiest way to obtain copies of GAO documents at no cost is through GAO's Web site (www.gao.gov). Each weekday, GAO posts newly released reports, testimony, and correspondence on its Web site. To have GAO e-mail you a list of newly posted products every afternoon, go to www.gao.gov and select "Subscribe to Updates."
Order by Mail or Phone	The first copy of each printed report is free. Additional copies are $2 each. A check or money order should be made out to the Superintendent of Documents. GAO also accepts VISA and Mastercard. Orders for 100 or more copies mailed to a single address are discounted 25 percent. Orders should be sent to: U.S. Government Accountability Office 441 G Street NW, Room LM Washington, D.C. 20548 To order by Phone: Voice: (202) 512-6000 TDD: (202) 512-2537 Fax: (202) 512-6061
To Report Fraud, Waste, and Abuse in Federal Programs	Contact: Web site: www.gao.gov/fraudnet/fraudnet.htm E-mail: fraudnet@gao.gov Automated answering system: (800) 424-5454 or (202) 512-7470
Congressional Relations	Gloria Jarmon, Managing Director, JarmonG@gao.gov (202) 512-4400 U.S. Government Accountability Office, 441 G Street NW, Room 7125 Washington, D.C. 20548
Public Affairs	Paul Anderson, Managing Director, AndersonP1@gao.gov (202) 512-4800 U.S. Government Accountability Office, 441 G Street NW, Room 7149 Washington, D.C. 20548

PRINTED ON RECYCLED PAPER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes and
Digestive and Kidney Diseases
Bethesda, Maryland 20892

June 22, 2007

The Honorable F. Pete Stark
Chairman, Subcommittee on Health
Committee on Ways and Means
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Thank you for your letter of June 18 regarding trends in dosing of erythropoiesis stimulating agents in the treatment of anemia associated with dialysis in patients with end-stage kidney disease. Your questions concern data presented in the 2006 Annual Data Report of the U.S. Renal Data System (USRDS). I have directed members of my staff with detailed knowledge of the USRDS to prepare the enclosed responses to your questions. The responses indicate that use of erythropoiesis stimulating agents has increased over the past 15 years and that patients undergoing dialysis display variation in their hemoglobin levels.

I welcome the opportunity to share information about NIDDK's research efforts with the Committee, and I hope that you find this information helpful.

Sincerely,

Griffin P. Rodgers, M.D., M.A.C.P.
Director

Summary of NIDDK Responses to Questions on the United States Renal Data System

1. How are patients distributed by mean monthly hemoglobin (USRDS Chart 5.27)? What percentage of patients exceed the recommended maximum hemoglobin (Hb) of 12 grams per deciliter (g/dl)? What percentage of patients are below Hb of 10 g/dl. How have those trends changed over time?

In general, the percentage of patients with hemoglobin levels lower than 10 g/dl has declined, while the fraction of patients with hemoglobin levels above 12 g/dl has increased over time. By 2005, over half of patients had hemoglobin levels of 12.0 g/dl or greater. About 6 percent were below 10 g/dl.

2. How has mean EPO dose per week changed over time (USRDS Chart 5.30)?

Between 1991 and 2005, the average weekly dose of EPO more than doubled.

3. Page 198 of the 2006 USRDS Annual Report states, "We assessed provider practice patterns on dosing changes and found that DaVita tends to adjust the least and DCI the most when hemoglobin levels exceed 12–13 g/dl." How was this assessment conducted? What information was reviewed? Did NIH review anemia management guidelines? In what manner does DaVita make adjustments as compared to DCI? How do the other chains, such as Fresenius, compare?

This assessment examined patient months in which hemoglobin levels exceeded 12 g/dl, and determined the frequency with which such patients subsequently had their EPO dose reduced by at least 12.5 percent. Dialysis providers made appropriate dose reductions in about half of cases; frequency ranged from 55.2 percent for Gambro to 44.3 percent for Davita.

4. How does patient hemoglobin vary across dialysis centers (USRDS chart 10.21)? Which chains have the most patients exceeding Hb of 12 g/dl? Which chains have the largest proportion of patients within the target range of 10 to 12 g/dl?

The percentage of patients whose hemoglobin exceeds 12 g/dl varies widely across dialysis providers, ranging from 65 percent (Davita) to 20 percent (DCI) The chains with the largest proportion of patients within the target range of 10–12 g/dl are DCI (65 percent) and National Nephrology Associates (54 percent).

5. What are the trends for Medicare spending on erythropoiesis stimulating agents (ESAs) in recent year (USRDS Chart 11.26)? How does growth in spending on ESAs compare to spending on other parts of ESRD care? How do ESA costs per member month vary by dialysis chain?

The cost of services associated with dialysis increased by 72 percent between 1991 and 2004. The two primary components of this cost are the dialysis itself and erythropoiesis stimulating agents (ESA). Over this time period, dialysis costs increased 17 percent and ESA costs increased 235 percent. ESA costs by chain range from $654 per patient month for Gambro to $516 for hospital-based dialysis.

NIDDK Responses to Questions on the United States Renal Data System

1. How are patients distributed by mean monthly hemoglobin (USRDS Chart 5.27)? What percentage of patients exceed the recommended maximum hemoglobin (Hb) of 12 grams per deciliter (g/dl)? What percentage of patients are below Hb of 10 g/dl. How have those trends changed over time?

Figure 5.27, shown on the next page, is from the 2006 Annual Data Report of the United States Renal Data System (USRDS). It shows the 15 year trend in average hemoglobin levels of kidney failure patients on hemodialysis whose treatment is reimbursed through Medicare. Normal hemoglobin values in adults range from 13.5 to 16.5 grams per deciliter (g/dl) of blood for men and 12 to 15.5 g/dl for women. Based on end-of-year figures for each year from 1991 to 2005, the following trends are displayed. In 1991, 52.4 percent of patients had a hemoglobin level of less than 10 g/dl, 16.4 percent of patients had achieved the target hemoglobin level of 11.0 g/dl, and 1.9 percent had a level of 12.0 or greater. By 2005, the percentage of patients with a hemoglobin level below 10.0 dropped to 6.4 percent, 30.5 percent of patients achieved the target hemoglobin level of 11.0, and the percent of patients with a level of 12.0 or greater increased to 50.1 percent.

The USRDS is a national data system that collects, analyzes, and distributes information about end-stage renal disease (ESRD) in the United States. The USRDS is funded directly by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in conjunction with the Centers for Medicare and Medicaid Services (CMS).

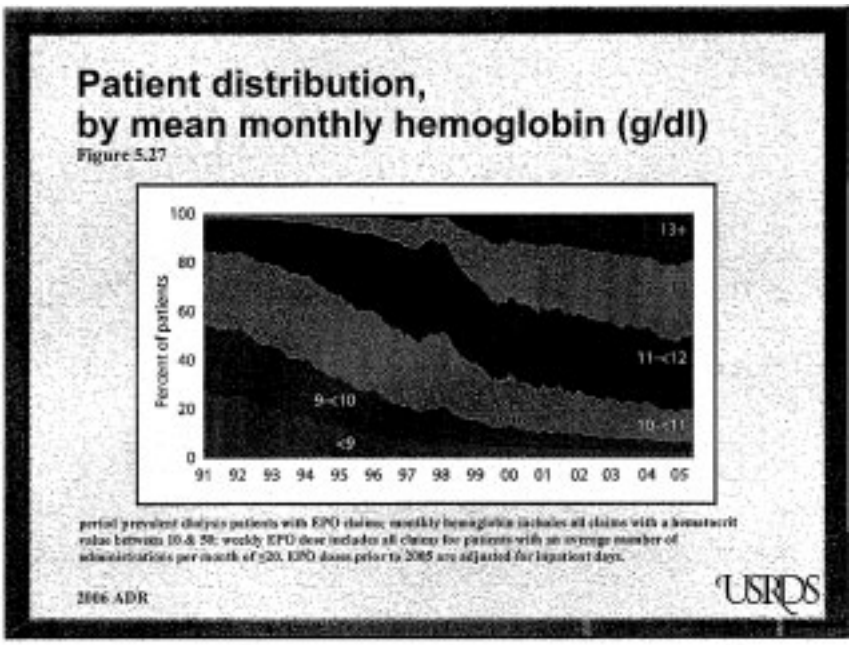

Patient distribution,
by mean monthly hemoglobin (g/dl)
Figure 5.27
Percent of patients
100
80
60
40
20
0
91 92 93 94 95 96 97 98 99 00 01 02 03 04 05
13+
11-<12
10-<11
9-<10
<9
2006 ADR
USRDS

Figure 5.27

2. How has mean EPO dose per week changed over time (USRDS Chart 5.30)?

Figure 5.30, shown on the next page (top), from the 2006 Annual Data Report of the USRDS, shows the EPO dosing and hemoglobin experience of new patients during the 6 months following the initiation of dialysis. These analyses are based on billing data, therefore, only patients for whom Medicare was the primary payer are included.

The left panel shows EPO dosing during the first 6 months following initiation of hemodialysis by year. For patients who started dialysis in 2000, the average weekly EPO dose in the first month was 12,298 units. This increased to 19,392 units in the second month and gradually decreased to 17,055 by the sixth month. The same pattern is seen in 2002 and 2004, although the EPO dose levels are higher in these years. The first, second, and sixth month weekly doses were 14,377, 22,738, and 18,495 units in 2002, and 16,783, 21,086, and 20,801 units in 2004. The maximum weekly dose occurred in the third month of 2004 and was 25,635 units.

The center panel shows EPO dosing as it relates to the patients' hemoglobin levels at the initiation of hemodialysis. Patients with the lowest initial hemoglobin levels had the highest levels of EPO dosing. For example, patients with less than 9 g/dl had first, second, and sixth month average EPO doses of 16,383, 26,006, and 21,672 units. EPO dose levels with patients with initial hemoglobin levels of greater than 12 g/dl were 10,858, 17,603, and 15,092 over the same time period.

The right panel shows EPO dosing as it relates to the patients' hemoglobin levels at the initiation of peritoneal dialysis. EPO dosing levels were approximately one-half the amount as for hemodialysis patients. As with hemodialysis patients, higher doses were given to those patients with the lowest starting hemoglobin levels.

Figure 5.28, shown on the next page (bottom), illustrates the overall trend in average weekly dose of EPO from 1991 to 2005. In 1991, the average weekly dose was 8,184 units. By 2005, the weekly dose doubled to 18,673 units.

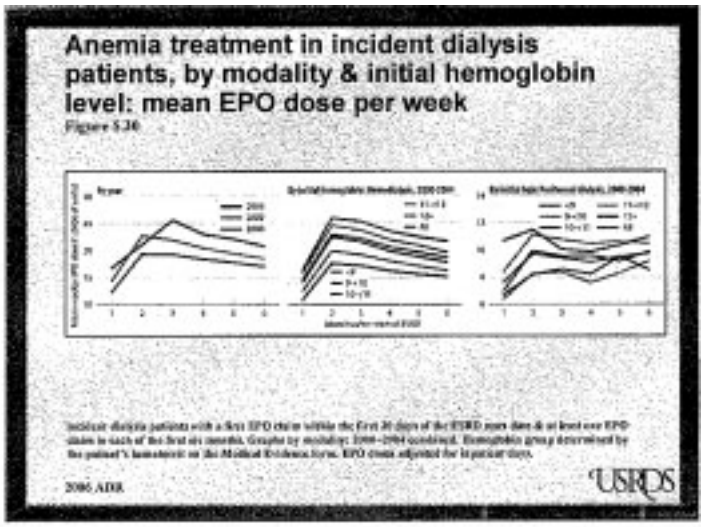


Figure 5.30

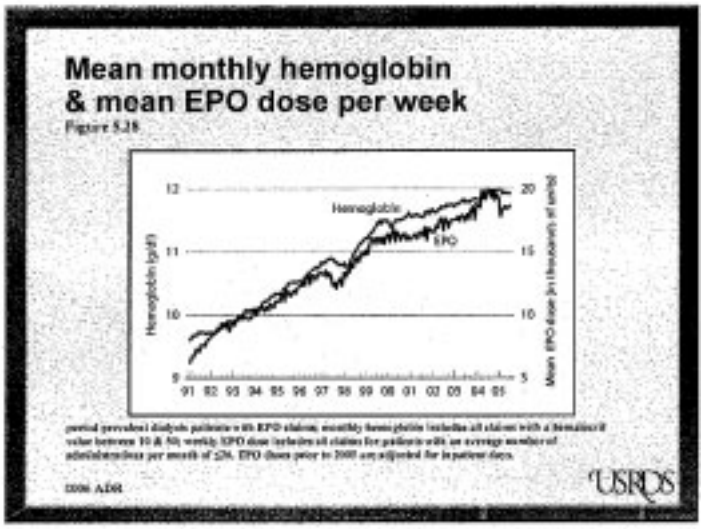


Figure 5.28

3. Page 198 of the 2006 USRDS Annual Report states, "We assessed provider practice patterns on dosing changes and found that DaVita tends to adjust the least and DCI the most when hemoglobin levels exceed 12–13 g/dL." How was this assessment conducted? What information was reviewed? Did NIH review anemia management guidelines? In what manner does DaVita make adjustments as compared to DCI? How do the other chains, such as Fresenius, compare?

It is expected that a reduction in EPO dose should occur following a month in which the hemoglobin level exceeds the K/DOQI (Kidney Disease Outcomes Quality Initiative) upper limit of the target range—12 g/dl. The manufacturer recommends reducing the dose of EPO by 25 percent when hemoglobin is rising and approaching this limit. Dose and hemoglobin data used here—derived from the Medicare billing data—contain only monthly detail, and because dose adjustments can occur at any time during a given month, a monthly dose reduction of 12.5 percent was used to define an appropriate response. For each month in which an EPO claim reported hemoglobin exceeded 12 g/dl, the following month's EPO claim was examined for a dose reduction of at least 12.5 percent. If the reduction was found, this was judged to be an appropriate response.

Based on the definition above, about 50 percent of all potential response months resulted in an appropriated dose reduction. As shown in Figure 10.16, from the 2006 USRDS Annual Data Report, the results by chain affiliation were as follows:

- Gambro – 55.2 percent
- DCI – 54.1 percent
- Fresenius – 51.1 percent
- Renal Care Group – 49.5 percent
- National Nephrology Associates – 48.6 percent
- Non chain units – 46.6 percent
- Hospital based units – 45.5 percent
- DaVita – 44.3 percent

Because this analysis was based only on observational billing data, it is not possible to determine the manner, or process, by which adjustments are made. The enclosed peer reviewed version of this analysis was published in the January issue of the *American Journal of Kidney Diseases*. The citation for this analysis is as follows: Collins AJ, Ebben JP, and Gilbertson DT. EPO Adjustments in Patients with elevated Hemoglobin Levels: Provider Practice Patterns Compared with Recommended Practice Guidelines. *Am. J. Kidney Dis.* 49:135–142, 2007.

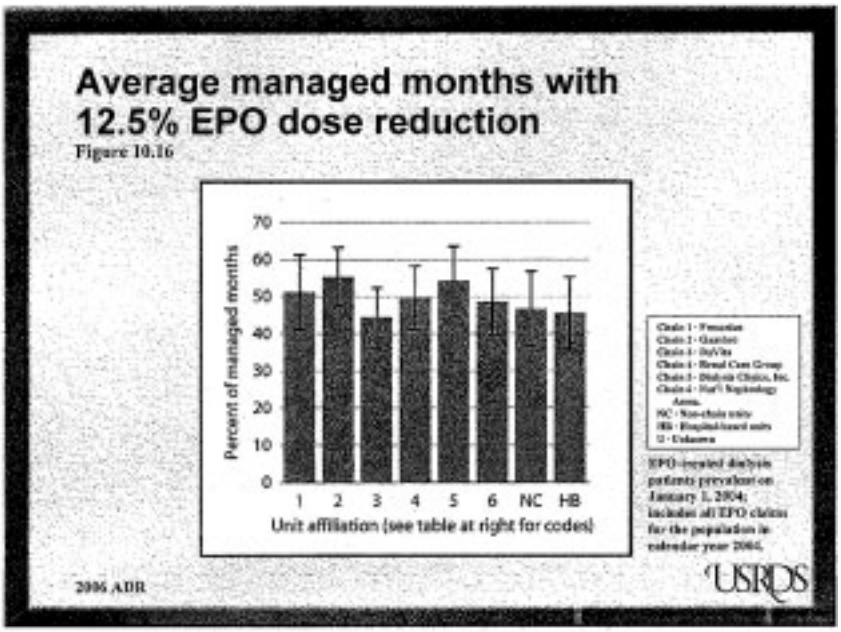

Average managed months with
12.5% EPO dose reduction
Figure 10.16
Percent of managed months
70
60
50
40
30
20
10
0
1 2 3 4 5 6 NC HB
Unit affiliation (see table at right for codes)
2006 ADR
USRDS

Figure 10.16

4. How does patient hemoglobin vary across dialysis centers (USRDS chart 10.21)? Which chains have the most patients exceeding Hb of 12 g/dl? Which chains have the largest proportion of patients within the target range of 10 to 12 g/dl?

Figure 10.21 from the USRDS 2006 Annual Data Report shows the distribution of patients at various hemoglobin levels by chain. In descending order of frequency, chains have the following percent of patient months greater than 12 g/dl:

- DaVita – 65.1 percent
- Gambro – 50.9 percent
- Renal Care Group – 47.3 percent
- Fresenius – 46.0 percent
- Hospital based – 43.1 percent
- Non chain – 42.4 percent
- National Nephrology Associates – 33.4 percent
- DCI – 20.3 percent.

In descending order of frequency, chains have the following percent of patient months in the target range of 10 to 12 g/dl:

- DCI – 64.8 percent
- National Nephrology Associates – 54.1 percent
- Non chain – 44.4 percent
- Fresenius – 43.6 percent
- Renal Care Group – 42.5 percent
- Hospital based – 40.6 percent
- Gambro – 40.3 percent
- DaVita – 27.5 percent.

These data represent aggregated monthly data. Most patients will be measured more than once, and some as many as 12 times. A patient could fall into one category for a few months, and one or more hemoglobin levels in other months. Therefore, these averages could be more accurately termed "patient months" of therapy. The data are self-weighting; that is, a patient with 12 months of hemoglobin data will contribute 12 data points to the final assessment, whereas a patient with only 3 months of data will contribute only 3 data points.

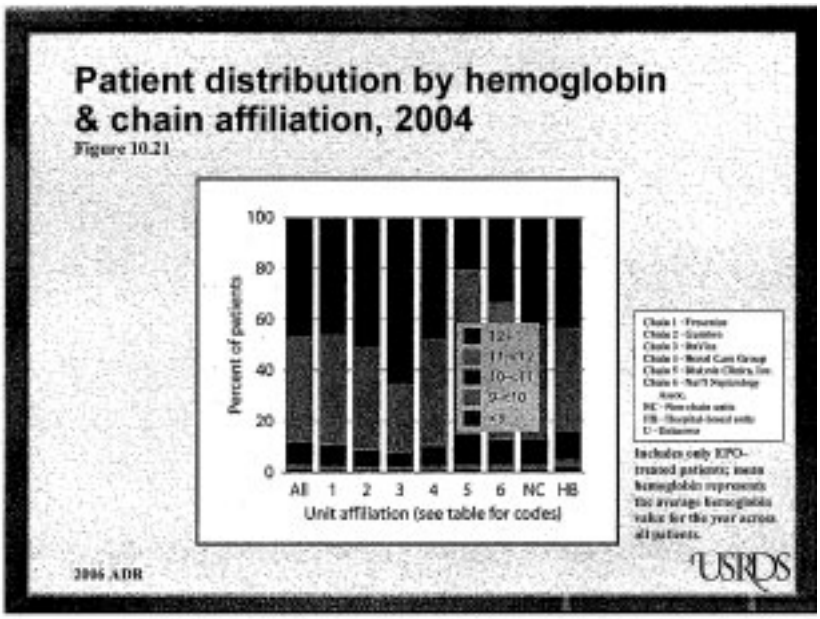

Patient distribution by hemoglobin & chain affiliation, 2004
Figure 10.21
100
80
60
40
20
0
Percent of patients
All 1 2 3 4 5 6 NC HB
Unit affiliation (see table for codes)
2006 ADR
USRDS

Figure 10.21

5. What are the trends for Medicare spending on erythropoiesis stimulating agents (ESAs) in recent year (USRDS Chart 11.26)? How does growth in spending on ESAs compare to spending on other parts of ESRD care? How do ESA costs per member month vary by dialysis chain?

Services provided as part of a dialysis session include dialysis, ESAs, intravenous iron, intravenous vitamin D, other injectibles, and laboratory procedures otherwise covered by the composite rate. In 1991 these services averaged $1,244 per patient month. By 2004, this had increased by 72 percent to $2,134. The two major cost components of the dialysis session are dialysis and ESA. Dialysis increased by 17 percent, from $970 to $1,135, whereas ESAs increased by 235 percent, from $173 to $580. ESAs accounted for 14 percent of dialysis-related costs in 1991 and 27 percent in 2004.

Medicare expenditures for ESAs per patient month by chain affiliation are as follows (in descending order), and are also illustrated in Figure 11.26 (next page, top panel).

- Gambro – $654
- Renal Care Group – $606
- DaVita – $588
- Fresenius – $576
- DCI and independents – $550
- National Nephrology Associates – $543
- Hospital based – $516

More detail is provided in figure 11.28 (next page, bottom panel).

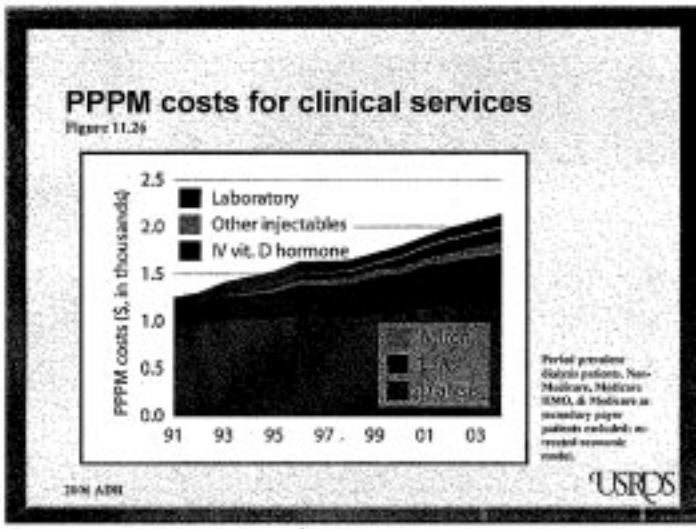


Figure 11.26

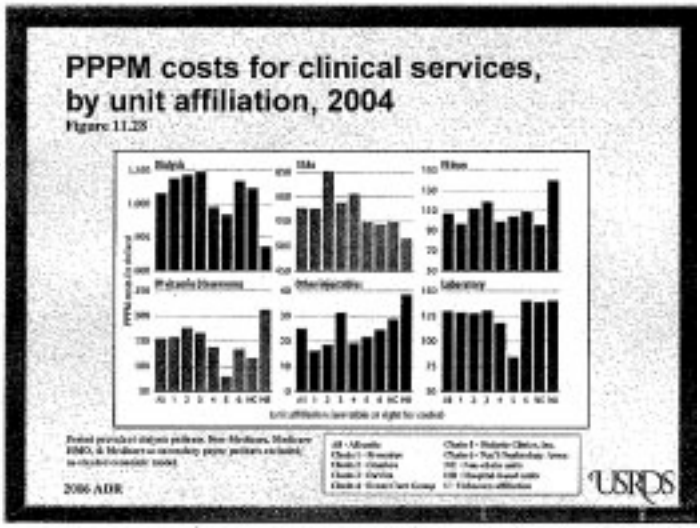


Figure 11.28

EPO Adjustments in Patients With Elevated Hemoglobin Levels: Provider Practice Patterns Compared With Recommended Practice Guidelines

Allan J. Collins, MD, FACP, James P. Ebben, BS, and David T. Gilbertson, PhD

Background: This study investigates provider practices regarding recombinant human erythropoietin (rHuEPO) dose when patient hemoglobin levels exceeded National Kidney Foundation–Dialysis Outcomes Quality Initiative target levels and reached 13 g/dL or greater (≥130 g/L).

Methods: The study population (N = 167,796) was hemodialysis patients prevalent on January 1, 2003, who were on renal replacement therapy at least 90 days with Medicare as primary payer and rHuEPO claims in 2 or more consecutive months. Patient characteristics were obtained from the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Report, and comorbid conditions were determined from Medicare claims. Providers and rHuEPO claims were linked by using CMS-assigned provider numbers and the CMS Annual End-Stage Renal Disease Facility Survey. Between-provider differences in patient characteristics were examined by using chi-square test, and provider effect on appropriate response, by using logistic regression.

Results: DaVita's percentage of monthly claims for patients with hemoglobin levels of 13 g/dL or greater (≥130 g/L; 16.7%) and mean monthly rHuEPO dose (54,299 units) were highest. Dialysis Clinic Inc's percentage of such claims (2.0%) and mean monthly dose (38,687 units) were lowest. Dialysis Clinic Inc, Fresenius, and Renal Care Group had the highest percentage of recommended dose adjustments (mean, 70% of units); hospital-based units had the lowest (59%). By adjusted odds ratio, adjustments were 20% more likely for Dialysis Clinic Inc, Fresenius, and Renal Care Group compared with DaVita, National Nephrology Associates, hospital-based units, and independents (17% to 28% less likely).

Conclusion: rHuEPO dose reduction practices are dependent on specific dialysis providers and whether units are hospital based or independent.

Am J Kidney Dis 49:135-142. © 2006 by the National Kidney Foundation, Inc.

INDEX WORDS: Hematocrit; hemodialysis (HD); hemoglobin; recombinant human erythropoietin.

The introduction of recombinant human erythropoietin (rHuEPO) into clinical practice for the treatment of anemia related to end-stage renal disease (ESRD) led to substantial improvements in hemoglobin levels.[1,2] The dramatic increase in mean hemoglobin levels from the early 1990s to 2003 is paralleled by similar increases in rHuEPO doses and iron management.[3]

Target hemoglobin levels became an important aspect of care in autumn 1997, with the introduction of clinical practice guidelines by the National Kidney Foundation under its Dialysis Outcomes Quality Initiative. These guidelines, which were developed from the US Food and Drug Administration (FDA) labeling indication for epoetin, intervention trials, and expert opinion, suggested a target hemoglobin level of 11.0 to 12.0 g/dL (110 to 120 g/L) with rHuEPO treatment.[4] Providers' ability to maintain hemoglobin levels within the target range has been a matter of concern, given natural variability and other clinical factors that interfere with rHuEPO effectiveness.[5,6] Centers for Medicare & Medicaid Services (CMS) payment policies requiring medical justification for rHuEPO treatment when hematocrit levels exceeded 37.5%, with possible auditing for repayment, also may have contributed to variability. Cross-sectional data gathered

From the Chronic Disease Research Group, Minneapolis Medical Research Foundation; and Department of Medicine, University of Minnesota, Minneapolis, MN.

Received May 10, 2006; accepted in revised form September 22, 2006.

Originally published online as doi:10.1053/j.ajkd.2006.09.030 on December 1, 2006.

Support: This study was supported by an unrestricted research grant from Amgen Inc, Thousand Oaks, CA. Potential conflicts of interest: A.J.C. and D.T.G. have received consulting fees from Amgen. J.P.E., none.

Address reprint requests to Allan J. Collins, MD, FACP, Chronic Disease Research Group, 914 South 8th St, Ste S-206, Minneapolis, MN 55404. E-mail: acollins@cdrg.org

© 2006 by the National Kidney Foundation, Inc.

0272-6386/06/4901-0016$32.00/0

doi:10.1053/j.ajkd.2006.09.030

monthly indicate that approximately 30% of patients have hemoglobin levels less than 11 g/dL (<110 g/L), 36% have levels between 11 and 12 g/dL (110 to 120 g/L), and the remaining third have hemoglobin levels greater than 12 g/dL (>120 g/L). Although this overall distribution appears to be consistent month to month, few patients remain within a particular group, such that by year end, only 5% are still in their original groups.[3,6]

The increasing percentage of patients with hemoglobin levels exceeding the current National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (KDOQI) target level of 12 g/dL (120 g/L) has been accompanied by a decreased percentage of patients with hemoglobin levels less than 11 g/dL (<110 g/L).[7] These developments appear to be the result of many factors, including concurrent illnesses, fluid overload leading to hemodilution, and rHuEPO hyporesponsiveness. However, as reported by the US Renal Data System (see *Annual Data Report* chapters on providers and economic costs),[3] there is considerable variation among dialysis providers in the distribution of patient hemoglobin levels. The increasing percentage of patients with hematocrits greater than 39% has caused concern because findings in at least 1 clinical trial suggested that high hematocrits (close to 42%) may constitute a risk for vascular access thrombosis and potentially increased mortality.[8] The recommended hemoglobin level range was defined on the basis of clinical trials suggesting safety at lower levels, but providers may not always decrease doses accordingly. Lack of attention to these targets, particularly at the upper end of the range, may lead to overuse of rHuEPO, driving hemoglobin to higher levels and overshooting the target range.

Recently, a new policy for rHuEPO use was implemented by the CMS.[9] It requires reduction in payment for rHuEPO doses for patients with hematocrits of 39% or greater. It is unclear how frequently providers adjust doses and whether there are differences across large groups. In this study, we investigate provider practice patterns related to rHuEPO dose and its adjustment when patient hemoglobin levels were at least 13 g/dL (130 g/L), a level consistent with CMS monitoring policy for use by fiscal intermediaries.

METHODS

The study population (N = 167,796) consisted of hemodialysis patients prevalent on January 1, 2003, who had been receiving renal replacement therapy for at least 90 days as of January 1, 2003; had Medicare as primary payer; and had rHuEPO claims in at least 2 consecutive months. Patient characteristics (age, sex, race, primary cause of renal failure, and dialysis vintage) were obtained from the CMS Medical Evidence Report (CMS-2728). Comorbid conditions were determined from Medicare Part A institutional and Part B physician/supplier claims, using *International Classification of Diseases, Ninth Revision, Clinical Modification*, codes according to a previously described method.[10] Conditions characterized included atherosclerotic heart disease, congestive heart failure, cardiac arrhythmia, other cardiac disease, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, chronic obstructive pulmonary disease, cancer (including melanoma, but not skin cancer), liver disease, and gastrointestinal bleeding.

All rHuEPO claims for the study population for 2003 were analyzed to characterize anemia management, with specific attention to claims with a reported hemoglobin level of at least 13 g/dL (130 g/L). For each such claim, the rHuEPO dose was compared with the dose reported on the rHuEPO claim for the next month. To reduce the potential for incomplete dosing information, only claims for months in which the patient was not hospitalized were considered. KDOQI guidelines and the FDA-approved manufacturer's recommendations for anemia management call for a dose reduction of 25% for patients with a hemoglobin level of at least 12 g/dL (120 g/L). Recognizing the difficulty maintaining levels at the upper end of the recommended range (12 g/dL [120 g/L]) without exceeding it and based on the new CMS payment policy, we used a cutoff point for dose reduction 1 g/dL greater than the recommended level. Because claims data generally yield rHuEPO dosing information for 1 claim per month, we could detect dosage changes only from one month to the next, but the dose could have changed at any time during the month. To accommodate this imprecision, we classified a month-to-month dose reduction of one half the guideline (ie, 12.5% reduction) as an appropriate response to a hemoglobin level of at least 13 g/dL (130 g/L).

Using the CMS-assigned provider number included on the rHuEPO claim and the CMS Annual ESRD Facility Survey, rHuEPO claims were linked to individual dialysis providers, which were analyzed by chain (DaVita, Dialysis Clinic Inc, Fresenius, Gambro, National Nephrology Associates, and Renal Care Group). Providers not part of a chain were classified as hospital based or independent, defined from the CMS facility survey. If CMS identified a unit as hospital based, we classified it as hospital based. If CMS identified a unit as freestanding and it was not a part of 1 of the major chains named, we classified it as independent. Provider numbers that could not be linked to ESRD Facility Survey data were classified as "unknown affiliation." Providers with fewer than 10 qualifying rHuEPO claims were excluded from analysis.

For each provider, a measure of anemia management was calculated as the number of appropriate responses (rHuEPO

dose reduction ≥ 12.5% in the month after a reported hemoglobin level of at least 13 g/dL (130 g/L)) divided by the number of claims with a reported hemoglobin level of at least 13 g/dL (130 g/L), for which an rHuEPO claim was present for the following month and the patient had no hospital days in either month. Results for individual providers were aggregated into the provider classifications described. Chi-square tests were used to examine differences in patient demographics and comorbid conditions between providers. A logistic regression model was used to examine the effect of provider on appropriate response (1 or 0), adjusted for patient age, sex, race, primary cause of renal failure, and 10 comorbid conditions.

RESULTS

As listed in Table 1, patient characteristics generally were consistent across provider groups, with some variation in racial mix. Statistical differences were not clinically significant because recommendations are irrespective of demographic variables. As listed in Table 2, comorbidity was very similar among provider groups; statistical differences among comorbid conditions were not clinically significant, with the possible exception of liver disease, for which values varied widely among providers. For each provider, mean rHuEPO dose in response to a reported hemoglobin level of at least 13 g/dL (130 g/L) was as follows: DaVita, 54,299 U/mo; independent, 49,634 U/mo; hospital based, 49,598 U/mo; Fresenius, 49,407 U/mo; Renal Care Group, 48,772 U/mo; Gambro, 42,629 U/mo; National Nephrology Associates, 41,992 U/mo; and Dialysis Clinic Inc, 38,687 U/mo. Each provider was significantly different from every other provider with the following exceptions: Fresenius versus Renal Care Group, Fresenius versus hospital based, Gambro versus National Nephrology Associates, and hospital based versus independent.

Table 3 lists the total number of qualifying rHuEPO claims and the percentage of claims with a reported hemoglobin level of at least 13 g/dL (130 g/L). DaVita units had the highest percentage (16.7%) of claims with high hemoglobin levels, and Dialysis Clinic Inc units had the lowest percentage (2.0%).

Figure 1 shows means and SDs of the anemia management measure (percentage of managed months) for the provider groups. There was considerable variation among provider groups; Dialysis Clinic Inc, Fresenius, and Renal Care Group had an average anemia management measure of more than 70% and hospital-based units had a measure of 59%. Error bars, representing SDs of the percentages of managed months, show the range of variation.

Figure 2 shows the distribution of the anemia management measure for individual units within each provider group. The width of the frequency distribution curves shows the variation. The peak of the curve represents the approximate mean, and the width represents the SD. For example, the curve for Renal Care Group peaks sharply at 70% to 80%, indicating close adherence to the guidelines, whereas the curve for Dialysis Clinic Inc has a very broad peak, stretching from 60% to 70% to more than 90%, indicating a more varied adherence.

Figure 3 shows results of logistic regression analysis of the anemia management measure. In response to high hemoglobin levels, rHuEPO dose reductions were 20% more likely to occur in Dialysis Clinic Inc, Fresenius, and Renal Care Group units than Gambro units. Dose reductions were significantly less likely to occur in DaVita (19%), National Nephrology Associates (20%), hospital-based units (28%), and independent units (17%) than Gambro units. The distribution of units adjusting doses based on recommended practice was broad, ranging from a low of 10% to 20% to a high of 90%. The odds of a provider reducing the rHuEPO dose by the KDOQI-recommended 25% was significantly lower for DaVita, National Nephrology Associates, hospital-based units, and independent units compared with Gambro units.

Mean monthly hemoglobin levels were stable during the course of the year, remaining within ±0.1 g/dL for each provider group (data not shown). SDs also were stable within provider groups, but there were differences in means and SDs between provider groups. The highest was DaVita at 12 ± 1.5, and lowest was Dialysis Clinic Inc at 11.4 ± 1.2.

Sensitivity analysis results show that the effect of specifying a dosage percentage reduction less than the recommended 25% is to shift distributions to the right, with little or no effect on the shape of the distribution. Similarly, specifying a larger percentage of change shifts the distribution to the left with little or no effect on the shape.

Table 1. Patient Characteristics

Characteristic	All	DaVita	DCI	Fresenius	Gambro	NNA	RCG	Hospital	Independent	Unknown
No. of patients	167,796*	25,025	7,638	47,585	25,382	3,160	13,372	20,496	35,794	1,425
Age, y										
Median	64.0	63.0	63.0	64.0	64.0	64.0	64.0	66.0	65.0	65.0
Mean	61.9	61.4	60.9	61.6	61.9	61.9	61.5	62.8	62.3	62.2
SD	15.3	15.2	15.5	15.0	15.2	14.9	15.5	15.9	15.3	16.2
Distribution (%)										
0-19	0.3	0.3	0.4	0.2	0.2	0.1	0.3	0.8	0.2	1.7
20-44	14.3	14.7	15.6	14.4	14.3	13.9	15.1	13.5	14.1	13.5
45-64	36.4	37.2	37.7	37.4	36.6	37.7	36.3	33.0	35.2	34.0
65-74	25.9	26.3	25.2	26.3	25.7	25.4	25.7	26.0	25.8	25.8
≥75	23.1	21.6	21.1	21.6	23.2	22.9	22.7	26.7	24.7	25.0
Sex (%)										
Male	52.3	52.7	51.5	52.1	52.3	51.2	51.9	53.4	52.6	52.0
Female	47.7	47.3	48.5	47.9	47.7	48.8	48.1	46.6	47.4	48.0
Race (%)										
White	53.0	51.0	48.4	52.3	47.2	49.0	55.5	60.7	57.3	62.0
Black	40.8	40.3	47.6	43.2	48.0	47.7	39.4	29.9	35.9	29.3
Native American	1.6	3.1	2.1	0.8	0.9	0.7	3.1	2.5	1.1	1.1
Asian	3.7	4.9	1.5	2.6	3.3	1.9	1.5	6.0	4.5	6.4
Other/unknown	0.9	0.7	0.4	1.1	0.7	0.7	0.4	0.9	1.1	1.3
Primary cause of renal failure (%)										
Diabetes	42.2	42.6	40.4	42.3	41.6	41.8	42.7	40.8	41.9	41.2
Hypertension	29.6	30.1	28.9	30.7	31.5	31.2	29.9	25.4	28.5	24.4
Glomerulonephritis	12.0	11.5	12.6	11.6	11.5	12.2	11.9	14.2	12.6	13.8
Other	12.8	12.2	14.4	12.1	12.3	12.0	12.5	15.4	13.5	15.0
Unknown	3.5	3.5	3.7	3.3	3.1	2.9	3.0	4.2	3.5	5.6
Vintage (y)	4.3 ± 4.2	4.2 ± 4.2	4.6 ± 4.6	4.3 ± 4.3	4.2 ± 4.1	4.2 ± 4.1	4.2 ± 4.3	4.3 ± 4.4	4.1 ± 4.2	4.1 ± 4.1

Note: Values expressed as mean ± SD or percent unless noted otherwise. All P less than 0.0001 for age, sex, race, and primary cause of renal failure, by chi-square test.
Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.
*The sum of patients for each provider type does not equal the total number because patients who switched providers were counted in each.

Table 2. Cumulative Comorbid Conditions

Condition	All	DaVita	DCI	Fresenius	Gambro	NNA	RCG	Hospital	Independent	Unknown
Atherosclerotic heart disease (%)	55.2	54.1	50.2	54.8	54.6	62.1	53.0	57.2	56.9	53.1
Congestive heart failure (%)	60.4	59.9	56.8	61.4	59.9	60.4	58.3	59.8	60.4	59.5
Cardiac arrhythmias (%)	42.2	42.1	41.3	41.3	42.7	40.5	39.4	43.5	42.9	42.3
Other cardiac disease (%)	53.7	53.4	51.6	54.4	53.4	56.6	52.9	52.9	53.8	51.1
Cerebrovascular accident/transient ischemic attack (%)	28.4	28.3	26.7	28.3	28.7	28.8	27.6	27.9	28.4	27.0
Peripheral vascular disease (%)	52.5	52.5	50.1	52.1	51.8	50.8	52.5	54.2	52.4	51.8
Chronic obstructive pulmonary disease (%)	27.3	26.5	26.7	27.2	27.3	27.3	26.8	27.6	27.4	30.1
Cancer (%)	12.9	12.7	12.7	12.8	12.5	12.3	11.8	14.4	13.8	13.0
Liver disease (%)	23.7	32.1	10.5	26.0	15.7	23.8	16.4	22.1	26.8	19.8
Gastrointestinal bleeding (%)	25.7	25.1	28.2	25.8	25.8	26.1	24.5	25.4	26.1	24.0

Note: Within each comorbid condition, all *P* less than 0.0001 by chi-square test.
Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.

DISCUSSION

The continued growth in rHuEPO dosing and the increase in hemoglobin levels have raised concerns among payers and policymakers that providers may not be achieving optimal anemia management. Monitoring of care under the ESRD Clinical Performance Measures Project[11] and the unit-level reports distributed under Medicare's Dialysis Facility Compare show that providers have varying percentages of patients who meet or exceed target hemoglobin levels. The US Renal Data System's *2004 Annual Data Report* shows that in some provider groups, at least half the patients have an average hemoglobin level of at least 12 g/dL (120 g/L) during the entire year.[9] Our study shows that some provider groups have a high percentage of patients with hemoglobin levels not only greater than 12 g/dL (>120 g/L), but greater than 13 g/dL (>130 g/L). In other groups, less than 8% of patients have a hemoglobin level of at least 13 g/dL (130 g/L). This wide variation in achieved hemoglobin levels suggests that some providers have targets different from those recommended in the KDOQI guidelines, which are consistent with FDA recommendations. Even within a single group of providers, there is a wide range of adjustment patterns, suggesting inconsistent adherence to the recommended dose modification.

A more detailed assessment indicates that provider practice patterns associated with rHuEPO dose reduction are highly dependent on the specific large dialysis organization and whether dialysis units are hospital based or independent. Although there are small differences in demographic characteristics of patients served by the individual dialysis chains, hospitals, and independent dialysis providers, DaVita, National Nephrology Associates, and hospital-based units appear to adjust doses 20% less than the reference chains and as much as 40% less than other large dialysis organizations. These findings are based on a minimal dose reduction of 12.5% across 2 months with a reported hemoglobin level of at least 13 g/dL (130 g/L). These minimal changes yielded, on average, a 70% rate of management (versus that recommended), but the variation is considerable. Results do not change across 3 months of claims.

We also found inverse relationships among the providers. For example, DaVita has the lowest number of managed months and the highest percentage of hemoglobin levels greater than 11 g/dL (>110 g/L), whereas Dialysis Clinic Inc has the highest number of managed months and lowest percentage of hemoglobin levels greater than 11 g/dL. Despite an inverse relationship between hemoglobin level greater than 13 g/dL (>130 g/L) and percentage of hemoglobin levels less than 11 g/dL (<110 g/L), the percentage of patients within the recommended hemoglobin level range of 11 to 12 g/dL (110 to 120 g/L) is highly dependent on the provider.[7] Dialysis Clinic Inc had the highest percentage of patients with levels within the recommended range and the lowest percentage with levels greater than 12 g/dL (>120 g/L). DaVita had almost 3 times as many patients with levels greater than 12 g/dL

Table 3. rHuEPO Claims

	All	DaVita	RCG	Fresenius	Hospital	Independent	Unknown	Gambro	NNA	DCI
Total claims	1,713,706	235,046	128,053	459,481	194,044	338,761	11,453	242,379	30,470	74,019
Claims with hemoglobin ≥ 13 g/dL										
No.	179,637	39,252	16,256	47,715	20,030	33,375	1,076	18,709	1,672	1,452
%	10.5	16.7	12.7	10.4	10.3	9.9	9.4	7.7	5.5	2.0

Note: To convert hemoglobin in g/dL to g/L, multiply by 10.
Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.

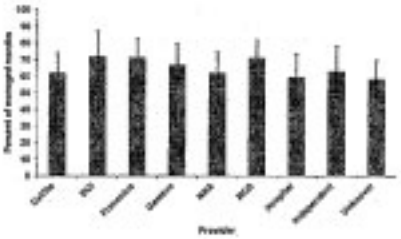


Figure 1. Anemia management measure (percentage of managed months) for the provider groups studied. Error bars are SDs. Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.

(>120 g/L), but the lowest percentage with levels less than 11 g/dL (<110 g/L). Provider practices appear to vary with regard to exceeding the guideline, raising the concern that practices focusing on a single component of the guideline recommendations (eg, hemoglobin level < 11 g/dL [<110 g/L]) may distort the more comprehensive FDA-approved package insert and KDOQI recommendations, which focus on keeping hemoglobin levels within 11 to 12 g/dL (110 to 120 g/L).

Reasons for the broad differences observed are not immediately apparent. One possibility is between-provider variation in the percentage of patients with medical indications for hemoglobin level to exceed recommended levels. A detailed analysis of diagnosis codes included on dialysis claims may help clarify this issue, but the justifications reported to fiscal intermediaries may not be passed on through the CMS system and may be unavailable for analysis. Also, parent corporations or owners may subject providers to performance measures linked to manager or staff compensation. Economic incentives to achieve certain targets may reduce the likelihood that rHuEPO doses would be changed, particularly if the percentage of patients for whom hemoglobin levels decreased to less than the KDOQI target is monitored, as opposed to the percentage of patients who were managed appropriately and those achieving a hemoglobin level of at least 11 g/dL (110 g/L). Provider efforts to reduce the percentage of patients with hemoglobin levels less than 11 g/dL (<110 g/L) may affect revenue streams. Finally, providers may be reluctant to reduce doses as recommended for fear that patients'

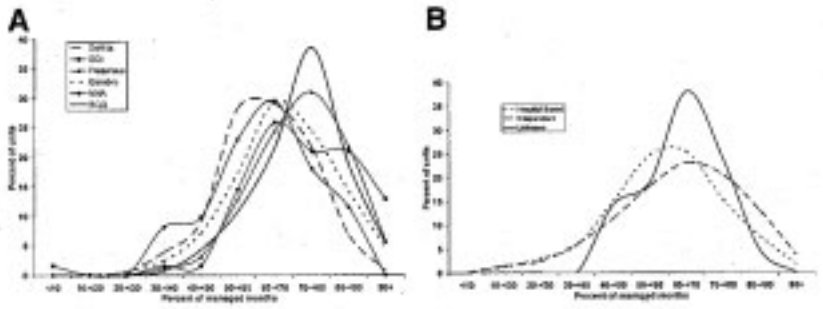


Figure 2. Distribution of anemia management by unit within provider group: (A) chain providers, (B) nonchain providers. Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.

levels may decrease further into and past the KDOQI targets, leading to cycling of patient hemoglobin levels as described by Fishbane and Berns.[12]

Clearly, provider practices are associated significantly with the likelihood of performing adjustments irrespective of age, sex, race, and comorbidity in the covered population. A more complete assessment of provider dosing practices is needed to determine whether these practices are associated with any positive, neutral, or adverse outcomes in patients. This complex assessment should address the greatest concerns, such as vascular access thrombosis and cardiovascular events, issues of concern in the normal-hematocrit trial by Besarab et al.[8] Because achieved hemoglobin levels may be highly confounded by disease burden, such advanced methods as a marginal structural model may be required.[13] Patient safety with hemoglobin levels exceeding the recommended range should be assessed further. Such analyses are beyond the scope of the current investigation, which focuses on describing patterns of practice and their potential variation.

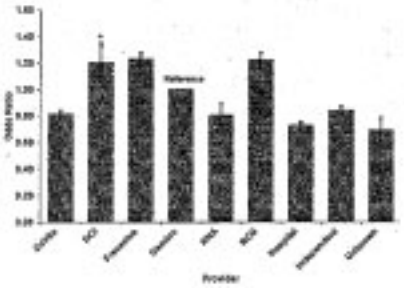


Figure 3. OPs for anemia management. $P < 0.0001$, except as noted. *$P = 0.0082$. Abbreviations: DCI, Dialysis Clinic Inc; NNA, National Nephrology Associates; RCG, Renal Care Group.

The limitations of our study deserve careful consideration. Only monthly hemoglobin levels are reported on rHuEPO claims. Providers may have access to multiple hematocrit values during the month that indicate a change in rHuEPO dose and allow for determination of the necessity of dose reductions for patients with a hemoglobin level that exceeds KDOQI targets. Because of hematocrit data limitations, determining the exact date during the month in which rHuEPO dose was decreased is difficult, and our ability to assess whether the total percentage of reduction was the suggested 25% is limited. To address this problem, we used a 12.5% reduction, reasoning that, on average, rHuEPO doses may change randomly throughout the month and the full amount of the change would not be reflected comparing it with the following month. Other unmeasured factors may influence a provider's likelihood of decreasing the rHuEPO dose, particularly in patients with high hemoglobin levels or with hospitalizations. Information regarding medical justifications offered for maintaining dosages in patients with higher hemoglobin levels is incomplete. To some ex-

tent, predictors of rHuEPO dose reduction show a greater likelihood in patients with cerebrovascular accidents and transient ischemic attacks. A more detailed analysis of indications for medical treatment exceeding the recommended levels is required to more accurately assess provider practices in rHuEPO dose reduction in patients with higher hemoglobin levels.

In summary, we assess the management of rHuEPO dose for patients with hemoglobin levels exceeding the KDOQI guidelines and find it to be highly related to the individual dialysis provider. In general, approximately 70% of providers' dialysis units adjust rHuEPO doses consistent with KDOQI guidelines and the FDA labeling instructions when hemoglobin levels exceed the recommended targets (13 g/dL [130 g/L]). The distribution is broad, suggesting that substantial improvement in the management of patients with elevated hemoglobin levels, with a decrease in rHuEPO dose, should be considered. Hemoglobin levels and rHuEPO dosing practices may change substantially with the recent changes in epoetin payment policies by CMS. Continued monitoring of these practices is warranted to determine whether providers are following recommended practices, thereby ensuring both safety and efficacy of anemia treatment for the dialysis population.

ACKNOWLEDGMENT

The authors thank our Chronic Disease Research Group colleagues Shu-Chang Chen, MS, for information-systems support; Stephan Dunning, MGIS, for project coordination; James Kaufmann, PhD, and Nan Booth, MSW, MPH, for manuscript editing; and Dana D. Knopic for manuscript preparation and administrative support.

REFERENCES

1. Eschbach JW, Egrie JC, Downing MR, Browne JK, Adamson JW: Correction of the anemia of end-stage renal disease with recombinant human erythropoietin: Results of a combined phase I and II clinical trial. N Engl J Med 316:73-78, 1987

2. Eschbach J, Abdulhadi MHJ, Delano B, et al: Recombinant human erythropoietin in anemic patients with end-stage renal disease. Results of a phase III multicenter clinical trial. Ann Intern Med 111:992-1000, 1989

3. US Renal Data System: USRDS 2004 Annual Data Report. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2004

4. National Kidney Foundation: NKF-DOQI Clinical Practice Guidelines for the Treatment of Anemia of Chronic Renal Failure. Am J Kidney Dis 30:S192-S240, 1997 (suppl 3)

5. Lacson E Jr, Ofsthun N, Lazarus JM: Effect of variability in anemia management on hemoglobin outcomes in ESRD. Am J Kidney Dis 41:111-124, 2003

6. National Kidney Foundation: NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease: Update 2000. Am J Kidney Dis 37:S182-S238, 2001 (suppl 1)

7. US Renal Data System: USRDS 2005 Annual Data Report. The National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2005, pp 24, 194

8. 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

9. Levy R: The new CMS monitoring policy for anemia drug reimbursement: Implications for providers. Dial Transplant 35:88-89, 107, 2006

10. Collins AJ, Li S, St Peter WL, 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

11. Centers for Medicare & Medicaid Services: 2004 Annual Report. End-Stage Renal Disease Clinical Performance Measures Project. Baltimore, MD, Centers for Medicare & Medicaid Services, Center for Beneficiary Choices, 2004

12. Pizzarelli S, Berni JS: Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin. Kidney Int 68:1337-1343, 2005

13. Robins JM, Hernan MA, Brumback B: Marginal structural models and causal inference in epidemiology. Epidemiology 11:550-560, 2000

MEDPAC Medicare Payment Advisory Commission

601 New Jersey Avenue, NW • Suite 9000
Washington, DC 20001
202-220-3700 • Fax: 202-220-3759
www.medpac.gov

Glenn M. Hackbarth, J.D., Chairman
Robert D. Reischauer, Ph.D., Vice Chairman
Mark E. Miller, Ph.D., Executive Director

June 25, 2007

The Honorable Fortney Pete Stark
Chairman, Subcommittee on Health,
House Ways and Means Committee
1102 Longworth House Office Building
Washington, D.C. 20515

Dear Chairman Stark:

Thank you for your inquiry regarding the Commission's findings about the adequacy of Medicare's payments for freestanding dialysis providers and our recommendations on modernizing the outpatient dialysis payment system.

The Medicare Payment Advisory Commission (MedPAC) has a long history in examining issues related to Medicare's payments for outpatient dialysis services. Each year, the Commission assesses the adequacy of Medicare's outpatient dialysis payments and makes recommendations about whether to update the composite rate. In addition, we have also examined and made recommendations on Medicare's method for paying for dialysis services, the quality of dialysis care, and beneficiaries' access to care.

In response to your inquiry, this letter summarizes our past research and recommendations on:

- Trends in the volume of outpatient dialysis services
- Medicare margins for outpatient dialysis services
- Modernizing the outpatient dialysis payment system

Trends in the volume of outpatient dialysis services

MedPAC has closely monitored changes over time in the volume of composite rate services (i.e., Medicare's prospective payment for each dialysis treatment) and dialysis drugs furnished by freestanding providers (who treat most dialysis patients). One way the Commission tracks utilization trends is by examining Medicare spending for both composite rate services and dialysis drugs. As described in our March 2007 report to the Congress, Medicare's spending for dialysis drugs, including erythropoietin, has grown more rapidly than composite rate services during the past decade (Figure 1 and Figure 2, page 3).

Between 1996 and 2004, the annual growth in payments for composite rate services generally kept pace with the increase in the dialysis population (8 percent versus 6 percent, respectively). The higher growth in composite rate payments between 2004 and 2005—14 percent—is due to the add-on payment mandated by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) and implemented by CMS in 2005. The MMA mandated shifting some of the profits from dialysis drugs to an add-on payment to the composite rate in 2005. The MMA also lowered the payment rates for most dialysis drugs closer to the prices provider paid in 2005. Spending for dialysis drugs grew much more rapidly—15 percent per year— than the growth in the patient population between 1996 and 2004. This is due to increases in the volume of dialysis drugs provided to patients and price increases for non-erythropoietin drugs. Drug payments declined by about 10 percent between 2004 and 2005 because of the MMA's changes in drug payment rates.

Although payments for dialysis drugs declined between 2004 and 2005, MedPAC's analysis suggests that the volume of drugs (in terms of the units furnished to beneficiaries) continued to increase for most dialysis drugs. Payments for dialysis drugs declined because the unit price Medicare paid for dialysis drugs declined between 2004 and 2005 due to changes mandated by the MMA. Our calculations find that erythropoietin volume increased by 2 percent and the volume of the other leading drugs increased by 7 percent in 2005.

Figure 1. Medicare's payments to freestanding dialysis facilities have steadily increased

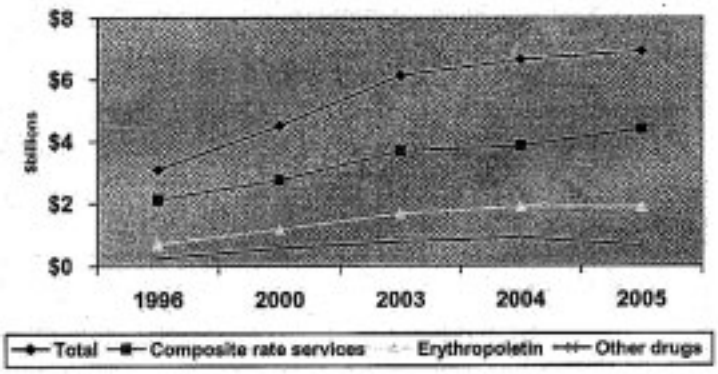
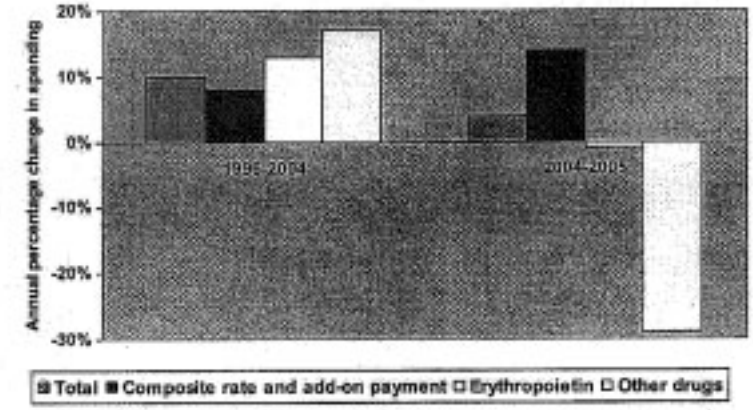


Figure 2. The MMA increased the annual growth in spending for composite rate services and decreased spending for dialysis drugs



Source: Compiled by MedPAC from 1996, 2000, 2003–2005 outpatient dialysis claims from CMS.

Why did providers increase the volume of dialysis drugs and is all of the growth in volume appropriate?

Use of dialysis drugs has grown for two reasons. First, the drugs—including erythropoietin, iron supplements, and vitamin D analogs—effectively treat conditions that result from the loss of kidney function, such as anemia and bone disease. The use of many of these medications has enhanced the quality of care furnished to dialysis patients.

However, some researchers have reported that erythropoietin use varies among providers and suggested that providers could furnish erythropoietin more efficiently. Thamer et al. (2007) concluded that, compared with other facility types, large for profit chains administered higher erythropoietin doses and higher dose increases.[1] Pizzi et al. (2006) estimated net savings (of $257 per patient per month) could be achieved by using an alternative mix of erythropoietin and intravenous iron.[2] In addition, randomized clinical trials have found adverse events among patients with chronic kidney disease who received a greater dose of erythropoietin to achieve a higher hemoglobin level (Singh et al. 2006).[3,4]

Paying according to the number of units given to patients means that providers have an incentive to provide more units (as long as Medicare's payment exceeds their costs). In addition, the profitability of most drugs under the pre-MMA payment method gave providers an incentive to use more. In 2005, the new drug payment method reduced but did not eliminate the profitability of drugs. Medicare's payment rate for the top dialysis drugs exceeded the average sales price in 2005 (MedPAC 2007).[5,6]

---

1 Thamer, M., Y. Zhang, J. Kaufman, et al. 2007. Dialysis facility ownership and epoetin dosing in patients receiving hemodialysis. *JAMA* 297, no. 15 (April 18): 1667–1674.

2 Pizzi, L. T., N. M. Patel, V. M. Maio, et al. 2006. Economic implications of non-adherence to treatment recommendations for hemodialysis patients with anemia. *Dialysis & Transplantation* 35, no. 11: 660–671.

3 Hematocrit measures a patient's anemia status by determining the percentage of red blood cells in the bloodstream.

4 Singh, A. K., L. Szczech, K. L. Tang, et al. 2006. Correction in anemia with epoetin alfa in chronic kidney disease. *New England Journal of Medicine* 355, no. 20 (November 16): 2085–2098.

Historical trends in the use of erythropoietin demonstrate the concerns about paying for profitable services on a per unit basis. After CMS changed its method of paying for erythropoietin from a relatively fixed payment per administration (of erythropoietin) between 1989 and 1991 to a per unit basis after 1991, per patient use of the drug substantially escalated—8 percent annually between 1991 and 2004 (from 7,100 units per week to 20,100 units per week) (USRDS 2006).[7]

As we discuss in more detail later in this letter, broadening the payment bundle and including drugs and other commonly furnished services might create more incentives for providers to furnish these services more efficiently.

The Medicare margin for outpatient dialysis services

Each year, the Commission assesses current payments and costs for dialysis services for freestanding dialysis facilities by comparing Medicare's payments for composite rate services and dialysis drugs with providers' Medicare-allowable costs. The latest and most complete data available on freestanding providers' costs are from 2005.

As we describe in our March 2007 report, we estimate that the aggregate Medicare margin for composite rate services and dialysis drugs is 8.4 percent in 2005, after an audit correction (Table 1).[8] The aggregate margin for the large dialysis organizations (LDOs) is greater than the margin for all other freestanding facilities (10.7 percent versus 2.6 percent, respectively). LDOs account for about 72 percent of Medicare's spending for dialysis services among freestanding facilities.

---

5 Average sales price (ASP) represents the amount drug manufacturers receive for their product. CMS calculates ASP using data submitted quarterly by pharmaceutical manufacturers and is net of rebates and discounts offered to purchasers by the manufacturers.

6 Medicare Payment Advisory Commission. 2007. *Medicare payment policy*. Washington, DC: MedPAC.

7 United States Renal Data System, National Institute of Diabetes and Digestive and Kidney Diseases. 2006. *USRDS 2006 annual data report*. Bethesda, MD: NIDDK.

8 The Commission determines payment margins using the results of CMS's 2001 audit of freestanding providers' cost reports. The audit process generally lowers the cost per treatment and thus raises the margin. We describe this correction in our March 2007 report. The Medicare margin without the audit correction is 5.5 percent in 2005.

This finding stems from differences in the cost per treatment and the share of total payments from dialysis drugs. LDOs have lower cost per treatment, on average, than their counterparts. Our regression analysis indicates that total cost per treatment was 6 percent lower for the LDOs than their counterparts after adjusting for patient case mix and other facility-level characteristics. In addition, LDOs derived a greater share of dialysis payments from dialysis drugs, which were more profitable than composite rate services in 2005, than non-LDOs.

Based on the 2005 payment and cost data, we estimate that the 2007 aggregate margin will be 4.1 percent. This estimate reflects the Congress's update of the composite rate in 2006 (by 1.6 percent) and in 2007. Beginning on April 1, 2007, the Tax Relief and Health Care Act of 2006 updates the composite rate by 1.6 percent. This estimate also reflects the update of the add-on payment in 2006 and 2007.

Table 1. Medicare margin in 2005 varies by type of freestanding provider

Provider type	Percent of spending by freestanding facilities	Medicare margin in 2005
All	100%	8.4%
LDOs	72	10.7
Non-LDOs	28	2.6

Note: LDO (large dialysis organization). LDOs are: Fresenius, DaVita, Gambro, and Renal Care Group.

Source: Compiled by MedPAC from 2001 and 2005 cost reports and 2005 outpatient claims submitted by facilities to CMS.

Modernizing the outpatient dialysis payment system

In our March 2001 report, the Commission recommended that the Congress broaden the payment bundle to modernize the outpatient dialysis payment system. Medicare would provide incentives for controlling costs and promoting quality care by broadening the payment bundle to include drugs, laboratory services, and other commonly furnished items that providers currently bill

separately and by linking payment to quality. A bundled rate would create incentives for providers to furnish services more efficiently. For example, a bundled rate would remove the financial incentive for facilities to overuse dialysis drugs under the current method. (However, a bundled payment might give some providers an incentive to stint, as we discuss below.)

A bundled rate would also simplify the outpatient dialysis system. The MMA created the add-on payment to the composite rate from some of the profits that Medicare previously paid providers under the pre-MMA drug payment method. The MMA requires that CMS update the add-on payment based on the previous year's increase in drug expenditures. Under a bundled rate, it would no longer be necessary for CMS to separately update the add-on payment to the composite rate.

There are several important design issues that will need to be addressed as the outpatient dialysis payment system is modernized. The first issue concerns determining the services to include in the expanded bundle. Along with widely used dialysis drugs and laboratory tests that are currently not covered by the bundle, policymakers should consider including other services needed by dialysis patients including:

- Nutritional therapy,
- Vascular access monitoring and surveillance services, and
- Vaccinations for influenza, pneumonia, and hepatitis C.

A broader bundle might give some providers an incentive to stint on care. Consequently, the Secretary will need to continue efforts to monitor, report on, and improve the quality of dialysis care in order to promote the delivery of clinically appropriate care. The Secretary should collect clinical information for each dialysis patient to reflect the services included in an expanded bundle. Currently, CMS collects dialysis adequacy and anemia status for all patients on the claims providers submit for payment. The Secretary might consider augmenting this information with patient-level information on:

- Nutritional, iron, and bone disease status, and other measures reflecting patients' clinical status;
- Use of the leading dialysis drugs, including erythropoietin and other erythropoiesis-stimulating agents, iron therapies, vitamin D therapies, alteplase, levocarnitine, and antibiotics;
- Occurrences of hospitalization and emergency department use;
- Cases of mechanical complications, such as thrombosis of the arteriovenous fistula in hemodialysis patients and intra-abdominal bleeding among peritoneal dialysis patients; and
- Cases of infection, such as septicemia, peritonitis, and methicillin-resistant staphylococcus aureus infections.

Under an expanded bundle, the Secretary will need to ensure that dialysis providers are not sending patients to other Medicare providers (such as outpatient hospital departments) for services covered under an expanded bundle. It will also be necessary to ensure that services covered under an expanded bundle are not obtained by patients under the Part D program. For example, Medicare covers doxercalciferol, a drug used to treat bone disease, under Part B when patients receive it intravenously and under Part D when patients receive it orally (by capsule). In addition, the Secretary will need to ensure that non-dialysis providers are not duplicating care, i.e., furnishing a service included in an expanded bundle.

Another design issue concerns equalizing the base rate between freestanding and hospital-based providers. Currently, Medicare pays hospital-based facilities $4 more, on average, for composite rate services than it pays freestanding facilities. This difference began with the Omnibus Budget Reconciliation Act of 1981, which mandated separate rates for the two types of facilities. In the 1983 rule implementing the composite rate, the Secretary attributed this $4 difference to overhead, not to patient complexity or case mix. This payment method is not consistent with the principle of paying the costs incurred by efficient providers who furnish appropriate care, regardless of the care setting. Consequently, the Commission recommended that the Secretary should implement a uniform payment policy across settings.

Other design issues that policymakers will need to address when designing a bundled payment include:

- Determining the unit of payment, which is currently a single dialysis session. Changing the unit of payment to either a week or a month might give providers more flexibility in furnishing care.
- Adjusting for factors that affect the costs of efficient providers. Currently, CMS adjusts payment for composite rate services by patients' age and two measures of patients' body mass. To assure that payments remain adequate in the future, both MedPAC and the Secretary should continue to explore whether additional factors are needed to adjust payment for factors that affect efficient providers' costs. In addition, Medicare's current payment method pays the same rate for the different methods of dialysis: conventional (thrice weekly) hemodialysis, more frequent hemodialysis, and peritoneal dialysis.

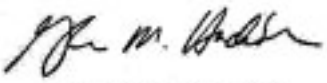
Finally, under an expanded payment bundle (as well as under the current payment method), the Commission believes that it is important for Medicare's payment systems to give incentives to providers investing in quality. Consequently, the Commission has recommended payment for performance in the outpatient dialysis setting (along with other fee-for-service providers and Medicare Advantage plans). Outpatient dialysis care is ready for pay for performance:

- Well-accepted measures are available
- Systems are in place to collect data
- Data are available to risk-adjust measures.
- Providers can improve upon measures.

The Commission supports implementing quality incentives budget neutral by explicitly linking a small proportion of total payments from facilities and physicians providing outpatient dialysis services to their quality performance. Possible quality measures that the Secretary could use include: adequacy of dialysis, other measures of patients' clinical status, and occurrences of hospitalization, emergency department use, complications (such as thrombosis), and infections (such as septicemia and peritonitis).

If you have any questions regarding this correspondence, please do not hesitate to contact Dr. Mark Miller, MedPAC's Executive Director, at (202) 220-3700.

Sincerely,



Glenn M. Hackbarth, J.D.
Chairman

DEPARTMENT OF VETERANS AFFAIRS
UNDER SECRETARY FOR HEALTH
WASHINGTON DC 20420

JUN 2 2 2007

The Honorable Fortney Pete Stark
Chairman
Subcommittee on Health
Committee on Ways and Means
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Thank you for your interest in knowing how Veterans Affairs (VA) administers erythropoiesis stimulating agents (ESAs) in the treatment of anemia for End Stage Renal Disease (ESRD). In response to your questions, the following information is provided:

1. How many dialysis patients does the VA treat? What proportion of those patients receive ESAs via subcutaneous versus intravenous (IV) administration?

Response: There are 2064 patients on hemodialysis in the VA dialysis units. Seventy-six percent of these patients receive ESA via subcutaneous (SC) route and 24 percent through intravenous (IV) route.

2. Does subcutaneous administration of ESAs require a lower dose than IV administration in order to reach the same anemia management goal? How much lower of a dose? How does the frequency of the dose compare to IV administration?

Response: The dose of ESA administered via the SC route is 71 units per kg/treatment and by the IV route the dose is higher with 88 units/kg/treatment. There are two ESAs available in the United States, epoetin-alpha (sold as Epogen® and Procrit®, the latter which is only marketed for subcutaneous injection) and darbepoetin (sold as Aranesp®). There is only limited data available comparing intravenous and subcutaneous darbepoetin and the two routes of administration appear to be equivalent in terms of dosing and efficacy. For erythropoietin-alpha, the largest clinical trial, which was done in the VA, demonstrated that the dose required to reach the same target hematocrit was achieved using 25-33 percent less medication when using a subcutaneous route compared to the intravenous route (Kaufman JS et al, N Engl J Med 339:578-583, 1998).

3. To the extent VA administers ESAs subcutaneously, how much has the resulting decrease in doses lowered the cost of patient care?

Response: These calculations have not been formally done. In the document summarizing VA anemia research (enclosure 1), we estimated an annual savings of $2,987 to $4,095 per patient.

4. Has VA completed and published research discussing the lower doses and costs associated with subcutaneous administration of ESAs? What were the conclusions of that research?

Response: Enclosure 1 summarizes the research done in the VA discussing the lower doses and costs associated with SC administration of ESAs. We concluded that subcutaneous administration of epoetin in the hemodialysis population results in dose reductions of up to 32 percent compared to intravenous administration with annual savings of $2,987 to $4,095 per patient.

5. Do patients express discomfort or complain of pain when they receiving ESAs subcutaneously?

Response: There are two preparations of epoetin-alpha, one packaged in single dose vials and one packaged in multi-dose vials that also contain a preservative, benzyl alcohol that acts as a local anesthetic. In the VA clinical trial, the preparation with the preservative was used. In the clinical trial 86 percent of the patients rated the pain associated with subcutaneous injection as ranging from mild to absent while 14 percent of the patients had moderate pain.

6. Has the VA's use of subcutaneous administration of ESAs resulted in incidences of pure red cell aplasia (PRCA)? How rare of an occurrence is PRCA for patients receiving ESAs subcutaneously?

The Honorable Fortney Pete Stark

Response: Pure Red Cell Aplasia (PRCA) has primarily been reported with subcutaneous administration of a specific preparation, Eprex®, which is not available in the United States, although cases have been reported with all available ESAs. Eprex® is an epoetin-alpha similar to Epogen®, but has a different stabilizer and packaging. The risk of PRCA with Eprex® was thought to be related to the stabilizer (Tween-80) and the packaging in pre-filled syringes. Once these components were changed in 2004, the incidence of PRCA decreased markedly. The most recent estimates are as follows (Cournoyer et al, J Am Soc Nephrol 2004; 15:2728-2734):

Eprex® old preparation, SC	26.9 cases per 100,000 patient years
Eprex® old preparation, IV	0 cases per 100,000 patient years
Eprex® new preparation, SC	0.63 cases per 100,000 patient years
Epogen®, SC	0.2-0.7 cases per 100,000 patient years

Thank you for your interest and concern on behalf of veterans' health care.

Sincerely yours,

Michael J. Kussman, M.D.

Michael J. Kussman, MD, MS, MACP

Enclosure

Enclosure

VA has completed and published important research addressing the lower doses and costs associated with the subcutaneous administration of ESAs.

1. ***Kaufman JS, Reda DJ, Fye CL, et al: Subcutaneous compared with intravenous epoetin in patients receiving hemodialysis. Department of VA Cooperative Study Group on Erythropoietin in Hemodialysis Patients. N Engl J Med 339:578-583, 1998.*** In an unblinded trial conducted at 24 hemodialysis facilities at Veterans Affairs medical centers, 208 patients who were undergoing long-term hemodialysis were randomly assigned to receive epoetin intravenously (n =101) or subcutaneously (n = 107) (10). The dose was reduced until the hematocrit level was below 30%, then increased gradually until the hematocrit level was between 30% and 33%, an acceptable range according to recommendations by the Food and Drug Administration. The average dose over a 26-week maintenance period was compared between patients who received epoetin intravenously or subcutaneously. Data on discomfort associated with the route of administration were also collected. Data were collected from August 1994 to January 1997. Results indicated that the average weekly dose of epoetin was 32% lower (95% confidence interval [CI]: 14% to 50%) for patients who received subcutaneous epoetin, and that 86% of patients rated the pain associated with subcutaneous administration as absent to mild.

2. ***Kaufman JS for the Department of Veterans Affairs Cooperative Study Group on Erythropoietin in Hemodialysis Patients. Subcutaneous erythropoietin therapy: Efficacy and economic implications. Am J Kidney Dis 32:S1-S5, 1998.*** This research reviewed prior studies that suggested that lower doses of erythropoietin (rHuEPO) may be required to achieve a target hematocrit when the biologic is administered subcutaneously (SC) compared with intravenously (IV). A particular focus was on the Department of Veterans Affairs multicenter trial comparing the two routes of administration. The discussion noted that the specific mechanisms that result in the greater efficiency of the subcutaneous route are unknown but are probably related to the prolonged half-life of the hormone with subcutaneous administration. It was suggested that possible mechanisms resulting in greater efficiency with subcutaneous therapy include sustained stimulation of the erythroid progenitor cells, diminished inhibition of erythropoiesis by proinflammatory cytokines, and prevention of neocytolysis, the hemolysis of newly formed red blood cells. Further, it was concluded that because most hemodialysis patients in the United States are receiving rHuEPO by the intravenous route, switching to the subcutaneous route may result in significant cost savings for the health care system.

3. ***Hynes DM, Stroupe KT, Greer JW, et al. Potential cost savings of erythropoietin administration in end-stage renal disease. Am J Med. 2002; 112(3):169-175. (CSP 392 Economic Impact Study).*** Based on results found from the VA clinical trial CSP392, this study posed the question: if Medicare end stage renal disease patients had their anemia managed similar to the way VA patients were managed, what impact would there be on Medicare costs? Using Medicare data from 1997-1998 the research found that 91% of Medicare patients were receiving their erythropoietin IV. The research estimated that the Medicare End-Stage Renal Disease Program could save $47 to $142 million annually as 25% to 75% of patients switched to subcutaneous administration of epoetin, assuming that the dose reduction matched the 32% reduction in the Department of Veterans Affairs randomized controlled trial. Centers for Medicare and Medicaid Services (CMS) collaborated on this study with VA researchers.

4. ***Hynes, DM, Stroupe, K, Browning, M, Kaufman, J, Reda, D. Chronic Care Delivery in End Stage Renal Disease: Adherence to Clinical Guidelines for Anemia Management. American Journal of Kidney Diseases. 2006; 47(3): 455- 461.*** Using data from a multisite prospective observational study of 308 hemodialysis patients from 8 VA medical centers from 2001 to 2003, the study examined compliance with National Kidney Foundation–Dialysis Outcomes Quality Initiative (NKF-DOQI) erythropoietin administration guidelines across Veterans Affairs (VA) versus private-sector dialysis facilities and implications for erythropoietin dose, anemia management, and cost. The research found that erythropoietin was administered predominantly subcutaneously for 52% of patients in the eight VA units in the study versus 15% in private-sector facilities and estimated costs for erythropoietin were lower in the VA compared to the private sector. Anemia management was similar. The findings indicate that potential annual savings of $2,987 to $4,095 per patient exist if NKF-KDOQI guidelines are followed and subcutaneous administration of epoetin is used, assuming a Medicare-allowed rate of $10/1,000 units.

KAISER PERMANENTE®

June 22, 2007

The Honorable Pete Stark
Chairman, Health Subcommittee
Ways and Means Committee
U.S. House of Representatives
1135 Longworth House Office Building
Washington, DC 20515

Re: Kaiser Permanente Southern California (KPSC) Renal Program Experience with Bundled Payment and Subcutaneous Use of EPO

Dear Chairman Stark:

In response to an invitation from your staff to submit information for the subcommittee hearing on June 26th, Kaiser Permanente Southern California (KPSC) Region is providing information from our experience regarding: 1) subcutaneous administration of erythrocyte stimulating agents (ESAs) for the majority of our hemodialysis patients; 2) bundling of payment for hemodialysis and dialysis-related services; and 3) provision of short daily hemodialysis.

Based on our experience in southern California, we have found that subcutaneous administration of Epogen is an efficient method of delivery and can lower dosing levels and costs. We have also found that bundled payments are an effective way to pay dialysis centers and are consistent with both positive health outcomes for beneficiaries and efficient use of Epogen.

Use of Subcutaneous Epoetin

Following the release of the original National Kidney Foundation DOQI guidelines in 1997 which supported subcutaneous administration of epoetin, KPSC undertook a quality initiative to convert hemodialysis patients from intravenous to subcutaneous use. The program allowed for exceptions based on medical considerations and patient preference. Most hemodialysis patients chose subcutaneous administration, and we have continued to maintain the majority of them on subcutaneous administration (80% as of 12/31/2006). Importantly, we have found that when given medical and cost information, most hemodialysis patients prefer to receive subcutaneous epoetin – for many it is a welcome chance to reduce the cost of their treatments which they recognize as being very expensive.

We have found and reported that the dose required for subcutaneous epoetin in hemodialysis patients is about 28% less than for intravenous epoetin (*American Society of Nephrology* abstract, 2001). This is similar in magnitude to several other published reports.

In addition, all KPSC patients on peritoneal dialysis utilize subcutaneous epoetin.

Dialysis and Dialysis-related Services Bundling

There is currently much interest and debate surrounding proposals to combine payment for medications and laboratory testing into a "bundled" Medicare dialysis payment. Some believe that such a strategy could lead to adverse patient outcomes, and further, that any bundled payment should be stratified to increase payment for patients with multiple co-morbidities. In this light, we wish to make the committee aware of our successful experience in the bundling of payment for dialysis and dialysis-related services.

The majority of our hemodialysis patients are either insured by Medicare (primary or secondary), most under the Medicare Advantage program (Kaiser Permanente Senior Advantage), or are enrolled in commercial Kaiser Foundation Health Plan coverage. Therefore, we are the direct payers for hemodialysis services, much the same as traditional Medicare is for the majority of beneficiaries needing dialysis.

KPSC adopted a bundled payment model for dialysis in 1999. This bundled payment model is now used for 53 percent of our hemodialysis patients (1957 out of 3675 hemodialysis patients, as of June 20, 2007).

The services included in these contracts have varied over time, but now include the dialysis treatment, non-oral medications including EPO, iron and vitamin D sterols, monthly routine laboratory tests and additional, non-emergent laboratory tests. Payment levels are not risk stratified for co-morbid conditions or other factors. In one contract with a dialysis provider, each facility is eligible for a performance incentive payment linked to patient satisfaction and nephrologist satisfaction.

Our quality monitoring, through both our internal quality program and our dialysis provider's quality programs, indicate that our hemodialysis patients have very good outcomes. Measured outcomes include the adequacy of the dialysis treatments, anemia outcomes, mineral metabolism outcomes and patient satisfaction.

The majority of dialysis services for our 400+ peritoneal dialysis patients are provided internally, so we do not have experience in the bundling of payments to third party providers for this modality.

More Frequent Dialysis and Home Hemodialysis

Your staff also asked about the KPSC experience with more frequent dialysis, particularly as utilized for short daily home hemodialysis (SDHHD). KPSC is gaining experience with SDHHD, and our program, based at our Los Angeles Medical Center, has recently published their results, showing positive outcomes, including improved quality of life (*Hemodialysis International*, Volume 11, Issue 2, pp. 225-230, April 2007).

Thank you for your interest in some of the innovative programs we have at Kaiser Permanente. Please do not hesitate to contact Fish Brown in our Washington, D.C. office with additional questions, as we would be happy to provide whatever information we can to assist you and your staff.

Sincerely,

Peter Crooks, MD
Physician Director, Renal Program
Associate Medical Director of Operations
Kaiser Permanente Southern California

Letter from the National Institutes of Health, "Between 1991 and 2005, the average weekly dose of Epo more than doubled. Furthermore, NIH data show that in 2005 over half of the dialysis pa-

tients had hemoglobin levels above twelve grams per deciliter," I guess it is, "or greater."

Keep in mind that the FDA recommends that hemoglobin levels not exceed 12 yet NIH data show that more than half of the patients are at 12 or higher.

The GAO writes that Medicare could realize greater system efficiency if all ESRD drugs and services were bundled under a single payment system.

The Medicare Payment Advisory Commission writes, "A bundled rate would create incentives for providers to furnish services more efficiently and would remove the financial incentive for facilities to overuse dialysis drugs. Bundled payments would encourage more efficient use of ESAs."

Please note here that we must, without question, and it should be of paramount importance that we are sensitive to patient-specific variations in the need for ESAs when we structure a bundled payment system. We are not recommending a one-size-fits-all system here.

The two large, for-profit chains have standardized dosing protocols and often they will encourage doctors to sign kind of a uniform dosing agreement without taking into effect the tests that should be done periodically during the course of treatment. We can address these sensitivities with steps such as aggressive monitoring and quality programs.

I'm sorry that CMS is unable to deliver their long overdue report on ESRD bundling. This report was due more than two-and-a-half years ago, and at our hearing on this topic last December CMS promised to report by summer of 2007. Guess what? For those of you who've been outside today, summer is here.

I understand that CMS will give us some insight on that report today. I look forward to that testimony and receiving a commitment from CMS as to when we'll receive the report.

Lastly, both Kaiser Permanente of southern California and the Veterans Administration have written letters to discuss their practice patterns. Each is able to safely and effectively treat patients with doses of up to 30 percent lower in Epo than we see used in Medicare. And I might add that Kaiser contracts with one of the for-profit chains to provide this service so that in effect they are paying a bundled rate to one of the for-profit operators and they are setting some standards such as "subcuetaneous" administrating of the drugs as does the VA and they are getting a one-third smaller dosage of ESAs in these programs.

Seventy-six percent of VA patients receive ESAs in this way, "subcuetaneous", and they have annual savings between $3,000 and 4,000 per patient. Now presuming that they buy Epo on the Federal schedule, they're probably paying half of what the for-profit chains are paying and you might then say that we could save from $6,000 to 8,000 per patient if we in fact followed the VA's protocol or Kaiser.

Kaiser in southern California does administer ESAs "subcuetaneous" and confirms that doing so requires a dose 30 percent smaller than needed for intravenous use. Of even greater interest, they do use bundled payments and write that bundled payments are an efficient way to pay dialysis centers and are con-

sistent with both positive health outcomes for beneficiaries and the efficient use of Epogen. They do suggest that they monitor it closely and they can feel comfortable with the results.

We must be certain that Medicare payments are structured to ensure the highest quality care to all beneficiaries, and I am confident that we can do so for dialysis services in a more efficient manner that safeguards against health risks of targeting the higher red blood cell levels. This should be the committee's goal for Medicare ESRD patients.

Now if there's anything left to say, Mr. Camp can say it.

Mr. CAMP. I'm sure I can find something.

Well, thank you, Mr. STARK. I also want to thank all of the witnesses from the three panels for being here today and also a special thanks to Leslie Norwalk, the acting administrator of CMS for her excellent and informative testimony before the Committee.

I appreciate you calling this hearing today. I agree that the safety of dialysis treatments is critically important. Coupled with the fact that 320,000 Medicare beneficiaries receive dialysis treatments, at a cost to taxpayers of 7.9 billion, this is a significant financial issue as well. Given the spread of diabetes and related conditions like kidney disease, these numbers are regrettably only going to increase.

We are all aware of the disturbing reports that have been published, which highlight how the current Medicare payment system may create incentives for providers to dose patients with unnecessarily higher levels of the drugs used to treat anemia in dialysis patients. This is alarming given the serious health concerns associated with the overuse of these same drugs.

In fact, the Food and Drug Administration recently released a "black boxed warning" that indicates an increased risk of death from blood clots, strokes and heart attacks in kidney patients and tumor growth in cancer patients from aggressive dosing of these drugs called ESAs.

In response to these events, policymakers have begun to consider proposals to reform the current Medicare payment system for dialysis. MedPAC has recommended bundling ESRD drugs into the larger payment rate.

As we consider making significant changes to how Medicare pays for dialysis I want to sound a note of caution. ESRD patients are a very sick population, often suffering from multiple chronic conditions, who may not benefit from a one-size-fits-all approach to this issue.

Any type of bundled payment must provide a proper adjustment to account for sicker patients. An appropriate bundled payment also needs to account for small dialysis facilities in rural areas, which have higher costs and may not be able to achieve the same efficiencies as the larger national dialysis providers.

In order to ensure that Medicare beneficiaries continue to receive access to high quality kidney care, we must also support adequate reimbursement to dialysis facilities. We need to maintain adequate payments to these providers, so that they can maintain their focus on prevention and care management of dialysis patients.

To address these issues, I introduced the Kidney Care Quality and Education Act of 2007. This bill provides a 3-year update to

the composite rate and rewards dialysis providers for quality improvement and attainment. Both the quality initiative and payment update have been continually recommended by MedPAC.

Through increased awareness and education on chronic kidney disease, both the patient and the provider can take steps to slow the progression and prevent the need for dialysis in the future. I have worked closely with the kidney care community to comprehensively address these issues, and I feel that it is important that Congress move forward. I certainly look forward to working with Chairman Stark to maintain quality care for kidney patients.

Thank you, and I yield back the remainder of my time.

Chairman STARK. Would the gentleman yield?

Mr. CAMP. Yes.

Chairman STARK. And perhaps we could stipulate something here at the beginning.

I don't think that either of us would suggest or that Chairman Thomas suggested or anybody else has suggested that we have a one-size-fits-all. I think we could stipulate that most medical treatment professionals would suggest that these are unique treatments for unique individuals and they vary, and that there are monitoring tests so you could tell fairly quickly how well they are doing, and that I don't think anybody on this Committee or I don't think any of the witnesses would suggest that we should just have a blanket treatment schedule.

And I just wanted—I don't know if that comes up in any of these——

Mr. CAMP. Well, that's very reassuring. Reading all the testimony yesterday I just thought it was important to put that out, and I think it's very——

Chairman STARK. I'm glad you did, but I think that you'd find——

Mr. CAMP. It's hard to know when you read the testimony exactly how they're going to come forward today, but I think it's very reassuring that we can both agree to that.

Chairman STARK. Is there anybody else who has a burning opening statement that can't appear in the record? And if not, I'm happy to recognize the Honorable Donna M. Christian-Christensen, a physician, a delegate to Congress from the United States Virgin Islands.

Donna, why don't you try and, in layman's language, educate us as best you can? Although we limit to 5 minutes, you'll have 5 minutes in the subsequent questioning to expand upon anything you'd like to tell us.

Ms. TUBBS JONES. Mr. Chairman, if you will, allow me, just a moment. For the record, I'd like to make it clear that Donna Christian-Christensen Chairs the Congressional Black Caucus Health Brain Trust and she's been doing that for a number of years. And she's experienced many years in Congress doing the work, and I just wanted to recognize the work of Dr. Christensen.

Chairman STARK. I thank the gentlelady for her comments.

STATEMENT OF MRS. CHRISTENSEN, CONGRESSIONAL DELEGATE, U.S. VIRGIN ISLANDS

Mrs. CHRISTENSEN. Thank you, Mr. Chairman, Ranking Member and Members of the Committee. Thank you, Congresswoman Tubbs Jones, for those generous comments. And I really welcome the opportunity to testify this morning.

I have my submitted testimony and I'm really going to speak from notes from that and from having a chance to have looked at some of the testimony that's submitted.

At the outset, I want to just start out by agreeing with you, Mr. Stark, that our priority is to ensure patient safety while also protecting taxpayers from unnecessary expenditures. And I also want to just agree with Ms. Norwalk who says in her testimony that the development of a new payment system is a significant endeavor that merits careful consideration and analysis.

And there's also other areas of the testimony that I really agree with, which is the need for reviewing the EMP and reimbursement and collaboration with the entire renal care community and the need for treatment decisions to be made by the patient and his or her physician. It's not the facilities that make those decisions. It's the patient and their doctor in consultation with each other.

And also on the advisory for the hearing there were certain facts that I want to just reference because I want to make sure that we're speaking from the same facts, and I stand to be corrected if I'm wrong, but first it was stated that ESAs account for about—almost 50 percent, and it's my understanding they account for 25 percent of ESRD costs.

Second, on the studies that raise the concerns that brought us here today and to reviewing the EMP, they were done in chronic renal disease patients not end-stage renal disease patients, and I think FDA will point out that they were done in conditions, for conditions not recommended on the prior labels and not treated for targets that are recommended. They were treated for higher targets of over 13 and over 14, so they really don't represent what happens in everyday chronic disease or end-stage renal disease practice.

And third, I don't think it's really been established that current CMS payment system incentivizes higher dosing. In fact, even Ms. Norwalk says in her testimony that it encourages really that all services that are needed be provided. And the only downside that she offers for the present system is that it may make providers more complacent and not willing to seek out innovative and new ways to provide more efficient treatment, but I doubt that. As a physician I know we're always looking for better, more effective ways to take care of our patients, which brings me to why I felt it was important for me.

I want to talk from the perspective of two groups, one, of course, and I am chair of the Health Brain Trust. We are finalizing our position on this issue, but this is where we are at this point. And we're speaking on behalf of the 32 percent of the ESRD patients who are African Americans and the other people of color who are disproportionately suffering from end-stage renal disease.

Although African Americans for example are 13 percent of the U.S. population we are 38 percent of all patients treated for end-

stage renal disease and we reach that point at younger ages. We are very disproportionately impacted by diabetes and hypertension as well, and we have higher risks when we have diabetes and hypertension to develop chronic renal disease and end-stage renal disease.

African Americans have an incidence that's more than three times that of whites, Native Americans—about two times that of whites and Hispanic Americans, 1.5, and that's by 2002 data. So whatever adverse consequences might occur, they would disproportionately impact people of color.

And I brought a couple of maps. The minority quality forum prepares maps really looking at renal disease—do you have them, these maps—across communities, and the lines, the ones with the lines across are those that have high minority populations.

And both, if we look at Congressman Stark and another Member of the Committee, Mr. McCrery's maps, you'll find that although, Mr. Stark, you have some green areas, which are sort of medium incidence rates, in some of your areas where you have high minority populations, those are mainly where you have high Asian populations who are—while they are slightly above the white population for ESRD, they are not as heavily impacted as African-American populations. And some of your highest end-stage renal disease incidences are in San Leandro and Hayward, where it appears by our looking at it that you have your highest African-American populations.

And in Mr. McCrery's, they have a mixed picture, but some of the areas where they have higher minority populations they also have higher incidences of ESRD patients. I'm not sure if I—do you have Mr. Camp's as well? Mr. Camp's is almost more green than anything else, and your population is 88 or better percent Caucasian and you have some of the lower rates of end-stage renal disease.

Those just go to underscore what I've been saying. And we can get other maps for other districts if you'd like, but I think across the board they're going to show that higher ESRD incidences exist in communities of color, and particularly where you have high population percentages of African Americans.

I'm also a family physician with more than 20 years of practice experience and I've been a hospital administrator with some degree of oversight, not a lot, but some degree of oversight for our dialysis unit. And I want to say on behalf of my fellow physicians, we went into this profession because we care about people. We care about their health and their overall well-being. So our greatest incentive is to have what we do result in a healthier individual, a healthier family. But we also have to keep our offices open in order to be able to do that.

The kind of strict and narrow EMP being considered not only ignores our years of study and dedication and our expertise as physicians but it also has the potential to tie our hands so as to cause us to under treat, not only in renal disease but even in some cancer patients so that we end up with hemoglobin below 11. We years ago, very wisely, put a lot of time and deliberation and moved away from that when we found that hemoglobins under 11 cause far

more morbidity and mortality than this current study that we're referencing suggests and the black box insinuates.

As a matter of fact, as I look at the block box, I think that in the first instance suggesting that they, ESAs, be used just to a level that would prevent transfusion is very shortsighted and ignores other benefits that are important to treat anemia as well as it adds risks that providers trying to treat just to the transfusion would tend to under treat and would end up with those hemoglobins 11 or under.

And I think it's a bit misleading because it doesn't clearly state that the untoward effects that occurred under higher than normally used dose regimens in targeting toward higher hemoglobin than is the current practice.

And the last thing I wanted to underscore about physicians is that they haven't had the commensurate increases in reimbursement compared to the increasing costs of care. So to now bundle the payments beyond what is now being done is to put them further behind the curve and really challenged to meet their overhead and perhaps to close.

And we note that in cases where dialysis facilities closed, those that closed, by and large treated higher percentages of African-American patients, so again we are mostly impacted.

On the incentive issue I think as I look at it, rather than incentivize for more Epogen as the current Erythropoietin protocols state, if they're targeted to meet the hemoglobin of between 11 and 12, which is the current practice, if they go over—CMS already decentivizes treating physicians from going over because they reduce your payment. There's a disincentive already present in the current EMP to overtreating patients, and I think that should suffice.

And again, I just want to underscore that we are here to heal, to do good and not to do any harm. And I think that's what we ought to also be focused on as we look at a new EMP, to do no harm.

I want to just end by—and I'm going to read from my prepared statement. I know, Chairman and Members, that as the cost of the healthcare continues to skyrocket the temptation is to do something quickly, and the easiest and quickest approach is to cut costs, but that's the kind of knee-jerk reaction that is not really worthy of this institution. More importantly it runs the very real and high risk of hurting patients. And because such large proportions of those patients with end-stage renal disease are African Americans we again will be the ones more adversely impacted by the decisions made without careful study of all the clinical implications.

We went through this in 1997 and we should take heed to the lessons learned back then. I would hope—and the CDC and all of our partnering organizations, universities and advocacy groups are working to this end, that we could get you, our colleagues and leaders on the issues of healthcare to see that the only way to cut costs is to emphasize prevention and increase the portion of the health budget dedicated to that and also to eliminate the disparities in health, a major one of which is end-stage renal disease, that cause people of color to seek care that is often uncompensated at late stages of their disease.

And that is really the only way that we can cut healthcare costs in the long run. Cost containment runs a real risk of creating an unjust, inequitable and ineffective system of healthcare in this country where some Americans, usually those—African-Americans and other people of color are left behind or left out, period.

And I want to thank the chairman again for holding this hearing and the Ranking Member, and I look forward to answering questions either from my written testimony or from my comments, from my notes. Thank you.

[The prepared statement of Mrs. Christensen follows:]

Statement of The Honorable Donna M. Christian-Christensen, M.D., a Delegate to Congress from the United States Virgin Islands

DONNA M. CHRISTENSEN
DELEGATE, VIRGIN ISLANDS

COMMITTEE ON
NATURAL RESOURCES

CHAIRWOMAN, SUBCOMMITTEE ON INSULAR AFFAIRS

MEMBER, SUBCOMMITTEE ON NATIONAL PARKS, FORESTS, AND PUBLIC LANDS

COMMITTEE ON
HOMELAND SECURITY

MEMBER, SUBCOMMITTEE ON EMERGENCY COMMUNICATIONS, PREPAREDNESS, AND RESPONSE

MEMBER, SUBCOMMITTEE ON EMERGING THREATS, CYBERSECURITY, AND SCIENCE AND TECHNOLOGY

Appointed Majority Whip

Member,
CONGRESSIONAL BLACK CAUCUS

MEMBER, CONGRESSIONAL CAUCUS FOR WOMEN'S ISSUES

Congress of the United States
House of Representatives
Washington, DC 20515–5501

PLEASE RESPOND TO:

WASHINGTON OFFICE

☐ 1510 LONGWORTH HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-1790
FAX (202) 226-1917

DISTRICT OFFICES

☐ STRUM NO. 36
SUNNY ISLE SHOPPING CENTER
P.O. BOX 5880
ST. CROIX, VIRGIN ISLANDS 00823
(340) 778-5900
FAX (340) 778-5911

☐ SUITE NO. 207
PEBBLY CENTER, 2ND FLOOR
ST. THOMAS, VIRGIN ISLANDS 00802
(340) 774-4403
FAX (340) 774-8033

☐ 4108 DANISH ESTATE
CHRIST ISLAND, ST. JOHN
U.S. VIRGIN ISLANDS 00831
(340) 776-1212

Testimony Presented by
Congresswoman Donna M. Christensen
Before the
U.S. House of Representatives
Ways and Means Subcommittee on Health
On
"Payment, Safety and Quality Issues in Treatment of Patients with ESRD"

June 26, 2007

Mr. Chairman, Members of the Ways & Means Subcommittee on Health and invited guests, I want to thank you for holding this hearing today on a very important issue - patient safety and quality of care for Medicare beneficiaries with End Stage Renal Disease (ESRD), a devastating chronic and debilitating illness. My remarks today will be concise and will focus on three key areas: (1) health disparities in ESRD, (2) the need to be cautious and judicious when considering any changes to Medicare ESRD reimbursement; particularly bundling separately billable services into the composite rate and major changes to the existing CMS Erythropoietin Monitoring Policy, and (3) the need for prevention of ESRD given the massive tidal wave of baby boomers that will soon enter the ranks of the Medicare program.

As a Member of Congress representing a district with significant incidence of Chronic Kidney Disease (CKD) and End Stage Renal Disease (ESRD), I am deeply concerned about the rapidly increasing numbers of patients on dialysis in my district as well as the United States overall. Each year CKD, a progressive condition that impairs kidney function, kills more than 14 people out of every 100,000, making it the nation's ninth leading cause of death.

PRINTED ON RECYCLED PAPER

There are approximately 470,000 people with ESRD, with 330,000 being treated with dialysis under Medicare in the United States today. Almost all ESRD patients –93%– are Medicare eligible creating a significant role for the Federal government in managing the care and expenditures for this very vulnerable and sick patient population. We have an obligation to Medicare beneficiaries with ESRD to ensure they receive the best available care.

As many of you may know, CKD and ESRD strikes people of all ages and races; however, it disproportionately affects minority populations, including African Americans, Hispanics, American Indians and Asians. Let me give you some statistics to convey the seriousness of this disease for communities of color. African Americans are 3.8 times more likely to suffer kidney failure than whites; for Native Americans, the rate is 2.0 times greater; and for Asian/Pacific Islander Americans, the rate is 1.3 times greater. The risk of kidney failure for Hispanics versus non-Hispanics is 1.5 times greater than the rate for whites.

For African Americans, who are susceptible to risk factors such as hypertension, diabetes, and obesity, and who may contend with socioeconomic factors that limit their access to health care services, the burden of CKD is disproportionately high.

Although African Americans only make up approximately 13% of the overall U.S. population, they represent approximately 38% of all patients treated for ESRD in the United States. African Americans also suffer kidney failure at an earlier age than their white counterparts: in 2006, the mean age for African Americans at the start of treatment for kidney failure was 56.4 years, compared with 59.6 for white Americans.

The leading causes of ESRD in the African American population are diabetes and hypertension. Diabetes, the leading cause, represents approximately 43% of all new cases each year. African Americans represented nearly one-third of new patients whose kidney failure was caused by diabetes.

The prevalence of diabetes has reached nearly epidemic levels in the African American community: 2.7 million (11.4%) of all African Americans, aged 20 or older, have diabetes; one third of these cases are undiagnosed. This phenomenon is reflected in the steadily rising incidence rate of diabetic ESRD among African Americans: African Americans with diabetes have 6 times the risk of kidney failure, in comparison with whites. Over the last decade, for Americans younger than age 40, the rates of diabetic ESRD have decreased among white Americans, but have increased among African Americans.

The second leading cause of ESRD – hypertension – affects one in every three African Americans. In African Americans under the age of 40, the rates of kidney failure caused by hypertension has increased over the last decade, while the rates of their white counterparts have decreased. Overall, African Americans

comprise 51% of new patients whose kidney failure was attributed to hypertension.

African American men ages 20 to 29 are 10 times more likely to develop kidney failure due to high blood pressure than white men in the same group; African American men ages 30 to 39 are approximately 14 times more likely to develop kidney failure due to high blood pressure than their white counterparts. Overall, rates of ESRD attributed to hypertension are up to 16 times greater in African Americans than white Americans.

The fact that these precursors to CKD are so prevalent in the African American community and in the family histories of most African Americans underscores the notion that all African Americans may be at risk and further heightens the importance of increased awareness, prevention, and screening among this population.

As a physician and Member of the Congressional Black Caucus, I am compelled to protect and ensure that correct policy choices are being made so that minority patients with ESRD who suffer from this terrible disease have access to the highest quality patient care.

In my testimony today I would like to comment on the policy proposal of quickly establishing a fully bundled payment system for ESRD – that is to bundle ESRD medications and other separately billable services into the composite payment rate. My concern is that patients on dialysis fall along a diverse spectrum of care and have distinct needs. This is especially true of African Americans who have more co-morbidities like diabetes, hypertension and obesity which impact dosing requirements. According to the Kidney Care Partners (KCP) African-Americans have a low response rate to anemia management therapy. These patients require higher doses of erythropoietin. According to KCP:

> *"A significant percentage of ESRD patients have a low response rate to anemia management therapy and, therefore, require higher doses of erythropoietin stimulating agents (ESAs) to achieve clinical performance targets. Thus, patient variability can be a major factor leading to variations in comparative data…the particular clinical needs of key patient groups, such as African Americans, can require higher levels of ESAs in order to generate red blood cell development."*

These differences among patients make it difficult to predict an average treatment regimen along a wide range of services and highly variable dosage of ESRD related medications. I want to urge my esteemed colleagues on this Committee that we must exercise extreme caution as we consider any policy changes so we don't affect patient care.

Additionally, we must be careful that ESRD payment policy changes do not adversely impact small dialysis organizations creating an access issue for many communities, but especially in the inner cities. This is a real concern in the African American community.

As the Medicare Payment Advisory Commission (MedPAC) suggested in their March 2007 report there are potential treatment access issues for African Americans. Many of the dialysis facilities that closed in 2005 treated a greater proportion of African Americans than facilities that opened (48 percent vs. 29 percent).

As the Chairman knows, the MMA required that CMS undertake a demonstration project that would examine the feasibility of bundling all dialysis services into one composite rate. During the December Ways and Means Hearing, we heard testimony from CMS about the difficulty of establishing an appropriate case mix adjuster—the tool needed to ensure that patient variation is adequately addressed in developing a bundled payment.

I am sure CMS can attest to the challenges that still exist in developing a fully bundled payment system. I am dedicated to developing a payment system that works well, provides the best quality care for Medicare beneficiaries, and strongly believe that any change should be tested first to understand the implications.

Ensuring that minority patients with ESRD have access to dialysis facilities and receive high quality patient care is one of my top priorities. Recently, CMS announced that it was reviewing the EMP, in light of the FDA's recent issuance of new warnings regarding Erythropoiesis Stimulating Agents (ESAs). I'm concerned that changes to the EMP, which has now been in effect for one year, could negatively impact minority patients. I do not want to see a repeat of the devastating effects that payment changes in ESRD had on patients in 1997, when CMS (HCFA at the time) issued the original Hematocrit Measurement Audit Program Memorandum (HMA-PM). That policy limited the ability of physicians to treat anemia and resulted in poor quality outcomes. The policy was subsequently changed and improved considerably after stakeholders voiced concerns. The current policy – the Erythropoietin Monitoring Policy was updated again in 2006, as a result of a thoughtful and transparent process with renal community input. Given the massive implications for patient care, any changes to the EMP should not be done in an arbitrary manner. CMS should establish an open and transparent process to allow external experts and stakeholders to consider the potential impact revisions would have on patient care. Further, Congress should not legislate a policy change on the EMP that CMS and the renal community have effectively been collaborating on for years.

We must be good stewards of taxpayers dollars, but instead of considering policies that may compromise care for some of Medicare's most

vulnerable patients, we should be looking at policies that emphasize disease prevention. Prevention of major medical conditions is of paramount importance for public health in the United States because of the increasing prevalence of conditions such as obesity, diabetes and heart disease... the very conditions that contribute to the onset of CKD. In light of the growing population eligible for Medicare and the baby boomers soon to come, we must look for policy solutions to keep Medicare beneficiaries healthy and avoid costly treatments instead of rationing care for patients after the onset of disease. As stewards of the Medicare program we must do what is best for Medicare patients first and foremost rather than letting raw economics make these determinations.

Mr. Chairman and Congressman Camp, as the costs of healthcare continues to skyrocket, I know the temptation is to do something quickly and the easiest and quickest approach is to cut costs. That is the kind of knee-jerk reaction that is not worthy of this institution. More importantly it runs the very real and very high risk of hurting patients. And because such a large proportion of the patients with ESRD are African Americans, we again will be the ones most adversely impacted by decisions made without careful study of all of the clinical implications. We should have learned that lesson in 1997.

I would hope – and the Congressional Black Caucus and all of our partnering organizations, universities and advocacy groups are working hard at it– that we could get you our colleagues and leaders on the issue of health to see that the only way to cut costs is to emphasize prevention and increase the portion of the health budget dedicated to it; and to eliminate the disparities in health - a major one of which is ESRD - that cause people of color to seek care that is often uncompensated at late stages of disease. This is the only way to really reduce health care costs.

Cost containment runs the real risk of exacerbating an already-unjust, inequitable and ineffective system of healthcare in this country where some Americans – usually those that look like me – are left behind or left out period.

I thank the Chairman for holding this hearing so we may learn more about this important issue and hope that we focus on what is best for chronically ill ESRD patients.

Chairman STARK. Thank you. Mr. Camp, would you like to——

Mr. CAMP. Thank you, Mr. Chairman.

Thank you very much for your testimony. Your written testimony has a lot of information in it that I think will be very helpful to the Subcommittee.

You correctly point out that African-Americans constitute 38 percent of dialysis patients in this country. And the complexity of finding a proper formula to account for differences in patient population is a difficult one. It's a complex issue. If CMS were to bundle ESRD drugs with a composite rate or make some other formula change how best can we do that in a way that does not result in poor outcomes, particularly for the entire patient mix, but for the vulnerable patient populations you testified about?

Mrs. CHRISTENSEN. I'm not sure that I have all the answers to that specifically right now, but there are a lot of people studying it. But there have been some suggestions that we either bundle everything and treat ESAs differently because of their importance to renal dialysis, which is something we all agreed to in one way or another. Either we include them with some specific issues addressed about their—the need for more individual titration or we exclude them from the bundle and put some other kind of cost-containment measure, a cap maybe, on the cost or change the cap on the costs or the amount that can be used per month or that we excluded entirely.

But I don't have the final answer on that. But there are many suggestions out there that I think we need to look at because Epogen and Procrit and the other ESAs are so critical to not only preventing transfusions but allowing patients to live a decent quality of life while on dialysis.

Mr. CAMP. Thank you, and thank you for your leadership on this and other health issues in the Black Caucus and in the Congress. I've enjoyed working with you on a number of issues and look forward to working with you on this as well. Thank you very much.

Mrs. CHRISTENSEN. Same here. Thank you.

Mr. CAMP. Thank you, Mr. Chairman.

Chairman STARK. Mr. Thompson.

Mr. THOMPSON. Yes, thank you very much for testifying. I too share many of your concerns, look forward to working with you as the Subcommittee takes this issue on.

Chairman STARK. Mr. Johnson.

Mr. JOHNSON. No questions.

Chairman STARK. Mr. Becerra.

Mr. BECERRA. Mrs. Christensen, thank you very much for your testimony. I'd like you to just give us a little bit more information on what you think we can do on any number of these issues that it appears that because we lack some of the data which could give us a better sense of some of the different populations and the outcomes and effects that some of these different populations will experience, whether it's with drugs or treatment, what we can do to try to address those disparities that occur in the healthcare field right now that make it very difficult for us to assess populations within the U.S. or part of the American fabric because we have not

yet reached out to all of these populations whether African American, Latino or otherwise.

I'm wondering what you can tell us in terms of what we are missing in terms of better legislating to make sure that the disparities are addressed.

Mrs. CHRISTENSEN. Thank you for that question, and we'll have a very specific answer for you probably later this week as the tri-caucus, the congressional black, Hispanic and Asian-Pacific caucuses introduce our minority health legislation, which addresses issues around language proficiency and making sure that those services are not only paid for but that we understand what is supposed to be done and the certification for those who will be doing the translation, better data collection.

The health professions issue is a big one, and reaching out to communities of color who are now under-represented in the healthcare profession workforce and finding ways to incentivize them and help them to get into those professions because it's been shown that—not only that people of color are discriminated against either when they get into the healthcare system but, in the converse, that when they are treated by people of the same cultural and linguistic background where they can develop a greater rapport—and that patient-doctor relationship is critically important, that they get better compliance and therefore better outcomes.

So we have a number of issues that we're going to address there, but you know, we're operating under some budgetary constraints and I just don't think that we can do it without an investment that starts to bring people up to at least a level playingfield in terms of where health status is. And you know, I would urge everyone to consider making that investment because we're paying for it on the other end, when you go to emergency rooms and seek care that is very expensive, you get there at late stages of the disease and the treatment costs more, and it's not being paid for—and of course, bringing everyone under coverage, because minorities make up more than half of the uninsured population in this country.

Mr. BECERRA. And your testimony points out that when we don't have that information at hand, when we haven't gone out there to try to solicit the full participation of some of these groups, populations, that we end up paying because we're not sure how to best administer, whether it's drugs or the therapies that are out there and we may make mistakes that actually cost people their lives. So I think you're absolutely right, and I hope that when the tri-caucus does come out with this information Congress takes it very seriously. So thank you very much.

Mrs. CHRISTENSEN. Thank you. And our message is to really proceed with caution. I think everyone wants to rein in costs, and I think everyone wants to make sure, obviously, that patients are taken care of safely and properly, but we want to make sure that we have all of the information that we need to make the best decision for everybody.

Mr. BECERRA. Excellent. Mr. Chairman, thank you very much. I yield back.

Chairman STARK. Ms. Tubbs Jones.

Ms. TUBBS JONES. Mr. Chairman, thank you very much. And Dr. Christensen, Congresswoman Christensen, thank you so much for coming this morning to present this testimony.

For the record, my sister died from kidney failure, my cousin is on dialysis right now, a lot of people in my family, and the issue becomes very personal for me, more than just on behalf of my constituency. Tell me, just so we have this in the record, it may be in writing, the proposed bundling puts in place—let me ask it like that. What will proposed bundling do to impact the physician's ability to prescribe or oversee his client's health?

Mrs. CHRISTENSEN. It depends on how it's done and whether there's any flexibility. And with some of the medications, you know, part of Medicare, part of ESRD payments are bundled now and part is not, and you might include some more and leave some out and may change—you may just want to change it from a 60/40 to an 80/20 with 80 percent being bundled.

But what it does is, depending on how—what the reimbursement is, if the reimbursement is too low, physicians may have to make choices that they ought not to have to make in terms of whether to prescribe Epogen or Procrit or the other ESAs as needed to have that patient achieve a better quality of life and to target their hemoglobin where we know that ought to be, and realizing that African Americans, obese patients and other patients require higher doses of Epogen. So you have to take all of that into consideration.

They may not have the ability to adjust to the different needs of different patients if the bundle is too tightly reimbursed. And that will harm patients, and it will likely harm those who are most dependent on end-stage renal disease treatment.

Ms. TUBBS JONES. And I think we've said this before, that sometimes a proposal that on its face appears neutral in its implementation it has a disparate impact.

Mrs. CHRISTENSEN. Oh yes.

Ms. TUBBS JONES. And so what you're saying to us as a Committee is that before you make your decision on this, understand the impact that could have and the disproportionate impact it could have on minority communities.

Mrs. CHRISTENSEN. And include everybody that has a stake in the decisionmaking process, whether it's the patients, the dialysis facilities, even those who provide the medication and the physicians of course, the treaters.

Ms. TUBBS JONES. And are you hearing that everybody is not having opportunity to be at the table to have that discussion?

Mrs. CHRISTENSEN. In looking through some of the reports or testimonies or white papers by patient groups, physician groups and other groups, that's the point that's most often made.

Ms. TUBBS JONES. Okay. Again, Dr. Christensen, thank you so much for coming this morning to testify. I believe your testimony has been eye-opening for us, the Committee as we make our decisions. And know that I'll call on you again sometime. Thanks.

Mrs. CHRISTENSEN. Thank you.

Chairman STARK. Thank you. Dr. Christensen, the best procedure, I believe, would be to treat each dialysis patient as a unique patient. There's no indication that anyone—that there's a certain amount for any racial group or any age group or for smokers or

non-smokers; that's up to, I presume, the physician's determination and the tests which would show the levels of their anemia or their blood count. Is that correct, so there is a unique measure for each patient as to how well they're doing?

Mrs. CHRISTENSEN. Yes, but I think studies have shown already that certain groups require more of certain medications.

Chairman STARK. But you're not proposing that we do this on a group basis, are you? You're proposing that we continue to have each individual patient measured. Wouldn't you agree that that's the best way to do it?

Mrs. CHRISTENSEN. Sure.

Chairman STARK. So that whether we are concerned with overutilization taking us above 12 if that's the agreed on upper level or below 11 if that's the agreed on lower level, we wouldn't want to create a payment system that takes us either too low or too high. Is that a fair——

Mrs. CHRISTENSEN. I think that's fair, and I think that the current EMP does that successfully now.

Chairman STARK. And we can measure that, can we not, and should measure it, I believe, as a patient goes through dialysis—and that there are other factors, I believe, such as do you do it—how often and how long? In other words, do you do it once a week for 5 hours or do you do it five times a week for 1 hour?

I don't pretend to understand but there are differences just in the dialysis protocol not to mention the—or whether you do it "subcut" or intravenous. All of these things can affect, as I understand it, the level of the person's blood level, whatever we call that.

Mrs. CHRISTENSEN. Right.

Chairman STARK. Okay. Is that a fair understanding?

Mrs. CHRISTENSEN. Yes, as well as certain disease events, if they develop infection or if they have some concurrent disease going on.

Chairman STARK. So would you agree that, as long as we can build in to the requirements for dialysis a monitoring program, a quality program that is current for each patient we would be doing the best job of ensuring that they get the proper treatment. Is that——

Mrs. CHRISTENSEN. As long as that monitoring is done over a long enough period of time to see the ups and downs that normally occur, because at any given time you may check a hemoglobin and it may be 13, but in the next few weeks it will be back down.

So there are fluctuations that occur that are totally acceptable and do not indicate that the person is being overtreated. And as long as the period of time of monitoring is long enough to encompass all of that, I would say yes.

Chairman STARK. And that should be in the judgment of the physician, should it not?

Mrs. CHRISTENSEN. Yes, the decision when to treat, how to treat and at what——

Chairman STARK. Yes. Well, I don't know as we have any disagreement, and I want to thank you for your testimony. I appreciate your concern. Thank you very much.

Mrs. CHRISTENSEN. Thank you very much.

Chairman STARK. Our next panel will consist of the acting administrator for CMS, Ms. Leslie Norwalk; Mr. Robert A. Vito, the regional inspector general for the Office of Evaluation and Inspection of the U.S. Department of Health and Human Services; Dr. John K. Jenkins, the director, the Office of New Drugs, Center for Drug Evaluation and Research, the FDA, from Rockville, Maryland.

I want to welcome the panelists and at least from the chairman's point of view if not the staff ask the panelists—in addition to Ms. Norwalk to please talk to us in layman's language and if they're Latin words say them slowly, and if they're big numbers, wait until I get my shoes and socks off.

And Ms. Norwalk, would you like to proceed to enlighten us in any way you're comfortable?

Without objection, by the way, all of your prepared testimony will appear in the record in its entirety.

STATEMENT OF LESLIE V. NORWALK, ACTING ADMINISTRATOR CENTERS FOR MEDICARE AND MEDICAID SERVICES

Ms. NORWALK. Thank you Chairman Stark, Representative Camp and the rest of the distinguished Members of the Committee. And I'd also like to thank you in particular for your kind words about my service. I appreciate it.

Medicare spends more than $8 billion annually on dialysis and dialysis-related drugs. Of this, 25 percent is spent on erythropoietin stimulating agents or ESAs. My testimony focuses on payment for the treatment of approximately 400,000 Medicare beneficiaries with end-stage renal disease.

CMS has dedicated a considerable amount of time and resources to researching the development of a prospective payment system or PPS for ESRD that bundles payment for services and dialysis as well as for drugs and lab tests, most of which are now paid separately.

Shortly we will release a report to Congress on the elements and features of such a payment system for ESRD. Today I want to highlight some of the major design issues in an ESRD bundled payment system and also talk about the use of ESAs.

In contrast to our current system, which pays separately for drugs and encourages their use, a bundled PPS would focus on appropriate delivery of the full range of ESRD services. Such a PPS would change the incentives for ESA use, potentially eliminating their overpromotion and overdosing and could obviate the need for a specific monitoring policy targeting ESA utilization, and with a collection of measures facilitate a broader focus on quality.

An ESRD bundled PPS would establish a fixed payment amount for a set of services furnished to a patient in an ESRD facility. The PPS would give facilities flexibility of managing ESRD patient care and eliminate incentives that have led to the overutilization of some medications.

As with any PPS, facilities could retain the difference if costs were less than the Medicare payment and would be liable for the difference in cost if costs were greater than Medicare payment. Our research has focused on the following, the unit of payment per

treatment or per month, case mix adjustment, a geographic adjustment, other payment adjustments such as outliers, special and technical design issues such as payment for home dialysis, setting and updating initial rates, quality, operational and administrative issues and the effective dates.

A key design issue in any payment system is a case mix adjustment that reflects the variation in resources for different kinds of patients. To date, our research indicates several case mix adjustment factors can be used in addition to the three used in the current system. Specifically, in addition to age, body surface area and low body mass index other factors could include duration of renal replacement therapy, co-morbid conditions and gender.

For example, the base payment amount could be increased for patients who have been on renal therapy for less than 4 months because treatment of patients new to renal therapy involves substantially more resources. Our regression analyses have shown that an increase in payment of about 50 percent relative to standard, ongoing treatment would be appropriate in such cases.

Similarly our research has found 12 co-morbid conditions for which payments should be increased to take into account the need for greater resources in treatment.

Prospective payment systems involve setting initial payment rates that are often based on expenditures that would be projected to occur in the absence of such a system. In this case, questions have been raised about the current use of in pricing of ESAs. For example, the Inspector General has provided data on how drug acquisition costs of ESRD facilities compare to current Medicare payment rates. Thus, payment rates based on expenditures that incorporate recent use in pricing may be too high.

Further, OIG studies on acquisition costs may guide us in this regard as we develop the payment system. In order to account for payment updates, CMS has researched an ESRD market basket for a bundled set of services. A market basket can be a starting point for determining an appropriate payment update mechanism since it is a measure of changes in input prices.

However an update mechanism can also take into account other factors such as productivity changes or changes in efficiency. With ESRD, a bundled PPS could, for example, provide incentives to achieve cost-reducing efficiencies, including movement to subcutaneous administration of ESAs.

In addition, the larger the bundle the PPS, the more opportunities there are to increase the efficiency of providing care. It is important to have a system for monitoring the quality of care so that providers furnish ESRD patients with appropriate services.

Today many argue that the reimbursement rate for ESAs lead to overutilization. The economic incentives under a PPS are opposite. Consequently the PPS should include safeguards from underutilization. These include paying for the quality of care furnished to ESRD beneficiaries.

CMS now has 18 quality measures for dialysis facilities covering several clinical areas, including hemodialysis and peritoneal adequacy, anemia management, vascular access and mineral metabolism as well as beneficiary satisfaction. The quality measures are

based on the National Kidney Foundation Kidney Disease Outcome Quality Initiative or KDOQI clinical practice guidelines.

One measure for anemia management recommends monitoring from adequate levels below 33 percent. We recognize that there is a delicate balance between low and high hematocrit levels, and monitoring for both under- and over-utilization is important.

We have submitted these and other measures to the National Quality Forum for their endorsement, and they are scheduled to consider them by the end of the year. Our proposed rule on the conditions of coverage for ESRD facilities requires reporting on quality. A final rule is targeted for publication in early 2008.

If the proposal were finalized all ESRD facilities would be required to report the NQF endorsed measures for 100 percent of their patients. In order to minimize the reporting burden we are developing a web-based reporting system to begin in February of 2009, enabling us to assess quality for each facility.

Until a bundled PPS changes incentives, effectively reducing overutilization of ESAs, we are taking action to strengthen our current ESA monitoring policy. Our current policy considers both hematocrit and dosage levels in order to promote appropriate administration.

We are examining the impact of the policy implemented last year, specifically the percent of patients for whom the reported hematocrit exceeded 39 percent both before and after the policy went into effect. Our primary concern is for the 5 percent of patients whose hematocrit levels are above 39 percent for three or more consecutive months—they're persistently at 39 or above.

Given the limited impact of our current policy, we are expanding our policy. Once implemented, CMS will reduce payment by 50 percent if a patient's hematocrit has exceeded 39 percent for three or more consecutive months. We will continue to review the impact that our monitoring policy has on ESA dosage and adjust accordingly.

Finally, I'd like to briefly comment on the use of ESAs for nonrenal care. As you know, the safety of our Medicare beneficiaries is paramount. Therefore, CMS plays close attention to FDA black boxed warnings.

Following the meeting of the FDA's Oncology Drug Advisory Panel on May 14, CMS promptly opened a national coverage decision to assess whether there is sufficient evidence to conclude that ESA treatment is not reasonable and necessary for beneficiaries under certain circumstances related to cancer. We have received input from interested public parties on all sides of this issue, including the physician community, patient groups and manufacturers.

The comment period for the national coverage decision closed on June 13. CMS and our physicians now are in the process of reviewing all of these comments. We will take them into account in developing a final national coverage decision, which is scheduled to be released in mid-August.

In conclusion, CMS has made significant progress in researching how best to develop a bundled PPS for ESRD services and we continue to improve and refine our monitoring policy to promote ap-

propriate ESA usage. We look forward to working with Congress on these critical issues. Thank you for your time this morning.

[The prepared statement of Ms. Norwalk follows:]

Statement of Leslie V. Norwalk, Acting Administrator, Centers for Medicare and Medicaid Services

Testimony of
Leslie V. Norwalk, Esq.
Acting Administrator
Centers for Medicare & Medicaid Services
Before the
U.S. House of Representatives
Ways and Means Subcommittee on Health
on
"Payment, Safety and Quality Issues in Treatment of Patients with ESRD"

June 26, 2007

Good afternoon, Chairman Stark, Congressman Camp and distinguished Members of the Subcommittee. Thank you for inviting me to discuss important developments related to payment, safety, and quality issues in the treatment of patients with End-Stage Renal Disease (ESRD), Medicare's only disease-specific program. Roughly 400,000 Americans suffer from ESRD and require either kidney dialysis or transplantation to survive. In addition, an estimated 20 million Americans have Chronic Kidney Disease (CKD) from various causes, creating the potential for substantial growth in the number of patients with ESRD unless ways are found to mitigate the progression of CKD. ESRD-diagnosed individuals of all ages are entitled to Medicare coverage, and this population has been growing steadily through the years, placing increased resource demands on the Medicare program.

As I mentioned briefly when I testified before the Committee last December, the Centers for Medicare & Medicaid Services (CMS) has spent a great deal of time and focused significant attention on the development of a prospective payment system for ESRD treatment that bundles payment for separately paid drugs and other items. I would like to discuss this work today. Additionally, I would like to provide the Committee with an update on our efforts to monitor hematocrit levels among ESRD patients, and discuss our efforts to examine the use of Erythropoietin Stimulating Agents (ESAs) in certain patient populations.

Developing a Bundled Prospective Payment System for ESRD

Medicare provides coverage to an estimated 400,000 beneficiaries with ESRD and spends about $8.1 billion annually for ESRD services. Currently, ESRD services are paid under a blended model. Approximately 60 percent of total payments to ESRD facilities are paid under a composite rate that has a basic case-mix adjustment. The remaining 40 percent of payments to ESRD facilities represent separately billed services (primarily drugs and clinical lab tests). Payments for one drug used in particular for ESRD care, erythropoietin, represents about 60 percent of these separately billable services or 25 percent of the total payment for ESRD services.

Many have urged a shift from the current model of paying independently for dialysis treatments and separately billable drugs, to a system of bundled prospective payment. CMS is generally supportive of such reform, depending of course on the specifics of the proposal.

As required by Section 623(f) of the Medicare Modernization Act (MMA), CMS will be issuing a report to Congress that covers the elements and features for the design and implementation of a bundled prospective payment system for ESRD services. Research conducted by CMS and contract researchers at the University of Michigan was complex; as a result, it took longer to complete than we anticipated. However, it has allowed us to make significant progress in assessing key design elements I would like to discuss today.

(1)—Scope of Services: A prospective payment system needs to have a scope of services that is included in the bundled rate. A potential bundle of services for an ESRD prospective payment system could include the following: composite rate services; separately billed drugs; separately billed lab tests; and other separately billed dialysis services paid under Part B, such as supplies and blood products.

(2)—Unit of Payment: A prospective payment system needs a defined unit of payment. In some prospective payment systems, such as the current ESRD composite rate, the unit is per treatment. In other prospective payment systems, such as home health, the unit is a

period of time over which services may be received. Each potential payment unit type has advantages and disadvantages that must be fully vetted. For example, payment per treatment generally encourages adequate provision of services, but could discourage innovative treatment methods that could improve quality outcomes. Monthly payments generally give providers maximum treatment flexibility and create incentives to furnish services in the most efficient manner. However, a monthly payment also can provide incentives to underserve patients.

(3)—Case-Mix Adjustment: Payment units in prospective payment systems have case-mix adjustments in order to reflect the variation of resources for different kinds of patients. There are a number of potential case-mix adjustment factors that could be used in a bundled ESRD prospective payment system. Our research will examine an analytic approach using multiple data sources including: claims data covering both billings for composite rates as well as separate billings for drugs and lab tests (for 2002 through 2004); cost report data (for 2004 supplemented with 2005 data); and enrollment and patient characteristics.

The current ESRD basic case-mix adjusted system includes adjustments to the facility's composite rate for five age groupings, body surface area, and low body mass index (an indicator of patients who are malnourished). Other prospective payment systems have different case mix adjustments based on other factors such as comorbid conditions or other clinical factors.

(4)—Geographic Adjustment: Prospective payment systems often entail some type of geographic adjustment to reflect relative differences in resource costs among geographic areas. The current ESRD payment system adjusts a portion of the composite rate for geographical differences in wages, similar to other prospective payment systems.

(5)—Other Payment Adjustments: Prospective payment systems often have special adjustments such as for outlier cases to account for very costly cases, or special characteristics of facilities, e.g., rural location.

(6)—Special Design Issues for ESRD: Prospective payment systems often have special design and implementation issues unique to the particular type of service. In the case of ESRD services, these special issues may include (a) whether there should be separate rates for hospital based and independent facilities or a consolidated single rate for all facilities; (b) treatment of oral Part D covered versions of Part B covered intravenous drugs; (c) billings for clinical laboratory tests furnished by independent laboratories; (d) payment for home dialysis including peritoneal dialysis; (e) treatment of currently-approved composite rate exceptions for pediatric facilities; (f) costs for self-dialysis patient training; and (g) application of beneficiary coinsurance under a bundled rate.

(7)—Setting and Updating Initial Rates: Prospective payment systems involve setting the initial payment rates, and a process for considering future changes and updates to these initial payment rates. Initial payment rates under prospective payment systems are often based on expenditures that would be projected to occur in the absence of the prospective system.

In the case of ESRD, questions have been raised about both the use and pricing of erythropoietin, particularly since payments for erythropoietin account for about 25 percent of total ESRD payments (this includes both payments for composite rate and separately billed items in 2005). The Department of Health and Human Services' Inspector General has found that acquisition costs for the ESRD facilities owned or managed by the largest providers is lower than the acquisition costs for other providers. Thus, questions have been raised about whether setting initial ESRD prospective payment system rates based on expenditures that incorporate recent use and pricing of erythropoietin would set such initial rates too high.

Prospective payment systems usually entail processes for consideration of updates. The current ESRD payment system does not provide automatic payment updates. Other prospective payment systems have updates based on a market basket and other factors. Since the statute requires the report to contain a methodology for appropriate updates under an ESRD prospective payment system, we will analyze the development of an ESRD

market basket for a bundled set of services. A market basket can be a useful starting point for determining an appropriate update mechanism. The market basket is a standardized assessment of the inputs involved with furnishing services. Thus, the market basket rate of increase is therefore a standardized measure of changes in input prices.

However, any update mechanism could take a number of other factors into account, such as productivity changes, changes in efficiency, changes in real and measured case mix, and any other variables that may determine appropriate changes to payment rates. For example, an ESRD prospective payment system could provide incentives to achieve efficiencies that would reduce costs, e.g., a movement to subcutaneous administration of erythropoietin. Such efficiencies could be considered in the context of an update. In addition, given that erythropoietin currently accounts for 25 percent of total spending on ESRD services, it presents an issue regarding what assumptions should be made for pricing growth. Finally, a market basket update could be considered in the context of pay-for-performance approaches, e.g., an update could be provided based on performance on quality measures.

(8)—Quality: Prospective payment systems encourage providers to efficiently furnish services. The larger the bundle the more opportunities exist for a provider to achieve efficiency. However, a bundled prospective payment also raises concerns that some providers may furnish fewer services than might be medically needed. An important feature of an ESRD prospective payment system is ensuring the quality of services furnished to beneficiaries, particularly that they receive all medically necessary services. This is especially important for this vulnerable patient population.

For the past 10 years, CMS has been working on quality measures for the quality of care furnished to ESRD beneficiaries. As required by the Balanced Budget Act of 1997, in 1998, CMS developed ESRD Clinical Performance Measures (CPMs) based on the National Kidney Foundation's Kidney Disease Quality Initiative Clinical Practice Guidelines. Sixteen CPMs were developed to measure and report the quality of dialysis services provided under Medicare in the areas of adequacy of hemodialysis and peritoneal dialysis; anemia management; and vascular access management (see

http://www.cms.hhs.gov/ESRDQualityImproveInit/03_Quality%20Measures.asp for more details).

Data on these 16 CPMs are collected on a national random sample of adult in-center hemodialysis patients, all in-center hemodialysis patients less than 18 years of age, and a national random sample of adult peritoneal dialysis patients. Thirteen of the CPMs are calculated, and released in the Department of Health and Human Services Annual Report of the ESRD Clinical Performance Measures Project.

CPM data are not currently collected in numbers sufficient for calculating dialysis facility-specific rates. Right now, they are collected on a 5 percent national sample by paper or electronic forms. However, CMS is currently implementing a system, referred to as the CROWN/Web system, that we expect will allow all ESRD facilities to report CPMs for all patients on or about February 1, 2009. Under this system, ESRD facilities would submit administrative and quality data electronically via the Internet. The CROWN/Web system will allow for the more timely, accurate, and efficient use of data to support administration of the ESRD program. This reporting requirement was included in the proposed rule updating the Conditions for Coverage for ESRD Facilities.

Currently, CMS calculates facility-specific measures using Medicare administrative data and reports these measures on the Dialysis Facility Compare location on www.medicare.gov. The three measures publicly-reported are (a) the percent of Medicare hemodialysis patients treated in the facility that received adequate dialysis treatments (e.g., treatments removing a sufficient amount of waste from the patient's system); (b) the percent of Medicare patients treated in the facility whose anemia was adequately managed; and (c) patient survival categories are reported as expected, better than expected, and worse than expected. These three measures are updated annually on Dialysis Facility Compare, using one year of data for the adequacy and anemia measure and four years of data for the patient survival measure.

Twenty-two measures are scheduled to be considered for endorsement by the National Quality Forum (NQF), a not-for profit membership organization that endorses voluntary consensus standards using agreed upon procedures. The NQF has a formal process by which it achieves consensus on standards or measures that it endorses. The endorsement process for these measures is scheduled to be completed by December 2007. Once endorsed by NQF, these measures would be required to be reported by facilities through the CROWN/Web system beginning in February 2009 if the proposal in the Conditions for Coverage for ESRD Facilities proposed rule were finalized.

(9)—Operational and Administrative Issues: A prospective payment system involves numerous operational, administrative, and systems issues. System changes generally take a minimum of five months to implement, and the considerable changes required for a new payment system could take significantly longer to complete. In addition, successful implementation of a new prospective payment system requires extensive provider education and it is likely that level of provider education would be needed for an ESRD prospective payment system. This timeframe for systems changes begins after a change request is written, which occurs only after final rulemaking, and that can happen only after the policy development needed for rulemaking is completed.

In the case of ESRD, operational and systems changes will likely be needed to expand data elements reported on the claim, and to implement consolidated billing (bundling) requirements. In addition, new payment systems often involve transitions between the old and new systems. While transitions allow facilities to adjust to new payment systems, they often involve administrative complexity.

(10)—Effective Date: The effective date for implementation of an ESRD prospective payment system involves consideration of a number of issues as indicated earlier. First, policy development and rulemaking would be involved. Second, systems changes are needed to ensure that accurate payments are made under the new payment system. All told, it is likely that 2 to 3 years from the date of enactment of authority to implement a prospective payment system would be involved in these activities.

We are also considering how potential changes to the ESRD payment system would interact with the statutorily required demonstration. The process of clearing a solicitation, obtaining and reviewing applications, selecting demonstration sites, and obtaining clearance for the demonstration award typically takes a minimum of 12 months to complete. The statute requires a 3-year demonstration. The final report for the evaluation of a demonstration is typically completed 1 year after the conclusion of the demonstration. Thus, if the demonstration is to be conducted first, before implementing an ESRD prospective payment system, about 5 years would pass before the new payment system could begin to be put into place. A demonstration could shorten somewhat the time required to implement a new payment system, but a new payment system may involve operational issues that the demonstration did not deal with. An alternative to a demonstration that could serve the same purpose would be to monitor and analyze the experience of patients and providers under the new system as it is being implemented.

Promoting Patient Safety and Appropriate Payment through Hematocrit Monitoring

As I indicated in December, nearly all ESRD patients suffer from debilitating anemia – much of which can be managed through drug therapy such as treatment with erythropoietin, an anemia-controlling compound, as an alternative to receiving blood transfusions. To promote appropriate erythropoietin usage, CMS' monitoring policy considers both hematocrit and erythropoietin dosage levels. The monitoring policy indicates that providers should adhere to the Food and Drug Administration (FDA) label instructions for erythropoietin, and not seek to achieve (or "target") a hemoglobin level in excess of 12 g/dL (a value that generally correlates with a hematocrit level of 36.0 percent). The instruction to carriers to initiate monitoring when the hematocrit exceeds 39.0 percent is not a new policy; rather, it establishes a marker at which payment must be reduced because the reported hematocrit was not maintained at levels consistent with FDA labeling.

While patients' therapeutic hematocrit targets are appropriately left to the clinical judgment of their physicians, the monitoring policy recognizes the difficulty of maintaining the hematocrit in the narrow clinical range of 33.0 to 36.0 percent, which is the target range set

forth in current kidney disease clinical guidelines. Because factors such as nutritional status, infection, and bleeding may cause the hematocrit to fluctuate, it is not easy to manage patients to this narrow target range. Some patients might be above (or below) the target in one month, for example, but below (or above) it in others. If frequent and significant changes in doses of anemia management drugs occur on top of these existing hematocrit fluctuations, such hematocrit fluctuations can become even more variable and difficult to interpret and manage, particularly within the narrow target range of 33.0 to 36.0 percent.

Accordingly, the monitoring policy does not immediately cut-off payment for a single reading that fluctuates above or below the 'guideline' value. However, the monitoring policy sets in motion a payment reduction when the hematocrit level exceeds 39.0 percent, and if the provider has not responded by reducing the ESA dosage as FDA labeling and national clinical guidelines indicate.

A provider submitting a claim for ESAs furnished to an ESRD patient with a hematocrit above 39.0 percent may indicate that a dose reduction has occurred, despite the continued high hematocrit, using a modifier on the claim form. If the provider fails to include the modifier, then Medicare will apply an automatic 25 percent reduction in amount of payment for ESAs.

We are in the process of analyzing the impact of this monitoring policy, looking specifically at the percent of ESRD patients for whom the reported hematocrit was above 39.0 percent since the monitoring policy went into effect. We are comparing these data to data for the same measure for periods before the new monitoring policy was in effect. This analysis will reveal whether the monitoring policy has resulted in a reduction in the percent of patients with hematocrits above 39.0 percent. Based on what these data show, we are prepared to consider potential revisions to the monitoring policy.

As mentioned above, the monitoring policy is based on data submitted on the claim form. A key limitation of this approach is that the base period is one during which a prior

monitoring policy was in effect. While this aggregate assessment of the monitoring policy can be done with existing data, it may not be possible to attribute changes to the monitoring policy. We are also assessing the aggregate number of units of erythropoietin that Medicare pays for per beneficiary each month. Here too while this is a macro assessment of erythropoietin use, from a research methodological perspective, it may not be possible to attribute changes to the monitoring policy.

For the longer term, a more detailed study would examine the hematocrits and erythropoietin use for specific beneficiaries; such approach has more potential to hold constant other intervening variables. We are currently developing the methodology for such a study. However, since the human physiologic response to erythropoietin is not immediate, and the effect of a given dosage on the hematocrit of a given individual can vary widely, even analysis of data for the same patient over time may make it difficult to attribute changes in the hematocrit to erythropoietin use.

As I mentioned in December, one possible approach is to collect data, such as the dosage of erythropoietin actually administered or additional hematocrit measurements, through clinical trials. Another approach might be to create registries of data submitted by hospitals and other facilities. Such registries could be a robust data collection mechanism, pursuing elements beyond what can be collected on the claim form. Before such an approach could be adopted, however, CMS must assess potential restrictions to requiring hospitals and facilities to report information to a registry. Provider burden also would be an important consideration.

It should also be noted that an ESRD bundled prospective payment system would focus on appropriate delivery of the full range of ESRD services included in the bundle for a beneficiary. In contrast, the current system, which separately pays for ESAs, encourages their use. An ESRD bundled prospective payment system would change incentives for use of ESAs.

Examining the Use of Erythropoietin Stimulating Agents (ESAs) in Certain Patient Populations

CMS pays close attention to FDA Black Box warnings because the safety of Medicare beneficiaries is paramount. Upon being advised of the March 9, 2007 Black Box warning for use of erythropoiesis stimulating agents (ESAs) in multiple clinical settings, CMS immediately began a dialogue with FDA. FDA conveyed serious concerns about potential dangers with the use of ESAs in some types of cancer/oncology management.

In wanting to protect Medicare beneficiaries from potential avoidable risks, CMS promptly opened a national coverage decision to assess whether there is sufficient evidence to conclude that ESA treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects related to ESA use.

Following the opening of this national coverage decision on March 14, 2007, CMS staff reviewed over 500 peer-reviewed articles (which are cited in the proposed national coverage decision) and consulted with FDA staff and other healthcare subject experts in this topic. The FDA held an Oncology Drug Advisory Panel (ODAC) meeting on May 10, 2007 to discuss the safety of recombinant ESAs and to inform possible further revisions to the labeling of these drugs. In addition, representatives of various cancer patient groups provided testimony expressing their concern about safe use of ESAs for treatment of anemia related to cancer. On May 14, 2007, CMS posted a "proposed" or "draft" coverage decision.

The national coverage decision process specifically involves the solicitation of public comment. Like all proposed national coverage decisions, public comment is solicited over a 30-day period following its publication. Ultimately, CMS uses the public comments received to inform its final decision, responding in detail to the public comments when issuing the final decision memorandum. The comment period for this national coverage decision closed on June 13.

We have received input from interested public parties on all sides of this issue, including the physician community, patient groups, and manufacturers. CMS is now in the process of reviewing all of these comments. Some of the comments suggested that ESA use not be restricted for specific conditions or situations as proposed. Many of the critical comments focused on a few specific conditions, e.g., our proposal that ESAs are not reasonable and necessary when used in conjunction with treating anemia of myelodysplasia (MDS) (which is an off-label indication of ESA usage). CMS also received many favorable comments that supported the approach in the proposed national coverage decision. Our physicians are carefully reviewing all of these comments and we will take them into account in developing a final national coverage decision.

At the same time, we are continuing to examine whether similar action is warranted with regard to the use of ESAs to treat patients with non-cancer conditions, namely ESRD patients. We have begun preliminary discussions with the National Institutes of Health about the possibility of collaborating on a large clinical trial to examine the effect of ESA treatment in ESRD patients. Further, we are awaiting the findings of the FDA's Cardiac and Renal Drug Advisory Committee, which will be meeting later this year to specifically examine the use of ESAs in treating the renal patient population.

Conclusion

CMS is committed to establishing and maintaining policies in all areas of the Medicare program that promote efficient and appropriate use of medical interventions, protect beneficiaries, and enable providers to furnish high quality care. As highlighted today, we have made significant progress in the research to develop a bundled prospective payment system for ESRD services, we continue to improve and refine our monitoring policy to promote appropriate erythropoietin usage, and we took prompt action with respect to Medicare coverage of ESAs following the FDA's issuance of a Black Box warning. As Congress considers ESRD payment reform and examines patient safety concerns, we look forward to continuing to work with this Committee on these important issues. At this stage we are continuing to devote significant resources to the substantial analytical and actuarial

development necessary to design a robust and accurate payment system. The development of a new payment system is a significant endeavor that merits careful consideration and analysis.

Chairman STARK. Thank you.
Mr. Vito.

STATEMENT OF ROBERT A. VITO, REGIONAL INSPECTOR GENERAL OFFICE OF EVALUATION AND INSPECTIONS, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. VITO. Good morning, Mr. Chairman and Members of the Subcommittee. I am Robert Vito, regional inspector general for the Office of Evaluation and Inspection at the U.S. Department of Health and Human Services Office of Inspector General.

For nearly 20 years, the OIG has devoted considerable resources, attention to end-stage renal disease-related services. I appreciate the opportunity to appear before you today to discuss our most recent report released to you today on the pricing of separately billable end-stage renal disease drugs.

The OIG work has involved ensuring the quality care of dialysis patients, conducting criminal and civil investigation of dialysis providers and examining pricing and utilization of dialysis-related drugs and services.

For example, since June of 2000, OIG has issued six reports examining ways CMS can better monitor the quality of care in dialysis facilities. We have also assisted in settlement agreements with national dialysis providers regarding violations of the False Claim Act and other statutes.

In addition, the OIG has been involved in pricing and utilization issues, including reviews in the early nineties of the end-stage renal disease composite rate and reimbursement for Epogen. In fact, in an October 1992 report we recommended that CMS consider including the cost of separately billable drugs into the composite rate to save on the administrative costs and to reduce payment errors.

We also audited Epogen claims at dialysis facilities where we identified inconsistencies between the number of units of Epogen prescribed in the written order, administered by the facility and built to the Medicare Program.

During this time period, the OIG issued a pricing report that found that the Department of Veterans' Affairs paid substantially less than Medicare for five high expenditure end-stage renal disease drugs. Most recently, in response to mandates contained in the Medicare Prescription Drug Improvement and Modernization Act of 2003, the OIG conducted two studies on Medicare reimbursement for end-stage renal disease drugs.

As required by the MMA, CMS used the data presented in the first report to set the 2005 reimbursement rate at freestanding facilities for ten high expenditure end-stage renal disease drugs. Reimbursement for drugs not included in our report was set at 106 percent of the ASP, the same method as the Part B drugs. At that time, hospital-based facilities were reimbursed at cost for most end-stage renal disease drugs.

As of January 1, 2006, CMS set the reimbursement for all end-stage renal disease drugs with a few exceptions at 106 percent of ASP. This change produced a consistent drug payment methodology among free-standing dialysis facilities and hospital-based dialysis facilities.

These changes prompted the OIG to conduct an additional review of Medicare reimbursement for end-stage renal disease drugs. For this review, we obtained third quarter 2006 average acquisition costs for 11 high expenditure end-stage renal disease drugs from a sample of freestanding and hospital-based facilities and compared these costs to the Medicare reimbursement.

Among the responding freestanding facilities, we found that the average acquisition cost for nine of the eleven drugs under review were below the Medicare reimbursement amount. The average acquisition costs for Epogen, a drug that accounts for three-quarters of the Medicare expenditures in freestanding facilities was 10 percent less than the Medicare reimbursement.

Our analysis also showed that chain freestanding facilities paid less for drugs than non-chain facilities. On average, drug acquisition costs at the chain facilities were 12 percent below the Medicare reimbursement amount for the entire basket of end-stage renal disease drugs compared to 7 percent below at the non-chain facilities. This difference can be attributed in large part to the pricing of Epogen as chain facilities receive larger discount rebates for the drug than non-chains.

For hospital-based facilities we found the average acquisition cost for six of the eleven drugs under review were less than the Medicare reimbursement amount. For the remaining five drugs, acquisition costs were slightly above Medicare reimbursement. However, on the whole, the hospital-based facilities were not being under-reimbursed as the average acquisition cost for the entire basket of drugs were 7 percent below the Medicare reimbursement amount.

In the hospital-based facilities, average acquisition costs for Aranesp and Epogen, the two drugs that account for the majority of Medicare spending in the hospital-based facilities were ten and 9 percent below the Medicare reimbursement amount respectively.

In conclusion, as our body of work in this area shows, the OIG has been involved in end-stage renal disease-related topics for many years, helping to ensure that Medicare beneficiaries receive quality care and that the care is reimbursed at appropriate levels.

CMS was able to use the results of our first mandated review to help set Medicare reimbursement amounts for separately billable drugs. We believe that our most recent study, a study not mandated by Congress, illustrates our commitment to continue providing current information on end-stage renal disease issues to policymakers.

This concludes my testimony, and I welcome your questions.

[The prepared statement of Mr. Vito follows:]

Statement of Robert A. Vito, Regional Inspector General for the Office of Evaluation and Inspections, U.S. Department of Health and Human Services, Philadelphia, Pennsylvania

Testimony of:
Robert A. Vito
Regional Inspector General for Evaluation and Inspections
Office of Inspector General, U.S. Department of Health and Human Services

Good morning, Mr. Chairman and Members of the Subcommittee. I am Robert Vito, Regional Inspector General for Evaluation and Inspections in Philadelphia at the U.S. Department of Health and Human Services' Office of Inspector General (OIG). For nearly 20 years, OIG has devoted considerable attention to end stage renal disease (ESRD)-related services. Our work has involved monitoring the oversight of the quality of care for dialysis patients enrolled in Medicare, conducting criminal and civil investigations of dialysis providers, and examining the pricing and utilization of dialysis-related drugs and services. I appreciate the opportunity to appear before you today to discuss OIG's work in this area and, in particular, summarize the findings of our recent review related to the pricing of separately billable ESRD drugs.

In short, our most recent report, released to you today, which is available on our Web site at http://oig.hhs.gov/, found that, on average, dialysis facilities could acquire the majority of ESRD drugs at prices 4 to 32 percent less than the Medicare reimbursement amount during the third quarter of 2006.[1] Acquisition costs for some ESRD drugs ranged from 1 to 9 percent above Medicare reimbursement amounts; however, on average, aggregate drug acquisition costs ranged from 7 to 12 percent below aggregate Medicare reimbursement amounts. This can be attributed, in part, to the average acquisition costs for the two most widely used ESRD drugs, epoetin alfa (Epogen) and darbepoetin alfa (Aranesp), for which acquisition costs were as much as 10 percent below Medicare reimbursement levels. Finally, acquisition costs varied substantially, with chain-owned freestanding facilities often paying less for ESRD drugs than nonchain freestanding and hospital-based facilities.

BACKGROUND

The Medicare program currently covers dialysis services for close to 400,000 patients under its ESRD benefit. Medicare covers all treatment methods for patients, including various methods of maintenance dialysis as well as renal transplants. ESRD facilities are paid based on a prospective payment system known as the composite rate, which covers most items related to dialysis services, such as labor costs, related supplies, routine tests, and certain drugs. Facilities receive a fixed composite rate payment for each dialysis treatment they provide to Medicare beneficiaries. However, the composite rate does not include many drugs that may be part of dialysis treatment and certain laboratory tests. These items are referred to as "separately billable." For example, the drugs Epogen and Aranesep, which stimulate the production of red blood cells in patients with anemia, are billed separately from the composite rate.

[1] "Medicare Reimbursement for End Stage Renal Disease Drugs: Third Quarter 2006." (OEI-03-06-00590). June 2007.

In 2005, Medicare spent close to $8 billion for the care of ESRD beneficiaries—approximately 60 percent of that amount was associated with dialysis services covered under the composite rate, with the remaining 40 percent attributable to separately billable items. Beneficiaries are responsible for 20-percent copayments for both composite rate services and separately billable items.

OIG work on ESRD services has identified vulnerabilities and inefficiencies related to quality of care and to the utilization, payment, and pricing of drugs and services.

MEDICARE REIMBURSEMENT FOR ESRD DRUGS: THIRD QUARTER 2006

Beginning January 1, 2006, the Centers for Medicare & Medicaid Services (CMS) instituted a new reimbursement methodology for both freestanding and hospital-based facilities. As of that date, all ESRD drugs—with the exception of certain vaccines, blood, and blood products—were reimbursed at 106 percent of the manufacturer-reported average sales price (ASP). CMS implemented this change because in 2005, as mandated by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), the agency had based reimbursement to freestanding facilities for 10 separately billable ESRD drugs on OIG's estimates of acquisition costs for those drugs. However, the agency believed it was inappropriate to continue to use older acquisition cost data provided by OIG (updated for inflation) as a basis for reimbursement and questioned the feasibility of continually obtaining acquisition cost data over the long term. This change also produced a consistent drug payment methodology among freestanding dialysis facilities and hospital-based dialysis facilities.

In our most recent review, OIG compared the Medicare reimbursement amounts for selected separately billable ESRD drugs to average acquisition costs of these drugs in freestanding and hospital-based dialysis facilities. We obtained third-quarter 2006 average acquisition costs for 11 high-expenditure ESRD drugs from a sample of dialysis facilities and calculated the percentage of facilities that had average acquisition costs below the ASP-based reimbursement amounts. We sent surveys to a random sample of freestanding and hospital-based dialysis facilities to collect data on the total amounts paid, discounts and rebates received, and total units purchased for these 11 drugs. We did not verify or validate the information provided by the responding facilities.

The 11 high-expenditure drugs accounted for nearly all of the $2 billion in Medicare reimbursement for ESRD drugs furnished by freestanding facilities and the $200 million for ESRD drugs furnished by hospital-based facilities in 2005. At the time of our review, 4,050 freestanding dialysis facilities and 310 hospital-based dialysis facilities were listed on Medicare's database of dialysis facilities. Approximately 71 percent of freestanding facilities are part of two large chain corporations, and another 11 percent are owned by smaller national or regional chains.

Acquisition Costs for Freestanding Facilities

We found that among responding freestanding facilities, third-quarter 2006 average acquisition costs for 9 of the 11 drugs under review were between 7 and 32 percent below the Medicare reimbursement amounts. For the remaining two drugs, acquisition costs ranged from 3 to 9 percent above the Medicare reimbursement amounts. However, reimbursement for these two drugs combined accounted for less than 1 percent of total Medicare expenditures for ESRD drugs in freestanding dialysis facilities in 2005. The average acquisition cost for Epogen, a drug that accounts for three-quarters of Medicare expenditures in freestanding facilities, was 10 percent less than the Medicare reimbursement amount ($8.56 per 1,000 units compared to $9.48). In total, 99 percent of freestanding dialysis facilities could purchase Epogen for less than the Medicare reimbursement amount.

Our analysis also showed that chain freestanding facilities paid less for the drugs under review than did nonchain freestanding facilities. On average, drug acquisition costs for chain facilities were 12 percent below the Medicare reimbursement amounts, compared to 7 percent below for nonchain facilities. This difference can be attributed, in large part, to the pricing of Epogen. Although chain facilities initially paid more than nonchain facilities for Epogen, the chain facilities received a much larger discount/rebate (27 percent, on average) than the nonchain facilities (5 percent, on average). As a result, the final price for Epogen among chain facilities was 5 percent less than the final price of the drug among nonchain facilities ($8.55 per 1,000 units compared to $8.99).

Acquisition Costs for Hospital-Based Facilities

Among responding hospital-based dialysis facilities, average acquisition costs for 6 of the 11 ESRD drugs under review were between 4 and 29 percent below the Medicare reimbursement amounts. For the remaining five drugs, acquisition costs ranged from 1 to 8 percent above the Medicare reimbursement amounts. These five drugs accounted for 29 percent of reimbursement to hospital-based dialysis facilities for ESRD drugs in 2005. This indicates that when compared to freestanding facilities, hospital-based dialysis facilities could potentially face larger gaps between acquisition costs and Medicare reimbursement when purchasing a number of highly utilized drugs. Average acquisition costs for Aranesp and Epogen (the two drugs that account for the majority of Medicare spending in hospital-based facilities) were 10 and 9 percent below the Medicare reimbursement amounts, respectively ($2.71 compared to $3.03 for Aranesp, and $8.66 compared to $9.48 for Epogen). On average, overall drug acquisition costs for responding hospital-based dialysis facilities were 7 percent below the Medicare reimbursement amounts—amounts identical to those of nonchain freestanding facilities.

Summary

We concluded that responding facilities, on average, could acquire the majority of ESRD drugs at prices below Medicare reimbursement amounts and that aggregate acquisition costs were below aggregate Medicare reimbursement amounts. However, acquisition costs for the same drug may vary based on the type and chain affiliation of the facility,

causing some dialysis facilities to potentially experience greater gaps in reimbursement than others. Therefore, we concluded that CMS should continue to monitor the situation closely to ensure that all facilities are reimbursed appropriately.

PREVIOUS OIG WORK RELATED TO ESRD SERVICES AND PAYMENTS

Prior Reviews of Medicare Reimbursement of ESRD Drugs

OIG's most recent report on ESRD reimbursement builds upon a body of work regarding the appropriateness of payments for ESRD drugs. Based on a 1990 audit in which we found that Medicare overpaid for ESRD services for nonroutine drugs, we recommended that the Medicare reimbursement rates reflect the cost of dialysis treatment in efficiently operated facilities.[2] In a 1992 audit, we further suggested that CMS consider folding all separately billable drugs into the composite rate to achieve savings on administrative costs and reduce payment errors.[3] A 1993 audit indicated that dialysis providers were being overpaid for Epogen and we suggested a reduction in the reimbursement rate.[4] In 1997, OIG conducted a follow-up review of Medicare reimbursement for Epogen and found that the reimbursement rate, which at that time was $10 per 1,000 units administered, exceeded the cost of purchasing Epogen by approximately $1 per 1,000 units.[5] In June of 2000, OIG issued another report specifically focusing on ESRD drugs.[6] This report found that the Department of Veterans Affairs paid between 37 percent and 56 percent less than Medicare for five high-expenditure ESRD drugs.

Based in part on OIG work, Congress included provisions to reform drug reimbursement in the MMA. These provisions created a new methodology for Part B drug reimbursement that is based on manufacturer-reported ASPs rather than problematic average wholesale prices (AWP). In addition, the MMA required that Medicare base payments for certain ESRD drugs on their acquisition costs as determined by OIG.[7] The MMA also mandated that OIG conduct two studies related to Medicare reimbursement for ESRD drugs.[8]

In the first MMA-mandated OIG report, which was issued in May 2004, "Medicare Reimbursement for Existing End Stage Renal Disease Drugs" (OEI-03-04-00120), OIG found that the four largest freestanding corporate dialysis providers and a random sample of freestanding nonchain dialysis facilities were able to acquire 10 high-expenditure drugs at costs averaging 14 to 22 percent below the Medicare reimbursement amounts.

---

[2] "Management Advisory Report - Reductions Continue To Be Needed in Medicare's End Stage Renal Dialysis Rates," (A-14-90-00215). July 1990.

[3] "Cost of Dialysis-Related Drugs," (A-01-91-00526). October 1992.

[4] "Review of Epogen Reimbursement," (A-01-92-00506). February 1993.

[5] "Review of Epogen Reimbursement," (A-01-97-00509). November 1997.

[6] "Medicare Reimbursement of End Stage Renal Disease Drugs," (OEI-03-00-00020). June 2000.

[7] Prior to 2005, the Medicare reimbursement amount for Epogen in both freestanding and hospital-based facilities was set by statute at $10 per 1,000 units.

[8] "Medicare Prescription Drug, Improvement, and Modernization Act of 2003." Public Law 108-173. § 623(c)(2)(A)-(B).

As required by the MMA, CMS used the data presented in this report to set calendar year 2005 reimbursement rates for the 10 drugs at the average acquisition costs as calculated by OIG. For all other drugs billed by freestanding dialysis facilities—with the exception of certain vaccines, blood, and blood products—CMS reimbursed freestanding dialysis facilities at 106 percent of the drugs' ASPs. During this same time period, hospital-based facilities were reimbursed at cost for most ESRD drugs.

For the second report, issued in March 2006, "Medicare Reimbursement for New End Stage Renal Disease Drugs" (OEI-03-06-00200), Aranesp was selected as the only drug for review because it accounted for 99.9 percent of Medicare reimbursement for new ESRD drugs. We found that, on average, responding freestanding dialysis facilities were able to acquire Aranesp for between 14 and 27 percent below the Medicare reimbursement amounts in 2005.

Improper Billing and Utilization

Through audits and investigations, OIG has also identified instances of improper billing and utilization of services in ESRD facilities, including inappropriate billing for services outside the composite rate and the provision of medically unnecessary services.

For example, in a 2004 audit of Medicare payments to DaVita, Incorporated, for Epogen services provided at one of its Philadelphia dialysis centers, we found that 44 of the 143 claims reviewed did not meet Medicare payment requirements for Epogen.[9] In some cases, we identified inconsistencies between the number of units of Epogen prescribed in the written physician order and the number administered by the facility and billed to Medicare. We also identified instances in which Epogen was still administered to the patient after the physician had ordered its discontinuation.

In another example, in 2005, as part of a global settlement with the Government, Gambro Healthcare, Inc. (GHI), owner and operator of over 500 renal dialysis centers, agreed to pay over $350 million to resolve civil and criminal fraud allegations in the Medicare, Medicaid, and TRICARE programs. To resolve its civil liability, GHI paid $310.5 million for allegedly submitting false Medicare claims and paying physicians improper remuneration related to their medical director services. In addition, Gambro Supply Corporation (GSC), a wholly owned subsidiary of GHI, agreed to plead guilty to health care fraud, pay a $25 million criminal fine, and be permanently excluded from Medicare and other Federal health care programs. To circumvent prohibitions applicable to durable medical supply companies, GSC made false statements to Medicare, allegedly enabling GHI to bill for ESRD-related services and equipment at a higher amount. GHI also agreed to pay the Government $328,286 to resolve its liability under the False Claims Act (FCA) for allegedly causing local laboratories to improperly bill separately for laboratory services that should have been covered under the facilities' composite rate. GHI also agreed to enter into a 5-year corporate integrity agreement with OIG.

[9] "Review of Medicare Payments to DaVita, Incorporated for Epogen Services Provided at Franklin Dialysis Center, Philadelphia, Pennsylvania," (A-03-03-00003). April 2004.

More recently, in 2007, Dialysis Clinic, Inc. (DCI), which provides health care services to Medicare beneficiaries with ESRD at its clinics located in more than 30 States, agreed to pay $1.8 million to resolve its liability under the FCA. The majority of the settlement was associated with DCI's administration and billing of Epogen when it was medically unnecessary. CMS authorizes the administration of Epogen to keep a patient's hematocrit blood level in the 33- to 36-percent range. The investigation revealed that DCI allegedly administered Epogen to patients whose hematocrit levels were in excess of 40 percent. Furthermore, DCI allegedly allowed hospital laboratories to bill Medicare separately for tests for DCI patients even though DCI was paid for the lab services as part of Medicare's composite rate payment. As part of the settlement agreement, DCI entered into a 3-year corporate integrity agreement with OIG.

Quality of Care Oversight

In addition to performing work on appropriate payment rates and billing, OIG has also identified concerns regarding CMS's oversight of the quality of care provided by ESRD facilities. In June 2000, OIG issued a report documenting problems with the oversight of these facilities.[10] OIG found that although CMS oversight using standardized performance measures encouraged improvements in quality of care, CMS did not use these measures to hold individual facilities accountable. OIG also found that Medicare certification surveys played a limited role in ensuring that ESRD facilities met minimum standards.

In January 2002, OIG issued a series of reports concerning the lessons learned by the five largest dialysis corporations in using clinical performance measures.[11] In those reports, we identified a number of methods the Medicare program could use to improve the quality of care in dialysis facilities. These included examining ways to foster a commitment to performance measures among attending physicians and developing more effective intervention strategies for facilities.

In 2003, GAO reported that problems with quality of care were prevalent at dialysis facilities, putting patients' health at risk and that limitations in the ESRD survey process inadequately addressed or failed to detect quality problems.[12] More recently, in a November 2006 report, OIG found that current sources of data have limitations in assisting CMS and its contactors in identifying quality improvement needs at ESRD facilities.[13] These limitations include lack of current, comprehensive, and facility-

---

[10] "External Quality Review of Dialysis Facilities: A Call for Greater Accountability," (OEI-01-99-00050). June 2000; and "Oversight of Kidney Dialysis Facilities Needs Improvement," (GAO/HEHS-00-114). June 2000.

[11] "Clinical Performance Measures for Dialysis Facilities: Building on the Experience of the Dialysis Corporations," (OEI-01-99-00052). January 2002; "Clinical Performance Measures for Dialysis Facilities: Practices of the Major Dialysis Corporations *Supplemental Report # 1*," (OEI-01-99-00053). January 2002; and "Clinical Performance Measures for Dialysis Facilities: Lessons Learned by the Major Dialysis Corporations and Implications for Medicare, *Supplemental Report # 2*," (OEI-01-99-00054). January 2002.

[12] "Dialysis Facilities: Problems Remain in Ensuring Compliance With Medicare Quality Standards," (GAO-04-63). October 2003.

[13] "Availability of Quality of Care Data in the Medicare End Stage Renal Disease Program," (OEI-05-05-00300). November 2006.

specific performance data. We recommended that CMS increase its efforts towards regularly collecting clinical performance data from patients and facilities. CMS has begun to develop a streamlined source of data that could assist contractors in identifying facilities with improvement needs, but this database has yet to be implemented.

CONCLUSION

Through a substantial body of work, OIG has examined the oversight of quality of care at ESRD facilities, appropriateness of payment systems, and improper billing and utilization of ESRD drugs. Our most recent work compared Medicare reimbursement amounts for ESRD drugs in third quarter 2006 to dialysis facilities' acquisition costs. We found that responding freestanding dialysis facilities could typically acquire the majority of the selected separately billable ESRD drugs for less than the Medicare reimbursement amounts. Drug acquisition costs varied among different types of freestanding dialysis facilities, with overall drug costs among chain facilities being somewhat less than those among nonchain facilities. In contrast, average acquisition costs among hospital-based dialysis facilities for almost half of the drugs under review exceeded the Medicare reimbursement amounts. We concluded that CMS should continue to monitor the situation closely to ensure that all facilities are reimbursed appropriately.

OIG remains committed to ensuring that Medicare ESRD beneficiaries receive quality services and that this care is being reimbursed at appropriate levels. Therefore, we will continue to conduct audits, evaluations, and investigations, as warranted, to oversee payment and quality of care at ESRD facilities. Currently, we are conducting audit work at individual dialysis facilities to review the appropriateness of Medicare claims submitted by dialysis facilities for Epogen administration, as well as identifying instances in which laboratory tests that should be included in the composite rate are being billed separately.

This concludes my testimony, and I welcome your questions.

Chairman STARK. Thank you.
Dr. Jenkins.

STATEMENT OF JOHN K. JENKINS, DIRECTOR, OFFICE OF NEW DRUGS, CENTER FOR DRUG EVALUATION AND RESEARCH

Mr. JENKINS. Good morning, Mr. Chairman and Members of the Committee. I am Dr. John Jenkins. I am the director of the Office of New Drugs at the Food and Drug Administration. Thank you for the opportunity to testify before you today about erythropoiesis-stimulating agents, which I will refer to as ESAs.

ESAs are manmade versions of a natural human protein known as erythropoietin. Erythropoietin is made by the kidney and stimulates the bone marrow to produce red blood cells. The main goal of treatment with ESAs is to increase the number of red blood cells in patients with types of anemia that are responsive to ESAs in order to decrease the need for blood transfusions.

The first ESA, Epoetin alfa was approved by FDA in 1989 for the treatment of anemia associated with chronic renal failure. Epoetin alfa is marketed under two trademarks, Epogen and Procrit.

Since their initial approval, Epogen and Procrit have also been approved for use in patients with certain cancers, with anemia due to chemotherapy and patients with HIV infection with anemia due to certain anti-viral drugs and in patients scheduled for certain types of surgery to decrease a need for blood transfusions.

The second ESA, Darbepoetin alfa, was approved by FDA in 2001 for the treatment of anemia associated with chronic renal failure. Darbepoetin alfa is marketed under the trademark Aranesp. Aranesp was also approved by FDA in 2002 for the treatment of anemia caused by chemotherapy in patients with some types of cancer.

Since the initial approval in 1989, the produce labeling for all marketed ESAs has been updated on several occasions to incorporate new safety information derived from clinical trials and from spontaneous reports of adverse reactions.

The details of the major safety-related labeling changes for ESAs are in my written testimony and I will focus for now on briefly describing the most recent safety-related labeling change.

The availability of extensive new safety information from clinical trials late in 2006 and early in 2007 prompted FDA to undertake a major revision of ESA labeling to include a boxed warning in March of 2007. As FDA became aware of the emerging safety information, we issued a series of public health advisories to alert healthcare providers and patients and to provide guidance on the use of ESAs.

The first advisory, which was issued in November 2006, alerted healthcare professionals that a newly published clinical study, referred to as the CHOIR study, showed that patients with chronic renal failure not on dialysis who are treated with ESAs to achieve a higher target hemoglobin level had a significantly increased risk of serious and life-threatening cardiovascular complications.

The second advisory issued in February 2007 notified healthcare professionals of the results of a large clinical trial evaluating the use of ESAs to treat anemia in patients with cancer who were not receiving chemotherapy. In that study, patients treated with

Aranesp had a higher death rate and no reduction in the need for transfusions compared to those treated with placebo.

The most recent public health advisory, which was issued in March 2007, outlined new safety information from several newly reported trials. As I said earlier, in March 2007, FDA also approved revised labeling for all ESAs that included updated warnings and new boxed warning and modifications to the dosing instructions.

The boxed warning advises physicians to use the lowest ESA dose that will gradually increase the hemoglobin level to a concentration sufficient to avoid the need for blood transfusions. The boxed warnings also highlight the major safety risks of ESAs in patients with renal failure and cancer.

To further evaluate the newly available data in patients with cancer treated with ESAs, FDA convened its Oncologic Drugs Advisory Committee on May 10 of this year. The advisory Committee recommended that the results of all ongoing trials of ESAs in patients with cancer be submitted for FDA review as soon as the data were available, that additional trials be conducted by the sponsors to further evaluate the safety of the doses of FDA's recommended in the approved labeling and that FDA consider additional changes in product labeling to ensure the safe use of ESAs in patients with cancer.

FDA is currently working with the sponsors of ESAs to address the advisory committee's recommendations. FDA is also planning discussion of ESA safety issues associated with the use in patients with chronic renal failure at a meeting of the Cardio-Renal Drugs Advisory Committee later this summer.

In closing, let me state that FDA's mission is to promote and protect the public health. The major component of that mission is to ensure that the American public has access to safe and effective medical products and that healthcare providers and patients have updated information about the benefits and potential risk of approved drugs on which to base individual treatment decisions.

FDA is continuing to carefully and thoroughly evaluate all available data for ESAs and will take additional regulatory actions in the future as warranted to ensure that the benefits of ESAs outweigh their risks when they are used according to the FDA-approved labeling.

Thank you, and I'll be happy to respond to questions.

[The prepared statement of Dr. Jenkins follows:]

Statement of John K. Jenkins, M.D., Director, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, Maryland

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT OF

JOHN K. JENKINS, M.D.
DIRECTOR, OFFICE OF NEW DRUGS
CENTER FOR DRUG EVALUATION AND RESEARCH

FOOD AND DRUG ADMINISTRATION

BEFORE THE

COMMITTEE ON WAYS AND MEANS

SUBCOMMITTEE ON HEALTH

UNITED STATES HOUSE OF REPRESENTATIVES

June 26, 2007

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Committee, I am John K. Jenkins, M.D., Director of the Office of New Drugs within the Center for Drug Evaluation and Research at the Food and Drug Administration (FDA or the Agency). Thank you for the opportunity to participate in this hearing regarding erythropoiesis-stimulating agents (ESA).

In my testimony, I will provide background information on the drug approval process in general, and will discuss FDA's regulatory history related to ESA products.

DRUG APPROVAL PROCESS

Before any new drug is approved for marketing in the United States, FDA determines whether the data submitted by the product's sponsor (usually the manufacturer) in the new drug application (NDA) or biologics license application (BLA) show the product to be safe and effective for its intended use. Prior to the submission of an NDA or BLA, a sponsor generally conducts a series of clinical trials to assess the effects of the experimental new product in humans. To conduct these clinical trials in the U.S., the sponsor submits an investigational new drug (IND) application to FDA. If FDA finds the manufacturing and supportive laboratory and animal data sufficient to support use of the experimental product in humans, clinical trials in humans can begin.

Generally, there are three phases of studies in the investigation of a new drug or biologic product. Phase I trials are conducted in a small number of people to gather early safety information that will support conducting studies in larger numbers of people and to determine how the drug works in humans (e.g. metabolism, absorption, and excretion). If those trials are successful, Phase II trials are designed to study the effects for a particular use of the new drug, including how people respond to various dosages or dose regimens. In Phase II trials, patients are monitored closely for any side effects or particular risks that might be associated with the product under study. If Phase II trials are successful, Phase III trials are designed to build on the information learned in the earlier trials in order to establish the safety and effectiveness of the new drug. If the new drug successfully completes all phases of the investigation, the sponsor assesses the data and decides whether to submit a marketing application (NDA or BLA) for the Agency's review. Following submission of an NDA or BLA, FDA must decide whether all of the information (clinical trial results and animal and laboratory data, and information on the manufacture of the product) submitted by the new drug's sponsor adequately demonstrates that the product is safe and effective under the conditions of use in the drug's proposed labeling.

It is important to realize, however, that no drug is absolutely safe. There is always some risk of adverse reactions with drugs. FDA's approval decisions, therefore, always involve an assessment of the benefits and the risks for a new drug. These approval decisions also apply when a previously approved drug is under consideration for a new use (i.e. a new indication). When the benefits of a new drug are thought to outweigh the risks, and if the labeling instructions allow for safe and effective use, FDA considers the new drug safe for approval and marketing.

DRUG SAFETY: A RISK-TO-BENEFIT BALANCE

FDA has a strong record on issues of safety and remains the world's gold standard for drug regulation. In reflecting on the concept of drug safety, it is important to remember not only that no drug is absolutely safe, but also to recognize that sometimes information about the safety of a drug emerges only after the drug is on the market. Because all possible side effects of a drug cannot be anticipated on the basis of pre-approval studies – which usually involve only several hundred to several thousand patients -- FDA maintains a system of post-marketing surveillance and risk assessment programs to identify adverse reactions and safety risks that did not appear in the clinical trials conducted to gain approval to market the drug. The Agency uses this information to update drug labeling, and, on rare occasions, to re-evaluate the decision to approve the drug.

FDA's role as a public health agency is to protect and promote the nation's health by assuring that patients and health care providers have access to safe and effective drugs as well as accurate benefit and risk information to make informed choices. Weighing the impact of the potential safety risks for drugs against their known benefits, for individual patients and the public health as a whole, is a multifaceted and complex process, involving scientific as well as public policy issues. As described below, FDA has approached the issues associated with ESA products mindful of our important role as a public health agency, and the need to make the best regulatory decisions we can for patients and health care providers.

ERYTHROPOIESIS-STIMULATING AGENTS (ESAs)

Erythropoiesis-stimulating agents are man-made versions of a natural protein known as erythropoietin. Erythropoietin is made by the kidney and stimulates the primitive cells in the bone marrow to produce red blood cells, the main oxygen-carrying cells in the blood. An increase in the number of red blood cells is commonly indicated by an increase in the laboratory measures known as the blood hemoglobin level and the blood hematocrit. An abnormally low hemoglobin or hematocrit value is one of the hallmarks of anemia.

Multiple conditions may cause anemia, including the loss of erythropoietin due to the destruction of kidney function by chronic kidney disease. Other conditions that may cause anemia are generally unrelated to a deficiency of erythropoietin and are exemplified by anemias due to iron deficiency, certain vitamin deficiencies, hemorrhage, and various intrinsic bone marrow disorders. Generally, regardless of the cause of anemia, blood transfusions may be necessary to relieve patient symptoms and maintain life when the anemic condition becomes severe. The main goal of treatment with ESAs is to increase the number of red blood cells in patients with the specific types of anemia that are responsive to the ESAs so that blood transfusions are not needed.

Procrit/Epogen (Epoetin alfa)

FDA approved Procrit/Epogen in 1989 for the treatment of anemia associated with chronic renal failure (CRF), (including end stage renal disease) patients and patients not on dialysis) to elevate or maintain the red blood cell level and to reduce the need for transfusions in these patients.

Epoetin alfa is manufactured by Amgen and marketed under the two proprietary names of Epogen and Procrit. Except for the difference in the marketing names for Epoetin alfa, the Epogen and Procrit labeling are identical.

The initial approval of Procrit/Epogen for use in treating anemia due to chronic renal failure was followed by approval for additional indications for use in patients with certain cancers with anemia due to concomitant chemotherapy, in patients with HIV-infection with anemia due to anti-viral drugs, as well as to decrease the need for transfusion in patients scheduled for certain types of surgery.

Epogen is distributed by Amgen for use in dialysis patients. Procrit is distributed by Ortho Biotech (a subsidiary of Johnson & Johnson) for use in anemic chronic renal failure patients who are not on dialysis, and for the three non-renal indications described above.

Aranesp (Darbepoetin alfa)

FDA approved Darbepoetin alfa (Aranesp) in 2001 for the treatment of anemia associated with chronic renal failure, including patients receiving dialysis as well as patients not on dialysis. The indication for Aranesp use was expanded in 2002 to include use treatment of anemia caused by chemotherapy in patients with some types of cancer. Aranesp is manufactured and marketed by Amgen.

FDA POST-MARKETING ACTIONS

Evaluating the benefits and risks of all drug products is a dynamic process—and FDA's ongoing evaluation of ESAs is no exception. FDA has received and is continuing to receive data from several different clinical trials studying the risks and benefits of ESAs, primarily in clinical trials of unique dosing regimens or clinical situations not described in the labeling (off-label unapproved uses). The product labeling for all U.S. marketed ESAs has been updated several times since the original approvals to incorporate new safety information. The most recent labeling is based upon the submission of extensive new safety information late in 2006 and early 2007. These data prompted a major revision of the ESA labels to include, for the first time, a boxed warning. I will discuss initially the major labeling safety updates and actions that preceded the activities of late 2006 and early 2007.

In 1996, FDA approved changes to the Procrit/Epogen labeling adding a new subsection in warnings regarding higher mortality with treatment regimens intended to maintain a higher hematocrit level in patients with anemia due to chronic renal failure who were undergoing dialysis. The Normal Hematocrit Study provided the first evidence of important cardiovascular safety risks, including a risk for death, when ESAs were administered in dosages that resulted in hematocrit levels that were closer to the normal range, and higher than the target levels stated in the product labeling. With respect to another safety concern, in May 2003 and in October 2005, FDA approved revisions to the Warnings and Adverse Reaction sections of the labeling to include information regarding pure red cell aplasia, a risk related to rare immunological reactions among all patients receiving ESAs.

1. Actions Related to Labeling for Anemia Among Cancer Patients

In late 2003 and early 2004, FDA received clinical trial reports of risks for tumor promotion and increased mortality among cancer patients who were receiving ESAs in the treatment of chemotherapy-induced anemia. These risks were discussed at a May 2004 Oncologic Drugs Advisory Committee and subsequently, in 2004, ESA labels were revised to describe these trials and the risks for tumor promotion and death. These activities were accompanied by requests for additional clinical trials to more thoroughly evaluate the risks for ESA use among cancer patients.

2. Most Recent FDA Actions

More recently, FDA issued a series of public health advisories (November 2006, February 2007, and March 2007) describing further emerging safety information that applies to all patients as well as specific risks in cancer patients. In November 2006, FDA alerted health care professionals that a newly published clinical study ("Correction of Hemoglobin and Outcomes in Renal Insufficiency" [CHOIR] study, *New England Journal of Medicine*, November 16, 2006, discussed in more detail below) showed that patients treated with ESAs and dosed to a target hemoglobin concentration of 13.5 g/dL are at a significantly increased risk for serious and life-threatening cardiovascular complications, as compared to use of the ESA to target a hemoglobin concentration of 11.3 g/dL. FDA public health advisories emphasized that the study's findings underscored the importance of following the currently approved prescribing information for ESAs including the dosing recommendation that the target hemoglobin NOT exceed 12 g/dL.

In February 2007, FDA notified health care professionals of the results from a large clinical trial evaluating the use of an ESA to treat anemia in cancer patients not receiving chemotherapy. In this trial, patients received either Aranesp according to the approved dosing regimen or a placebo. Patients treated with Aranesp had a higher death rate and no reduction in the need for transfusions compared to those treated with placebo. FDA warned that the findings in the Aranesp trial also may apply to other ESAs, and furthermore, that the finding show that treating anemic cancer patients NOT currently on chemotherapy with an ESA may offer no benefit and may cause serious harm.

The most recent public health advisory in March 2007 outlined new safety information based upon the CHOIR trial and several newly reported trials conducted among cancer patients that prompted extensive revision of the ESA product labels. Concomitant with this March advisory, FDA posted an "Information for Health Care Professionals" sheet to further inform prescribers and other health care professionals about these important new safety findings. See: *http://www.fda.gov/cder/drug/infopage/RHE/default.htm*.

The revised product labeling from March 2007 included updated warnings, a new boxed warning, and modifications to the dosing instructions. The boxed warning, the strongest warning for an FDA approved product, advises physicians to use the lowest ESA dose that will gradually increase the hemoglobin level to a concentration sufficient to avoid the need for blood transfusions. Also, the boxed warning highlights the major safety risks for ESAs and important dosing information.

The March 2007 ESA label revisions were based upon recently completed trials that described an increased risk of death, blood clots, strokes, and heart attacks in patients with chronic kidney failure when ESAs were given at doses that resulted in higher than recommended hemoglobin levels. The label revisions also addressed recently reported trial findings for cancer patients, both when ESAs were given at doses intended to result in higher than recommended hemoglobin levels, and when ESAs were given to cancer patients whose anemia was not chemotherapy-related. The revised labeling also summarized the information from the trial that showed an increased risk for blood clots in patients following orthopedic surgery when ESAs were administered without the blood clot prevention measures described in the product label.

Because all ESAs have the same mechanism of action, FDA believes these new concerns apply to all ESAs and is re-evaluating how to safely use this product class. The new label changes are specifically summarized below:

- A new boxed warning states that prescribers should use the lowest dose of Aranesp/Epogen/Procrit that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid the need for red blood cell transfusion.
- The boxed warning also notes that Aranesp /Epogen/Procrit increased the risk for death and for serious cardiovascular events when administered to target a hemoglobin of greater than 12 g/dL.
- For cancer patients, the boxed warning notes that use of ESAs
  - shortened the time to tumor progression in patients with advanced head and neck cancer receiving radiation therapy;
  - shortened overall survival and increased deaths attributed to disease progression in patients with metastatic breast cancer receiving chemotherapy; and
  - increased the risk of death in patients with active malignant disease not under treatment with chemotherapy or radiation therapy. ESAs are not indicated for this patient population.
- The boxed warning also notes that patients treated before surgery with ESAs to reduce allogeneic red blood cell transfusions had a higher incidence of deep venous thrombosis. Only Procrit/Epogen is approved for this indication.

Additional Warnings section information describes these increased risks for mortality, cardiovascular events, and tumor progression:

- *Increased Mortality and Cardiovascular Events* – the warnings now describe the results of new studies showing an increased incidence of cardiovascular and thrombotic events in patients with chronic renal failure, cancer patients on chemotherapy, and surgical candidates.
- *Potential for Tumor Growth Progression* – A new subsection in Warnings describes the new data and emphasizes the evidence for increased rate of tumor progression.

In addition, FDA has issued letters describing the new data to all active IND holders investigating new uses of ESAs. These letters described the new trial data and revised ESA labeling, advised discussion of this information with patients, investigators, and investigational review boards, and recommended re-consideration of the safety of studies in light of these new data.

FDA ADVISORY COMMITTEE INPUT

FDA often seeks advice from its advisory committees regarding emerging safety issues. Advisory committees provide independent, expert advice on scientific, technical, and policy matters related to the development and evaluation of products regulated by FDA. The advisory committee system enhances FDA's ability to protect and promote the public health and maintain the public trust by enabling the Agency to obtain the benefit of independent, professional expertise. Although advisory committees provide recommendations to the Agency, final decisions are made by FDA.

As previously noted, FDA convened a meeting of the Oncologic Drugs Advisory Committee (ODAC or the Committee), on May 4, 2004, so that FDA could present and seek advice regarding safety signals (evidence of adverse effects on survival and shorter time-to-tumor progression) observed in two studies. In addition to presenting data from these two studies (the ENHANCE and BEST studies discussed below), FDA presented the results of a study conducted under an agreed-upon post-marketing commitment to assess the tumor-stimulating potential of Procrit/Epogen. The Committee agreed that the results of these studies raised concerns that should be investigated through additional studies.

FDA convened ODAC again on May 10, 2007, to discuss the recently reported information on risks of ESAs, specifically, Aranesp, Epogen, and Procrit, for use in the treatment of anemia due to cancer chemotherapy. The results of the trials in patients with cancer were presented. The results of trials that have completed accrual but have not been analyzed were identified, and it was noted that these trials may provide additional information on tumor progression, mortality, and thromboses when ESAs are used at doses higher than recommended in patients with cancer.

ODAC recommended that the results of these trials be submitted for FDA review as soon as the data are available, that additional trials be conducted by the sponsors to evaluate the safety of the recommended doses, and that further marketing authorization be contingent upon additional changes in product labeling and additional trials. ODAC also recommended revisions to product labeling to provide more direction on safe use among cancer patients, as follows:

- That product labeling should specifically state that ESAs are not indicated for use in specific tumor types (breast cancer, head and neck cancer, and non-small cell lung cancer) studied in trials that showed adverse safety signals. The Committee did not specify which tumor types should be added.

- That product labeling should define a hemoglobin level in asymptomatic patients at which ESA should be initiated.
- That the hemoglobin level at which dosing should be suspended should remain, as described in the March 2007 revised labeling, at 12 g/dl..
- That product labeling should recommend discontinuation of ESAs following the completion of a chemotherapy regimen and re-evaluation of the degree of anemia with subsequent chemotherapy regimen(s).

FDA is working with the companies to address ODAC's recommendations. Also, FDA is planning discussion of ESA safety issues associated with the chronic renal failure indications at a Cardio-Renal Drugs Advisory Committee meeting later this summer.

DATA SUMMARY

I will now briefly review the clinical trials that have provided important new safety information since the original approval of ESAs. These trials may be grouped into three categories based upon the treated patient population: 1. Patients with chronic renal failure; 2. Patients with cancer; and 3. Patients undergoing surgical procedures.

1. Trials in patients with chronic renal failure

a. Normal Hematocrit Study Evaluating Patients with CRF

The first trial to raise serious concerns about the risks of ESAs was a report from a trial entitled, the Normal Hematocrit Study. FDA was informed of the results of the Normal Hematocrit Study in 1996 and incorporated the important safety information into the product labeling shortly following the review of the information. The Normal Hematocrit Study was designed to evaluate whether certain patients with chronic renal failure undergoing dialysis had fewer

cardiovascular complications if the ESA was administered to attain a higher hematocrit level as compared to a lower hematocrit level. However, the trial was terminated early because of the unexpected finding of more deaths and non-fatal myocardial infarctions in the patients randomized to the higher hematocrit target level. The 1996 labeling revision based upon this study recommended that the ESAs not be used to achieve hematocrit in excess of 36 percent, a value that corresponds to a hemoglobin level of 12 g/dL. This label revision was also accompanied by the sponsor's commitment to conduct a study that further examined the risk for thrombotic events (blood clots) among patients receiving ESAs. An increased thrombotic risk in association with ESA use was thought to be one of the potential causes for the safety risks detected in the Normal Hematocrit Study.

b. Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) study and Cardiovascular Risk Reduction by Early Treatment with Epoetin Beta (CREATE) study

Two clinical trials and an editorial published in the *New England Journal of Medicine* in November 2006, addressed safety concerns about the use of ESAs in the treatment of anemia of chronic renal failure (CRF). The 1,400 subject Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) study demonstrated increases in serious and potentially life-threatening cardiovascular events when Epoetin alfa (Procrit) was administered to reach higher target hemoglobin levels than lower target hemoglobin levels. The 600-subject Cardiovascular Risk Reduction by Early Treatment with Epoetin Beta (CREATE) study trended toward more cardiovascular events in a pattern similar to the CHOIR study, thus strengthening the findings of the CHOIR study. The CREATE study examined the use of Epoetin beta, a product not approved in the USA.

The CHOIR study was an open label study in which patients with anemia due to chronic kidney disease subjects were randomized to be dosed with Procrit to either a higher target hemoglobin (13.5 g/dL) or a lower target hemoglobin (11.3 g/dL). The primary endpoint was a time to event analysis for a composite cardiovascular endpoint (all cause mortality, congestive heart failure (CHF) hospitalization, non-fatal myocardial infarction [MI], or non-fatal stroke).

Procrit was administered as 10,000 U SC weekly and titration allowed to a maximum dose of 20,000 U weekly. Overall, 715 subjects were randomized to the high hemoglobin target and 717 randomized to the low hemoglobin target. At the end of the study, the average hemoglobin was 12.6 g/dL for the high target group and 11.3 g/dL for the low target group. The primary endpoint showed statistically significantly worse cardiovascular outcomes in the higher target hemoglobin group ($p = 0.03$ by log rank test) with a hazard ratio of 1.3 (95 percent CI 1.03, 1.74). The rates for the individual components of the composite primary endpoint were (high target hemoglobin vs. low target hemoglobin):

Death:	7.3% vs 5.0% ($p = 0.07$)
CHF hosp:	9.0% vs 6.6% ($p = 0.07$)
Non-fatal MI:	2.5% vs 2.8%
Non-fatal stroke:	1.7% vs 1.7%

The findings from the CREATE trial were generally less notable with respect to safety risks than the CHOIR trial, a finding that may relate to the smaller patient population enrolled in the CREATE study and other design features. In the CREATE trial, anemic patients not undergoing dialysis were treated with Epoetin beta to attain a hemoglobin level of 13 to 15 g/dL

or a level of 10.5 to 11.5 g/dL. The primary endpoint was similar to that for the CHOIR trial but included a few additional cardiovascular complications. Specifically, the endpoint consisted of any occurrence of sudden death, MI, acute heart failure, stroke, transient ischemic attack, angina pectoris resulting in hospitalization, complications of peripheral vascular disease, or cardiac arrhythmia requiring hospitalization. Overall, the primary endpoint events occurred in 19 percent of the patients in the high hemoglobin target group and 16 percent of the patients in the low target group, a result that was not statistically significantly different (p=0.20).

The published CHOIR and supportive CREATE study findings underscore the importance of the warnings previously described in the labeling for Procrit, Epogen, and Aranesp regarding cardiovascular risks that include thrombotic events and increased mortality in hemodialysis patients who participated in the Normal Hematocrit Study. Importantly, the new data from the CHOIR study, combined with the findings previously reported from the Normal Hematocrit Study, showed that patients with anemia due to chronic renal failure (whether or not receiving dialysis) were at increased risk for serious cardiovascular complications when ESAs were administered to attain hemoglobin levels in excess of the 12 g/dL level recommended in the ESA product labels.

2. ESA Trials in Cancer Patients

Between 2001 and 2003, FDA became aware of the results of new trials that raised safety concerns for the use of ESAs in patients with cancer. Specifically, during this period, FDA received reports from three trials of ESAs in patients with cancer receiving chemotherapy. While one trial (N93-004) did not suggest harmful effects of the use of ESAs, the other two trials

(BEST and ENHANCE) demonstrated higher mortality and more rapid tumor progression when the ESAs were given in an unapproved manner, i.e., to maintain hemoglobin levels of greater than 12 g/dL. These findings were discussed at a May 2004 meeting of the ODAC and the new safety data were added to product labeling for ESA products shortly following that meeting. ODAC recommended that additional data be gathered to further evaluate these new safety concerns in patients with cancer receiving ESAs.

In late 2006 and early 2007, FDA was informed of several new trials in cancer patients that raised additional safety concerns. We have described these trials below.

a. Danish Head and Neck Cancer Study

In December 2006, the manufacturer of ESAs informed FDA of the interim results of the Danish Head and Neck Cancer Study Group trial (DAHANCA 10). This open-label, randomized trial compared radiation therapy alone to radiation therapy plus Aranesp in the treatment of advanced head and neck cancer. The trial assessed whether treating anemia to achieve and maintain a hemoglobin concentration of 14.0-15.5 g/dL during radiotherapy would improve local-regional disease control. The DAHANCA 10 data monitoring committee found that 3-year local-regional control in patients treated with Aranesp was worse than for those not receiving Aranesp ($p=0.01$). Overall survival time also favored those not treated with Aranesp, though this finding was not statistically significant ($p=0.08$). The data monitoring committee recommended the ESA treatment be stopped in the experimental arm on December 1, 2006. The DAHANCA 10 trial was similar in design and in outcomes to the ENHANCE trial noted above.

b. Study in cancer patients NOT receiving chemotherapy

FDA was notified in January 2007 of the results of a 989 patient, multi-center, double-blind, randomized, placebo-controlled trial of Aranesp (Darbepoetin alfa) in cancer patients with anemia who were not receiving chemotherapy. The target hemoglobin in the Aranesp treatment group was 12 g/dL. FDA's analysis of the primary study data demonstrated that Aranesp did not significantly reduce the need for red blood cell transfusions and showed an increase in mortality in patients receiving Aranesp compared to those receiving placebo (hazard ratio 1.30; 95 percent confidence interval: 1.07, 1.57).

c. Study in non-small cell lung cancer patients

FDA was notified in February 2007 of the final results of a double-blind, placebo controlled study that was designed to evaluate whether Epoetin alpha improved the quality of life for patients with non-small cell lung cancer who were not receiving chemotherapy. The Epoetin alfa dose was titrated to maintain a hemoglobin level of 12 to 14 g/dL. Though planned to enroll 300 patients, the study was closed to accrual in December 2003, after enrolling only 70 patients because its data monitoring committee found higher mortality in those treated with Epoetin alfa. It should be noted that although the study size was small, prognostic factors and extent of previous cancer treatments were reported to be well balanced between the study arms. Median time to death in those treated with Epoetin alfa was 68 days and significantly shorter than the median time to death of 131 days in those treated with placebo ($p = 0.04$), with the majority of deaths reported as due to disease progression. Also, treatment with Epoetin alfa did not significantly reduce the need for red blood cell transfusion or improve quality of life.

3. Trial in patients undergoing surgery

In 1996, the indication for use of Procrit/Epogen was broadened to include its use to reduce transfusion in patients with hemoglobin values between 10 and 13 g/dL scheduled to undergo non-vascular, non-cardiac surgery. In these patients, the ESA reduces the need for blood transfusions. The approval of this peri-surgical indication was accompanied by a commitment to complete a post-marketing study that explored the risk for thrombotic events among patients who were not receiving preventive therapy with anti-thrombotic drugs. As previously noted, the Normal Hematocrit Study had suggested that ESAs may increase the risk for thrombotic events in certain patients. The results of this post-marketing study were supplied in 2007. Specifically, FDA was notified in February 2007 of the preliminary results of a 681-patient, multi-center, randomized, open-label, non-inferiority trial of Procrit compared to the standard of care in adult patients undergoing elective spinal surgery. In this trial, the frequency of deep venous thrombosis in patients treated with Procrit was 4.7 percent (16 patients), a rate more than twice that of patients who received usual blood conservation care (2.1 percent, seven patients). Hence, this trial suggested that, in the peri-surgical setting, ESA use increases the risk for thrombotic events.

CONCLUSION

FDA's mission is to promote and protect the public health. A major component of that mission is to ensure that the American public has access to safe and effective medical products. At this time, FDA continues to believe that ESAs are safe and effective when used according to the recently revised product labeling, at the recommended dose and approved indication. The

revised labeling reflects the current knowledge regarding risks and benefits that patients and their physicians should consider. FDA continues to assess data as it becomes available.

Thank you for the opportunity to testify before the Committee today. I will be happy to respond to questions.

Chairman STARK. Thank you. Dr. Jenkins, is it FDA's position that Epogen, the dose of Epogen should be reduced by 25 percent if the hemoglobin levels approach or exceed 12 grams? Is that still where you are?

Mr. JENKINS. That's the current dosing recommendations in the approved package labeling.

Chairman STARK. And is there any reason that it should take three months to adjust a level that exceeds 12?

Mr. JENKINS. Mr. Chairman, the ESAs take two to 4 weeks for each dose to have their effect on the bone marrow to raise the red blood cell count. So some of these drugs are administered as often as three times a week in patients who are on dialysis, so you can imagine that it's very difficult to carefully titrate the dose to achieve an exact hemoglobin level of 12. Plus, there are other factors of impact on the patient's hemoglobin level at any given time.

So we recognize that there might be occasional excursions over 12, but our advice is to try to maintain hemoglobin at or below 12 as much as possible.

Chairman STARK. Okay. Now DaVita's anemia management guidelines recommend a 25-percent increase in the dose if hemoglobin is near or at 12 grams, and they recommend a small decrease in the dose of 10 percent if it's between 12 and 13. And they recommend continued dosing up until a patient reaches a hemoglobin of 15. And it's only at the hemoglobin level of 15 grams that they finally recommend to stop dosing.

Now would that management guideline be consistent with the FDA's recommendations?

Mr. JENKINS. Mr. Chairman, no, they would not. Our dosing recommendations recommend that you start reducing the dose of ESAs as you start to approach a hemoglobin level of 12, recognizing that you have to be very cautious in patients with end-stage renal disease about completely stopping the use of ESAs because they don't make much if any of their own erythropoietin. So sometimes stopping completely can lead to an undershooting of the hemoglobin and then you have to use higher doses of erythropoietin to get their bone marrow started again.

So it's a careful titration but those recommendations you read would not be consistent with our approved labeling.

Chairman STARK. And is it generally—you mentioned that people are dosed several times a week, and are they also tested several times a week so that the physician in charge can monitor these levels closely and should, as a matter of course, adjust the levels for each individual patient? Is that——

Mr. JENKINS. That's true. The hemoglobin or hematocrit is a readily available laboratory test that can be measured frequently to help adjust the dose of erythropoietin.

Chairman STARK. Well, then my question to Ms. Norwalk is, while I appreciate CMS being Johnny-on-the-spot, why did you go to a 13 level, which I gather is what—39 percent would be about the equivalent instead of the 36 percent that FDA recommends and that you—that CMS used to be 36-and-a-half in '97 or '98? Why the bump to 39?

Ms. NORWALK. I think there are a number of different points to make with regard to that, Mr. Chairman. The first is that when you have a target level—and the CHOIR study actually looked at this; they were targeting 13-and-a-half; the average actually came in at 12.6. Our target is the FDA label, between 11 and 12 or our 33 to 36. That is our—in fact, that's our policy.

Chairman STARK. Okay.

Ms. NORWALK. But from a payment perspective, if you're looking at payment changes, as Dr. Jenkins noted and as you noted the importance of an individual. So it could be at any particular time an individual may have a level that bumps up and it can take—I think actually the label says two to 6 weeks to change as opposed to two to four, but whatever it happens to be, our payments are monthly. And wanting to take into account the variation between payment between individuals not only over time but certainly between patients and not wanting to penalize a facility for doing what is correct, our monitoring policy really focuses now, and the changes that I announced this morning really focus on a persistent level at 39 or higher because that's where we really see a concern.

From information that we received yesterday on the progression of dosage for patients who persistently have a hematocrit level of over 39, we've noticed that in the months following the first measure of 39 that dosages in fact do come down over time so that you'll have—if the dose in January is equal to one or 100 percent, the dosage in February, most recently with our new policy, has come down to under 70 percent of the initial dosage; the dosage in March under 50 percent; the dosage in April under 40 percent, so that our policy, we do think, has had some impact because these figures are better than what they were in '05 and '06.

But I'm still concerned that the impact is not sufficient given the information that we've seen in the CHOIR study. But I think to do something more precipitously may have an adverse impact on patients that we're unaware, and so I think we need to be very careful in having people focusing on the payment side for something that's more of an outlier rather than allowing patients over time who may be 39 1 month and 36 the next.

Chairman STARK. Would you then agree that a robust risk adjustment program and a good outlier policy could—would be a useful tool in managing this program?

Ms. NORWALK. Oh, absolutely. That, coupled with appropriate quality indicators, yes.

Chairman STARK. Mr. Vito, I don't know if you're the person to ask, but I'll try it anyway. Is there a—the Veteran's Administration, as I mentioned in my opening remarks, says that they save $3,000 to $4,000 a patient on their dosages. Do they pay—under the Federal supply schedule, do they pay a lot less for Epo than Fresenius or DaVita or John Jones Hospital?

Mr. VITO. We haven't done that review recently. We had done a review, I believe, in 2004, around that time, where we compared the end-stage renal prices that the VA paid compared to what the Medicare was and we found that the VA prices were lower.

Chairman STARK. Do you know about how much lower? I mean do you want to make a stab at that; half?

Mr. VITO. I do not recollect that. I can provide that to you and I will be glad to do it after.

Chairman STARK. Let's assume for a minute that it were half, okay, the VA is paying half of what the major providers are paying. And if we take the VA at face value and say they're saving $3,000 to $4,000, if somebody in fact is paying twice what the VA is paying for the drug, is my logic correct that therefore we might save

$6,000 to $8,000, assuming the drug costs half? Does that make sense to you?

Mr. VITO. I did not completely understand the question.

Chairman STARK. Well, let's try this. The VA says, under their program of "subcutaneous" treatment and the level at which they use Epo, they're saving $3,000 to $4,000 per patient per year as opposed to using intravenous and more aggressive dosing.

Okay, now if we accept that, and if they're paying half for the Epo that Fresenius is, wouldn't one assume that if Fresenius could buy the drug at 50 percent less and use the VA's protocols that they'd save $6,000 to $8,000 a year per patient?

Mr. VITO. Well, we did not do that analysis, but it makes sense to me.

Chairman STARK. Is my logic pattern there——

Mr. VITO. Yes.

Chairman STARK. Dr. Jenkins, you must have had a lot of math before you went to med school, is that——

Mr. JENKINS. I still have my shoes on. It sounds fairly logical, but I'm not familiar with the difference between the VA protocol and the Fresenius protocol as far as their dosing strategy.

Chairman STARK. Well, I think most of that savings they think comes from "subcutaneous" dosage instead of intravenous, but I don't know that.

I want to thank the panel. Mr. Camp.

Mr. CAMP. Thank you, Mr. Chairman. Mr. Vito, you mentioned the VA prices being lower, and as you get that information to the Committee would you please also include a patient mix analysis because I do think it's important, given the testimony we've had from Dr. Christensen that we understand, does the VA patient population mirror what we find in the private sector. I mean that's going to be a very important factor here in determining whether their prices are lower because of what they've done.

But I think this testimony that we've had has really given us the intersection between medical treatment standards and payment policy standards and those are very different. I thank you, Ms. Norwalk, for making that distinction there.

The Medicare Modernization Act in 2003 required a demonstration that would look at the feasibility of bundling all dialysis services into one composite rate. And I understand CMS has a report that's going to be coming out soon which will talk about the complexities of this issue, and I was wondering when this report might occur and why there have been delays in implementing a bundling demonstration.

Ms. NORWALK. Two points. I promise that—I said this summer last December. I will be here through three or four more weeks, and it's still the summer when I leave. You will have it before I leave if it's the last thing I do.

Now we appreciate that it's—it's a long process in administration to get policy out, but I appreciate the importance of it, and I made the promise. I intend to stick to it.

Part of the reason why it took up longer than the October 2005 deadline really relates to the research and wanting to be sure that before we put together a report to Congress, given the critical nature of the fact that 93 percent for ESRD is through Medicare, the

importance of all the different indicators that could impact it, I think we were concerned with our initial research and felt more needed to happen before we could put together a report to Congress that recommended the bundled payment system.

Now when it comes to the demonstration, clearly if we were to do a demonstration we should do it after we had the information from our researchers, but I will tell you that it is certainly my opinion that a demonstration is not necessary in order to go forward.

Of the six prospective payment systems that we have done in the past seven years or so, four of them have not had a demo to have. And for a number of reasons, the demonstration, because of it's voluntary nature, may not provide the information that we would need, and we may be better off simply taking a look at what happens over time as we have with other case-mix adjusted systems and monitoring that and adjusting from 1 year to the next as we go forward, that it may be a more accurate assessment of what is required because everyone participates and it's not voluntary.

Mr. CAMP. You touched briefly on the—not briefly, but you talked about ESA-monitoring policy that CMS has put in place. Are there any results of that that you can share with us that might be helpful?

Ms. NORWALK. Well, I got—and I apologize for not, I literally got this in email last night, so it has taken us a bit to put together the data, particularly because it was very recent data, as recent as April and May of this year, and we looked at a number of different things, including the claims that were submitted, and what beneficiaries were in what range, what were the dosages that they were receiving and so forth.

And we also took a look at those who had persistently higher—levels at 39 of above of hematocrit and wanting to take into account, well, what happened; did they actually reduce the dosage as our monitoring policy intended and what happened when you compared it to the similar cohort from 2005 and 2006 over the same months. And we have, in fact, seen some change, although I am concerned that the percentage of patients who were persistently at 39 or above remains about the same, in fact, is slightly higher.

So it's—I think we need to do a little more work internally to figure out what these data mean so that we can put that into account as we develop the case mix adjustments on a go-forward basis.

Mr. CAMP. Thank you. Thank you, Mr. Chairman.

Chairman STARK. Mr. Doggett.

Mr. DOGGETT. Thank you very much. Ms. Norwalk, you've talked about getting the study completed before you depart. I believe in your written testimony you estimate that it will take what seems to me like a longer period of time to actually implement a bundled payment system than it took to roll out Part D prescription drug, which you and I have discussed, from start. Do you—isn't there a way to get this job done quicker?

Ms. NORWALK. I think, forgive me for interrupting. I think it's a very similar time period, so if the end—December 8, 2003 versus the beginning of 2006 is about 2 years, and I would—to be fair to the staff who do our information systems I think we would be better served if we had slightly more time than that to ensure that

our computer systems work and that we resolve whatever remaining issues there may be around case-mix adjustment for example.

So two to 3 years is our requested timeframe, and part of that is just the amount of time it takes to do the proposed rule, get the comments, ensure that we are well informed from commenters, have time to reply to those, do any listening sessions that need to be done, work with the Committee certainly, before we put out a final rule, and then implement it.

Now our systems changes from a computer perspective really depend on what else is going on and what else is changing and often that is a result of what happens here on Capitol Hill and what legislation changes because they fight for computer time, all the changes that we have. So two to 3 years, which is in line with where we were in the drug benefit.

Mr. DOGGETT. Well, I usually find with CMS two to 3 years means four to five, but your best estimate and testimony today, is that 3 years from today?

Ms. NORWALK. Well, it would be three—two to 3 years, three years if you pass legislation tomorrow. So it really is based on when the legislation passes as opposed to any particular other point.

Mr. DOGGETT. Related subject. As you know, MedPAC attributes part of the increase in the ESRD population to the epidemic of diabetes that we have in this country, which is a major risk factor for ESRD. Given the importance of preventing the progression of both diabetes and ESRD, do you think it makes sense for CMS to expand coverage of nutrition therapy to target groups that have not fully developed diabetes as a preventive step?

Ms. NORWALK. I know that we added a nutrition therapy benefit under the MMA, and it would be good for—I'm happy to go back and take a look and talk to staff as to whether or not it's been sufficient and how well it's been utilized. If it hasn't been well utilized is it because we need to do more education; what are the reasons? And is it broad enough that we're taking into account this particular vulnerable population? So let me get back to you with some answers on that, because I don't know.

Mr. DOGGETT. Okay. Could you report back to our Subcommittee on that and whether you're able to do everything that you need on this nutrition therapy without any additional legislative authority, and if you feel any legislative authority is needed, whether you support that and what you support?

Ms. NORWALK. Okay.

Mr. DOGGETT. And then just one final followup on our discussion from your testimony last Thursday. You referenced me to a document that you said dealt with this prompt payment for community pharmacists. And I've looked at the document since then. As I understand it, the plans are reported back to you on their payment policies, is that right?

Ms. NORWALK. Correct.

Mr. DOGGETT. And did you collect any data regarding monitoring whether the payments were being made in accordance with the plans that you got reports on?

Ms. NORWALK. Well, I can say this. I don't know if we did any systematic collection, but the beginning of 2006, probably for the

first five, six months, a significant number of pharmacists were free to tell us and in fact did tell us on a fairly regular basis how unhappy they were with the timing of the payments.

Since that time it has settled down quite significantly and I personally spent a fair amount of time working with the pharmacy community on a whole host of issues which are before CMS and I have—that issue really has not risen to the—really at all compared to where it was last year.

Mr. DOGGETT. What you're saying is you're not getting as many complaints now as you got then?

Ms. NORWALK. Well, almost no complaints now compared to a high volume then.

Mr. DOGGETT. Have you done any—following your review of what the plans said they were doing, have you done any satisfaction study or survey of pharmacists to see whether they're satisfied with how the plans are being implemented or are you relying solely on the variation in the volume of complaints?

Ms. NORWALK. I don't know that we've done a study but I will go back and—not that I'm aware of, but I'll go back and ask that question.

Mr. DOGGETT. Thank you. Thank you, Mr. Chairman.

Chairman STARK. Mr. Johnson.

Mr. JOHNSON. Thank you, Mr. Chairman.

Ms. Norwalk, you know, any changes in payment policy can affect patient care, so I'm sure you're extremely cautious. A 2005 report shows that '97 to 2004, the number of dialysis patients with hemoglobin below 11, a level associated with a higher risk of mortality and hospitalization, has decreased by 40 percent. I'd say that's a significant achievement.

I fear this could be reversed if reverted back to a restricted payment policy for ESRD patients. Can you walk us through how the payment policy in '97 affected hemoglobin outcomes and why you changed the policy to give physicians more flexibility in treating anemia and do you think any changes, further changes, need to be made with respect to CMS policy?

Ms. NORWALK. I believe that the policy 10 years ago was touched on a bit earlier, which is a rolling average of 36-and-a-half percent. And then that was changed to 37-and-a-half percent.

A couple of issues we had with that, one was the ability to actually implement that policy. Our carriers didn't understand it and the dialysis facilities also had difficulty figuring out how to make that work. So that's one of the reasons why we changed where we are now to focusing on a particular point in time and having a persistent level of hematocrit above 39 percent.

But I agree with your overarching point, which is, having a bundled payment system, one of the things that we need to be very concerned about is under-utilization so that we don't have hemoglobin levels below 11.

One of the things that is important to do when we are working from a timing perspective to ensure that we have both quality metrics in place where we can measure for all facilities and all patients hematocrit levels over time or we can focus on other things like subcutaneous administration and other things that we think are better for the patient and really letting the physician treat that

patient individually, so taking that into account by having both patient-focused risk adjustment factors as well as facility-focused risk adjustment factors.

A combination of these things should lead us to a path where we don't have underutilization and don't have over-utilization. But I think hopefully the next thing that we'll discuss is perhaps the evidence, what are those target numbers, where should we be focusing and are there differences in patient populations that we need to be concerned about so that we can consider that for case mix adjustment.

Mr. JOHNSON. Thank you. You know, I think and I believe you believe market forces do a better job controlling prices than the government. What can we do to foster competition since we only have two therapies available at this time?

Ms. NORWALK. Well, one of the things that we did for the third quarter of 2007 that—particularly if you're looking at the OIG numbers I think it's important to recognize the OIG for the similar time period a year ago had 9.58 for 1,000 units. Our recent pricing has $9.10.

So the issue for a unit of Epo, for example, is what do—you have to consider all the different provider types. You've got hospitals; you have the large chains, you have the smaller chains and so forth; profits, not-for-profits, et cetera, and wanting to take into account if you're having a single payment policy, particularly for acquiring ESAs, wanting to be sure that we can take into account what does it cost any of those facilities to acquire it and how can we let the market move in that direction.

I suspect that over time there will be other ESAs to the market, and they may foster additional competition. And that's something that we should also take into account when we're setting our initial rates for a bundled payment system on a go-forward basis.

Mr. JOHNSON. You know, I don't think that you cover home dialysis and yet people say there's a higher savings and better patient outcomes. Can you give me a reason why you don't cover that?

Ms. NORWALK. We do cover home dialysis. Most of the dialysis today provided in the Medicare setting is, in fact, done in a facility. I think one of the things that the report to Congress will touch on is the home dialysis piece, too, and I can't actually—see if I can find my notes. Because the vast majority is otherwise, our focus really has been from a facility perspective, but I think we want to take into account different payment methods in as much as something is done at home and you're working with a different supplier to provide the equipment that you would need and the drugs that you would need at home.

So it's really a different fix for the issue, but since—oh, so we do pay the same rate for both. So there we go, thank you.

When you're doing a bundled system it might be—it's something I think that we have to take into account that differences in resources that you may have from one or the other. So our report to Congress will focus on that a bit more.

Mr. JOHNSON. Thank you, ma'am. Thank you, Mr. Chairman.

Chairman STARK. Thank you. Mr. Thompson.

Mr. THOMPSON. Thank you, Mr. Chairman.

Ms. Norwalk, I am interested in this idea of bundling payments that we've spent so much time on, and I'm concerned as to how that would be handled with different providers in different areas. And as I understand it, the big providers would have a fairly easy time with this, but I also understand that small, independent, rural providers may not and that they wouldn't be able to—maybe not even stay in business if we went to this form.

So I'm interested in hearing from you, maybe the percentage of rural dialysis facilities that are independent as opposed to those that are affiliated with one of the larger organizations. Or maybe it would be better if I had an idea how many patients are served in rural areas by independents vis-a-vis the larger corporate ones. And what I'm really trying to get at is the impact that this would have on not just the rural providers but also the spillover effect that it may have on rural hospitals.

Ms. NORWALK. My recollection is that about 70 percent of the reimbursement goes to the large dialysis organizations. So that gives you some sense of the percentage difference. About, is it 70 percent?

Mr. THOMPSON. Yes, I'm told it's about 70 percent; the large guys control about 70 percent.

Ms. NORWALK. Right, I think 70 percent is hospital-based.

Mr. THOMPSON. And about 25 percent of all dialysis facilities are located in rural areas.

Ms. NORWALK. Right. I think you raise a very good point, and there are a number of different things to take into account. One of the things that I suspect we ought to consider is whether or not something is called an isolated essential facility. And obviously in a number of our other payment systems, as you well know, we often will have differences in payments if something is in a rural area.

Now in the report to Congress our main focus is based on resources; what does it cost to treat a patient and can we predict—what factors would we need to include in order to better predict the cost of a particular patient? And they're preliminary——

Mr. THOMPSON. But this seems to me that it's different because some folks can internalize some of those costs, can absorb those, but this could have a very serious impact on not just the independent folks but other medical services that are provided in rural areas.

Ms. NORWALK. Right, and you will find in our report that there is a—we do, in a sense, some impact analysis around rural areas, the large dialysis facilities, the hospitals, so it has—and I apologize; it would have been my preference for you to have that today, so I apologize that you don't in terms of looking at it, but the report does go through a number of different pieces.

So when the Committee is considering legislation, they can take that into account, whether or not you might want to have an adjustment for both. But the size of the facility and so forth, in terms of resource use as well as whether or not something is rural, which is slightly different from your question, didn't have a significant impact through our cost analysis, so it doesn't help predict future costs.

But that's not to say that it might not be an important consideration given, to your point, other healthcare facilities within a rural area and the ability to access that.

Mr. THOMPSON. If the folks in a rural area take a hit in this area of their business it's going to affect something else that they're doing or something that they're not going to be able to do, and I'd like to know more about that. And if you any of you could provide information to the subcommittee on that, I would appreciate it.

The other issue is I want to talk about the monitoring program. It's my understanding that this was put in place to get at the issue of over-prescribing and that there's a pretty significant hit, about 25 percent hit on this?

Ms. NORWALK. That's the current policy, but as I noted in my oral testimony today, if someone is—a couple points. One is they need to have a modifier, and they would not have that payment reduction if they have reduced the dosage of the ESA. So the payment hit only occurs if they haven't reduced the dosage.

The second policy that I noted in my testimony earlier——

Mr. THOMPSON. Before you reiterate your other testimony, I'm running out of time. My concern is, is bundling going to bring about providers to underdose patients?

Ms. NORWALK. It is a concern that we have.

Mr. THOMPSON. How big of a concern?

Ms. NORWALK. It's a very big concern, which is why I think it's critical we do quality monitoring at the same time that we do the implementation of the ESRD bundled payment.

Mr. THOMPSON. But all you would do is find out that patients are put in a dangerous——

Ms. NORWALK. No, I would suggest that we pay for performance, so in as much as a facility is underdosing an individual, their payment be reduced.

Mr. THOMPSON. I would suggest rather than putting the program in place and then monitoring it to see if patients are put in a dangerous position that we do something to make sure they aren't underdosed.

Ms. NORWALK. Sure.

Mr. THOMPSON. Thank you, Mr. Chairman.

Chairman STARK. Mr. Hulshof?

Mr. HULSHOF. Thank you, Mr. Chairman. Let me just follow up on a couple of points my colleagues on both sides have raised. First of all, Mr. Camp, Dr. Jenkins, I think it was to you, or maybe Mr. Vito, talking about a study comparing the VA patient population mix and making sure that it is in fact consistent with the patient population at large.

Dr. Jenkins, it's my understanding as a lay person that normal hemoglobin values are different for children than for adults. Is that true.

Mr. JENKINS. There are different normal ranges for hemoglobin based on gender and age, so that is correct.

Mr. HULSHOF. Even kids as they grow older as they grow older. Those values change. Is that not also correct?

Mr. JENKINS. The normal range is different. I don't have then in my head right now, but the normal range is clearly different from infants up to adults. And it also is different by gender.

Mr. HULSHOF. Just curiously, I probably could have gotten this before the hearing. I know that there are 400,000 patients Medicare covers. Does anyone now approximately how many 18 or younger population that are served or that have ESRD? I'm just curious.

Leslie?

Ms. NORWALK. Someone here probably has that. It's quite small in terms of the population. It is, however, one of the things that we've taken a look a look at in our report to Congress, they're very expensive. The young patients are as expensive as the very old patients. So, it may have something to do with the ESRD or EPA required as well.

Mr. HULSHOF. I'm not sure, Ms. Norwalk, in your remaining days how many more times we can bring you here. So let me take this quick opportunity to thank you for your service and what an extraordinary job that you've done, and wish you well in the future.

One of the advantages that we have is that we get to examine testimony of the next panel. And I know you've probably been focused primarily on your own notes and the follow-up on something my friend from Texas, Mr. Johnson, asked. I think we're going to hear from the next panel from the Director of the American Association of Kidney Patients regarding home dialysis. Not only are there cost savings, but I think the testimony's going to be better patient outcomes.

Is that something that is also going to be included in the long-awaited report?

Ms. NORWALK. I think there is some detail there, but we really focused more overall on the bundled payment system and it's probably less on that. But I'd be more than willing to have staff come and brief the Committee on some what we've seen and we can figure out whether or not we would do a supplemental.

Mr. HULSHOF. One of the things to that you mentioned in your presentation as you were trying to get as much information in on the five minutes allotted to you, you mentioned briefly the subcutaneous administration of EPO and you talk about. Well, you didn't get a chance to talk about it. Let me give you just a few minutes. We've seen studies that that type of administration would be safer, maybe cheaper.

Are there some problems that you foresee in that regard, or what are your thoughts?

Ms. NORWALK. Now, in fact, we think it is terrific to use subcutaneous, and we would like to promote that and would expect and anticipate if we went to a bundled policy that me may well see significantly more of it. But in one of the things that we have done for the past number of years is really focus on something called our fistula first policy, which encourages subcutaneous administration of ESAs.

And we have a whole package around that, wanting to promote that, and are working with our quality improvement organizations to do just that so that patients may be slightly uncomfortable for them. So, maybe that's the, if there were a drawback, but I'd have to ask my favorite just behind me to answer that question, but we think clinically it makes a lot of sense and would like to encourage it.

Mr. HULSHOF. Mr. Vito, in a few seconds, I've got remaining, following up a bit on what my friend from California, Mr. Thompson raised concerned that he and I and others share as far as putting our role providers in a very difficult situation. And I know that you mentioned, you all, the Office of Inspector General, sent surveys to a random sample of free-standing and hospital-based dialysis facilities and you've talked about that a little bit. In some of the things, specifically, to hone in on the price differences and acquisition costs which you talked about, in fact, you said that the chains are cheaper. Non chains don't get the group rate, if you will. And at least anecdotally, in a congressional district like the 9th District of Missouri, those non-chains are often in rural areas.

If we were to bundle ESRD drugs in the composite rate, you think that rural areas are going to be put at risk, Mr. Vito?

Mr. VITO. Well, our work did not break out the rural areas from the urban areas. Our work did demonstrate that there was variation depending upon whether it was a chain, a non-chain or a hospital. And just to use EPO as an example, if you were a chain facility, you were able to purchase that product for $8.55.

If you were a non-chain facility, it would be 8.99. Hospitals would get it at 8.66, the average acquisition cost. Therefore, there are various pricing points. You have to be careful how you would bring that cost in, because if you would bring it in, for example, at the cost of the chain, then some of the other people will be disadvantaged, because they might not be able to purchase the drug at that price.

So, clearly, it has to be thought out very carefully and we have to go through all those ramifications when you're establishing this.

Chairman STARK. Thank you.

Mr. Becerra.

Mr. BECERRA. Thank you, Mr. Chairman. Thank you all for your testimony and let me focus first with you, Dr. Jenkins, and see if you can give me a better sense of something. Much of this has been very technical, and I suspect that for most people it's unclear what's been said and what the outcome of this hearing will be.

When the FDA made its determinations that we should try to reduce the levels that we see when it comes to the hematocrit and to try to make sure that we don't cause other consequences for the health of others being treated for the various diseases, whether it's diabetes or other things, for EPO and these other drugs. Did you all come to the conclusion that you were very certain that we need to start reducing the levels that these drugs were being prescribed at and do it quickly?

Mr. JENKINS. The decision we made was based on the data, primarily from two large studies, which in both cases were targeting hemoglobin levels higher than our labeling had recommended. And in both of those studies, one study was in patients on dialysis, the other study was on patients who were not on dialysis. Both showed an increase on adverse outcome, such as death, cardiovascular events such as heart attack stroke.

So our concern was that we did not want patients to be exposed to higher doses to get their hemoglobin to higher levels, because we had clear evidence that higher was causing worse out comes. I

think one of the major remaining questions and could really benefit from a lot more study is what is the optimal target, hemoglobin. Our labeling advises that you not go over 12.

That's based on the data we have that showed studies that went over 12 had worse outcomes than patients who were treated under 12. But I think it's still a big uncertainty from our perspective what the optimal target hemoglobin might be for patients with renal disease.

Mr. BECERRA. And you've sounded the alarm to some degree saying anything over 12 and we may start to run some ancillary risks to the patients. And, Ms. Norwalk, I hear what you're saying. As we try to treat these patients and get their various conditions under some control, we don't want to be driven so much by pricing or reimbursement rates in making those decisions about what ultimately their hemoglobin count should be, but there is a concern that if the alarm's been sounded and if we don't move quickly, we may continue to have this fairly large range under which we could see people prescribe the different drugs for the various conditions they may suffer.

So, I'm wondering if you can tell us, do you feel comfortable having heard what FDA has said that CMS is moving quickly enough to give us an accurate read on where we should be on the hemoglobin count?

Ms. NORWALK. We've done a couple of things. First, it's important to note we spend a fair amount of time talking with folks at the FDA as well as NIH and other sister agencies at the department just to make sure that we can have the most updated understanding about what their concerns are, so we can take that into account as we make policy about what's reasonable and necessary for Medicare payment, which of course is a different standard than safe and efficacious.

From the payment policy perspective, there are two things: one, the black box warning, and one of the things it focused on was cancer or the non-renal setting; and we did make some immediate adjustments. In that particular regard, what we proposed in final will be forthcoming shortly. And the ESRD setting; I do think that our revised monitoring policy, we have seen some changes in prescribing patterns for patients who have hematocrit levels that are persistently high. But still wanting to take into account the fact that physicians need to have—this is an individualized issue—physicians really do need to treat the patient and not be necessarily penalized when it's a patient issue as opposed to one of consistently doing something that may be not in the patient's best interest.

So, maybe this patient takes 6 weeks to change hematocrit levels for whatever reason, because who knows what is going on physiologically. And because of that, because their payments are monthly, wanting to take into account monthly payments as well as physiological changes and not penalize a physician who's already done the right thing, but it may not yet be seen in the hematocrit level.

So I do think that our payment policy is where it needs to be, and we will continue to monitor it over time and make adjustments if these changes haven't brought down the hematocrit levels to the point where they would be more in the range of the FDA label.

Mr. BECERRA. And I hope we are able to get some clear movement on this, because for someone who's asking very pedestrian questions and still is trying to understand that's being said, I know that we do have to try to find savings, and I know we don't want to extract them at the expense of letting patients get the treatment they need. But now you have the FDA weighing in. So I'm hoping that at some point those who are the experts who understand this well, medically, technically, can give us some answers that make us feel comfortable that we can proceed quickly and that CMS can move as quickly as possible to give us what we ultimately want, which is a good reimbursement rate for those providing a very quality service to our patients.

Ms. NORWALK. Agreed.

Mr. BECERRA. Thank you. I yield back, Mr. Chairman.

Chairman STARK. Ms. Tubbs Jones?

Ms. TUBBS JONES. Mr. Chairman, thank you. To the panel, good afternoon. Well, good morning, still. And to the next panel, I've got to go be speaker pro tem, so I'm going to miss you.

But I have in my hand a statement from a Dr. Peter D'Orio, who is from Cleveland Ohio, my congressional district. Having practiced internal medicine and nephrology for 27 years, he serves as medical director for dialysis facility for centers for dialysis care, nonprofit. But this is his statement. Additionally, results from Oncology trials have raised safety questions about dosing and hemoglobin targets. While none of these trials included dialysis patients, these results have also been applied to the question of managing renal anemia. None of these studies showed any harm to dialysis patients treated to the currently accepted target range, but none of these studies show any benefit, however, from treating patients to targets over 13.

The recent FDA revision and imposition of a black box warning causes serious problems for practicing nephrologists. If we are to interpret them literally, we are allowed to use ESAs only for the purpose of preventing transfusion. None of us would use blood transfusions to support the same hemoglobin ranges that we can achieve with ESAs. Would you agree or disagree, Ms. Norwalk, with that statement; Dr. Jenkins with that statement?

Ms. NORWALK. One of the things that we've done at CMS is differentiate our payment policy on the basis, at least from a coverage decision, non-renal and renal. So, if your constituent is saying what I would be willing to bet my nephrologist, who is our chief medical officer, would agree with, there in fact are differences in treating those who are non-renal, i.e. cancer patients versus who are in ESRD. And we have taken those into account at CMS and do think those distinctions may be important, particularly given the duration of treatment. If you have anemia due to cancer treatment, you would use ESAs for a much shorter time period than you would if you are an ESRD patient.

Ms. TUBBS JONES. Dr. Jenkins?

Mr. JENKINS. We recognize that there are significant differences in the use of ESAs for cancer patients versus in-stage renal disease patients. We've heard some of the same comments that you just read in that letter when we met with some of the renal physician societies and patient groups, and some of the dialy-

sis providers a couple of months ago. And we are considering whether we should modify some of the language and are labeling to make some technical adjustments to avoid misunderstandings.

For example, we recognize that it's impossible to always maintain every patient at 12 or below, given the variability of response and the other factors. So the fact that someone might occasionally have readings that are over 12, we didn't intend to imply that that was evidence that, you know, something was being done incorrectly. So, we've heard those comments and were considering whether to make adjustments. And we also have the cardiorenal advisory Committee coming up later this Summer to discuss some of these issues as well.

Ms. TUBBS JONES. Mr. Vito, I didn't mean to leave you out, but I just thought the answer was better directed to Ms. Norwalk and to Dr. Jenkins. I'm going to yield my time, because I have to get to the floor. But I just want to say for the record, this is an issue that is of paramount importance to a whole lot of people, people that are patients, the physicians rendering the service, the people who run the dialysis center, the people who make the medication, and on, and on, and on. And all I want to lay on the table is caution that as we proceed down this road that we make sure that we have the best information we can with regard to making decisions so the people out there are getting the best service.

My time's up anyway. I thank you very much for the opportunity, Mr. Chair. I give you 30 seconds back.

Chairman STARK. Thank you. Mr. Pomeroy, want to use up those 30 seconds?

Mr. POMEROY. Thank you, Mr. Chairman. I really don't know much about the subject of today's hearings, so I found this discussion quite interesting. And so, Mr. Vito, if we get back to the figures you talked to Mr. Hulshof about, the procurement costs between the chains, the non-chains, and the hospitals, you have figures. What are they?

Mr. VITO. Okay, yes, we have the actual or the average acquisition cost as we calculated it. At the chain facilities for EPO, it was 8.55. At the non-chain, free-standing facilities, it was $8.99. And at the hospitals it was $8.66.

Mr. POMEROY. That's just basically volume purchasing?

Mr. VITO. I believe that the rebates, the chains started out with the higher price from the manufacturers, but got greater rebates to bring their prices lower than the non-chains.

Mr. POMEROY. The reimbursement rate is under the reformulation about $9.10?

Mr. VITO. When we did our review, it was $9.48. I believe that they're changing the reimbursement to make it $9.10.

Mr. POMEROY. When is that? Has that occurred? Is it occurring?

Ms. NORWALK. It's implemented for July 1st. So those are the rates we announced June 15 for July 1.

Mr. POMEROY. At the earlier rate of reimbursement, or the present rate of reimbursement before its upcoming change, was there differential in practice patterns indicating some kind of differential application of people?

Ms. NORWALK. Well, certainly, one of the things that happened in preparing for this hearing is that I saw what the NIH submitted. So, I do think there are some variations and practice patterns, at least according to the NIH review of the U.S. RDS.

Mr. POMEROY. And were those practice patterns subject to groupings, chain, non-chain hospital?

Ms. NORWALK. At least, I think what the U.S. RDS reviewed is more chain specifically. So that's my recollection of their letter to the chairman. I would not be surprised, of course, if there are differences in some of these settings, hospital versus non-hospital. We see them occasionally, but the question is whether or not our revised payment policies can ensure that all of them are dosing at the appropriate amounts over time, and we can take into account differences in acquisition costs through a single reimbursement mechanism.

So part of the concern and part of the reason that we're grateful that the OIG has done this study is focusing on making sure that all of the people who provide ESAs, we can reimburse something at least slightly above their acquisition cost, so they can acquire the ESA. I think the Medicare Modernization Act focused on having the OIG do the study on the average acquisition cost, but it's not practical for CMS to implement that over time.

And so we used an average sales price. And what we're seeing is that the average sales price plus 6 percent has actually come down over time and now looks more like what the OIG focused on in terms of their review of third quarter '06 data. So I don't know if that makes sense, but the conception is corporate.

Mr. POMEROY. So, your take is they probably got the cost figures about right, chain, non-chain, hospital.

Ms. NORWALK. Yes, we have no reason to disagree with that analysis. Correct.

Mr. POMEROY. Do you believe that the $9.10 rate is going to make these differentials in application less likely?

Ms. NORWALK. It really depends on whether or not the average sales price and what the manufacturers or those who are marketing the product, whether it's AmGen or Johnson & Johnson, how much they're selling and what rebates and discounts. Now, rebates and discounts are included in the definition of average sales price, so we take that into account. The question is, whether or not those mixes change from one quarter to the next.

Another thing that happened that may have an impact here is also for July 1st, and we've included the use of these products in both settings. So we'll both have the cancer setting as well as ESRD. And this is a change that will have just occurred on July 1, which may have had some impact and some reason for bringing that price down to 9.10. So, not exactly sure how that might impact the average sales price in the future, but at least for the next quarter, it does have an impact of bringing that down a bit. And we did that implementing section 1847(a), the statute in terms of bundling those two different treatment types together.

Mr. POMEROY. I would conclude, Mr. Chairman, by observing—I wish we had more information. The information you're going to bring to us is going to be very important, I think, given the policy considerations before the Subcommittee. Thank you.

Chairman STARK. Thank you. I wanted to just follow-up on this issue of payment. Mr. Vito raised it for non-chains who may very well be the smaller or the hospitals.

Ms. Norwalk, you're familiar with the argument that's been proposed that we dare not use the Federal supply schedule, the VA's purchasing program to purchase pharmaceuticals, because the pharmaceutical companies will all hold their breath, turn blue and die and go away. However, where you have one supplier and one customer, we're the customer and AmGen is the supplier.

I suspect that that argument wouldn't hold if we said to the supplier of EPO, you got to sell to everybody at the same price. We're talking 8.55 to 8.99, so if we said, if you're going to sell to the big chains at 8.55, you ought to sell to the smaller providers at that same price to give them some additional margin to stay in business.

Other than the idea of not liking price regulation, but I don't believe the arguments on setting prices for other pharmaceuticals would hold if we did something to protect the smaller providers or the rural providers.

Ms. NORWALK. I have to think about that. Certainly typically that argument has come up in the Part D setting and I do think the VA system and the Medicare system under Part D are vastly different. So there are reasons there for this. I'd have to give it a little more thought. I do think, ultimately, that there will be other drugs that come to market as these patents expire. So this is not a long-term issue. This is more likely to be in terms of how short-term, I have to check the patents; it probably depends in fact on litigation. But I do think that over time this will not be an issue that we're currently seeing. I'm not sure that we would want to put something in statute that would perpetuate something that the market can take care of later.

Chairman STARK. Okay, a couple of questions very quickly, if I may, with Dr. Jenkins.

AmGen will argue that research for pre-dialysis patients can't be used to extrapolate the dialysis patients. How do you respond to the argument that research for pre-dialysis patients can't be applied?

Mr. JENKINS. Mr. Chairman, we understand that there are significant differences in the care and the physiology of patients who have in-stage renal disease who require dialysis, and those who are not on dialysis. I would just point out that as I mentioned earlier, there are two large studies. One that was reported in 1996 that was in dialysis patients and one that was reported last year, and non-dialysis patients, both of which raised concerns about adverse outcomes when they were treated to hemoglobin levels above 12.

So that's why our labeling and our blocks warning addresses both to groups of patients recommending that you not target hemoglobins to those high levels.

Chairman STARK. AmGen will also argue that there was a study for better health outcomes from trying to reach the hematocrit levels of a normal, healthy adult, and this AmGen argued that the research is not relevant because it was cut short. So I understand it was cut short for ethical reasons. Is it appropriate to use

this research in guiding decisions about health risks? And would it be appropriate to recreate this study?

Mr. JENKINS. Mr. Chairman, I'm not sure I'd know which study you might be referring to. Do you have any additional information?

Chairman STARK. All I have to reference here is the normal hematocritic study tested whether there was better health outcomes for dialysis patients in trying to reach the hematocrit levels of a normal, healthy adult.

Mr. JENKINS. Right, right. Okay, I do know about that study. That's the study that was reported in 1996. That study was intended to try to show that higher levels of hemoglobin or hematocrit were better and actually improved outcomes such as heart attack, stroke. In fact, that study was stopped early. It was stopped technically for what was called futility, meaning they could not show that higher was better. Our interpretation though is that there was asignificant worrisome trend that higher was worse. And that's why it was added to the labeling in 1996 to state that the mortality, the death rate in people treated with the higher levels of hemoglobin was higher than those treated at the lower level. So we do find that study to be informative, even though it was stopped early.

Chairman STARK. Okay, and then there's an issue about quality of life and higher hemoglobin levels. Now, as I interpret that as a lay person, if you stoke me up with this stuff and I get way above 12, I'm going to feel great, but I may die.

[Laughter.]

Chairman STARK. It's like my mother wouldn't have the cancer operation. She said, "As long as they don't run out of morphine, I ain't going to be operated on." Now, the quality of life from her standpoint is probably pretty good, never so good in her life. But, it did her in, finally.

How do you assess this quality of life issue, I guess it's a doctor's responsibility to make damn sure that the patient knows that overdosing might make him feel better, but also might kill him. How does that wash?

Mr. JENKINS. Well, Mr. Chairman, it's important to go back and recall that the basis on which we approve these drugs for use on patients with chronic renal failure was that it decreased the need for transfusions. Before these drugs were available, it was not uncommon for dialysis patients to have hemoglobins of 6, 7, 8, and be symptomatic from their anemia.

In the studies that led to the approval, there was not an attempt to bring the hemoglobin or hematocrit back to normal. In fact, most of those studies brought the hemoglobin back up to 10, 11, and 12. And in those studies, we did see improvements in some of the measures are referred to as quality of life. And that information is in the Procrit and Epogen labeling. I don't know that we have evidence that treating to 12, 13, 14 has been shown to improve quality of life above and beyond treating to 10, 11, 12.

There is a point at which anemia is asymptomatic. You have the abnormal lab value, but you may not be symptomatic of the fact that your hemoglobin is below the normal range. So, our view is that there has been evidence shown in renal failure patients that bringing hematocrit up improves those measures and it's in the la-

beling. But I don't think we have seen any data suggests that going above the current target of 12 further improves those quality of life measures.

Chairman STARK. Thank you. If there are no further questions of the panel, I want to thank the panel very much for your enlightenment this morning. And we'll call the third panel.

Chairman STARK. I want to welcome Dr. A.J. Singh, Clinical Director of the Renal Division, Director of Dialysis Services and Associate Professor of Medicine at Brigham and Women's Hospital, Boston, Massachusetts;

Mr. Kris Robinson, Executive Director and CEO, the American Association of Kidney Patients from Tampa Florida; and

Dr. Alan Kliger, President of the Renal Physicians Association, Rockville, Maryland.

Thank you for your patience. If you'd like to summarize your written testimony as previous witnesses have, your written testimony will appear in the record without objection.

Dr. Singh, would you like to start?

STATEMENT OF AJAY K. SINGH, M.D., CLINICAL DIRECTOR, RENAL DIVISION, DIRECTOR, DIALYSIS SERVICES, ASSOCIATE PROFESSOR OF MEDICINE, BRIGHAM AND WOMEN'S HOSPITAL, BOSTON, MASSACHUSETTS

Dr. SINGH. Thank you Chairman Stark, Mr. Camp and Members of the Subcommittee on Health for the privilege of being asked to testify. My testimony will address three issues. The first is the target hemoglobin in patients with kidney disease.

Chairman STARK. Excuse me just a minute. Could I get, if you could pull the mike there. The sound system is very 20th century here. Thank you.

Dr. SINGH. My testimony will address three issues. First, the target hemoglobin in patients with kidney disease; second, the extensive off-label use and over utilization of reported in the United States, and three, thoughts on bundling of ES30 services. With respect to the target hemoglobin concentration in patients with kidney disease, I fully support the recent FDA box advisory that a hemoglobin level should be maintained to less than 12 grams per deciliter.

Randomized control studies have shown both in dialysis patients and in non-dialysis patients that this is a prudent recommendation. Indeed, the normal hematocrit study that Dr. Jenkins has already discussed was published in 1998 in the New England Journal of Medicine, and at the time, and I have a quite from that study. The study was halted when differences in mortality between the groups is the dialysis patients were recognized, sufficient to make it very unlikely that the continuation of the study would reveal a benefit. And the results were nearing the statistical boundary of higher mortality.

So clearly both in the non-dialysis patient population and in the dialysis population, increased risk has been demonstrated. In our own study in the choir study, published in November of 2006, we not only demonstrated a 34 percent higher risk of death and cardiovascular complications, but also a 48 percent higher rate of death among those treated or targeted to a higher hemoglobin.

We also found that there was no incremental benefit in quality of life. Since the publication of these studies, the National Kidney Foundation, Kadokey panel will state in revised guidelines that the target hemoglobin should generally be 11 to 12 grams per deciliter, a recommendation which I think would be compatible with the FDA. It's reassuring that the FDA has recommended caution in using ESAs, but past experience both with respect to this issue and with other drugs teaches us the powerful factors can stimulate continued and even increased off-label use of drugs. I would like to refer to the study by Dr. Cotter's group published in German, which document overuse of Epoetin in for-profit dialysis chains as compared to not-for-profit chains. And I think there are potentially several explanations for this off-label overuse of Epoetin that's generated much higher doses be used.

First, flaws in the current CMS reimbursement system. The new reimbursement schedule launched in April 2006 in fact facilitates over utilization of Epoetin. In our own dialysis chain, DCI, when we looked at data from prior to the Medicare changes and compared them to the more recent schedule, we found that the proportion of patients with higher hemoglobin values, above 13 grams, actually increased. And I was interested to hear Ms. Norwalk's testimony that in fact supported this at a more general level.

We also have some data that will be published soon that suggests that the current CMS reinvestment system facilitate over utilization of hemoglobin above the FDA recommended level and higher Epoetin use. Second, I think another explanation for this over utilization is the use of standing orders that are based on corporate guidelines in dialysis facilities.

Chairman Stark, you stated a Davita protocol, which actually recommends changes that Dr. Jenkins from the FDA didn't think were compatible with their recommendations. In other words, reductions that were less aggressive than the FDA would consider to be compatible with their recommendations. There's also marketing and rebate activities by pharmaceutical providers in driving off label use, which I won't go into details about. But it's certainly very present in the current marketplace.

The other issue is with regards to ESA reimbursement is that the current reimbursement system facilitates over utilization, and therefore I would recommend and fully support the notion of bundling. I believe bundling of drugs such as ESAs will remove incentives for overtreatment. It will reduce the escalating cost for injectible drugs. It will encourage the use of subcutaneous administration of Epoetin, a practice which is widely utilized in the veteran administration system in Kaiser, and is certainly the case in Canada and other European countries.

I believe that the Kaiser experience with ESRD bundling is really a live demonstration project, and I do agree with Ms. Norwalk that I do not necessarily see the need to actually have another demonstration project. We can learn a lot from Kaiser's system where they in fact do bundle and contract with for-profit dialysis providers and there's large-scale use of subcutaneous Epoetin.

And, finally, I believe that if bundling takes some time, CMS should modify its reimbursement policy so that the current over

utilization that has accrued since and higher hemoglobin levels above 39 that have occurred since April 2006 gets corrected.

I want to thank the Chair and Members of the Committee for listening to my testimony.

[The prepared statement of Dr. Singh follows:]

Statement of Ajay K. Singh, M.D., Clinical Director, Renal Division, Director, Dialysis Services, Associate Professor of Medicine, Brigham and Women's Hospital, Boston, Massachusetts

This testimony addresses 3 issues*:*

1.) The Optimal Target Hemoglobin In Patients with Kidney Disease

2.) The Extensive Off-Label Use and Over-Utilization of Epoetin in the United States

3.) Bundling of ESRD services

The Optimal Hemoglobin Concentration in patients with kidney disease.

• I fully support the recent FDA Black Box Advisory[1] that the hemoglobin level should be no higher than 12 grams per deciliter. Randomized controlled studies (RCTs), both in dialysis and in predialysis patients, demonstrate an increased risk of cardiovascular complications and death in patients targeted to a hemoglobin level that exceeds 12 grams per deciliter. In dialysis patients this was demonstrated in the Normal Hematocrit Study, published in 1998,[2] and in non-dialysis CKD patients, this was demonstrated in the CHOIR study, published by us in 2006[3] The CREATE study[4] reinforced the findings from CHOIR.

• Randomized controlled studies are superior to retrospective observational studies. While these retrospective studies have suggested benefit for cardiovascular outcomes or survival with targeting of a higher hemoglobin concentration, they are confounded by co-morbid factors and illness[5] Continuing to cite these studies without providing RCT's contextually, as companies have continued to do is unnecessary, generates confusion, and undermines the FDA's strong safety message embodied in its Black Box advisory[6]

• Aiming for and achieving a hemoglobin concentration in a narrow band of 11 to 12 g/dL may only be possible in approximately 2 out of every 3 patients. As I have discussed elsewhere, expanding the target range to 10 to 12 g/dL seems not only prudent but also practical. This approach is prudent because of the safety concerns with hemoglobin concentrations greater than 12 g/dL as suggested by the RCT's and further reinforced by a recent meta-analysis published in the Lancet.[7] This Lancet analysis aggregated studies of patients with kidney disease, whether on dialysis or not, and demonstrated a 17% increased risk of death with targeting a hemoglobin concentration of greater than 12 g/dl. While I agree with the notion that the target hemoglobin concentration level should b individualized based on patient need, in general, expanding the range to aim for a hemoglobin concentration greater than 10 g/dL but less than 12 g/dL should not result in a higher rate of blood transfusion, nor should it result in a worsening in quality of life.

• We should accept that the proven benefit of erythropoetic stimulating agent (ESA) therapy is in preventing blood transfusions. Although, the FDA has recently

---

[1] www.fda.gov/cder/drug/advisory/RHE2007.htm.

[2] Besarab A, Bolton WK, Browne JK, Egrie JC, Nissenson AR, Okamoto DM, Schwab SJ, Goodkin DA. 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. 1998 Aug 27;339(9):584–90.

[3] Singh AK, Szczech L, Tang KL, Barnhart H, Sapp S, Wolfson M, Reddan D; CHOIR Investigators. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006 Nov 16;355(20):2085–98

[4] Drueke TB, Locatelli F, Clyne N, Eckardt KU, Macdougall IC, Tsakiris D, Burger HU, Scherhag A; CREATE Investigators. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. N Engl J Med. 2006 Nov 16;355(20):2071–84

[5] Regidor DL, Kopple JD, Kovesdy CP, et al. Associations between changes in hemoglobin and administered erythropoiesis-stimulating agent and survival in hemodialysis patients. *J Am Soc Nephrol.* Apr 2006;17(4):1181–1191.

[6] http://www.anemia.org/professionals/resources/slides/

[7] Phrommintikul A, Haas SJ, Elsik M, Klum H. Mortality and target haemoglobin concentrations in anemia patients with chronic kidney disease treated with erythropoietin: a meta-analysis. Lancet 2007; 369:381–88

pointed out that blood transfusions are much safer than ever before[8] chronic kidney disease patients benefit from transfusions because of the avoidance of antibody sensitization (the latter decreases the likelihood of kidney transplant eligibility) and in reducing the risk of iron overload. Therefore, I continue to believe strongly that ESA treatment should be used to minimize the risk for blood transfusions; however, expanding the target hemoglobin range from 11 to 12 g/dL to 10 to 12 g/dL is reasonable, and should not meaningfully increase the proportion of patients requiring blood transfusion. On the other hand, quality of life benefits of a higher hemoglobin concentration are, at best, inconsistent. Studies have been dogged by methodologic issues, open label design, and the variable use and reporting of quality of life instruments. The CHOIR study showed no incremental benefit in quality in life with targeting a higher hemoglobin concentration and showed an increase in adverse events and complications.

• The FDA issued a Black Box for all ESA's because of RCT data in kidney disease patients and because of emerging data from studies in cancer patients that suggested increased risk. The National Kidney Foundation (NKF) Kidney Disease Quality Initiative (KDOQI), in newly updated guidelines will also state that the target hemoglobin concentration in patients with kidney disease should generally be 11 to 12 g/dL.

• It is reassuring that the FDA, empowered with evaluating the efficacy and safety of drugs in the United States, has recommended caution in using ESA treatment. However, past experience both with respect to this issue and with other drugs teaches us that power factors can stimulate continued and even increased off-label use of drugs. Every effort should be made to avoid continued off-label use of ESA's. Minimizing off-label use of ESA's will not only reduce CMS expenditure but will also be beneficial to ESRD beneficiaries and CKD patients collectively by reducing risk of higher hemoglobin concentrations and possibly higher doses of ESAs.

2) The Extensive Off-Label Use and Over-Utilization of Epoetin in the United States

• As a recent New York Times Editorial,[9] as well as articles by others[10], has pointed out, trends in ESA utilization illustrate much that is wrong with reimbursement of ESAs. Off-label use of ESAs, and its over-utilization, are common-place and largely driven by flawed reimbursement, rebates, and over-zealous marketing of the drug.

• In 1998, approximately 10% of patients had hemoglobin levels that exceeded 12 g/L, whereas by 2000 this had rapidly grown to 40% of all dialysis patients. Surprisingly, this steep increase in average hemoglobin levels occurred after the publication in 1998 of the Normal Hematocrit Study (NHS) showing a higher risk of death or myocardial infarction in aiming for a hematocrit of 42%. The authors of NHS indicated that concerns regarding excess mortality precipitated the decision to prematurely terminate the study.[11] Two years before the publication of NHS—in 1996—the FDA added a new subsection in the Warnings section in the label of epoetin regarding higher mortality with hemoglobin levels of 12 to 140 g/L in patients with chronic renal failure (reviewed most recently at an FDA oncology advisory committee meeting). The steep increase in hemoglobin levels from 1996 onwards, coupled with a 50% increase in the average epoetin dose administered to dialysis patients during this time, needs to be further scrutinized.

• The study by Thamer and co-workers documents the overuse of epoetin in for-profit dialysis chains as compared to not-for profit chains, with for-profit facilities administering roughly a third more units of epoetin per week. Indeed, the for-profit chain DaVita utilized higher doses of epoetin at both lower and higher hemoglobin levels. Thamer and colleagues also confirmed an earlier observation that for-profit chains especially DaVita had a higher proportion of their patients achieving hemoglobin levels greater than 12 g/dL when compared to the non-profit chain DCI.

• **There are several potential explanations for the Off-Label Overuse of Epoetin.**

• **Pervasive incentives for ESA Overuse in current CMS reimbursement guidelines.** The current CMS reimbursement schedule, launched April 2006, facili-

[8] www.fda.gov/OHRMS/DOCKETS/AC/07/briefing/2007-4301b2-02-FDA.pdf

[9] New York Times, May 14, 2007 Late Edition—Final, Section A, Page 18, Column 1

[10] Marlene Busko Is Medicare Reimbursement Policy for Erythropoietin in ESRD Flawed? http//www.medscape.com/viewarticle/550594

[11] The NHS study was stopped because: "Our study was halted when differences in mortality between the groups were recognized as sufficient to make it very unlikely that continuation of the study would reveal a benefit for the normal-hematocrit group and the results were nearing the statistical boundary of a higher mortality rate in the normal hematocrit group".

tates over-utilization of epoetin [12] In work that has been submitted for publication, we assessed the impact of the change in CMS guidelines on hemoglobin levels and EPO usage in DCI, the largest not-for-profit dialysis chain in the United States. We evaluated [13] the effect of a new protocol implemented on May 1, 2006 to reflect the CMS policy change. We found that reducing rather than discontinuing epoetin supplementation at hemoglobin > 13 g/dL (the current CMS reimbursement schedule) was associated with a significantly greater proportion of hemodialysis patients at higher hemoglobin levels, higher cumulative epoetin use, and had no effect on the number of individuals with lower hemoglobin levels. Given recent studies that have demonstrated potential harm with higher hemoglobin targets, our study suggests that discontinuation rather than reduction of epoetin is appropriate when hemoglobin reaches 13 g/dL.

• **The use of anemia protocols by dialysis providers and facilities.** Administration of epoetin to patients at dialysis has both a facility and a physician component. Dialysis facilities have centralized corporate committees that formulate an anemia algorithm. This algorithm defines anemia targets and formulates epoetin and hemogklobin measurement orders that are instituted as part of the patient's standing orders. In addition, in many dialysis facilities, the dialysis facility has a designated employee who oversees anemia. In most facilities this is a nurse who evaluates the hemoglobin and iron values of individual patients, supervises the epogen over-fill utilization program, and ensures patient's compliance with the anemia protocol. The dialysis facility also expects the medical director, who receives a stipend or medical director fee from the dialysis facility, to ensure adherence to the anemia goals of the facility and of the dialysis chain. Individual dialysis physicians can and sometimes do over-ride the standing orders of the dialysis facility since they are ultimately responsible for the treatment of the patient under their care. Dialysis chains vary by the extent to which they provide autonomy to their medical directors and treating dialysis physicians in regard to the anemia protocol. The more aggressive dosing of epoetin recommended by DaVita is the likely explanation for the over-utilization of epoetin in the DaVita chain as compared to DCI. For example, a corporate DaVita anemia protocol dated February 2007, recommends only a 10% reduction in epoeitin dose for hemoglobin concentration greater than 13.1 g/dl and less than 14 g/dL (and a dose reduction of 25% for hemoglobin concentration greater than 13.1 g/dl and less than 14 g/dL). In contrast, DCI recommends and immediate decrease in epoetin by 25% when the hemoglobin concentration exceeds 13 g/dL. In our own dialysis unit in Boston, we discontinue epoetin when the hemoglobin exceeds 12 g/dl. Since these anemia goals and epoetin dosing recommendations are protocolized and managed by the facility, the current structure of anemia management in dialysis chains is a powerful driver for off-label use of epoetin and over-utilization of epoetin.

• **Marketing and Rebate Activities by Pharmaceutical providers in driving Off-Label use.** The pervasive effect of marketing and rebates to physicians have driven physician off-label use of ESAs. This is supported by recent press articles in both the New York Times [14] and the Wall Street Journal [15] and the British Medical Journal [16] This is currently being investigated by the Senate Committee on Finance [17] This has been discussed extensively in the scientific literature with regards to the promotion of gabapentin [18] The influence of marketing activities on molding opinions about epoetin use is also concerning and has also been brought to light [19]

---

[12] Cotter D, Thamer M, Narasimhan K, ZhangY, Bullock K Translating Epoetin Research Into Practice: The Role Of Government And The Use Of Scientific Evidence. Health Affairs, 25, no. 5 (2006): 1249–1259

[13] Weiner DE, Miskulin DC, Seefeld K, Ladik V, Zager PG, Singh AK, Johnson HK, Meyer KB: Erythropoietin Use and Hemoglobin before and after 2006 Changes in Medicare Reimbursement Guidelines. 2007. Submitted for publication

[14] Alex Berenson and Andrew Pollack, "Doctors Reap Millions for Anemia Drugs" The New York Times, May 9, 2007

[15] Heather Won Tesoriero and Avery Johnson, 'Suit Details How J&J Pushed Sales of Procrit, Wall Street Journal, May 10, 2007

[16] Tonks A. Too much of a good thing. *BMJ*. 2007 May 12;334(7601):978–80. Singh AK: Marketing Epoetin: Too Much of a Good Thing. http://www.bmj.com/cgi/eletters/334/7601/978

[17] http://www.google.com/search?q=epogen+rebates+2007&hl=en&start=20&sa=N

[18] Steinman MA, Bero LA, Chren MM, Landefeld CS. Narrative review: the promotion of gabapentin: an analysis of internal industry documents. Ann Intern Med. 2006 Aug 15;145(4):284–93. (Letters and Response Ann Intern Med. 2007 Feb 20;146(4):313; author reply 313–4.)

[19] Dyer O. Journal rejects article after objections from marketing department. BMJ. 2004 Jan 31;328(7434):244.

• **The limited use of subcutaneous epoetin in dialysis chains in the United States** Evidence shows that approximately ⅓ less epoetin is used when it is administered subcutaneously (SC) as compared to the IV route[20] The SC dosing is certainly commercially less attractive and will influence profits for both pharma and dialysis providers. However, it will save the CMS substantial amounts of money because cumulative epoetin doses will be lower. The saving is likely to be in the range of 500 million or more. While some have argued that it is less convenient to patients and provider this issue does not seem to have adversely affected the VA population or those insured by Kaiser or for that matter thousands of patients in Canada and Europe. As well the use of lower doses of epoetin if given SC could be important if high doses of epoetin are shown to be associated with worse outcomes.

3) Bundling of injectibles, including ESAs, by including its reimbursement into the ESRD composite reate should be adopted.

• **Bundle of injectible drugs into the reimbursement of the dialysis procedure, i.e., into the composite rate offers several benefits and should be adopted.**

a.) It removes incentives for over-treatment—aiming for higher hemoglobin levels using higher and higher doses of epoetin.

b.) It will reduce the escalating costs for injectible drugs, particularly ESAs, in the treatment of dialysis patients.

c.) It will encourage the use of subcutaneous administration of epoetin—a practice widely used in Europe, Canada, and in the VA system.

d.) This should facilitate lower doses of ESAs in the treatment of anemia.

• **Utilize the Kaiser Experience with ESRD Bundling.** As I have pointed out elsewhere,[21] the Kaiser Permanente system provides an accessible and functioning model of ESRD bundling. This system functions without risk adjustment of payments and has resulted in largescale use of subcutaneous epoetin administration.

• **In the near-term, CMS should modify its reimbursement policy**. This will be important in reducing epoetin over-utilization and to conform more robustly with the FDA Black Box Advisory. Indeed, CMS has done this with reimbursement of the oncology indications for epoetin therapy.

Summary

I recommend that the importance of following the FDA Black Box for epoetin in the treatment of anemia of kidney disease should be followed.

a.) The hemoglobin target should be less than 12 grams per deciliter.

b.) The extensive off-label use of epoetin and its overutilization requires greater scrutiny.

c.) Medicare should modify its reimbursement policy to adopt a bundled reimbursement approach. This will, at least in part, remove the incentive for higher epoetin use, increase subcutaneous administration of epoetin, and restrain spending on ESAs.

Chairman STARK. Thank you.

Ms. Robinson.

STATEMENT OF KRIS ROBINSON, EXECUTIVE DIRECTOR AND CEO, AMERICAN ASSOCIATION OF KIDNEY PATIENTS, TAMPA, FLORIDA

Ms. ROBINSON. Thank you, Mr. Chairman, and Members of the Committee for inviting me here to testify. My name is Kris Robinson and I am the Executive Director and CEO of the American Association of Kidney Patients. AAKP is the only national, non-profit

---

[20] (a. Kaufman JS, Reda DJ, Fye CL, Goldfarb DS, Henderson WG, Kleinman JG, Vaamonde CA. Subcutaneous compared with intravenous epoetin in patients receiving hemodialysis. Department of Veterans Affairs Cooperative Study Group on Erythropoietin in Hemodialysis Patients. N Engl J Med. 1998 Aug 27;339(9):578–83. b. Parker KP, Mitch WE, Stivelman JC, Macon EJ, Bailey JL, Sands JM. Safety and efficacy of low-dose subcutaneous erythropoietin in hemodialysis patients. J Am Soc Nephrol. 1997 Feb;8(2):288–93. c. Kaufman JS. Subcutaneous erythropoietin therapy: efficacy and economic implications. Am J Kidney Dis. 1998 Dec;32(6 Suppl 4):S147–51.

[21] Singh AK et al Letter to JAMA. 2007. In press.

organization founded and directed by kidney patients for kidney patients. Our organization is dedicated to serving the needs and interests and welfare of all kidney patients and their families. And this is the very reason I am here before you today.

In 1971, our organization's then Vice President, Shep Glazer, made history here in the House Ways and Means Committee Room, testifying while he was actually hooked up to a kidney dialysis machine and receiving dialysis. Within a year, our government took action, passing landmark legislation in 1972 to cover the cost of kidney dialysis through Medicare.

As a kidney transplant recipient myself, I am well aware of the human and financial cost of kidney care. Let me begin by stressing how important it is to get the dosing of ESA's right for kidney patients. AAKP supports achieving a hemoglobin level of 11 to 12 grams per deciliter, as indicated by the FDA label for ESAs. We view current CMS monitoring policy as somewhat out-of-sync with where the FDA is and where the mainstream medical community is.

Although each case is different from a patient perspective, there is very little medical reason for a patient to remain at levels above 13 grams, especially in light of the current literature citing safety issues. I myself receive Epogen for anemia, and my doctor would not delay before titrating me down from a level of 13.

AAKP strongly adheres to the principal that a physician and patient must be permitted to decide a care plan best suited for that patient. Separate Medicare reimbursement for ESAs potentially distracts from the doctor/patient decisionmaking relationship. So we support bundling Medicare reimbursment for ESAs into the overall Medicare reimbursement rate. We believe that bundling the payment would not only result in cost savings, but also result in more appropriate dosing of ESAs and draw more attention to the comprehensive nature of kidney care.

Let me emphasize that underdosing of ESAs is a danger too. Many kidney patients remember the difficult times before the ESAs were available, suffering the debilitating fatigue associated with anemia. We don't want to scare patients away from being treated with this valuable life-enhancing medication. Nor would we want to create a perverse incentive that causes providers to skimp on doses of ESAs because they would no longer be receiving separate reimbursement.

What we need is a Medicare policy that strives for a goldilocks solution to ESAs; not too much; not too little; but just right. So we believe Congress should 1) establish guidelines regarding the proper dosage of ESAs, and 2) link reimbursement to meeting those guidelines. Let me say just a few words about potential subcutaneous administration.

We surveyed 3700 patients about "subcut" administration of Epoe and found that patients are very willing to do "subcut". An overwhelming majority of patients told us they wouldn't mind getting an Epoe shot and even giving themselves the shot. Many of these patients are already receiving administration shots because of diabetes.

Mr. Chairman, let me briefly mention three quality recommendations and not that I have included others as well in my written

statement. First, we strongly support legislation that would extend Medicare coverage to patient education services and would allow patient education for predialysis patients. The earlier we can start educating patients regarding behavior, nutrition and other matters in their stages of chronic kidney disease, the fewer health problems will result later.

Second, there is currently no standard for training and certification of technicians in the centers. Some states, like Texas, have strong standards they must meet. Other states, like my home state of Florida, have none at all. AAKP would like to see standard training requirements that at least set a minimum for dialysis technician training.

Finally, some patients choose the option of daily home dialysis, which can be administered six times a week for 2 hours a day. Unfortunately, Medicare will cover three dialysis sessions per week. If Medicare were to cover more frequent home dialysis, patients would have better outcomes and we believe there would be a cost savings to the program. Home dialysis patients use one-third less hospitalization; one-third less EPO; one-third less hypertension medicine, and more of them can stay in the workforce.

Mr. Chairman, we applaud your leadership over the years on these issues that are so important to us as kidney patients. We offer ourselves as a resource to you as your Subcommittee works on these issues.

Thank you and I look forward to responding to your questions.

[The prepared statement of Ms. Robinson follows:]

Statement of Kris Robinson, Executive Director and CEO, American Association of Kidney Patients, Tampa, Florida

Mr. Chairman, Ranking Member Camp, and members of the Committee, thank you for inviting me before you today to testify. My name is Kris Robinson and I am the Executive Director and CEO of the American Association of Kidney Patients (AAKP) headquartered in Tampa, Florida.

AAKP is the only national non-profit organization founded by kidney patients, for kidney patients. AAKP serves over one million Americans annually who have either lost kidney function (and live with dialysis or transplant) or have chronic kidney disease (CKD). Our organization is dedicated to serving the needs, interests, and welfare of all kidney patients and their families.

And this is the very reason I am here before you today. It was 36 years ago, in 1971, when our organization's Vice-President, Shep Glazer, made history here in the House Ways and Means Committee Room *testifying while he was actually hooked up to a kidney dialysis machine and receiving dialysis*. Within a year our government took action, passing landmark legislation in 1972 to cover the costs of kidney dialysis through Medicare.

Mr. Chairman, we thank you for holding this important hearing because, as you know, the government's policies towards kidney care today have room for improvement. As a kidney transplant recipient myself, I am well aware of the human and financial cost of kidney care. Our nation has the unique opportunity to provide better outcomes for kidney patients—and this can lead to substantial cost savings because better outcomes translate into less reliance on the drugs, dialysis, and hospitalization currently covered by Medicare.

I want to begin by addressing issues regarding anemia management for kidney patients and then also raise several quality improvement recommendations for your Subcommittee's consideration.

Appropriate Use of ESAs

Let me first stress how important it is to get the dosing of ESAs (erythropoiesis stimulating agents) right for kidney patients. AAKP supports achieving a hemoglobin level of 11 to 12 grams per deciliter, as indicated by the FDA label for ESAs.

We view current CMS monitoring policy as somewhat out of sync with where the FDA is and where the mainstream medical community is. Although each case is dif-

ferent and there will always be outliers, from a patient perspective there is very little medical reason for a patient to remain at levels above 13 grams, especially in light of the current literature citing safety issues. I myself receive epogen for anemia and my doctor would not delay before titrating me down from a level of 13; nor would AAKP's Medical Advisory Board recommend waiting before doing so.

Yes, we realize that CMS' monitoring policy is a payment policy and not a policy to set therapeutic targets, but payment policies can often affect decisions regarding treatment options. Since we know overdosing can lead to potentially severe outcomes, we are concerned the current payment policy could provide incentives for overdosing.

Bundling:

Because every medical case is unique, AAKP strongly adheres to the principle that *a physician and patient must be permitted to decide a care plan best suited for that patient*. Averages and other statistics are fine for certain purposes, but let's remember that medicine is fundamentally about the treatment of a unique individual.

In this light, we worry about any policy that clouds the doctor/patient decision-making relationship for treatment options. Separate Medicare reimbursement for ESAs potentially distracts from the doctor and patient deciding which course to pursue. That is why we support bundling Medicare reimbursement for ESAs into the overall Medicare composite reimbursement rate for ESRD. We believe that bundling the payment would not only result in cost savings, but also would result in more appropriate dosing of ESAs and draw more attention to the necessarily comprehensive nature of kidney care. It is important, however, to ensure that any bundling structure include risk-adjustment so as not to inadvertently create a disincentive for providers to cover the sickest patients.

ESA Guidelines:

Having said that, let me emphasize that underdosing of ESAs is a danger too. Many kidney patients remember the difficult times before ESAs were available, suffering the debilitating fatigue and adverse health affects associated with anemia. None of us want to return to those days and we do not want to scare patients away from being treated with these valuable life-enhancing medicines. We also do not want to create a perverse disincentive that causes providers to "skimp on" doses of ESAs because they would no longer be receiving separate reimbursement.

What we need is a Medicare policy that strives for a "Goldilocks" solution on ESAs: not too much, not too little, but "just right."

We believe, therefore, it would be useful to: 1) establish guidelines regarding the proper dosage of ESAs, and 2) link reimbursement to meeting those guidelines. AAKP has long supported linking quality of services to payment for those services.

Subcutaneous Administration of ESAs:

Before leaving the discussion of ESAs, let me say a few words about potential subcutaneous administration of ESAs. As you know, one-third less dosage can be used in subcutaneous administration versus intravenous administration, resulting in substantial cost savings and better outcomes. The Veterans Administration typically administers ESAs subcutaneously.

AAKP surveyed 3,600 patients when the NKF–DOQI guidelines were first released. At that time, DOQI stated that patients should receive their EPO subcutaneously as opposed to intravenously. We surveyed patients concerning the factors they felt doctors should consider when deciding which route (subcutaneous or IV) to administer EPO.

- 93% felt it was "very" or "extremely" important that the doctor make the decision based on "how EPO works best for me."
- 67% felt that it was ″very" or "extremely" important for doctors to consider the patient's preference with regard to route of administration.
- 74% wanted to be involved in the decision making process.
- Patients also were willing to have EPO administered subcutaneously if they felt it worked best, was more economical, and they could be trained.
- Patients overwhelmingly told us they didn't mind getting a shot—even giving themselves a shot—if it would make them feel better. Most of these patients are already self-administrating medication due to their diabetes, so one more shot doesn't faze them.

My point is that our survey of 3,600 patients shows that they would readily accept subcutaneous administration of ESAs. As far as I know, ours is the only such survey data on this question.

Quality Improvement Recommendations

Mr. Chairman, as you know, AAKP has been intimately involved with how kidney care is delivered since the advent of kidney dialysis a generation ago. Based on our 36 years of experience, we offer the following programmatic recommendations for your Subcommittee's consideration:

1) *Patient Education*:

AAKP is one of the nation's leading providers of patient education materials and services. Medicare currently does not cover patient education services. We strongly support legislation that would extend Medicare coverage to patient education services and would allow patient education for pre-dialysis patients. The earlier we can start educating patients regarding behavior, nutrition, and other matters in their stages of chronic kidney disease, the fewer health problems will result later.

2) *Standards for Dialysis Technicians*:

The quality of services varies considerably in dialysis centers across the country. There is currently no standard for training and certification of technicians in the centers. Some states, like Texas, have strong standards that must be met. Other states, like my state of Florida, have none at all. AAKP would like to see standard training requirements that at least set a minimum for what training dialysis technicians should receive.

3) *Coverage for Home Dialysis*:

Dialysis patients typically receive treatment three times a week for four hours a day at a dialysis center. Some patients, however, choose the option of daily home dialysis, which can be administered six times a week for two hours a day. Unfortunately, Medicare only covers three dialysis sessions per week even though more frequent home dialysis can promote better outcomes and save money.

Studies show that daily dialysis translates into lower cardiovascular event rates, which is the leading cause of death in kidney patients. Patients undergoing daily dialysis felt much better, especially noting increased energy, better physical functioning, clearer thinking, better control of their anemia and reduced symptoms related to their kidney disease and the dialysis treatments.

Daily dialysis can result in savings because: 1) four times as many nurses are needed for conventional dialysis as opposed to home dialysis; 2) hospitalization for daily dialysis patients is reduced by 34%; 3) weekly EPO dosage is reduced by an estimated 41%; and 4) the number of antihypertensive drugs is reduced by 46%. Further, patients undergoing home dialysis have a much greater flexibility in their schedule and are more likely to stay in the workplace.

4) *Lifetime Coverage for Immunosuppressive Drugs*:

Medicare coverage for immunosuppressive drugs can expire after 36 months even though kidney transplant recipients need to take the drugs for the rest of their transplanted lives. Many patients who no longer can afford the costs will stop taking the drugs. This leads to graft failures, which cause patients to go back on dialysis and wait for another transplant.

Considering that immunosuppressive drug coverage costs approximately $1,000 per month while dialysis costs $4,000 per month and a transplant costs 100,000, it makes fiscal sense to extend Medicare immunosuppressive drug coverage for life.

5) *Extending Medicare Coverage to Stage 4 of ESRD*:

Medicare only covers the fifth (and final) stage of ESRD, but this is clearly not in the best interests of the patients. The Renal Physicians Association has stated, "Proactive preparation for RRT (Renal Replacement Therapy) is recommended to facilitate the transition and reduce the burden of clinical risk factors known to be associated with worse outcomes in ESRD patients." Out of the 28 guidelines the RPA recommends in their physician practice guideline manual, 27 include treatment in both stage 4 and 5, not just in stage 5.

A demonstration project would serve to quantify the health and fiscal benefits of stage 4 coverage.

6) *Medicare Coverage for Fistulae Before Stage 5 Eligibility*:

The benefits of AV fistular access are already recognized by CMS, who recently enacted a "Fistula First" policy geared towards increasing the number of people who choose this treatment. AAKP strongly endorses the "Fistula First" policy. Fistulae last longer, need less rework, and are associated with lower rates of infections, hospitalization, and death for Medicare beneficiaries than other types of access.

However, Medicare coverage does not begin until a patient is at stage 5 of ESRD and an AV fistula should be put in months earlier. We believe this is why fistular access rates are lower than they should be—substantially lower in the United States than in Europe and Japan. Medicare should cover surgical placement of fistulae in stage 4.

7) *Medicare Secondary Payer*:

Lastly, AAKP opposes proposals to make Medicare the secondary payer for ESRD services. We believe that the health of patients is enhanced by receiving the comprehensive spectrum of services covered by Medicare. Some proposals would delay Medicare coverage for as long as 60 months. Mr. Chairman, 60 months is five years, and kidney patients in Stage 5 have an annual mortality rate of 25% and a life expectancy of only five years. So making Medicare the secondary payer would mean only the healthiest patients even make it to Medicare coverage. Delaying Medicare coverage increases cost-sharing for patients, and we believe it would undermine patient well-being in many cases.

Mr. Chairman, we applaud your leadership over the years on these issues so important to kidney patients. Our government can vastly improve the quality of care for kidney patients while saving money in many areas. Thank you for having me here to testify today and we offer ourselves as a resource to you for further information as your Subcommittee works on these issues in the months ahead.

Chairman STARK. Thank you.

Dr. Kliger.

STATEMENT OF ALAN S. KLIGER, M.D., PRESIDENT, RENAL PHYSICIANS ASSOCIATION, ROCKVILLE, MARYLAND

Dr. KLIGER. Thank you, Mr. Chairman, and Member of the Committee. My name is Alan Kliger. I'm a kidney specialist and a Clinical Professor of Medicine at Yale University School of Medicine, and I'm chairman of the Department of Medicine at the Hospital of St. Raphael in New Haven, Connecticut.

I'm an employee of a not-for-profit hospital, and for the record, I'm not in the employ of any drug companies or other commercial enterprises. I'm also President of the Renal Physicians Association, the professional organization of nephrologists, whose goals are to ensure that patients suffering from kidney disease receive the best care delivered under the highest standards of medical practice. And last, I'm the past president of the Forum of ESRD Networks, a national organization of regional networks under contract with CMS to promote and oversee quality improvement at dialysis and kidney transplant facilities, and to ensure access of care for all patients who need dialysis.

First I'd like to thank you, not only for inviting me to be here, but for allowing me to give voice to those whose real world practical experience has sometimes been overlooked—the practicing nephrologist who cares for kidney disease patients every day.

Today you're examining the safety concerns regarding dosing of ESAs, variations in utilization and reimbursement. Nephrologists have a long record of experience with safe and effective use of these agents. Nearly 15 years ago, the kidney community helped to develop evidenced-based clinical guidelines passed on a systematic review of the published evidence. I served on the steering Committee of the National Kidney Foundation's DOQI, which was charged with developing guidelines for dialysis patient care, including anemia management.

I also participated in the then-HCFA-funded development of 16 clinical performance measures designed to measure what doctors actually do, give them feedback, and help them to refine their patients in order to do what works best. The dividends we saw from that effort were that most nephrologists used to effectively use

practice guidelines, and we saw measurable improvements in the quality of care.

In the past year, several new publications on the effect of ESAs have drawn everybody's attention to these safety and efficacy questions. Our patients read and hear these stories. Many have asked us what these findings mean to them, should it change their treatment, and should they be concerned?

We owe it to them to carefully review each new study, critically analyze its findings, and based on that analysis, revise guidelines to conform with the latest scientific medical knowledge. For example, the latest evidence warns us that kidney failure patients should not have high blood counts.

Dr. Singh's study showed us that a group of patients with high blood counts in general carried a higher risk than patients with lower blood counts. The challenge to nephrologists is how to best adjust their medicine to achieve these safe and effective blood levels. Every patient is unique. When it comes to ESA dosing, each patient must be considered individually, not in the aggregate. A dose of EPO that works in one patient will not necessarily work in another. Focusing on dosing levels at the aggregate rather than the patient level does not take into consideration the very real issue of patient variability. Responses to ESAs may vary from patient to patient and even change from one patient—in one patient from one time to another. This biologic variation requires individual fine tuning to get the best results.

Also, please understand that guidelines are not rules. They're in place to give doctors and their patients advice on the best practice to follow. But since each patient and their response to treatment is different, clinical decisions and prescription choices are made one patient at a time, based on what options provide that patient with the best care and treatment possible.

Most of the time, that's what the recommendations suggest. But sometimes it's not. Mr. Chairman, I have a 52-year-old patient I'll call Ted, who has kidney failure. When his blood count is less than 36 percent, he feels tired and washed out. He has difficulty getting up to work in the morning, and experiences chest pain. When EPO raises his blood count to 38 percent, he feels like a healthy man again. He functions better and feels more productive. In fact, the differences are so prominent to him that he tells me what his blood counts are before I have a chance to measure them.

So while the most recent guidelines say I should keep his blood count at less than 36 percent, he understands the risks of a higher blood count, and he and I both know that what he needs in order to function as normally as he can is a higher level.

Yes, absolutely, doctors must be held accountable for best practice. But they must also be allowed to use professional judgment, weigh the evidence, consider their patient's wishes, and then decide what's best one patient at a time.

I agree there should not be financial incentives to overuse drugs like ESAs. I want to underscore the fact that in dialysis units, the financial incentives are not given to the doctors. The dialysis owners have financial arrangements with the drug companies, but the doctors who prescribe these medicines receive no such incentives.

Mr. Chairman, we know that kidney failure can be delayed or prevented. We know that finding and treating high blood pressure in its earliest stages, treating diabetes and high cholesterol, getting patients to stop smoking, all lead to better kidney health. Nearly 20 million Americans have some form of kidney disease, but most don't know it. To help identify these individuals and get them into treatment as early as possible, some states now require medical laboratories to report to doctors on the estimated kidney function when routine blood tests are being performed. The earlier the intervention, the less chance they will eventually need dialysis or a transplant.

Those are the goals that the RPA endorses and that individual nephrologists strive for. As this Subcommittee considers all of the evidence surrounding this very complex issue of anemia management, I urge you not to lose sight of one very critical factor in this equation; biologic variability makes dosing an individual challenge. Each physician's clinical judgment plays a critical role in achieving the highest quality of care for his or her patients.

I'd like to take this opportunity to recognize and thank Congressman Camp and Congressman Lewis for their leadership in advancing the Kidney Care Quality and Education Act championed by the Kidney Care Partners, a coalition of kidney partners of which RPA is a member. And I'd also like to recognize the commitment over the years that you, Chairman Stark, and Congressman McDermott have made to improve the health of all kidney patients.

Thank you.

[The prepared statement of Dr. Kliger follows:]

Statement of Alan S. Kliger, M.D., President, Renal Physicians Association, Rockville, Maryland

Mr. Chairman and Members of the Subcommittee.

My name is Alan Kliger. I am a kidney specialist, a Clinical Professor of Medicine at Yale University School of Medicine, and I am Chairman of the Department of Medicine at the Hospital of St. Raphael in New Haven, Connecticut. I am an employee of a not-for-profit hospital, and am not in the employ of any pharmaceutical manufacturers or other commercial enterprises.

I am currently President of the Renal Physicians Association (RPA), the professional organization of nephrologists whose goals are to ensure optimal care under the highest standards of medical practice for patients with renal disease and related disorders. RPA acts as the national representative for physicians engaged in the study and management of patients with renal disease. In addition, I am the past president of the Forum of ESRD Networks, a national organization of regional networks under contract with CMS to promote and oversee quality improvement at dialysis and kidney transplant facilities, and to ensure access to care for all patients who need dialysis treatments.

I want to begin by thanking you, Mr. Chairman and Ranking Member Camp, first for your leadership on an issue that affects the lives of the millions of Americans suffering from kidney disease. Secondly, I want to thank you for giving me an opportunity to inform this discussion with some perspectives on the issue of anemia management that I believe have sometimes been overlooked—those of the front-line physicians who are actually treating patients suffering from kidney disease and kidney failure.

This is a complex issue. I know because for more than 15 years RPA has been directly involved in helping to develop evidence-based clinical practice guidelines, based on systematic reviews of the published evidence. In fact, I served on the steering committee of the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative, or KDOQI, which was charged with developing guidelines for dialysis patient care, including anemia management. I also participated in the development of 16 clinical performance measures designed to measure what doctors actually do, give them feedback, and help them refine their practices to reflect what works best.

The dividends we saw from that effort included an improvement in the quality of care as well as documented evidence of better adherence to practice guidelines.

Clinical Practice Guidelines and Physician Prescribing Autonomy

RPA believes that clinical practice guidelines in renal care, like those in other medical disciplines, should be evaluated on the basis of the strength of evidence, an assessment of harms and benefits, and should benefit from robust physician and other multidisciplinary input and review. Guidelines developed with these considerations in mind can only enhance the delivery of high quality patient care and help ensure kidney patient safety. RPA also believes that the current body of literature in the area of anemia management fulfills these criteria, and forms a solid foundation for public policy making efforts such as the Centers for Medicare and Medicaid Services (CMS) EPO Monitoring Policy (EMP). Further, it is our opinion that the CHOIR and CREATE studies published in the *New England Journal of Medicine* last year, once subjected to the full measure of robust scientific review, will likely represent an important addition to this already significant body of literature, and should be considered thoughtfully and thoroughly by care providers and policymakers.

However, it is important to remember that clinical practice guidelines are just that: guidelines, not required protocols. Because every patient is unique, when it comes to ESA dosing, each patient must be considered individually—not in the aggregate. *Clinical decisions and prescription choices must be made one patient at a time—based on what options provide that patient with the best outcomes possible.*

The most important determining factor in the care of the patient, above all, should be the physician's clinical judgment considered in the context of the physician-patient relationship. We believe that it is of paramount importance to maintain the physician's autonomy and ability to exercise clinical judgment in prescribing for the individual patient. Decisions for the individual may be different than practice guidelines advise because of individual clinical evaluation and specific patient needs, taking into account a wide range of factors, including the age of the patient and the severity of kidney disease. This is a fundamental and well-recognized clinical principle in medicine, and it is mandatory that it be maintained and protected. RPA believes the CMS' EPO Monitoring Policy accounts for such use of the physician's clinical judgment.

Variability in ESRD Patient Hemoglobin Levels

Recent studies warn that kidney failure patients should not have high blood counts, noting that a group of patients with high blood counts in general carried a higher risk than patients with lower blood counts. But my experience with one of my patients shows how patient-centered care sometimes should deviate from guideline-advised care. I have a 52-year-old patient who is in kidney failure. When his blood count is less than 36 percent, he feels tired and washed out and experiences chest pain. When EPO raises his blood count to 38 percent, he feels like a healthy man; he functions better and feels more productive. The differences are so prominent to him that *he* tells me what his blood count is before I have a chance to measure it. For this particular patient, a higher blood count is what he needs in order to function normally. My patient knows that the recent studies warn about the long-term side effects of these higher blood counts, but he also knows he needs these levels to function normally. His choice and mine for enough EPO to maintain higher blood counts is the right choice.

RPA believes that in the recent discourse on national coverage of EPO, the critical issue of variability of individual patient response to EPO dose has been understated. As we have noted in correspondence to CMS, attempts to assess or quantify individual sensitivities (i.e. responsiveness) to EPO at a narrow level have not been successful. Therefore, there is no single, predictable response to a given dose of EPO, a fact that accounts for the wide range in individual responses to treatment. As a result, in the aggregate it is physiologically not rational to tailor a normal distribution of patient responses to a payment limit: such a paradigm cannot be successful in delivering optimal treatment with sophisticated agents to complicated patients. Payment limits structured in this fashion place emphasis on the wrong arm of therapy: emphasis should be placed rather on *reducing* the number of patients with low hematocrits/hemoglobins (>30%/10 gm/dL). At the same time, Medical coverage policy should strive to maintain levels in all patients > 11 gm/dL, given the ample data disclosing the adverse short and long-term effects to patients with persistent anemia. Simply put, overemphasis on monitoring patients at the upper end of the range should not create problems for patients at the lower end, and RPA believes that the current CMS EPO Monitoring Policy strives to avoid such problems in the broad Medicare ESRD beneficiary population.

Misperceptions Regarding EPO Reimbursement

Finally, RPA would also like to take this opportunity to dispel some common misperceptions regarding reimbursement for erythropoietin. There have been articles in both the mainstream and medical trade press implying that nephrologists have a financial incentive to prescribe higher doses of erythropoietin to ESRD patients. This is simply not true. Nephrologists prescribe EPO based on their clinical judgment of what will optimize the individual patient's hemoglobin level. Moreover, it is the dialysis facility that receives reimbursement for EPO prescribed to ESRD patients, not the nephrologist. Any inference that the nephrologist will personally benefit from prescribing higher doses of EPO, or any drug, to ESRD patients is flat wrong.

Conclusion

In conclusion, RPA supports the use of clinical practice guidelines in the development of protocols enhancing the delivery of high quality patient care, but believes they must be considered in the context of the physician's clinical judgment. RPA believes that physician prescribing autonomy must be maintained, and that the variability in ESRD patient hemoglobin levels must be taken into account in the development of national coverage policy for EPO.

As always, RPA stands ready to serve as a resource as the Committee works to ensure the best possible health outcomes and quality of life for Medicare beneficiaries with ESRD. (Check this out)

Chairman STARK. Thank you. I agree with you, Dr. Kliger, it seems quite obvious that the physician should establish a protocol for each individual patient, variations. But what about physicians who sign standing orders with the two big—with DaVita and Fresenius? Is that—do you approve of that?

Dr. KLIGER. The standing orders, as I understand them, largely were established according to the evidence-based guidelines that came down from the original KDOQI plan. But I certainly agree with you that signing on to something that is set up somehow outside of a physician's judgment is not appropriate.

Physicians are responsible for all of the orders they sign. The algorithms of care that some of the chains have, and in fact some of the drug companies have as well, were done according to the recommendations of the guidelines and were meant to be an aid to physicians in making the best prescriptions. But I surely agree with you that in the final analysis, it is the physician who has that responsibility.

Chairman STARK. Dr. Singh, you've talked about the differences in management practices in two dialysis chains, really what we're talking about this morning. Can you comment on what—how you observe these practices and whether—what's beneficial and what's harmful?

Dr. SINGH. Chairman Stark, generally what happens in dialysis chains is that there are centralized corporate Committees that take into account some of the prevailing guidelines as well as some opinions of their own individual medical directors, as well as corporate staff, and formulate guidelines for anemia management. These guidelines generally get translated into standing orders, which is signed off frequently by the medical director of a dialysis facility and then subsequently monitored at many dialysis facilities by an anemia nurse.

Different dialysis chains have different ways to put together these guidelines, and these guidelines differ from one chain to the other. If you look at the dialysis guidelines with regard to ESAs at

DCI, a not-for-profit facility, the company gives medical directors a lot of autonomy in deciding what they should be doing in their own patients. So, for example, in our DCI unit, we hold EPO at hemoglobin levels above 12 grams per deciliter. We do not give EPO. We discontinue it at that level or higher.

In contrast, for example, in the DaVita chain, the corporate guidelines say that hemoglobin levels can—certainly should be targeted between 11 to 12 grams, but that there is only a 10-percent reduction in EPO when the hemoglobin level exceeds 13 grams. So there is tremendous variability between different chains and what is in the standing orders between different chains.

My own perspective is exactly the same as actually Dr. Kliger's, that dialysis physicians need to be able to individualize the anemia management for their patients, because patients are different. And I think that there have been some unfortunate consequences of instituting standing orders and these rather restrictive guidelines with respect to anemia in terms of the hemoglobin levels that are achieved, and I think in part explains why hemoglobin levels and EPO doses at the DaVita units, for example, as shown by Dr. Cotter's research, are much higher than in DCI, which is much lower.

Chairman STARK. Okay. Let me try this. In Southern California, Kaiser contracts with Fresenius, okay. Same centers that other people walk into that Medicare may be paying for directly. But Kaiser has—first of all, it requires ″subcutaneous", and also it has their own guidelines in terms of dosage and monitoring. And I don't know that anybody's ever complained, and I'd ask any of you, that theirs is lower quality. As a matter of fact, I suspect it's rather high quality. And they're saving a couple of grand, two, three, four grand per patient per year, with a bundled payment.

Now, help me there. Why is what Kaiser is doing bad? Dr. Kliger?

Dr. KLIGER. I wouldn't characterize it as bad.

Chairman STARK. No, and it saves money.

Dr. KLIGER. Right. You know, first of all——

Chairman STARK. Okay. But then—now help me. I look at that and say, well, why couldn't we do that? Assuming some very strict assumptions. I have a hunch that Kaiser may do its own monitoring. So it has its own quality standards. Maybe they're the same, but they supervise it perhaps more closely than some Medicare intermediary might. Item one.

Two, they are willing to vary the payments. Now I'm as a—people have talked today about, oh, dear me, if we have bundling, we will underserve. We'll cut the dosage. Well, that hasn't happened in this case, and my guess is we could protect against that, and we'd probably get AMGEN's help in designing a system that would guarantee we don't under-dose.

You know, it seems to me, the pendulum, we can overdose or under-dose, and we can have financial incentives that push us either way, and we shouldn't. We should let you and you decide what's best and hit for that standard. Now, I'm going to talk to you about the guy with the quality of life, because my medical marijuana people would like to enlist your help on this idea of quality of life on the same rubric. But—and I understand. As I say, a pa-

tient feels good. That's an important thing, and if the patient understands, and I gather you've said that he or she does, whatever risks might be there, and really clearly understands them, I think that's great.

If I could get to one other issue that's come up, the issue of basically of minority or non-white patients and the difference in treatment. Ms. Robinson, your group and the groups—are you representative of the patient population in terms of minority members and——

Ms. ROBINSON. We are. We represent over a million patients a year with our services and by our own survey of data, we represent the population almost identically to the population at large in renal disease.

Chairman STARK. Dr. Singh, in my district in Alameda County, I perhaps have a third of my constituents—40 percent are either Asian or Indo-American. I think most of the physicians in my district are Indo-American. But is there, as our first witness today indicated, for African Americans, are there different general characteristics among various ethnic or racial groups that you all—between Asian or Native Americans or African Americans? Is that——

Dr. SINGH. With regards to achieving certain quality parameters such as anemia management of dialysis adequacy or iron management, or vitamin D management, these are important complications of kidney failure, there is no evidence that has made the compelling case that we should treat certain races differently than others.

Certainly you could argue that we need to investigate more and do studies that explore this issue more robustly. But there's certainly no evidence that I'm aware of with respect to anemia management, for example, that African American individuals or individuals of Asian origin should be treated differently or to different hemoglobin levels than patients who are all white Americans.

Chairman STARK. Would you agree with that, Dr. Kliger?

Dr. KLIGER. I surely agree with that. There is one interesting study that was published in 2005 looking at the ESA requirements for African Americans versus whites was interesting in that among the nonsmokers——

Chairman STARK. Yeah.

Dr. KLIGER. You had alluded to that before.

Chairman STARK. Yes.

Dr. KLIGER. This one study suggest that the dose of ESAs required to get to the same hemoglobin level was somewhat higher in nonsmoking African Americans.

Chairman STARK. And it seems to me that kind of a study would alert both of you physicians to say, if I have a smoking African—can't talk about a smoking, I at least ought to be monitoring the dosage levels very closely, because this could cause a problem. Is that—I mean, that's the way doctors think, I believe.

Dr. KLIGER. Sure. Sure. And also alert us that it may be that those patients might require somewhat higher doses of ESAs to get to the same level.

Dr. SINGH. Can I just add to that? I think it's very important to emphasize that there are major limitations with observational or

retrospective data that emerges with respect to kidney disease patients. So, for example, observational data had suggested that higher hemoglobins are beneficial to patients with kidney disease, and in fact the randomized control study showed precisely the opposite.

So I think before we conclude, based on observational data, that one group should be treated differently to another group, we really do need to try and get it confirmed in randomized control studies, and I think this would be a plea for us to actually get more support for funding of research that allows us to do these type of investigations.

Chairman STARK. Agreed. Let me ask if you'd like to inquire. Mr. Johnson has been waiting patiently.

Mr. JOHNSON. Thank you, Mr. Chairman. Dr. Kliger, I understand that fluctuations in hemoglobin are fairly common, and I think it's important that we try to keep that in mind when we make changes. In fact, I've heard the analogy that adjusting hemoglobin levels in patients is from my viewpoint kind of like landing on an aircraft carrier at night. It's tough.

So you can provide your views as a nephrologist on the difficulty of maintaining patients in this range? In addition, what are the situations where patients with ESRD could still experience temporary excursions above 12?

Dr. KLIGER. Well, there's always going to be, because of the biologic variation in response to the ESAs, there will always be a distribution of blood counts, given the same overall approach to therapy. So that trying to maintain all patients, for example, in the very narrow range between say 11 and 12 grams percent, would really prove to be very difficult or perhaps even impossible. So that the truth is that any policy that you make that will tend to stop the upper end dangers will also shift the curve toward the left and undergo the possibility of more patients with the lower blood panels, with the lower hemoglobin levels.

Because of that variability, we really have to be critical in watching the responses, monitoring the responses of our patients and acting accordingly. Dr. Singh, of course, is right. In fact, as Kris was, that when patients get into those upper levels that reducing the does is important, but the response to that reduction varies. Some patients stay for a longer time at higher levels. Some fold very quickly. It's that variability that's really at the heart of the patient-doctor decisions about the best care.

Mr. JOHNSON. Thank you. Ms. Robinson, I think it's important to focus on ways to improve the quality of care, as I'm sure you do, and there's been a ton of studies on—that suggest more frequent dialysis, which is often provided in the patient's own home, might significantly reduce the need for EPO and other medications.

Can you tell us how often home dialysis is used by dialysis patients and what are the benefits for the patient and what can we do to increase the utilization by Medicare?

Ms. ROBINSON. It's a very small population who are currently dialyzing at home, whether that's home hemodialysis or——

Mr. JOHNSON. What kind of percentage would you guess?

Ms. ROBINSON. Probably less than 10 percent, including peritoneal dialysis. But there are a lot of benefits.

Mr. JOHNSON. But it's a fairly recent thing, too?

Ms. ROBINSON. It is. Absolutely. The home daily hemodialysis is really quite recent. And what patients are finding is not only are their outcomes better, but they're feeling better. They're able to be—continue with their work. They're able to be active in their community. And one of the best things is they can dialyze on a schedule that is good for them, whether it be when they come home in the evening.

So they really do have much better outcomes, and they're in the hospital less, and they use less medication, and they cost less money because they don't use the nursing population as much.

Mr. JOHNSON. Okay. So you're an advocate of that?

Ms. ROBINSON. I'm a huge advocate, correct.

Mr. JOHNSON. So am I. So am I.

Ms. ROBINSON. Thank you.

Mr. JOHNSON. Dr. Singh, in your testimony last December before the Ways and Means Committee, you talked about bundling, and there's been a good deal of discussion on that today. The difficulties of establishing the proper case mix to account for certain patient variability parameters. Have you considered how the case mix adjust a bundled payment to avoid unintended consequences for small providers and patients?

Dr. SINGH. Thank you. I continue to believe that there needs to be adjustment according to risk and geography for—in designing a system, a bundled system of payment, because I agree with you that we should not place at risk providers who provide care for patients in remote areas, rural areas, or in inner city indigent areas where it may or may not be easy to treat these patients.

But I do believe that one can achieve that. One can accomplish that by modeling current CMS data. And I was interested to hear Ms. Norwalk talking about this, that they have in fact developed regression models which adjust for a number of these factors to try and accomplish this.

I think that the best way to do it is to actually implement a system, because there are certain limitations with doing demonstration projects. Because these demonstration projects select different regions or tend to select different regions, I think that one needs to implement a system, one needs to have an open mind about what that—about adjusting that system to handle some of the issues that come out of it.

But I do think that a key aspect of that will be to adjust for factors such as case mix, geography, so that you don't put certain people out of business because they happen to provide care in an area where it may not be feasible to otherwise provide care. And I do believe a system can be designed to accomplish that, and I believe—and I was very pleased to hear that in fact CMS appears to have accomplished that.

Mr. JOHNSON. Thank you, sir. Thank you, Mr. Chairman.

Chairman STARK. Mr. Camp?

Mr. CAMP. Well, thank you, Mr. Chairman. Thank you all for your testimony and for being here today. Dr. Kliger, does Medicare currently address either education or prevention programs for patients with chronic kidney disease? And how should we modify existing programs to ensure that patients receive the best care possible?

Dr. KLIGER. It's a great question. We surely don't have sufficient funding for education programs. With so many Americans with kidney failure, most of whom don't even know that they have it yet, we clearly need to invest more of our resources at getting at the roots of renal disease early. Educating people into knowing what their number is, knowing what their estimated kidney function is. Knowing whether they have high blood pressure, knowing whether they have diabetes, that they're getting appropriate treatment for each.

And then for those people who have chronic kidney disease and approach the need for dialysis, critically important is the education about patient-centered choices, the choices that they have about modes of treatment, including home dialysis, home peritoneal dialysis, hemodialysis, kidney transplantation.

So I surely think that we need to do more and that CMS should do more to support those.

Mr. CAMP. We heard Mr. Johnson mention the CMS published proposed national coverage decision for the administration of ESAs in regard to hemoglobin and hematocrit levels for cancer patients with anemia. But you state in your testimony that it's paramount to maintain the physicians's autonomy and ability to exercise clinical judgment in prescribing for the individual patient.

And from your experience, have you found that dialysis facilities disregard physician ESA recommendations on dosing, or do they insert their own judgment in those areas?

Dr. KLIGER. Both physicians and facilities I believe are guided by the evidence-based guidelines that have been published that use the best evidence that we have to come up with algorithms of care. It's not a matter of done independent of neither group, neither physicians nor facilities make up their own minds or should be making up their own minds about that, but rather be utilizing those evidence-based guidelines.

As new evidence comes along, like Dr. Singh's study, those evidence-based guidelines need to be revised, considered but continue to be the main source of the authority for both facilities and physicians to be making those best decisions.

Mr. CAMP. And, Ms. Robinson, do you have any comment on the new CMS guidelines?

Ms. ROBINSON. For ESA dosing?

Mr. CAMP. Yes, for ESA dosing.

Ms. ROBINSON. We feel very strongly that they should coincide with the FDA guidelines for ESA dosing. That's extremely important to us. We don't want to see patients under-dosed or overdosed, but we do want to see them in the 11 to 12 range, understanding that there is variability and sometimes they'll go over.

Mr. CAMP. Well, aren't those different approaches, one is a payment guideline and one is a treatment guideline? Do you see those as—you don't see those as different approaches?

Ms. ROBINSON. Not necessarily, because if there's the opportunity to pay at a higher level, then you want to ensure that the physician is still dosing with regard to the FDA guidelines. So, that, you know, based on the payment policy, you'd still want to make sure that the physician isn't dosing above 13 for several months.

Mr. CAMP. Well, given the testimony we heard earlier, it may take several months to come down to that level. And so, therefore, the reimbursement rate is a bit higher, at least in their advisory panel. Either Dr. Singh or Dr. Kliger, do you want to comment on that?

Dr. SINGH. I think that it is true that it does—that you cannot immediately see a response when you adjust the dose of ESAs, but I think it's remarkable that there are still a fairly reasonable number of patients that have persistently elevated hemoglobin levels, and that this number seems to have grown since the Medicare reimbursement guidelines were changed in April 2006.

So I think that if the intent of the Medicare reimbursement guidelines was to reduce people who had hemoglobin levels persistently above 13, that hasn't worked, because Ms. Norwalk herself in testimony today indicated that the percentage has actually increased somewhat. And in fact, in DCI's, our own data which we've looked at, the amount has—you know, the proportion has gone up since these guidelines were introduced.

Mr. CAMP. Yes. And, Dr. Kliger, if you could comment. But it does seem to me that everything we've heard in terms of medicine is about individualizing medicine in the future, and if we have a national standard at a certain level, what does that do to the individual patient? But Dr. Kliger, I'd like to hear your comments.

Dr. KLIGER. Well, Congressman, I think that your point is very well taken. That is that we clearly need to have targets of therapy, good clinical guideline targets. But the payment policy needs to take into consideration that variation, that targets are not hit as a bullseye. Targets are hit in a wider range, and the payment policy needs to be there to encourage the appropriate use and prevent the harmful effects of the medicine, but nonetheless recognize that variability.

Mr. CAMP. All right. Thank you. I see my time has expired. Thank you, Mr. Chairman.

Chairman STARK. I just wanted to make sure that I emphasize that Ms. Robinson, your group supports the use of ″subcutaneous" administration?

Ms. ROBINSON. Yes we do.

Chairman STARK. There may be cases when that's not called for by the physician.

Ms. ROBINSON. Right.

Chairman STARK. But in general, you don't have an objection?

Ms. ROBINSON. We do. When we surveyed patients, they were willing to do it, overwhelmingly willing to do "subcut". If they understood from their physician in a discussion why it was more effective, which it is, why it might be cost efficient and how they'll have better outcomes overall. So, yes.

Chairman STARK. And you support bundled payments but also strong review of—to ensure quality if we are involved?

Ms. ROBINSON. Absolutely. And also to ensure that patients aren't discriminated against by facilities because they may be sicker patients.

Chairman STARK. Okay. If I can digress for a minute, Dr. Kliger, you had suggested that we want to educate and be alert to the causes of kidney problems. Do you think—and Dr. Singh can—

that those of us who are on various cholesterol-lowering medicine are reasonably alerted to the fact that in some cases, that could cause kidney problems? Do you think in general that we are—those of us who are trying to keep our cholesterol down using these drugs, knowing that in some cases they can cause kidney problems. Is there enough information abroad in the land?

Dr. SINGH. I think certainly one of the issues that we do rely on is the FDA to try and alert us, because they have a very—a good system of—a Medwatch system that allows us—the FDA to monitor side effects after post-marketing of a drug. And there were reports that in fact there was some concerns with regards to certain statin or a certain statin agent that might be associated with increased risk. However, I feel that the systems that we have in place currently are good at at least detecting these issues.

I think the much more challenging issue is, once you detect this, what does the FDA do about it? And I think that that's something that has been addressed most recently by the Institute of Medicine. That's something that I think the Congress is also considering whether to empower the FDA to deal with this in different ways.

I think that's even germane to the ESA issue. The first study on ESA safety was published in 1998 in the New England Journal, showing increased risk in dialysis patients, and we are 9 years later, and we're debating this issue when the first study showing increased risk was over, you know, was 9 years ago. So I do think that, you know, post-marketing surveillance is important, whether it's important for statins, as you suggest, or it's important for ESAs. And I think we should rely on Federal agencies such as the FDA adequately empowered to work on our behalf to make sure that patients are kept safe.

Chairman STARK. Are you comfortable with that, Dr. Kliger?

Dr. KLIGER. Yeah, I surely agree. I guess one of the things that it points out is really how complex this is. Because what you have is confounding of people with heart disease, high cholesterol, those other things, all of which predispose to kidney disease and kidney failure. And understanding and sorting out what is a side effect of a medicine or a result of the complex medical conditions can be very difficult.

Chairman STARK. Okay. Let me digress one more time while I have two nephrologists here. You both are familiar with AIDS treatment, right? We had some testimony not so long ago that in the Part D program, some of the providers, the benefit providers, are in effect discriminating against the anti-retroviral drugs, and either they're raising the price or not being too excited about enrolling patients with AIDS.

Should we not, in your opinion, in any of our pharmaceutical programs, make sure that these anti-retroviral drugs are available to AIDS patients? Is there any reason we shouldn't?

Dr. KLIGER. Yes, sir. I agree with you.

Chairman STARK. Okay.

Dr. SINGH. I agree with you.

Chairman STARK. One more. And you may not agree to this one. Are we close, and could you make a case, and if there's any research, let me know, that perhaps we ought to treat HIV in terms of how we pay for it the same way we do end-stage renal disease?

Dr. KLIGER. You're not going to get an easy answer from me. I'd have to think about it, what you mean by that and how——

Chairman STARK. Well, it's a disabling disease. It's the only, if you will, socialized medicine that we have in this country. End-stage renal disease, young, old, the government pays for it, right? I mean, there's a little bit of private insurance at the beginning, but basically, it's the only thing I know of that we pay for universally.

Should—can you make a case that it would be good both social and economic, and/or economic policy? And you may not know. I'd love to hear your opinion, that we ought to include HIV patients and treat them in the same way? Not necessarily under the ESRD, but that if you've got it, your insurance may cover it for a year or two and then we pay for it in a Federally funded program?

Dr. SINGH. Chairman Stark, I would suggest to you that in fact the Federal support for the ESRD program is really a beacon of what can and should be considered for a number of conditions where groups of patients are affected. I think that it's been an absolutely huge success that the government has paid for dialysis and related services in patients, and I think that it just shows that it can be done. And I think if you are arguing that HIV is a condition, like many other conditions, chronic diseases, where it's very difficult to get support from either private insurers or to get help if you're uninsured. And I do think that the Federal Government has an example in ESRD where it can be done, and it can be done successful, you know, not withstanding tweaking that needs to be done, of course.

But it's been a hugely successful program in terms of its achievement of quality, where I think—tell me a program where the government pays for it and there's people, you know, there are quality measures and there's attempts by large numbers of doctors and providers to try and achieve quality parameters in patients. I think it's just an inspiring example of what can be done.

Dr. KLIGER. Well, actually, you know, as a physician, I'd love to see HIV underwritten and supported for all. I'd like to see diabetes underwritten and supported for all. I'd like to see hypertension underwritten and supported for all. So the truth is, of course, as an advocate of my patients, I tell you guys here on Capitol Hill, you bet. That's what I'd want. But, obviously, the practical question then is where do you really draw the line and how do you know how to best invest the limited resources that we have?

Chairman STARK. Thank you. Thank you very much. If there are no further comments or questions, I want to again thank the panel for their participation and patience. You've been very helpful. And the hearing is adjourned.

[Whereupon, at 1:05 p.m., the Subcommittee was adjourned.]

[Submissions for the record]

Statement of Amgen

Amgen is pleased to submit this written testimony for the record with regard to the use of Erythropoiesis-Stimulating Agents (ESAs) in Medicare beneficiaries with End-Stage Renal Disease (ESRD).

Amgen has pioneered the development of innovative medicines—ESAs—that safely and effectively treat anemia when used according to the U.S. Food and Drug Administration (FDA)-approved prescribing information. EPOGEN® (Epoetin alfa) is

an ESA developed by Amgen scientists using recombinant DNA technology which has the same biological effects as naturally occurring erythropoietin. Nearly every patient with ESRD does not produce adequate amounts of erythropoietin, and consequently suffers from anemia (lack of red blood cells). EPOGEN® has been shown to increase hemoglobin levels (amount of red blood cells) and reduce the need for red blood cell transfusions; indeed the development of EPOGEN® as a therapeutic has been hailed as one of the major breakthroughs in treatment for dialysis patients.

Over recent months, new clinical trials published in November 2006 have raised important questions regarding the safe and appropriate use of ESAs in patients with kidney disease. These questions primarily arose from two studies conducted in non-dialysis patients with kidney disease,[1] and were also influenced by an earlier study, the Normal Hematocrit Cardiac Trial (NHCT) published in 1998, that was conducted in hemodialysis patients with pre-existing chronic heart failure or ischemic heart disease.[2]

It is important to note that all three of these studies evaluated ESAs when used to target hemoglobin levels that are higher than those recommended in the FDA-approved product labels.

Additionally, several recent oncology studies highlighted important potential safety risks of ESAs when used in off-label and experimental conditions—related to the potential for tumor progression and decreased survival. These issues are not directly relevant to dialysis patients who receive ESAs as physiologic replacement therapy, a very different situation that in cancer patients receiving cytotoxic chemotherapy.

On March 9, 2007, the FDA and Amgen announced that a black box safety warning was being added to all ESA labels, including new guidance for dosing and administration. Amgen immediately sent letters to all prescribing physicians and directed our professional staff to communicate these changes in full to prescribers. Amgen also sent letters to all physician prescribers in November 2006 communicating the results of two recent studies in non-dialysis patients with kidney disease.

These important safety issues will be discussed at a joint meeting of the FDA Cardiovascular and Renal Drug Advisory Committee and the Drug Safety Advisory Committee in September.

Amgen is committed to ensuring that our ESA medications are used in the most safe and effective manner. Amgen takes the recent questions that have arisen based on the results of the clinical trials conducted in patients with kidney disease not on dialysis targeting hemoglobin levels above 13 g/dL very seriously, and has undertaken a thorough review of all available clinical evidence. We appreciate this opportunity to comment on these important questions about the safe and appropriate utilization of ESAs in ESRD in this written testimony.

THE BENEFITS OF EPOGEN® AND ANEMIA THERAPY IN ESRD

EPOGEN® has revolutionized the treatment of anemia in dialysis patients, while virtually eliminating the need for red blood transfusions that compromise the potential for subsequent successful kidney transplantation.

Anemia affects approximately 9 out of every 10 dialysis patients, and is a consequence of reduced production of the hormone erythropoietin by the kidney. ESRD patients with anemia can suffer from fatigue and weakness. Dialysis patients with anemia are at significantly higher risk for cardiovascular events, such as heart attack or stroke, and are more likely to die than dialysis patients without anemia. Anemia, defined as a hemoglobin concentration below 11 g/dL, is associated with increased risk of hospitalization and death. As a result of this increased risk for hospitalization, Medicare beneficiaries with hemoglobin concentrations less than 11 g/dL incur higher costs and healthcare utilization: Collins et al demonstrated that Medicare member-per-month expenditures for patients with hematocrit values 30% to > 33% (hemoglobin 10 to > 11 g/dL) were 10.6% higher than for patients with hematocrit values 33% to > 36% (hemoglobin 11 to > 12 g/dL).[3]

---

[1] Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med. 2006*;355:2085–98; Drüeke 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*. 2006;355:2071–84.

[2] 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*. 1998;339(9):584–90.

[3] 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. 2001*;12(11):2465–73.

Before the availability of EPOGEN® more than a decade and a half ago, physicians had few options for treating anemia in dialysis patients, and had to rely on blood transfusions. Unfortunately, blood transfusions put patients at risk for complications such as blood-borne infections, iron overload, and antibody responses that limit the chances for a successful kidney transplant.

EPOGEN®, a genetically engineered form of erythropoietin, has the same biological effect as naturally occurring erythropoietin. EPOGEN® dramatically reduces the need for red blood cell transfusions. In the EPOGEN® registrational clinical trials that targeted hematocrit levels between 32% and 38% (hemoglobin 10.7 to 12.7 g/dL), the percentage of patients requiring red blood cell transfusions was reduced from 55% at study inception to 0%–4% following 13–24 weeks of therapy.[4] When used as directed by the FDA-approved package insert, EPOGEN® has been shown to be safe and effective in multiple clinical trials, and has over a decade and half of safety monitoring in real-world use in almost 1.4 million dialysis patients for a total exposure of approximately 3.8 million patient-years.

PATIENT SAFETY AND QUALITY OF CARE ISSUES RAISED BY THE COMMITTEE

The nephrology community consensus is that a hemoglobin target range of 11 to 12 g/dL minimizes risk and maximizes benefit in ESRD patients, but due to the severity of additional disease burden and inherent natural hemoglobin variability, dialysis patients are difficult to consistently maintain within this relatively narrow hemoglobin range.

Recently, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI™) Anemia Working Group reviewed all of the published clinical trial data to date. This analysis included the two recent trials and the one older trial that have raised these safety issues. They examined clinical outcomes associated with higher or lower hemoglobin targets including the NHCT in hemodialysis patients with chronic heart failure or ischemic heart disease, the Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) study, and the Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta (CREATE) study. Based on this review, the NKF–KDOQI™ Anemia Work Group recommended that physicians *target* a hemoglobin in the range of 11 to 12 g/dL, and also stipulated that the *target* not be above 13 g/dL.[5]

It is important to recognize that dialysis patients are seriously ill. Seventy percent of patients are on dialysis as a result of diabetes and hypertension.[6] These two conditions are also risk factors for cardiovascular disease. Cardiovascular complications are endemic in dialysis patients, and account for the high rate of morbidity and mortality in this fragile population.[7] In addition, inter-current events such as hospitalization and infection often lead to frequent episodes of inflammation, a condition which can dramatically decrease an individual patient's responsiveness to ESAs.

Because of the general poor health status of a typical dialysis patient and the natural variability in patient hemoglobin levels, it is difficult to consistently maintain hemoglobin within a narrow band such as between 11 and 12 g/dL.[8] Consequently, physicians write anemia management protocols to *target* a specific hemoglobin range with the intent of maximizing the number of patients with *achieved* hemoglobin concentrations within this targeted range. However, due to hemoglobin variability, patients targeted to a specific hemoglobin range will at various times have *achieved* hemoglobin concentrations that are above and below the target at various times.

Worse patient outcomes such as cardiovascular events or death have been consistently shown to be associated with hemoglobin levels below 11 g/dL compared with temporary excursions above 12 g/dL.

It is well documented in both domestic and international studies that hemoglobin levels of less than 11 g/dL in dialysis patients are associated with increased hospitalization, healthcare expenditure, and mortality.[9]

---

[4] Amgen data on file.

[5] National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF–KDOQI™). KDOQI clinical practice guideline and clinical practice recommendations for anemia in chronic kidney disease: 2007 update of haemoglobin. (Draft under review).

[6] USRDS Annual Data Report 2006.

[7] Sarnak MJ. Cardiovascular complications in chronic kidney disease. *Am J Kidney Dis.* 41(S5):S11–S17.

[8] Fishbane S and Berns JS. Hemoglobin cycling in hemodialysis patients treated with recombinant human erythropoietin. *Kidney Intt.* 2005;68(3):1337–43.

[9] Wolfe RA, Hulbert-Shearon TE, Ashby VB, et al. Improvements in dialysis patient mortality are associated with improvements in urea reduction ratio and hematocrit, 1999 to 2002. *Am J*

Continued

In a recent study using United States Renal Data System (USRDS) data, Gilbertson et al demonstrated that patients with hemoglobin concentrations below 11 g/dL have the greatest risk for adverse clinical outcomes, and even transiently low hemoglobin concentrations are associated with worse outcomes than transiently high or persistently high hemoglobin concentrations above 12.5 g/dL.[10] Thus, these temporary high excursions must not be confused with the risks observed with targeting patient hemoglobin levels greater than 13 g/dL as was done in both the NHCT study in dialysis patients and the CREATE and CHOIR studies in nondialysis patients with kidney disease.

As a result of the numerous analyses demonstrating that achievement of hemoglobin levels below 11 g/dL is associated with adverse clinical outcomes, physicians strive to achieve maximum benefit by decreasing the percentage of patients with hemoglobin levels less than 11 g/dL at any time. Furthermore, CMS has independently established the percentage of patients with hemoglobin levels above 11 g/dL as a Clinical Performance Measure (CPM) for all dialysis clinics, and publishes this data on its website. Finally, the community and CMS recognize that when striving to achieve hemoglobin levels above 11 g/dL, hemoglobin concentrations fluctuate and often exceed the upper bound of the target range, temporarily.

The majority of patients are not being maintained at hemoglobin levels above 12 g/dL.

As discussed above, dialysis patients exhibit extensive variability in hemoglobin levels. ESAs are titratable drugs and ESA doses are adjusted in response to changes in patient hemoglobin concentrations over time in dynamic fashion. Targeting a hemoglobin in a dialysis patient is not like setting the cruise control in your car; it involves constant monitoring and ESA dose adjustments when hemoglobin values fall out of range. A number of studies in dialysis patients have provided a cross-sectional, or "snapshot", view of hemoglobin concentrations for the entire dialysis population showing that at a *single* point in time, 50% of patients may have hemoglobin levels above 12 g/dL. However, because the majority of these hemoglobin concentrations above 12 g/dL are only transient, this snapshot view of the data does not accurately describe the natural fluctuations in patient hemoglobin levels over time, nor does it capture the consistent pattern of physician-directed ESA dose adjustment in response to out of target hemoglobin levels. The majority of physicians seek to achieve hemoglobin levels of greater than 11 g/dL and less than or equal to 12 g/dL.

Due to hemoglobin variability, 90% of patients have hemoglobin levels that move from within the recommended targeted hemoglobin range (11 to 12 g/dL) to above or below the targeted range over time when the data are looked at longitudinally instead of cross-sectionally. This is the difference between a "snapshot" (cross-sectional point in time) versus a "movie" (longitudinal view over time).[11] This critically differentiating concept was illustrated by Ebben et al in an analysis examining 152,846 patients over a 6 month period in 2003. The study found that only 2.0% of patients had hemoglobin levels that were persistently maintained at greater than 12.5 g/dL for a six month period, but 68.4% of patients had hemoglobin levels that were above 12.5 g/dL at least once during the same timeframe.[12] Similarly, Amgen has analyzed data and found that 83% of hemoglobin excursions above 12 g/dL return back below 12g/dL within 3 months.[13]

When hemoglobin levels exceed the upper bound, physicians adjust ESA doses downward, with the objective of returning hemoglobin levels to within target.

Kidney Dis. 2005 Jan;45(1):127–35; Locatelli F, Pisoni RL, Combe C, et al. Anemia in haemodialysis patients of five European countries: association with morbidity and mortality in the Dialysis Outcomes and Practice Patterns Study (DOPPS) *Nephrol Dial Transplant*. 2004 Jan;19(1):121–32; Volkova N and Arab L. Evidence-based systematic literature review of hemoglobin/hematocrit and all-cause mortality in dialysis patients. *Am J Kidney Dis*. 2006 Jan;47(1):24–36; 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*. 2001;12(11):2465–73.

[10] Gilbertson D, Ebben J, Bradbury B, et al. The effect of hemoglobin variability & trends on mortality. American Society of Nephrology 39th Annual Scientific Meeting. San Diego, CA. November 14–19, 2006. Poster SA PO032.

[11] Ebben JP, Gilbertson DT, Foley RN, et al. Hemoglobin level variability: Associations with comorbidity, intercurrent events, and hospitalizations. *Clin J Am Soc Nephrol*. 2006;1:1205–10; Rubin RJ and Mendelson DN. Translating guidelines into policy. *Clin J Am Soc Nephrol*. 2007;2:209–10.

[12] Ebben JP, Gilbertson DT, Foley RN, et al. Hemoglobin level variability: Associations with comorbidity, intercurrent events, and hospitalizations. *Clin J Am Soc Nephrol*. 2006;1:1205–10.

[13] Amgen data on file.

An important finding is that the tendency to decrease ESA doses in response to hemoglobin levels being above 12 g/dL has increased as a result of recent ESA label changes and the CMS Erythropoietin Monitoring Policy (EMP).

As of April 2007, 81% of hemoglobin excursions above 13 g/dL are followed by a dose reduction within 30 days compared to 72% in November 2005 when the EMP was announced. Data also demonstrate more ESA dose reductions occur following hemoglobin excursions between 12 g/dL and 13 g/dL since the ESA label change was communicated in March 2007. In April 2007, 49% of hemoglobin excursions between 12 g/dL and 13 g/dL are followed by an ESA dose reduction within 30 days, as compared with 37% in January of 2007. In addition, in some instances physicians implement a dose reduction after 30 days. There is a corresponding increase in the number of patients with hemoglobin levels in the 11 to 12 g/dL range, and the percentage of patients with hemoglobin levels above 13 g/dL has declined from 26% in January of 2007 to 23.6% in April of 2007.[14]

Surveillance data from U.S. dialysis patients does not suggest evidence of increased mortality when ESAs are a routine component of care for dialysis patients.

Surveillance of nearly 100% of the U.S. ESRD population via the USRDS shows that mortality rates have declined since the introduction of EPOGEN® (approximately 250 per 1,000 patient years at risk in 1989 versus 220 in 2004), coincident with the rise in population hemoglobin levels. While not proof of causality, these data do not suggest evidence of increased mortality when ESAs are a routine component of care for this very fragile dialysis patient population.[15]

These associations from the entire population level data appear to be at odds with correlations of individual patient data. One publication has suggested that patients receiving higher ESA doses are more likely to die, and has suggested that the high ESA doses cause these adverse events.[16] Similar correlations can be found between doctor visits and hospitalizations and death: the more one visits a doctor or is hospitalized, the greater the likelihood of death. It does not follow, however, that doctors and hospitals *cause* death. On the contrary, it is common sense that those individuals who require physician and in-patient care are more likely to die than those who do not require medical attention.

This paradox is called "confounding-by-indication", and it occurs when there is an underlying factor (i.e., being ill) that is associated with two parallel outcomes (hospitalization and mortality). Those parallel outcomes will then also be correlated: both hospitalization and mortality rates increase with more seriously ill patients. A similar effect can be seen in the association between ESA dose and mortality. Dialysis patients who are relatively more ill have lower hemoglobin levels and may be relatively less responsive to ESAs, and thus physicians prescribe higher ESA doses in the attempt to achieve target hemoglobin levels. However, these relatively more ill dialysis patients are simultaneously more likely to die in addition to receiving higher ESA doses. This does not provide conclusive evidence that higher ESA doses *cause* increased mortality.

Fortunately, specific analytical methods have been developed to address the epidemiological problem of confounding-by-indication. They adjust for the degree of underlying illness in the population. When these appropriate techniques are applied to dialysis patients, they do not reveal an association between higher ESA doses and increased mortality. In fact, these adjusted analyses demonstrate that the achieved hemoglobin is a stronger predictor of better or worse outcome than is the ESA dose administered.

While there does not appear to be a causal relationship between ESA dose and mortality, Amgen recognizes that there remain unanswered questions regarding hemoglobin and ESA dose, especially in patients who require high doses of ESAs to achieve modest increases in hemoglobin (i.e., hyporesponsive patients). Amgen is evaluating ESA therapy in hyporesponsive patients based on all available data and is updating the FDA in an ongoing manner regarding the insights and findings. We are also informing CMS and the renal community on our findings.

PAYMENT POLICY ISSUES RAISED BY THE COMMITTEE

ESA doses have increased in the U.S. in concert with substantial improvements in the quality of care, growth in the ESRD population, increased comorbidity burden, and increased racial disparities in ESRD—not due to inappropriate physician utilization or financial incentives.

---

[14] Amgen data on file.

[15] *USRDS Annual Data Report 2006*.

[16] Zhang Y, Thamer M, Stefanik K, et al. Epoetin requirements predict mortality in hemodialysis patients. *Am J Kidney Dis*. 2004;44:866–76.

Medicare spending, as well as doses of EPOGEN® administered to U.S. dialysis patients, has increased since the introduction of this life-changing therapy due to four primary factors:

- *Improvement in hemoglobin outcomes*—According to the USRDS 2006 Annual Data Report and the CMS 2005 Annual Report for the ESRD Clinical Performance Measures Project, the percentage of patients with hemoglobin concentrations below 11 g/dL has decreased from 84% in 1991 to 17% in 2004.[17] This is a remarkable achievement by the nephrology community and a benefit to patients.
- *Comorbidity burden*—The percentage of ESRD patients with diabetes has increased over time from 59% to 66% in whites and from 60.6% to 66.3% in blacks respectively from 1995 to 2004. It has been observed that diabetic patients and patients with other comorbidities often require higher ESA doses.[18]
- *Increased racial disparities*—Racial minorities are also disproportionately represented in the ESRD population and this trend has increased over time: approximately one-third are African-American, and 1 in 7 are Hispanic. African-Americans in particular receive higher ESA doses to achieve similar hemoglobin levels as other patient subgroups.[19]
- *Growth in the number of patients on dialysis*—USRDS reports that prevalent dialysis patients have more than doubled since 1988. This growth in dialysis patients means that more patients require treatment which increases Medicare spending.[20]
- A recent article in the New York Times indicated that ESA doses in the U.S. are twice that observed in Europe.[21] However, the article did not describe the achieved hemoglobin levels in the U.S. compared with EU countries, or other differences in the U.S. and EU patient populations that impact ESA dose requirements.
- The U.S. had the second highest hemoglobin level, a marker of quality care, of all the countries studied (the best hemoglobin outcome was observed in Sweden, which had the second highest unadjusted mean ESA dose).[22]
- The differences in ESA dose across world regions can be explained in part by differences in patient comorbidities, race, and dialysis vascular access type.[23] This has been shown in the Dialysis Outcomes and Practice Patterns Study (DOPPS), the largest global registry of dialysis patients.

The most recent data suggests that ESA doses are stabilizing. The Medicare Payment Advisory Commission (MedPAC) indicated in its March 2007 Report to Congress that there has been a 0.6% decline in the EPOGEN®dose from 2004 to 2005.[24]

Current Medicare payment policy for ESRD drugs, average sales price (ASP) + 6%, has reduced Medicare expenditures for ESRD drugs in general, and for ESAs specifically, thereby minimizing incentives for ESA overutilization.

As already discussed above, the evidence demonstrates that most ESA dosing decisions are appropriate; i.e., ESA doses are adjusted up or down in response to out-of-target hemoglobin levels, and there is no compelling evidence of inappropriate utilization. However, the announcement for this hearing suggested the existing Medi-

---

[17] USRDS 2006 Annual Data Report, CMS' 2005 Annual Report ESRD Clinical Performance Measures Project.

[18] USRDS 2006 Annual Data Report; Bárány P, Divino Filho JC, Bergstörm J. High C-reactive protein is a strong predictor of resistance to erythropoietin in hemodialysis patients. *Am J Kidney Dis.* 1997;29(4):565–8; Del Vecchio L, Pozzoni P, Andrulli S, et al. Inflammation and resistance to treatment with recombinant human erythropoietin. *J Ren Nutr.* 2005;15(1):137–41; Hsu SP, Peng YS, Pai MF, et al. Influence of relative hypoparathyroidism on the responsiveness to recombinant human erythropoietin in hemodialysis patients. *Blood Purif.* 2003;21(3):220–4; Ifudu O. Patient characteristics determining rHuEPO dose requirements. Nephrol Dial Transplant. 2002;17(Suppl5):38–41.

[19] USRDS 2006 Annual Data Report.

[20] USRDS 2006 Annual Data Report.

[21] Berenson and Pollack The New York Times, May 9, 2007.

[22] Pisoni RL, Bragg-Gresham JL, Young EW, et al. Anemia management and outcomes from 12 countries in the dialysis outcomes and practice patterns study (DOPPS). *Am J Kidney Dis.* 2004;44(1):94–111.

[23] Goodkin DA, Bragg-Gresham JL, Koenig KG, et al. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *J Am Soc Nephrol* 14:3270–3277, 2003; Pisoni RL, Young EW, Dykstra DM, et al. Vascular access use in Europe and the United States: Results from the DOPPS. *Kidney Int* 61:305–316, 2002.

[24] Medicare Payment Advisory Commission. Report to the Congress: Medicare Payment Policy. March 2007.

care system may incentivize overutilization of ESAs, at higher costs to taxpayers and risk to patients. The data suggest otherwise.

In fact, Medicare spending on ESRD drugs has been reduced under the ASP+6% system. According to MedPAC in its March 2007 report to Congress, the use of the ASP+6% methodology lowered Medicare payment for ESRD drugs by about 10% from 2004 to 2005 (a $300 million reduction) and shifted drug profits to the dialysis add-on payment.[25]

The Medicare per unit payment limit for EPOGEN®also has decreased under the ASP+6% system, declining almost 7% since ASP-based reimbursement was instituted (Q4 2005 versus Q3 2007). Furthermore, while MedPAC did not provide a dollar amount for total Medicare EPOGEN® spending in its 2007 March report to Congress, figures included in the report show a slight decline in total EPOGEN® spending between 2004 and 2005.

Changes to ESRD drug reimbursement from the ASP+6% methodology may result in serious unintended consequences to specific dialysis populations, in particular those patients that are treated by smaller, independent dialysis facilities, including in rural areas and centers located in underserved urban areas. Small dialysis providers may just be breaking even on ASP+6% reimbursement. ASP is a weighted average of all prices and the Department of Health and Human Services Office of the Inspector General has found that smaller providers have higher drug acquisition prices than larger providers.[26] If the payment rate were changed or lowered, smaller dialysis facilities may lose money in an effort to provide needed drugs to their patients, potentially forcing these facilities to close and inhibiting sustained access to quality care for dialysis patients nationwide.

New analyses of ESA utilization data since the FDA updated the ESA labels in March 2007 reinforce the recommendation that a change in the EMP is not necessary at this time.

CMS developed the EMP after several years of extensive deliberation and consultation with the nephrology community. CMS and the nephrology community have long recognized the need for CMS ESA payment policies in ESRD to account for the temporary fluctuations of hemoglobin levels that commonly occur. When physicians target hemoglobin levels between 10 g/dL and 12 g/dL (consistent with the prior FDA-approved label hemoglobin target), the majority of those patients—even those on a stable dose of EPOGEN®—can experience temporary elevations above 12 g/dL, as discussed earlier.

Prior to the implementation of the EMP, analyses demonstrated that ESA dosing decisions were generally consistent with the FDA-approved product labels. Although patients may have temporary excursions above 12 g/dL, 83% of hemoglobin concentrations above 12 g/dL return below 12 g/dL within three months, and thus it does not appear that physicians are maintaining patient hemoglobin levels persistently above 12 g/dL.[27]

Early results post-EMP implementation demonstrate stability of population hemoglobin levels and ESA doses.[28] Amgen analysis of data collected since the EMP implementation suggests that 81% of physicians are reducing ESA doses within 30 days when hemoglobin exceeds 13 g/dL, compared to 72% at the time the EMP was announced in November 2005.[29]

Additionally, newly analyzed data collected following the recent ESA label changes show the percentage of patients with hemoglobin concentrations above 13 g/dL has been reduced with a corresponding increase in the number of patients in the 11 to 12 g/dL range, and there is an increased frequency of ESA dose decreases made in response to achieved hemoglobin between 12 and 13 g/dL, as well as above 13 g/dL. As of April 2007, 49% of hemoglobin excursions between 12 g/dL and 13 g/dL are followed by an ESA dose reduction within 30 days, as compared with 37% in January of 2007.[30] In addition, in some instances physicians implement a dose reduction after 30 days. We anticipate that additional changes to physician ESA prescribing trends will continue.

Payment changes for ESAs in ESRD based on an insufficient analysis of scientific data could lead to negative outcomes for patients and for health care in the U.S.

---

[25] Medicare Payment Advisory Commission. Report to the Congress: Medicare Payment Policy. March 2007.

[26] Department of Health and Human Services Office of the Inspector General. Medicare Reimbursement for Existing End stage Renal disease Drugs. May 2004. OEI 03–04–00120.

[27] Amgen data on file.

[28] Ofsthun NJ and Lazarus JM. Impact of the change in CMS billing rules for erythropoietin on haemoglobin outcomes in dialysis patients. *Blood Purif*. 2007;25:31–5; Amgen data on file.

[29] Amgen data on file.

[30] *Amgen data on file*.

Amgen believes that any change to the ESRD payment system should have a strong policy or clinical rationale, and any new system should maintain patient quality of care, ensure patient access, and be financially viable for dialysis providers, patients, and taxpayers. As this document describes, there does not appear to be a compelling policy or clinical rationale to make fundamental changes to the ESRD payment system based on the best available scientific evidence and utilization data. Congress should carefully consider the potential for negative patient outcomes as an unintended consequence of payment changes that are not carefully designed, considered, and implemented.

Accordingly, Amgen does not believe that Congress should consider implementing a single bundled payment for drugs and dialysis services in dialysis until the Medicare Prescription Drug, Modernization, and Improvement Act (MMA) mandated CMS demonstration project to test a bundled payment in ESRD is completed. As bundled payment systems create powerful financial incentives to save money by underutilizing and withholding needed medical services, bundling methodologies must be balanced by a robust and clinically valid risk-adjustment system, as well as an agreed-upon set of quality safeguards, lest they result in the under-treatment of vulnerable dialysis patients. In particular, there may be serious unintended consequences to specific dialysis populations, such as those residing in rural areas and those receiving dialysis care in centers located in underserved urban areas from independent dialysis centers. Ultimately, if there is under-treatment of dialysis patients, not only would dialysis patients be harmed, it could cost taxpayers more money in hospitalizations and other patient care expenses. Congress recognized these complex issues, and mandated the conduct of a demonstration project before implementing a bundled dialysis and drug payment rate.

ESRD patients represent a seriously ill and vulnerable patient group, at high risk of death, with minorities disproportionately represented. Even among ESRD patients, there are some who are more gravely ill and require significantly greater health care intervention. Unless Medicare appropriately reimburses for these patients, even one or two such patients in a single dialysis center can literally "tip the scales" and cause a provider to lose money and even risk closure. Many believe that the risk is highest for the small dialysis organizations that serve poor patients in rural areas.

Other changes to ESA reimbursement policy could also have serious consequences for patients and providers. Changes to ASP+6% reimbursement, a system that has reduced spending and saved taxpayer dollars, could in particular harm smaller dialysis providers and the patients they service. Changes that mandate specific physician treatment decisions, such as mandating a particular ESA route of administration, also should be avoided.

Any of these changes could lead to unintended consequences including:

- Poorer quality of care, as dialysis providers may need to make compromises to offset lower overall reimbursement.
- Higher overall Medicare costs as a result of poor quality dialysis care.
- Threats to access to quality care for patients treated in small dialysis facilities in both rural and underserved urban areas. Small clinics may begin to avoid more ill/costlier patients in order to control costs, or even close as a result of financial burden.

Finally, given the evolving data on physician prescribing of ESAs since the announcement of the revised FDA product labels and implementation of the EMP, it may inappropriate for Congress to implement new legislation or direct CMS to alter the existing reimbursement paradigm for ESAs prior to allowing the Agencies and community to review and respond to this most recent and highly relevant information.

Conclusion

In conclusion, Amgen thanks the Committee for the opportunity to submit written testimony. We are proud of EPOGEN®'s long history of safely and effectively treating anemia in ESRD patients. We stand alongside the physicians, nurses and other healthcare providers in supporting the best possible care for highly vulnerable kidney disease patients. Amgen remains concerned that legislation based on an insufficient analysis of relevant clinical data could result in unintended negative consequences for patients and for U.S. health care.

Statement of Kidney Care Partners

Introduction

Chairman Stark, Representative Camp, and distinguished members of the Subcommittee, the undersigned members of Kidney Care Partners (KCP) thank you for the opportunity to provide written testimony regarding anemia management and the continuing effort to ensure safe and appropriate care for patients with End Stage Renal Disease (ESRD). KCP is a nationwide alliance of representatives from the entire kidney care community, including patients and their advocates, nephrologists, nurses, dialysis care providers, and manufacturers who have joined together to improve the quality of care and quality of life for individuals suffering from kidney disease and kidney failure.

KCP recognizes the serious and important questions that have been raised by recent analyses in the area of anemia management. KCP applauds the efforts of those who have demonstrated concern for the safety of different patient populations within the ESRD program and remains committed to the need for careful consideration of drug utilization patterns as new research is released. Advancements within the kidney care community during the last ten years have been well documented, and KCP desires to build on this history by volunteering the collective knowledge, experience, and perspective of its members as Congress reviews issues related to anemia management and endeavors to improve the ESRD program.

Commitment to Safe and Appropriate Anemia Management

The kidney care community believes strongly that there should be one motivation for determining utilization of drugs used to treat anemia, and that motivation is patient well-being. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Guidelines and the Clinical Performance Measures (CPMs) developed by CMS and the ESRD Networks provide critical guidance for physicians to use as they work to keep patients feeling well, while also meeting important medical standards. KCP also believes there should be one goal for anemia management policy, and that goal is ensuring safe and high quality care. To those ends, KCP puts forth the following guideposts as essential to a proper consideration of anemia management and related policy.

First, drugs used to treat anemia have a history of enhancing patient care by improving clinical conditions and quality of life while reducing the risks from transfusions. In particular, KCP would like to point out with pride the continuous improvement in the mortality rate of ESRD patients for the past 10 years that has been repeatedly highlighted in the USRDS data. KCP believes any well-balanced consideration of anemia management and related policy should be attentive to this reality and this record.

Given the kidney failure patients on dialysis have experienced, treatment with erythropoietin stimulating agents (ESAs) ensures that dialysis patients have the hemoglobin levels necessary to sustain their energy levels and physical functioning, thereby improving patients' ability to engage in typical daily activities, including a parents' capacity to raise their children and an employees' potential to head to work.

Moving from the patient to the aggregate level, ESAs have been part and parcel of the kidney community's ability to advance the quality of care during the past ten years. As the Centers for Medicare and Medicaid Services (CMS) stated, "Since 1994, [CMS] has documented continued improvements, specifically in the adequacy of dialysis and anemia management. The providers of dialysis services are to be commended for their ongoing efforts to improving patient care."[1] CMS' findings reflect the fact that most ESRD patients meet the CPM benchmarks developed by the Agency in consultation with independent experts. Ensuring that patients meet the core standard of the CPMs (i.e. hemoglobin levels > 11g/dL) means that there are fewer hospitalizations and lower expenses for the Medicare program.

More directly, ESAs have reduced the rate of transfusion in the dialysis population, which has helped reduce the risk from transfusion, lower the impact on antibodies in transplant candidates, and mitigate the chance of infection and iron overload. These benefits, as well as ESAs' ability to improve patient quality of life, should be considered in striking a safe and appropriate balance for individual ESA use.

Second, the entire kidney care community is committed to the highest standards and the most current science on anemia management. The community, however, is also acutely aware of the need for anemia management policy to be sensitive with respect to patients' varied physiologic responses to ESAs and responsible with re-

[1] Centers for Medicare and Medicaid Services, *2005 ANNUAL REPORT ESRD CLINICAL PERFORMANCE MEASURES PROJECT* 35&38 (2005).

gard to the unanswered questions that overlay current anemia management research.

Because each patient receiving dialysis responds differently to the drugs used to treat anemia, it is not possible to determine a single dosing regime that works for all patients at all times. This means that physicians must establish unique dosing regimes for each patient for whom they provide care. Ultimately, a system impeding this flexibility is a system impeding its own goals of safe and appropriate care.

This point underscores the need for responsible action when reacting to current research on drug utilization in anemia management. There can be no doubt that current research raises many significant questions, but not all of the questions raised may be fully applicable to ESRD patients. The study results of CHOIR and CREATE, as reported in the New England Journal of Medicine (NEJM), for example, focused on patients with kidney disease, but not those in full kidney failure (ESRD). As CMS has noted, "Anemia management for patients with ESRD cannot be assumed to be the same for patients, often younger, with chronic kidney disease who do not require dialysis—Patients receiving dialysis are exposed to clinical situation that patients with [Chronic Kidney Disease] CKD not requiring dialysis are not exposed to, including artificial kidney membrane exposure, large fluid shifts during dialysis—" and other situations.[2] In addition, the NEJM studies looked at patients intentionally maintained at hemoglobin levels outside the target range of 11–12 g/dL.

Although we believe it is important to review these studies in the context of current treatment protocols, policy-makers should not rush to judgment and implement broad policy changes based upon only a few studies where experts have yet to determine how they relate to patients with kidney failure and current practice protocols. Policy-makers must have access to the best cumulative data to answer properly the question of appropriate anemia management policy, and KCP is committed to maintaining a proactive dialogue as new research becomes available.

As part of this cautious approach, KCP firmly and steadfastly rejects any effort to use current research on anemia management as a justification to withdraw funding from the ESRD program. The trail of concern leading to this hearing has been paved with the logic of structural reform, not the need for payment cuts. If one is convinced that the incentives are misaligned with respect to drug utilization, then it is the incentives that need to be fixed. Resources should not be taken away from the ESRD program.

Commitment to Overall Quality in Patient Care

To the extent that questions about safe and effective care are driving the reform agenda, the discussion should not end with consideration of drug utilization alone. On the contrary, a genuine commitment to appropriate care should be carried through with respect to ensuring that the ESRD program as a whole continues to be structured so as to provide the highest quality care to patients with irreversible kidney failure.

At the broadest level, policies affecting patients with ESRD must be based upon the goal of ensuring continued improvements in the quality of care provided, and any changes to the system must reflect and advance this goal. More specifically, this means that policies impacting care for ESRD patients should ensure there are no incentives driving utilization. This requires equal vigilance against the possibility that patients will be under-provided essential drugs and services, or worse yet, selected against by a structural impetus to "cherry pick" relatively healthier patients with advantageous treatment scenarios.

Put another way, any reform effort should seek to enhance the existing high quality of the community and not hinder it. According to the most recent data collected by CMS, more than 90 percent of patients attain dialysis adequacy, approximately 83 percent have hemoglobin levels above 11, 82 percent have albumin levels (an indicator of nutrition) greater than 3.5 g/dL, and 54 percent of patients have an AV fistula as their access. These data demonstrate the quality has improved substantially over the years; yet, there is more that can be done. To that regard, KCP strongly supports implementing a continuous quality improvement program, as outlined in legislation introduced by Representatives John Lewis and Dave Camp.

Quality in patient care is also a product of the stability and sustainability of the treatment system. At present, however, there is a piece missing from a stable programmatic foundation. While every other prospective payment system within Medicare is provided an annual update mechanism tied to inflation, so that the commitment to quality in those programs is paired with the resources necessary for its at-

[2] Statement of Leslie V. Norwalk, Acting Administrator, Centers for Medicare and Medicaid Services, Before the House Committee on Ways and Means, December 06, 2006.

tainment, the ESRD program does not include such an assurance. Moreover, ESRD providers operate in a competitive marketplace with other health care providers that receive annual updates under their payment systems. Providers receiving annual updates enjoy a significant advantage in their ability to offer compensation designed to attract and retain nurses and other professional staff, for example. Over time, the lack of an annual update mechanism could impede ESRD providers' ability to remain competitive with other health care sectors.

It is equally critical that any reform effort look beyond the clinical aspects of the ESRD program to consider the broader potential to make strides by renewing the community's capability to focus on education, prevention, technology, and how services are delivered. Today's reform agenda may rightly reflect today's concerns, but insofar as the ERSD program has not been comprehensively reexamined since its creation in 1973, there is strong reason to believe we are not adequately considering tomorrow's opportunities. KCP believes that reform should not be locked into a responsive mode, but should be proactive in achieving innovations and interventions that can save lives and conserve resources.

Beginning with education, the ERSD program should provide mechanisms to inform patients about the ways to delay and prepare for the onset of irreversible kidney failure. Specific educational initiatives include protocols for patients with Stage IV chronic kidney disease; other prominent efforts involve the training of patient-care dialysis technicians. Prevention efforts are quite similar in concept, but operate earlier and more broadly. These seek to halt the development of risk factors and instances of early-onset, but also extend to initiatives that prevent older patients from developing such extensive co-morbidities as to irredeemably "crash into dialysis."

Alongside education and prevention, the ESRD program should prioritize and incentivize new technological breakthroughs in pharmaceuticals, devices, and delivery mechanisms alike. The creation of the "fistula"—a surgically enlarged vein (usually located in the wrist or elbow) that provides access to the bloodstream for hemodialysis—offers a prime example of the cost savings and quality benefits that flow from innovation. The successful "Fistula First" initiative, sponsored by CMS, further exemplifies the latent potential of collaboration to improve technology—and with it the efficiency and quality of patient care.

Finally, policies to advance flexibility in service delivery are also critical given the weakened condition and regular treatments that characterize ERSD patients. All dialysis modalities should be adequately funded, and studies should proceed as to why some remain underutilized. For example, home dialysis and more frequent dialysis should be studied so as to improve both patient access and quality of clinical outcomes.

Conclusion

KCP is committed to the goals of safe, appropriate, and high-quality care for ESRD patients. In turn, KCP operates under the conviction that any anemia management reform should be well balanced, well grounded, and well considered. This means taking into account the advances and achievements in anemia management brought about by ESAs, alongside any concern regarding their utilization, as one derives motivation and methods for reform. It also means that current research, given its preliminary state, should be viewed as an urgent call for further inquiry, but not as a springboard for precipitous action. It finally leads to the conclusion that reform, when achieved, should be responsive to its animating goals of safety and efficacy, and not to a desire for payment cuts.

KCP is also of the mind that a commitment to the goal of safe and effective care is not well served when it ends with anemia management alone; on the contrary, KCP believes this commitment should extend to all those elements of the ESRD program relating to the quality of patient care. This means, first and foremost, that any reform should strive to ensure continued improvements in the quality of care. More specifically, this means ensuring stable and sustainable system economics and an update mechanism while ensuring there are no non-clinical incentives for utilization. It also means endeavoring to proactively reform the ESRD program, to strengthen our commitment to education, prevention, technology, and flexibility in order to improve not only the care we deliver to those patients served by the ESRD program, but also the quality of life for those individuals who can avoid kidney failure.

In closing, KCP wishes to recognize and thank Representatives Camp and Lewis for their leadership in advancing the Kidney Care Quality and Education Act and to also recognize the commitments over the years by Chairman Stark and Representative McDermott to improve care for all kidney patients. We are committed

to working with Congress to strengthen the Medicare ESRD program and welcome the opportunity to serve as a resource to the Committee in that regard.

Abbott Laboratories
Advanced Magnetics, Inc.
American Kidney Fund
American Nephrology Nurses' Association
American Regent, Inc.
American Renal Associates, Inc.
American Society of Nephrology
American Society of Pediatric Nephrology
California Dialysis Council
Centers for Dialysis Care
DaVita, Inc.
DaVita Patient Citizens
Diversified Specialty Institutes
Fresenius Medical Care North America
Genzyme
Kidney Care Council
National Kidney Foundation
National Renal Administrators Association
National Renal Alliance, LLC
Northwest Kidney Centers
Renal Advantage, Inc.
Renal Physicians Association
Renal Support Network
Renal Ventures Management, LLC
Satellite Health Care
U.S. Renal Care
Watson Pharma, Inc.

Statement of National Renal Administrators Association

On behalf of the National Renal Administrators Association (NRAA), I am pleased to submit the following statement for the record of the Subcommittee hearing on safety concerns regarding the dosing of erythropoiesis stimulating agents (ESAs), variation in utilization of ESAs across providers, and reimbursement issues. We commend the Committee for its interest in the health and safety of dialysis patients and the current system for reimbursing providers.

The NRAA is a voluntary organization representing professional managers of dialysis facilities and centers throughout the United States. Our membership includes free-standing and hospital-based facilities, which are for-profit and non-profit providers located in urban, rural and suburban areas and serving dialysis patients in all settings. Many of our members are small providers and treat patients in underserved inner city and rural locations. NRAA members are located in virtually every congressional district.

We welcome the opportunity to comment on the appropriate dosing of erythropoietin (EPO) and its impact on reimbursement. We see the effects of anemia and of adequate management every day. It is a serious matter and we applaud the Committee's interest and concern.

Patients with ESRD suffer from anemia because their kidneys do not produce a hormone that regulates red blood cell production. Anemia seriously affects every organ system, including the brain, and has a direct impact on a patient's quality of life. Anemic ESRD patients have more difficulty performing every day activities, including working. They experience lower vitality and may suffer from depression.

A patient's degree of anemia is measured by hemoglobin or hematocrit levels. A healthy man, for example, has a hemoglobin level of 15 (a hematocrit level of approximately 45 percent), with slightly lower values in healthy women. Before effective treatment was available an ESRD patient on dialysis would typically have severe anemia: A hemoglobin level lower that 10 (hematocrit level lower than 30). This could be treated only through blood transfusions.

There is no definitive consensus within the scientific community regarding optimal anemia management, or hemoglobin levels for the ESRD population. There is, however, an extensive volume of peer-reviewed literature discussing what the optimal target hemoglobin/hematocrit level for patients with ESRD should be. The Food and Drug Administration (FDA) label recommends a target hemoglobin of 12 grams per deciliter.

As everyone knows, recent studies in the New England Journal of Medicine have created renewed controversy and discussion. These studies found in kidney disease patients not yet on dialysis an association between higher hemoglobin levels and increased risk for adverse effects ranging from cardiovascular morbidity and death to episodes of elevated blood pressure and headaches.

We firmly believe, as does everyone involved in the care of patients with kidney disease, that anemia management in ESRD patients should be medically appropriate and designed to maximize benefits and minimize risks. We also believe that all care-givers should comply with the FDA labeling requirements. We urge the Committee to recognize, however, that determining and maintaining optimal hemoglobin levels is not straightforward, but is complex and inextricably linked to patient variability. Health care providers and policy makers are accustomed to the fact that providers treat patients with conditions across a wide range of acuity: some patients are more severely ill and some have more co-morbidities than others. It is also important to note that it is very common for the same ESRD patient to experience variations in hemoglobin level, resulting from co-morbidities, hospitalizations and unique physiology. Because of the variability, optimal anemia management requires a highly flexible and individualized approach to treatment.

The recent CMS EPO Monitoring Policy recognizes the need for the reimbursement policy to take into account patient variability. When reviewing this policy, it is important to note that it is not a treatment guideline. Rather, it is a reimbursement auditing tool. Under the policy, if a patient's hemoglobin reaches 13 and the dose is not reduced, CMS will reduce the payment 25 percent. It does not call for, nor recommend, that patients' hemoglobin levels be maintained above 12.

Because of the scientific and clinical complexity surrounding anemia management in ESRD patients, the NRAA believes that Congress and CMS should take all available studies, as well as the FDA label, into account when setting Medicare payment policy. Further, we urge great caution in making policy decisions based on recent studies, which focus on patients undergoing chemotherapy not dialysis, or with chronic kidney disease and not yet in need of dialysis treatments. More research is needed, focusing exclusively on patients with ESRD. Until there is indisputable scientific evidence that the current parameters of anemia management in ESRD patients are inappropriate, it would be premature for the Congress or CMS to revise Medicare reimbursement policy based on these considerations.

We also wish to point out the recent recommendations of a work group of the National Kidney Foundation.

"The Hb target is the intended aim of ESA therapy for the individual CKD patient. In clinical practice, achieved Hb results vary considerably from the Hb target.

2.1.1 In the opinion of the work group, selection of the Hb target and selection of the Hb level at which ESA therapy is initiated in the individual patient should include consideration of potential benefits (including improvement in quality of life and avoidance of transfusion) and potential harms (including the risk of life-threatening adverse events.) (Clinical Practice RECOMMENDATION)

2.1.2 In the opinion of the work group, in dialysis and non-dialysis CKD patients receiving ESA therapy, the selected Hb target should generally be in the range of 11.0 to 12.0g/dL. (Clinical Practice RECOMMENDATION).

2.1.3 In dialysis and non-dialysis CKD patients receiving ESA therapy, the Hb target should not be above 13g/dL. (Clinical Practice Guideline—MODERATELY STRONG EVIDENCE)"

CMS reimbursement policies, including the monitoring policy to ensure reimbursement for anemia management is medically appropriate and in adherence to FDA label specifications, should be consistent with current medical standards of care and should not create incentives to over-or-under prescribe, and should allow doctors the flexibility to manage anemia on a per-patient basis. Medical decisions should be made on the basis of the best patient care and should not be driven by reimbursement considerations.

We also want to comment on one specific aspect of the current reimbursement system. We are aware of and fully appreciate the costs of the current program to Medicare. There were an estimated 290,000 patients on dialysis who are covered by Medicare, according to a 2004 report of the U. S. Renal Data System (USRDS). We also know that the increase in the rates of diabetes and hypertension, particularly in the minority community, will, unfortunately, lead to a continued growth in the number of patients needing dialysis. While we are concerned with increasing Medicare expenditures and the need to stabilize the program, we do not believe that taking action to reduce reimbursement rates for dialysis providers or failing to address the current inequities in the program is the answer.

Inadequate reimbursement is a particularly acute problem for the smaller provider (SDO) that has to absorb increases in pharmaceutical costs and medical prod-

ucts, employee compensation and benefits, utilities and other requirements simply to continue to serve their patients. Smaller providers do not have the ability to cost shift to commercial carriers to offset inadequate Medicare reimbursement. For most SDOs, Medicare and Medicaid account for nearly 80 percent of their revenue.

Nor do the SDOs have the purchasing power to gain the discounts that are available to the large dialysis organizations (LDOs). Currently, the majority of independent dialysis providers purchase through one of two specialty Group Purchasing Organizations (GPOs). The largest of these purchases for more than 80 percent of the independents but still cannot achieve the discounts afforded to the LDOs. Additionally, the small providers do not have the ability to share profits or losses among a number of facilities.

Unfortunately, because of the lack of adequate Medicare payments, some providers are being forced to close their doors, requiring patients to seek care in other facilities, which in rural areas can require hours of driving time. Given the fact that most patients must receive treatment for the better part of the day—three times or more a week—the additional driving time is a tremendous hardship. It is a very sad commentary that, in some instances, patients have decided to stop treatment rather than place the burden of travel on their loved ones.

Let me take a few minutes to review the history of the Medicare ESRD program. In 1972, Congress expanded Medicare coverage to include all patients suffering from kidney failure, no matter what their age. Dialysis was a new, life safe-saving procedure. In 1983, because of the unexpected costs of the program, Congress created the composite rate for dialysis services, which was Medicare's initial prospective payment system. In response to a proposed reduction in the composite rate by the Centers for Medicare and Medicaid Services (CMS), then the Health Care Financing Administration (HCFA), Congress intervened and limited the reduction. But there was no statutory provision for updating the reimbursement rate. As a result, for over two decades, the composite rate payment system has not kept pace with costs, leaving many providers inadequately paid for their dialysis services.

From 1983 until congressional intervention in 1986 to stop a significant reduction in the composite rate payment, the Centers for Medicare and Medicaid Services (CMS) continually expanded the bundle through the "folding in" of previously separately billable items such as common volume expanders and laboratory services. The composite rate payment recognized none of these "folded in" services. In fact, the payment for freestanding dialysis providers decreased from $138 to $123 per treatment. Additionally, despite annual recommendations by first the Prospective Payment Assessment Commission and then the Medicare Payment Advisory Commission (MedPAC) for an increase in the composite rate, neither Congress nor the Administration supported increases except on two occasions.

In a 2003 report to Congress entitled "Toward a Bundled Outpatient Medicare End-Stage Renal Disease Prospective Payment System," CMS acknowledged that the current system has not addressed the increases in costs and the losses that providers have incurred in treating Medicare patients.

The following table is a summary of the increases in the Consumer Price Index (CPI), the Medical Care Component of the CPI from 1996 to 2006 and the corresponding increases in Medicare reimbursement for hospital and for dialysis providers.

Year	Consumer Price Index CPI	Medical Care Component	Hospital Update	ESRD Composite Rate
1996	3.0%	3.0%	1.5%	0.0%
1997	2.3%	2.8%	2.0%	0.0%
1998	1.6%	3.4%	0.0%	0.0%
1999	2.2%	3.7%	0.5%	0.0%
2000	3.4%	4.3%	1.1%	1.2%
2001	2.8%	4.7%	3.4%	2.4%
2002	1.6%	4.7%	2.8%	0.0%
2003	2.3%	4.1%	3.4%	0.0%
2004	2.7%	4.5%	3.3%	0.0%

Year	Consumer Price Index CPI	Medical Care Component	Hospital Update	ESRD Composite Rate
2005	3.4%	4.3%	3.7%	1.6%
2006	2.5%	4.5%	3.4%	1.6%
Average	2.5%	4.0%	2.28%	0.61%
Cumulative Total	27.8%	44.0%	27.3%	6.8%
Sources	Bureaus of Labor Statistics—Department of Labor	Bureaus of Labor Statistics—Department of Labor	Medicare	.

As you can see, the table shows that hospitals have received total increase of 27.3 percent, reflecting the overall increase in the CPI, versus 6.8 percent for dialysis providers. This lack of adequate reimbursement for dialysis providers has established a perverse arrangement in which providers, to survive, continuously have had to squeeze productivity and margins. Furthermore, as we noted earlier, since commercial coverage represents such a small portion of income for dialysis providers, the Medicare losses cannot be shifted to private insurers.

On January 9, 2007, MedPAC convened a session on the "Adequacy of Outpatient Dialysis Payments." Staff reviewed the Medicare margins for the two largest dialysis providers and all other providers. The data showed that the two largest providers have a 10.7 percent margin and the other providers only a 2.6 percent margin. SDOs clearly have unique financial concerns and many have been forced to sell or shut down, which is one of the reasons that the two largest chains now serve more than 70 percent of the dialysis patients.

Any changes in reimbursement policy should address the need to create a statutory mechanism for an annual update. It is only fair that dialysis providers be granted the same statutory right to an annual update as all others who participate in Medicare. We firmly believe that the Medicare reimbursement system must be based on two fundamental principles: providing the highest quality of care to our patients and guaranteeing a sound financial footing for our members.

We thank you for the opportunity to present our views and look forward to continuing to work together to ensure that whatever action is taken is fair to patients, providers and the Medicare program.

Statement of Renal Support Network

The Renal Support Network strives to help patients with chronic kidney disease (CKD) improve their employability and develop their personal coping skills and special talents by educating and empowering them, as well as their family members, to take control of the course and management of the disease. We who have CKD are very grateful for the ESRD program and how it has helped both prolong our lives and improve the quality of our lives. I am writing to provide the patient's perspective on two aspects of care for patients with CKD that are currently being considered by your Committee—namely, appropriate anemia management and the bundling of dialysis services.

Patients with kidney disease often have anemia because their kidneys do not produce enough of the hormone erythropoietin. This hormone stimulates red blood cell production. Anemia is common in patients with CKD and is almost universal in patients with stage 5 CKD who are on dialysis.

The introduction of Erythropoiesis Stimulating Agents (ESA) to treat anemia in patients with renal disease has dramatically improved patient quality of life. In addition, patients no longer have to be transfused on a regular basis. Before ESAs were available, we commonly received red blood cell transfusions, which carried the risks of infection, iron overload, and potentially reducing the chances of receiving a kidney transplant.

Please keep in mind the following when making decisions:

- All drugs carry risks. **Patient safety, coupled with respect for patient quality of life concerns, should always be paramount in drug prescribing and dosing.** A dialogue between the patient and physician is critical to determine what is best for each individual patient.

- Patients with CKD, especially those on dialysis, are exposed to conditions **that make their anemia significantly different than patients with cancer** (e.g., ongoing need for ESA therapy versus temporary need for those with cancer, ongoing blood loss from the dialysis procedure, etc.).
- ESAs remain the **best treatment for anemiain patients with CKD.**
- Given the major loss of blood inherent with dialysis, **ESA treatment sustains the hemoglobin level and allows patients to have higher levels of energy.**
- Based on the newest safety data, RSN agrees with the latest recommendation from the National Kidney Foundation's Kidney Dialysis Outcomes Quality Initiatives (KDQOI™) panel of experts that calls for **targeting patients' hemoglobin levels (the blood test used to measure anemia) between 11 and 12 g/dL.** In making this recommendation, the KDOQI™ states that actual Hb levels may fluctuate to above or below this target range because of natural variations in Hb.
- In its most recent report, CMS found that 83 percent of all patients with ESRD had a mean hemoglobin ≥11 g/dL and that **the mean hemoglobin for patients was within the 11–12 g/dL range.**
- Patients want to make sure that **the progress in anemia outcomes that has been made over the past two decades is not reversed.**
- Patients want to make sure **that the therapies they receive are being administered safely**, but also **do not want to sacrifice the quality of life benefits associated with an appropriate hemoglobin, or run the risk of an increase in blood transfusions if Hb levels are kept inappropriately low.**

I, among fellow patients in our organization, have witnessed firsthand the evolution of anemia management in patients with kidney disease. With the introduction of ESAs, thousands of patients have been spared the risks associated with multiple blood transfusions. The quality of our life and level of functioning has improved markedly. This has been shown in many clinical studies and evidenced by the patients themselves. I would specifically like you to give high priority to considering the issue of quality of life as it pertains to the guidelines that will be used to manage anemia in patients with CKD.

Although some say that quality of life should not be considered when administering care, RSN supports the position stated in the 2007 Medicare handbook that the Medicare program is helping patients to "**stay healthy and active."** The importance of quality of life is also eloquently stated in the mission statement of the National Center for Chronic Disease Prevention and Health Promotion which states that they strive to **"promote health and quality of life by preventing and controlling disease, injury, and disability."**

Anemia is one of the most devastating and potentially debilitating conditions that affect those with CKD, and it can dramatically affect our quality of life. Many people who have CKD can relate experiences of how anemia has affected them personally (please visit our website to hear their personal stories). Symptoms include chest pain, feeling cold, feeling tired, low energy levels doing routine activities of daily living, poor appetite, shortness of breath, depression, a poor sense of well-being, and an inability to work, manage a home, or volunteer—in short, loss of a meaningful quality of life. Patients visit doctors out of what they sense about some symptom that is affecting our quality of life (i.e. "how we feel"). We simply have no other way to communicate. While preservation of life is certainly a primary focus of medical care, **an equally important goal is to help us preserve or regain our quality of life. An illness is too demanding when you don't have hope!**

There is much to be learned about anemia management in the CKD patient population, and more analyses and studies need to be conducted. We hope that quality of life will not be ignored in the current dialogue and decision-making—to do so is tantamount to ignoring the patient.

A second issue that is currently under discussion by your Committee is potentially changing the dialysis payment process in favor of a bundling approach. We are concerned that sudden revisions in the reimbursement policy may unintentionally lead to a decrease in our quality of care or quality of life. We would like to bring up a few points to consider to ensure that the new policy remains focused on the patient:

1. Ensure that the new policy **does not result in the disappearance of patient care services** that dialysis facilities currently provide.

2. **Laboratory testing must be done in the dialysis setting to ensure patients receive optimal care.** This is crucial for dialysis patients to remain viable candidates on the transplant list. In addition, for every extra stick a kidney patient

receives to draw blood is counterproductive to CMS's Fistula First and National Vascular Access Initiative. We need to preserve our veins.

3. Ensure that all people who have ESRD **have access to quality care,** as jointly defined by medical professionals and patients.

4. Ensure that any newly implemented policies include provisions for **ongoing and timely modifications in the definitions of quality of care and quality of life based on current data and the newest therapies.**

5. Ensure that all patients **continue to receive education on the differences between modality options** (including home dialysis and kidney transplantation).

6. Include provisions that will continue to **allow patients real choices on where they dialyze** and have the ability to travel throughout the United States.

7. Include provisions and a financial model that will **allow both small and large providers to remain viable**, thereby providing patients with true choices on where to dialyze.

8. Provide reimbursement structures that will continue to allow and motivate dialysis facilities to **employ the best professional staff, upgrade dialysis machines, and integrate new equipment based on technological innovations.**

9. Provide a reimbursement structure that will continue to **motivate researchers to develop innovative therapies that will improve our quality of care and overall well-being.**

10. Develop safeguards to **prevent companies from "cherry picking" patients** to avoid treating those who require the most expensive care.

11. Ensure that safeguards are in place to allow medical professionals to provide care **based on individual patient needs**, while **protecting patients from needlessly being sent to the hospital** or for additional physician office visits for care that can be provided in the dialysis facility.

We salute CMS and Congress for their past and ongoing efforts to improve the quality of care and quality of life for patients with CKD. Prominent examples of how CMS continues to protect the interests of patients include Fistula First, National Vascular Access Improvement Initiative the Dialysis Facility Compare Website, Know Your Numbers, and the Clinical Performance Measures. These efforts are currently benefiting hundreds of thousands of individuals, and may positively affect millions in the future. We urge CMS and Congress to continue and expand these efforts.

We respectfully request Congress to resist making a premature reimbursement decision that may not include complete or accurate information on the impact of such a change on patient outcomes. Demonstration projects are currently underway or being planned that will test whether proposed changes in reimbursement will preserve the quality of care for patients with kidney disease. **As stated in the Medicare handbook**, these demonstration projects are designed to **reduce health risks, improve quality of life, and provide savings.** It is critical to have an understanding of all the complexities that may impact how care is provided under a bundled model before such a model is implemented. In addition, when any new system is implemented, it is vital that there are regular reviews that allow for evaluation and prompt correction of the new payment system if problems arise.

The reality is that the ESRD program has a flawed reimbursement system and the incentives are wrong. Renal Support Network recognizes the need for the system to be changed. We urge Congress to take the necessary steps to ensure that any change does not unintentionally lead to an increase in mortality, decrease in our quality of life, or decrease in access to care.

Thank you for taking the patients' concerns into consideration. Please feel free to call if you have any additional questions.

Sincerely,

Lori Hartwell
RSN President and Founder

Research Utilization Project Proposal

Quality of Life Outcomes Related to Anemia Management of Patients with Chronic Kidney Disease

Nancy Newbold and Evelyn N. Reyes
University of Phoenix
Research Utilization Project
NUR/598
Margaret L. Colucciello, PhD, RN

Table of Content

Abstract.....5
Research Utilization Proposal.....7
1. Problem Statement: Inadequate Anemia Management Strategies.....7
2. Proposed Solution for Anemia Management Strategy.....8
Section A: Problem Identification:.....9
1. Problem identification/Description.....9
2. Importance of the Problem.....10
3. Developing Project Objectives.....11
4. Brief Proposed Solution Description and Rationale.....11
Section B: Innovation Description:.....12
1. Solution Description.....12
2. Consistency of Solution with Research Support.....12
3. Feasibility of The Solution.....13
4. Consistency of Solution with Resources.....13
Section C: Research Support:.....14
1. Sufficient Research Support Base.....14
2. Compelling Research Support Base.....15
3. Types of Research Articles.....15
a. Quantitative.....15
b. Qualitative.....16
4. Discussion of Research Studies.....16
a. Scientific merit.....16
b. Strengths and limitations.....17
c. Relevance and rationale for inclusion.....18
Section D: Implementation Plan.....18
1. Solution Implementation Plan.....18
a. Involvement of formal and informal leaders.....18
b. Timing of implementation.....19
c. Inclusion of personnel.....19
d. Obtaining approvals.....19
e. Communication Methodologies.....19
2. Resources Needed for Solution Implementation.....20
a. Timing of implementation.....20
b. Involvement of key personnel.....21
c. Equipment and materials.....21
d. Consideration of Costs.....21
3. Monitoring Solution Implementation.....22
4. Utilization of Planned Change Theory.....22
5. Feasibility of Implementation of Solution.....23
Section E: Evaluation Plan.....24
1. Developing or Revising Outcome Measure.....24
a. A copy of the measure needs to be included in the Appendix.....
2. Determining Outcome Measure Value.....24
a. Validity.....25
b. Reliability.....25
c. Sensitivity to change.....26
d. Appropriateness for use.....26
3. Data Collection and Analysis.....27
4. Resources Needed.....27
5. Feasibility of the Plan.....28
Section F: Decision-Making Strategies.....29
1. Maintenance of the Solution.....29
2. Extending the Solution.....29
3. Revising the Solution.....29
4. Discontinuing the Solution.....30
5. Plans for Work Setting and Professional Feedback.....30
References.....30
SF–36 Appendix A.....33
The SF–36v2™ Health Survey Appendix B.....36
Quality of Life Outcomes Related to Anemia Management of Patients with Chronic Renal Failure. Appendix C.....40
CNS AMP Projected Budget. Appendix D.....48

Abstract

The main reason for writing this proposal was to bring attention to the need of having an Advanced Practice Nurse take on the role of a Clinical Nurse Specialist (CNS). Working in dialysis as a Clinical Manager, and managing an anemia man-

agement program has brought effective results in anemia management patients. A patient in dialysis by the name of Mack is an 80 something women that comes to dialysis three times a week. Mack wears bright clothes with stripes or poke-a-dots and a beach hat. When she wheels through the doors of the clinic she smiles at everyone she meets and if asked how she is, she will go into detail about her day. Real or unreal her stories are sweet and all the while she is talking there is a big smiling on her face. She is a tiny women the size of a child, small and fragile. A short six months ago Mack's hemoglobin was critical low and now she has stable hemoglobin levels. Her hip fracture is healed and she is not in traction anymore. She can pivot to the chair to sit down for her treatments. Anemia management helped Mack improve her active daily living. Her improvements did not go unnoticed by her daughter, or the Nephrologists and mostly her Clinical Manager who was the CNS of the AMP at Mack's clinic. Mack, like so many patients in dialysis needs a CNS who cares about their future. A future that is unsure, but still lives in every one of the patients receiving dialysis. The needs of end-stage renal disease (ESRD) patients are many due to the existing co-morbidity of life threatening diseases that compound these patients' health problems. This proposal recommends that a Master's level nurse be hired for a position as Clinical Nurse Specialist (CNS). The proposal requests that the Clinical Manager of the dialysis unit take on the role of the CNS. By giving the responsibility to the Clinical Manager the organization can save resources and still provide a high quality performer to manage an anemia program. The rationale for this Research Utilization Proposal is found in Hamilton and Hawley's, 2005 quantitative research. (Appendix C). (Hamilton, R., & Hawley, S., 2006).

Research Utilization Proposal; Quality of Life Outcomes Related to Anemia Management of Patients with Chronic Renal Failure

1. Problem Statement: Inadequate Anemia Management Strategies

The National Anemia Action Council and Healthy People 2010 have identified anemia as a significant public health concern. At least 3.4 million Americans have been diagnosed with anemia, and millions more may be undiagnosed or at increased risk of developing anemia. Anemia is associated with lower functional ability, self-care deficits, and depression. Even though the body tries to compensate for the effects of anemia, almost every organ system is eventually affected. Even mild anemia adversely affects the patient's quality of life (Lipschitz, 2003). Blood loss, decreased red blood cell lifespan, uremia byproducts that inhibit erythropoiesis, decreased levels of erythropoietin, and deficiencies in essential nutrients such as foliate acid or iron all contribute to the anemic state in CKD patients (Eschbach & Adamson, 1985; Kulzer et al 1994). Severe anemia (hematocrit (hct) less than 28%) has been shown to be present in about 50% of patients at the start of dialysis, but only 20% had received recombinant human erythropoietin (EPO) treatment (Obrador, Ruthazer, Port, Held, & Pereira, 1997). Patients treated in the Anemia Management Program (AMP) have anemia related to chronic kidney disease (CKD). "As kidney function declines, the likelihood of anemia associated with erythropoietin deficiency increases because the deceased kidneys are unable to produce sufficient quantities of erythropoiesis. Frequently, anemia manifests early in the spectrum of CKD and worsen over time" (Lipschitz, D. (2003) p, 140). Effective treatment of the anemia in CKD improves survival, decreases morbidity, and increases quality of life (Sowers, McClellan, & Schoolwerth, 2005). Quality of life can be difficult to define because it means different things to different people. For the purpose of this Nursing Research Utilization Proposal the emphasis will be on health-related quality of life because it impacts every aspect of a person's life (National Kidney Foundation, Inc). This finding highlights the need for more proactive treatment of this condition in the more advanced stages of CKD.

2. Proposed Solution for Anemia Management Strategy

The selection of a clinical nurse specialist (CNS) in a nephrology office and dialysis clinic is essential in early detection of the anemia condition for the patient population pre-End Stage Renal Disease, (ESRD which would coordinate Erythropoiesis Stimulating Agent ESA therapy changes based on algorithms supportive of recommendations by National Kidney Foundation (NKF), Kidney Disease Outcome Quality Indicators, (KDOQI). NKF/KDOQI came out in 2006 with guidelines for the clinical nurse specialist (CNS) as the anemia manager monitoring hemoglobin levels using an AMP to treat CKD. ESA's therapies are found to improved quality of life for the ESRD patient by improving the patient's ability to maintain independent for Activities of Daily Living (ADL's). (NKF, 2006, para 2). According to the NKF KDOQI guidelines the CNS will work with an interdisciplinary team which is aliened with the mission statement of the Kidney Disease Indicators and Global

Outcomes (KDIGO) which states "Interdisciplinary approach: Work Group members will be chosen for leadership in their respective fields, commitment to quality of care and expertise in clinical practice, with due consideration of international representation reflecting the mission statement of KDIGO." (NKF, KDIGO, 2006, par 2). The CNS who manages the AMP identifies earlier referrals by primary care providers as the intervention with the greatest potential to impact positively the quality of life for patients with anemia. Research supports the CNS's outcome objectives of stable Hgb. Levels at 11 to 12 and uses ESA's to accomplish this. The symptoms of chronic renal failure appear late in the course of the disease, and earlier referrals to a nephrologists by the CNS can lead to a better quality of life for patients with renal disease (Frimat et al 2004). The CNS has an opportunity to make a positive impact on patient outcomes by educating other members of the healthcare team, such as physicians, case managers, and diabetes educators, regarding the advantages of identifying and screening high-risk patients. Earlier screening can lead to earlier referral. With the continued increase in CKD and the anemia that accompanies it, organizations may find the CNS's to be a valuable resource for managing this patient population. A CNS is well prepared and qualified to manage patients with chronic health problems, and the positive impact of a CNS-managed program need not be limited to anemia. By controlling anemia the CNS has opened up an increase quality of life for the pre ESRD patient as well as the ESRD patient receiving dialysis.

Section A: Problem Identification:

1. Problem identification/Description

The problem of health related symptoms of the ESRD patient can be addressed by the Clinical Nurse Specialist (CNS) in treating anemia for the end-stage renal disease (ESRD). Patient who are afflicted with ESRD are linked to the disease pathology and patient compliance issues increasing risk factors for anemia. The CNS has his or her work cut out for them. This is due in part to patients not showing up for treatments, not follow aseptic techniques for vascular access, ignoring diet and fluid restrictions, and not taking medication supplement or take prescribed medication as directed are all at risk behaviors for increase inflammation and infections leading to a reduction in red blood cell (RBC) production anemia. The loss of kidney function impedes the production of red blood cells (RBC's) or a low hemoglobin level, for the ESRD patient and therefore, must be compensated through replacement therapy. In the past replacement was only available through blood transfusions. **Blood transfusions were problematic in that the patient had to rely on supply, type, correct delivery and not having an allergic reaction that could be fatal to the blood product.**

This proposed solution to unstable hemoglobin levels for the dialysis patient is to stabilize the levels through drug interventions using Epogen. Epogen is a Erythropoiesis Stimulating Agents (ESAs) an anti-anemia biologics, distributed as Epogen®, Procrit ®, and Aranesp®. ESA's are man-made versions of erythropoietin, a hormone that is produced in the kidney and stimulates the bone marrow to make more red blood cells. ESAs are Food and Drug Administration (FDA) approved for the treatment of anemia in CKF patients, in patients with cancer whose anemia is caused by chemotherapy, in patients with human immunodeficiency virus who are using Zidovudine (also known as (AZT) and to reduce the number of transfusions in patients scheduled for major surgery (except heart surgery)." (CMS, 2007, para 5).

A CNS can identify those patients at risk and place them on an Anemia Management Program. An AMP can consist of patients at risk for ESRD, ESRD patients, cancer patients and blood disorders. The NKF/KDOQI guidelines have evidence based research that target supplemental treatment for the ESRD patient in ESA dosing with subcutaneous or intravascular injection that can be an intravascular push through the dialysis system and have a direct affect on improvements in Hgb Levels. The solution of a CNS in an AMP is appropriate in treating anemia. A Clinical Nurse Specialist CNS using the ESA's in an AMP according to Hamilton and Hawley's quantitative research has long lasting benefits for compliance and quality of life improvements.

2. Importance of the Problem

Resolving anemia symptoms has improved the lives of ESRD patients for the last 10 years. In an effort to improve the treatment of anemia for ESRD patient even more is found in evidence based scientific research of ESA's as a treatment option. Treating anemia in ESRD patients has been improved with the use of ESA by 51% in the last 10 years according to NKF. (Best Practice, 2006 topic 4 para. 2) The ap-

pointment of a CNS to head up this project is necessary because they are an advance practice nurse with the management skills necessary to understand the complex issues related to anemia and the need for homeostasis in hemoglobin (Hgb) levels in the ESRD patient. In Hamilton and Hawley's study the presence of a CNS in an AMP resulted in a significant improvement in physical and mental conditions in patients. (Appendix C).

3. Developing Project Objectives

The developing project has objective based on the NKF/KDOQI that in turn developed these guidelines based on Agency for Healthcare Research and Quality (AHRQ) research. The NKF has developed guidelines to help in anemia manager or CNS support AMP presentations to a healthcare organization. The guidelines are evidence based practice from the (AHRQ) Evidence-Based Practice Center a well respected and reputable source.

4. Brief Proposed Solution Description and Rationale

Improvements in patients physical and mental levels is the outcome objective and the mode to achieve this would be in appointing a CNS to the position of an AMP for a patient population of pre ESRD and ESRD patients The individual to be hired would hold a Master in Nursing and certification in dialysis. The certification will be a Certified Nephrology Nurse CNN which is an accredited program highly respected by the nephrology community. CNN is dedicated to education and research for the dialysis patient's improvement through evidence based research. The CNN meets added requirements of advance education and on going Continuing Education Units (CEU's) above the minimal requirements of a non certified nurse. The CNN will review of monthly/post hospitalizations/infections/inflammation results reflecting a drop in hemoglobin/hematocrit levels (Appendix C). Further research is needed to evaluate the more accurate outcome to support a CNS involvement in an AMP for chronic ESRD. The CNS will prescribe/adjust/and stop ESA dosing for newly diagnosed ESRD patients and re-evaluating the effectiveness of the ESA doses by the changes in hemoglobin levels using an algorithm based on NKF/KDOQI guidelines.

Section B: Innovation Description:

1. Solution Description

The solution description is the implementation of a CNS to head up a well organized medical management AMP using a host of treatment modalities to reduce the erratic ups and downs in Hgb levels seen in ESRD patients.

2. Consistency of Solution with Research Support

The present system is reactive to patients currently experiencing anemic conditions. The new program called the AMP would be a proactive intervention for at risk anemic and ESRD anemic patients. In Robbins Study regarding the role of the CNS managing the AMP they support the concept. According to Robbins, Nephrology nurses often play a key role in managing patients with CKD. The advanced practice nurse or clinical nurse specialist may fulfill essential roles in identifying chronic kidney disease (CKD) patients at risk for developing anemia and managing the iron and epogen requirements of these patients (e.g., laboratory assessments of iron and hematology indicators, prescription for therapies, such as counseling and surgery). (Robbins, Kerhulas, Senger, & Fishbane, 1997).

3. Feasibility of the Solution

Data has shown that overall prognosis is improved by successfully managing and correcting anemia of chronic disease whether the symptoms are related to Chronic Kidney Disease (CKD), cardiovascular disease, or cancer (Lipschitz, D., 2003). In Lipschitz study the patients are managed by a CNS direct AMP for anemia and the results are positive. Lipschitz discusses the impact of a CNS that has the experience and expertise to provide direction for medical and mental support of the ESRD patient. These skills by the CNS make the critical difference in the AMP implementation process. (Lipschitz, D., 2003)

4. Consistency of Solution with Resources

Funding for the CNS presence some challenges. The salary requirements for a CNS are not cheap, and healthcare organizations are reluctant to hiring high paying salaries to specialty nurses without good cause. The decision to make a financial commitment will be solely based on the healthcare organization buying into the CNS managed AMP. Funding decisions motivated by profits can be an incentive for healthcare management to hire a CNS. The decrease of hospitalizations and reduction in procedures for this patient population can be lucrative. In today's re-

imbursement reality for healthcare cost under Diagnosis-Related Group (DRG's) a set amount is agreed upon by the facility and the insurance carrier.

Wikipedia's encyclopedia defines DRG as:

- **Diagnosis-Related Group (DRG)** is a system to classify *hospital* cases into one of approximately 500 groups, also referred to as DRGs, expected to have similar hospital resource use, developed for *Medicare* as part of the prospective payment system. **(Healthcare Cost and Utilization Project (C–HUP), 2007)**

According to C–HUP if the patient stays the exact amount of days as an inpatient the cost is minimal and profit predictable to the healthcare organization, staying less than the targeted days results in an increase profit margin for the health care organization, and staying too long then the hospital losses money. Since the ESRD patient is at risk for infections, heart disease, and electrolyte imbalances all requiring prolonged hospitalization an organization such as healthcare must look at ways to cut those cost. (National Statistic Archive, 2007). The proposal to hire a CNS is attractive to healthcare management because of the promise to minimize fluctuations in health related risk for ESRD patients resulting in hospitalizations. A reduction in hospitalizations reduces loss of revenue for the healthcare industry. According to H–CUP congestive heart failure (CHF) is reported to be the 5th top reasons for hospitalization. ESRD patients are a high risk for CHF due to fluid overload (National Statistic Archive, 2007).

Section C: Research Support:

1. Sufficient Research Support Base

According to Van Wyck's study anemia management is a highly specialized practice and requires advance practice skills to be able to run an AMP. The CNS as a successful anemia management will provide care to patients with CKD that requires them to target therapies including iron. Van Wyck believes that the goal of iron therapy another treatment modality for anemia is to achieve and maintain target Hgb levels, to avoid storage iron depletion, and prevent iron deficient erythropoietin. (Van Wyck, D.B., 2000). Van Wyck supports the hiring of a CNS because they would use protocols and algorithms in the AMP they are managing. A CNS would also know the NKD/KDOQI Anemia Management Guidelines and use them to serve as an enhancement to current clinical practice in the AMP. The CNS will studies the outcome results from controlled trials and evaluate if the reports are valid using proven resources such as NKF/KDOQI respected expert research of anemia management treating ESRD. Van Wyck believes that prospective, controlled trials are needed to determine the comparative safety of periodic and maintenance IV iron protocols and to explore the relationship between IV iron administration, body iron status, and risk of infection and ischemic heart disease (Van Wyck, D.B., 2000). The healthcare management team chosen to hire the CNS will have to use this and other research to test the knowledge and skill set of the CNS. The CNS will have to support his or her ability to handle this responsibility by knowing about these and other research studies.

2. Compelling Research Support Base

The innovation to assign a Clinical Nurse Specialist (CNP) to manage the Anemia Management Program (AMP) will have a measurable impact on the quality of life for Chronic Kidney Disease patients. Kimmel and Patel believed that an AMP would help improve patient outcomes in terms of cardiovascular function, quality of life, and morbidity/mortality. They believed that this would lead to better and improved patient compliance to dialysis treatment. (Kimmel & Patel, 2006).

3. Types of Research Articles

a. Quantitative

Hamilton and Hawley's quantitative study supports the increase number of patients who experience improvement in quality of life from having an AMP managed by a CNS. (Hamilton & Hawley, 2005). The qualitative studies support positive patient outcomes and improved patient compliance (Pruett, Johnson & O'Keefe, 2007). Pruett, Johnson and O'Keefe discussed the effectiveness of educating the nursing staff using a protocol of application and concluded that a well-trained and knowledgeable nurse can improve outcome results for the anemic patients. The CNS must be able to discern appropriate dosing of ESA's and Iron. "The primary conclusion from the analysis is that the seesawing effect of administering IV iron then withholding iron was stabilized as a result of the new IV iron protocol (Pruett, Johnson & O'Keefe, 2007, p 211).

4. Discussion of Research Studies

Many studies have been conducted which consider the impact of anemia on patients' quality of life. Decline in physical functioning because of anemia has an adverse effect on the patient's quality of life. Several clinical trials in young patients with renal disease or undergoing chemotherapy for various malignancies have reported a strong positive correlation between quality of life score and hemoglobin concentrations. Available data have shown that overall prognosis is improved by successfully managing and correcting anemia in patients with chronic disease such as congestive heart failure and end-stage renal disease (Lipschitz, 2003). The Lipschitz study supports the hiring of a CNS to manage an AMP because of the CNS's ability to focus on anemic conditions and treatment them aggressively. By treating anemia early the CNS has a better chance of bring the ESRD patient back to therapeutic levels in Hgb.

a. Scientific merit

Repeating, Hamilton and Hawley research study with a larger sample may show a greater increase in the mean scores for both the Physical and the Mental Component Score in each of the post treatment time frames, especially the 12-month survey. A more consistent, orderly approach in the administration of the SF–36 (Appendix A) would be beneficial in tracking the progress of patients in the Anemia Management Program, (AMP) and increasing sample size for future studies would give the result better scientific merit. (Hamilton, R., & Hawley, S., 2006). Giving Hamilton and Hawley's study more merit by repeating the study with a larger sample size would help improve attitudes of the healthcare organizations to comply with proven scientific merited research studies such as Hamilton and Hawley and motivate the present of CNS's in AMP's.

b. Strengths and limitations

The strength of appointing a CNS to an AMP would be consistency in care. The CNS would be observation, treating and gaining data from the SF–36 survey for review. This information obtained would go a long way in answering questions about the validity of a CNS managed AMP. In Hamilton and Hawley's study one limitation was that the research lacked a power analysis. A power analysis would have determined the number of patients needed to detect if an increase in quality of life was due to anemia treatment. In Hamilton and Hawley quantitative research the starting number of patients was 78 then after six months was less than 20. (Hamilton & Hawley, 2005). In this proposal the power analysis would take into consideration the amount of participants. A CNS would make this task a high priority and the results would become strengths for this program. A limitation that this program would have could be the nursing shortage. Due to many nurses being overwhelmed with their responsibilities already these nurse might not want to help out with an anemia management program. In Hamilton and Hawley's research they found that the staff nurses played a significant role in depleting the participants in their study. Because the nursing staff was suppose to make the SF–36 survey available to the patients at timed intervals not doing so had a direct impact on the study. A limitation in Hamilton and Hawley's research relates to administration of the Medical Outcomes Short Form 36 Item Health Survey (SF–36) (Appendix B). There were incidents when the staff failed to make the SF–36 available to the patients for self-administration at the designated intervals. In Ware and Kosinski they also experienced a lack of commitment by the nursing staff to distribute surveys. "There were also surveys that were excluded from the research due to missing data." (Ware & Kosinski, 2001).

c. Relevance and rationale for inclusion

Section D: Implementation Plan

The implementation phase of any clinical studies is critical for the success of the proposed program. The purpose of the implementation plan is to make systemic summary and necessary resources to start the program on clinical nurse specialist (CNS)-managed anemia management program (AMP) to elevate patient quality of life.

1. Solution Implementation Plan

The target populations for this program are ESRD patients with anemia. These patients are likely experiencing decline in physical functioning because of anemia and have an adverse effect on the patient's quality of life. The plan would be to have a CNS management the treatments for the ESRD patient and subsequently decrease the risk for anemia.

a. Involvement of formal and informal leaders

The CNS will actively manage the AMP in collaboration with a nephrologist who will serve as the program's medical director. The AMP is staff with registered nurses and one program assistant. Nursing director, the formal leadership of the nursing division will be involved in the initial planning of the AMP as well as the medical director. Any additions or changes to protocols or algorithms will be presented to the management team and physicians for approval.

b. Timing of implementation

The medical director together with and the head of nursing division and the Clinical Manager will schedule a meeting to discuss the program and get approval from the vice president of the hospital's patient services. Succeeding monthly meetings will be held for follow-up, review and re-evaluations of the AMP.

c. Inclusion of personnel

One vital role of the CNS is the training and coaching of staff nurses to become competent in providing care to patients with anemia related to CKD. The program protocol will be developed by the CNS in collaboration with the nephrologist for the staff to use, and when patient's condition fall outside norms then established protocols and algorithms will be followed by staff.

d. Obtaining approvals

Any treatment adjustments will be decided in a collaborative effort by the nephrologists and CNS. The recommendations of treatment will be initiated by the CNS who will submit the report to the nephrologists with recommendations and requiring approval. Any changed to protocols and algorithms will be presented to the healthcare management for approval.

e. Communication Methodologies

The methods of communication will be verbal between CNS and staff. A monthly meeting will be convened to hear monthly reports on hospitalizations, improvements in quality of life (quarterly), quality outcome reports outlining compliance to approved protocols and algorithms.

2. Resources Needed for Solution Implementation

Staffing needs will require the hiring of a CNS to head up the AMP within the nephrologists office and chronic dialysis clinic. The equipment needed will be a desk, phone, computer, printer, fax and office supplies. The space will be located either in the physician's office or the dialysis clinic. The educational and technical support will be supplied by the educational specialist from the dialysis unit and computer staff already in place at the dialysis clinic will support the needs of the CNS as well. The support staff for this program will be supplied by the existing RN staff nurse and the facility to operate this program will be integrated into the clinic area's resources or the physicians office. The access to telephones and computer will be located in the office of the CNS and are a part of the existing system found in both locations.

a. Timing of implementation

The timing for this implementation will start post agreement with management at the facility. Once management has approved hiring a CNS the full enactment of the program will follow. The priority items that the CNS will have to address are the present mental and physical state of the pre ESRD and ESRD patients they are managing. The lab results for each patient will be reviewed and the results of those labs will dictate how the treatment will start based on the algorithms. The interview with staff nurses will lend a substantial amount of data that the CNS can use to develop a plan for implementing the program and what training is needed by the Nurse Educator. The next step would be to start training staff members on how the SF–36 survey would be presented and completed by the ESRD patients. The implementation of the SF–36 survey would then be administered to give more data results for the CNS to evaluate a starting level to measure change in quality of living for the ESRD patients. A review of the data and reports would be presented to the physicians and a collaborative planning session would be held. This meeting would discuss methods of addressing issues that are expected to present during care in the clinic.

b. Involvement of key personnel

The procurement office will be in charge in the procurement of the assessment tool SF–36 forms and the Orion Outcomes Database that will store and analyze the data survey. The Information Technology (IT) will be responsible for the computer

wiring system and training on data input. An educator for staff will be the responsibility of the Education department from either the physician's office or the dialysis clinic. This personnel to provide training for the staff nurse. Human resource is in charge in the processing of the hired the CNS. A budget of cost for this program is outlined in Appendix D.

c. Equipment and materials

The equipment and materials needed for this program consist of office support, computers, printers, fax machines—or availability, and phones. These can be supplied by the existing office of the Clinical Manager if the CNS responsibilities become his or her or out of the physician's office. Having a Clinical Manager take on this responsibility would also alleviate the need for more office space which can be difficult to find in clinics and physician's offices.

d. Consideration of Costs

The primary resources needed for this program is the clinical nurse specialist (CNS) who will manage the program. The average annual CNS salary is 76,209 this is based on a salary for an Advance Practice Nurse. Other interdisciplinary personnel include the procurement department, IT, education and human resources.

3. Monitoring Solution Implementation

The clinical nurse specialist will monitor outcomes. It will be the responsibility of the CNS to provide the SF–36 survey to patients via staff nurses in the physician's office and in the dialysis clinic. The proof is in the pudding for monitoring solutions that are being implemented into any organization. The CNS must have a organized approach when setting up this program, staff must to educated and trained on the procedures they are responsible for and have competency in being able to perform those duties. The reactions to patients conditions and the treatments used to help them must be monitored by the CNS through direct exposure to the patients charts, or via the staff nurses.

4. Utilization of Planned Change Theory

The planned change theory selected for the CNS-managed AMP on patient quality of life is the Stetler model of research utilization to facilitate evidenced-based practice. As cited in Burns and Grove (2005), "the model has five phases: preparation, validation, comparative evaluation/ decision making, translation/ application, and evaluation". The preparation phase involves determining the purpose and potential outcomes of making an evidenced-based change in a clinical agency. The purpose of this innovation is to evaluate the impact of a CNS managed AMP on stable Hgb's and improvements in the quality of life for patients with anemia related to CKD. The validation phase involves research finding cited by Sowers et al (2005). As kidney functions decline, the likelihood of anemia associated with erythropoietin deficiency increases therefore, the hiring of a CNS to manage the AMP would be prudent for a healthcare organization to prevent the complications of anemia and reduce cost associated with ESRD such as long hospital stays. The comparative evaluation/ decision making phase is a time to view the end product found when a CNS manages an AMP. The responsibilities of the CNS is to report the results from SF–36 and the analyzing tool of the data by Orion Outcome Database. (Appendix A&B). The translation application phase in a proposal will put into practice the results found in research. The CNS will plan the application of applying practices of managing anemia for ESRD patients by working out the schedules of staff nurses for administrating the survey, evaluation of the lab results and scheduling the labs based on re-imbursement for these test, reviewing the results and changing doses for epogen per the algorithm established by the guidelines and approval of management. The CNS will also address different issues such as counseling, education and psychotropic drugs. The practice of managing anemia has to take into account a holistic approach to healthcare for the ESRD patient. (Hamilton & Hawley, 2005). The evaluation phase involves the CNS monitoring and reporting on outcomes, both clinical and financial. The CNS will report the results at monthly meetings attended by administration and physicians.

5. Feasibility of Implementation of Solution

The professionalism, education, and clinical expertise of a CNS make them an ideal solution for the AMP. In Hamilton and Hawley the positive effects of a CNS managed AMP are worthwhile to the patient's overall health and the healthcare community's ability to met those needs.

Tracking the quality of life outcomes of patients at various stages of the AMP provides greater insight into the effectiveness of the treatment program. In Hamilton and Hawley's research the patients' had pre and post results for comparison. This

was done because the pre results gave a baseline for measuring movement negative or positive about the quality of life. The CNS can use the SF–36 survey and analysis tool Orion Outcome Database to repeat the research and duplicate the results showing improvements in the quality of life for ESRD patients. (Appendix A).

Section E: Evaluation Plan

1. Developing or Revising Outcome Measure

The outcome measurement tool will be the Orion Outcomes Database designed to analyze data and based on results from research to evaluate whether or not the objective outcome goals were achieved. This will be used in this program to help the CNS evaluate the outcome goals and measure the trends for meeting those goals.

a. *A copy of the measure needs to be included in the Appendix*

The results from Orion Outcomes Database (Appendix A) showing that there was a significant improvement in the quality of living for the ESRD patient who had the support of a CNS in an AMP. The conclusion of Hamilton and Hawley's research study (Appendix C) found that CNS interventions for the CKD patient population was seen in the first 3 months as significant in physical improves in the patient's quality of life.

2. Determining Outcome Measure Value

The outcome tool Orion Outcome Database (Appendix A) has a proven reliability for scientific research that is used to evaluate outcome goals. The results in Hamilton and Hawley study inspirited further research seen in this proposal. The results of Orion Outcome Database found in Hamilton and Hawley's research separated two components of physical and mental both scored then analyzed showing significant improvements with an AMP managed by a CNS. (Appendix C). An example of Hamilton and Hawley research would be seen the score of a patient experiencing a low quality of life mentally, but has a high score physically which would require intervention by the CNS. The next survey would be evaluated for the effectiveness of that intervention. This proposal would follow that same pattern and use those same tools to determining outcome measure values of the AMP.

a. Validity

The validity that is in this plan is found in duplicating the efforts of Hamilton and Hawley's research. (Hamilton & Hawley, 2005). Validity should be obvious when a colleague looks at and measures outcomes from a study that is considered experts in the field. Examine the research and finding that it will show the same results when repeated proves validity. The measured outcome intended as seen when duplicating a study uses the same materials and methods. This is the aim of this proposal, to use the same research tools found in Hamilton and Hawley and duplicate the results to improve the quality of life for the ESRD patient. (Appendix A).

b. Reliability

The Orion Outcome Database (Appendix A) is a proven method of analyzing data created by the survey. In Hamilton and Hawley's research study the measurement was significant when the results were analyzed by Orion Outcome Database showing an upward trend of improved quality of living for ESRD. Using this tool would be advantageous when reporting the progress of an AMP managed by a CNS to healthcare management. Management could see the results of improvements in a proven scientific method when using Orion Outcome Database and rely on that information to base a judgment on the AMP's success with a CNS in control of the operation.

The CNS will take steps to analyze the results found at three month intervals based on Orion Outcomes Database (Appendix A) and crease a summary report for the healthcare management team and physicians using verbiage that helps to separate changes in physical and mental results. By separating the two fields the CNS report will more closely follow Orion's Outcome Database (Appendix A) to find the results of the effectiveness a CNS has on an AMP.

c. Sensitivity to change

This instrument has sensitivity issues: The survey results are simplistic for easy access, time constraints, and analyzing. The results seen in Hamilton and Hawley's study do not plan for complications, surgeries, declines in other co-morbidities, emotional stressors, and staffing problems. According to Burns and Grove, "This assessment of reliability is irrelevant or only partially relevant to assessing the suitability or precision of measures selected because of their sensitivity to change within the individual over time". (Burns & Grove, 2005, P.). This research was conducted using

a simple survey SF–36. The format made the SF–36 easy for the patients to compete quickly. The research information did not specify if the SF–36 survey was made available in English only, and therefore, an evaluation of appropriateness of language could not be evaluated. (Appendix B)

d. Appropriateness for use

According to Burns and Grove appropriateness is shown by the partnerships established by following guidelines formulated by established and respectable organizations. In this proposal the partnership between the AMP guidelines and the recommended guidelines from the NKF/KDQOI lends support for appropriateness. (Burns & Grove, 2005, P. 656).

3. Data Collection and Analysis

Hamilton and Hawley's research used a SF–36 survey (Appendix B) to collect the data and Orion Outcome Database for analyzing a research because the tools used were respected and valid for measuring the quality of life. The CNS must use a product like SF–36 so that they can collect data from the patients in the AMP and analyze the data resulting in a report that shows outcome goals are being met by the program. The idea that a CNS is the key factor in a successful AMP will be decided by the healthcare organization based on the results from tools such as OOD. According to Burns and Grove, "Data collection is the precise, systematic gathering of information relevant to the research purpose or the specific objectives, questions, or hypotheses of a study." Burns & Grove, 2005, P. 42).

4. Resources Needed

This proposal would ask that the CNS role will be the Clinical Manager. The benefits of having an existing employee of the clinic are cost saving and decreases the time required for orientation to the facility. The requirements for the CNS will include existing duties of maintaining a safe environment for patients, training programs for staff and using an implementation plan to guide staff in learning this new method of nursing practice. The staff nurses will administer the SF–36 survey and monitor the location, scheduled time to provide SF–36 survey's to participants, Submit to the CNS a completed survey, and make sure patients have an opportunity to fill out the SF–36 survey. The staff nurses are key stakeholders in compliance. These nurses have to add this responsibility to work loads that are already overwhelming. The nurses have to be able to locate the SF–36 survey easily, maintain a list of patients in the research project, schedule times for filling out the SF–36 survey initially, in 3 months, 6 months and 12 months. The SF–36 survey cost is $405. Orion Outcomes Database cost $500 for a license to use this product. The implementation of the AMP will be introduced in an in-service training program to staff nurses. The cost for training will include re-imbursement at the rate of pay per RN. RN Salaries range from $22/hr to $32/hr. The clinic has four staff RN's resulting in cost of 88/hr to 128/hr. The total amount of time projected to spend in training is 4 hours which will total 352/RN to 413/RN. The records of this project must be kept appropriate in a time frame to support the outcome goals to measure change in the patients' quality of life by the CNS to plan interventions based on the results.

5. Feasibility of the Plan

According to Burns and Groves, "feasibility of using research findings in practice involves examining the three R's." The two that relate to this portion of the proposal are potential risks and readiness of those involved (Burns & Groves, 2005, P. 644). The potential risks of implementing this change are that the staff RN will not want to perform the task of handling the SF–36 surveys'. Staff may have problems staying organized and remembering when to hand out the SF–36 survey. In Hamilton and Hawley's research study this problem resulted in over half of the 79 participants dropped due to a lack of staff RN's making the SF–35 survey available and giving the SF–36 survey to patients within the time frame set out by the study. The CNS will have to plan for interventions and training staff to make sure that this does not happen. The second R addresses the ability or timing of induction to staff ready to take on this task. A new RN trying to train in basic skills for the department is a poor candidate because this staff RN has so much to learn and adding a SF–36 survey to his or her schedule would not be wise. The CNS must evaluate the staff working in the clinic, what are the staff's strengths and weaknesses for conducting the survey.

Section F: Decision-Making Strategies

1. Maintenance of the Solution

The need to communicate and collaborate with administration and staff nurses is required to maintain the CNS-managed AMP. The importance of close contact and direction will result in a positive outcome of the project, particularly the achievement of upward trends in patients' quality of life outcome. This innovation can be done through: staff development or educational program held monthly and hospital committees developing practices that are incorporation into established policies and/or procedures. It is essential that once a CNS is hired that the hospital management team review outcome goals provided by Orion Outcome Database, reports of hospitalization trends for ESRD, a reduction in hospital stays for ESRD patients to evaluate the effectiveness of this program.

2. Extending the Solution

An annual evaluation of the results from research of report findings and measuring goals set out for the AMP will be a tool that management can use to make the decision to continue this program. A reevaluation of the CNS performance will be based on meeting outcome goals as seen in Orion Outcome Database results, hospital stay. The nurse manager in collaboration with the nurse educator would have to plan education and training sessions as new staff members were hired in the clinic. The development of an introduction program would be beneficial to this program and help the CNS provide training as new hires came into the clinic more easily.

3. Revising the Solution

As the program is managed the CNS will be evaluating the effectiveness of the practices, reporting methods and measurement tools. As nursing research continues the CNS may want to incorporate new guidelines that would change protocols and algorithms. The solution to revising the solution would be done by a collaborative effort of evidence-based practice and input from key stakeholders.

4. Discontinuing the Solution

It would be very difficult to discontinue an innovation that staff has acknowledged success. However, if the program continues to produce negative outcome, then it should be discontinued that will formally involved different departments in the hospital such as nursing, medicine, education, IT, human resources, and administration.

5. Plans for Work Setting and Professional Feedback

The plans for work setting will be a clinic of ESRD patients receiving dialysis. Professional Feedback would be collected by way of a questionnaire from staff and the SF–36 survey from the patients. These two tools will help the CNS evaluate the effectiveness of this program.

References

Best Practice, 2006, National Kidney Foundation, Kidney Disease Outcome Quality Indicators. Guiding principles for the KDOQI process. Retrieved 5/26/07 online: http://www.kidney.org/professionals/kdoqi/index.cfm

Eschbach, J. W., & Adamson, J. W. (1985). Anemia of end-stage renal disease (ESRD). Kidney International, 51, 622–630.

Frimat, L., Ayav, C. L., Panescu, V., Cordebar, N., Briancon, S., & Kessler, M. (2004). Early referral to a nephrologist is associated with better outcomes in type 2 diabetes patients with end-stage renal disease. Diabetes Metabolites, 30, 67–74.

Hamilton, R., & Hawley, S. (2006) Quality of life outcomes related to anemia management of patients with chronic renal failure. Nursing Center, (Vol 20 is. 3 PP 139–143).

Kimmel, P. L., & Patel, S. S. (2006). Quality of life in patients with chronic kidney disease: Focus on end-stage renal disease treated with hemodialysis. Seminars in Nephrology, (Vol. 26, PP. 68–79).

Kulzer, P., Schaefer, R. M., Krahn, R., Schaefer, L., & Heidland, A. (1994). Effectiveness and safety of recombinant human erythropoietin (r-HuEPO) in the treatment of chronic renal failure in non dialysis patients.

Lipschitz D. (2003) Medical and functional consequences of anemia in the elderly. Journal of American Geriatric Society (vol. 51(3): is. 10). Retrieved 6–3-07 online: http://www.americangeriatrics.org/search.

National Anemia Action Council. (2002) Anemia: Hidden epidemic. Retrieved June 4, 2007. Online: http://www.anemia.org/.

National Institutes of Health. Healthy people 2010. Retrieved June 3, 2007. Online: http://www.healthypeople.gov/.

National Kidney Foundation, Inc. Kidney disease outcomes quality initiative: Guidelines for anemia of chronic kidney disease. 2001. Retrieved June 2, 2007. Online http://www.kidney.org/.

Obrador, G. T., Ruthazer, R., Port, F. K., Held, P. J., & Pereira, B. G. (1997). Markers of quality of pre-ESRD care among patients starting dialysis in the U.S.Journal of the American Society of Nephrology, 8(145A)

Pruett, B., Johnson, S., & O'Keefe, N. (2007). Improving IV iron and anemia management in the hemodialysis setting: A collaborative CQI approach. Nephrology Nursing Journal, (34 (2), pp. 206–213). Retrieved 6/2/07 on-line http://web.ebscohost.com/ehost/detail?vid=9&hid=15&sid=a039dc14–4602–45c7-b252-c6481ca788df%40SRCSM2

Robbins, K. C., Kerhulas, S., Senger, J. M., & Fishbane, S. (1997). Iron management in ESRD and the role of the nephrology nurse. ANNA Journal, (Vol. 24, PP. 265–274).

Sowers J, McClellan W, Schoolwerth A. (2005) An Educational Monograph. Timing is everything; A proactive approach to CKD management. AdvancMed, LLC.; (vol. pp 1–44). Retrieved June 3, 2007 on-line http://www.advancmed.org/edu.php.

Van Wyck, D. (2000). Lessons from NKF–DOQI: Iron management. Seminars in Nephrology, (Vol. 20, PP. 330–334). Retrieved 5/14/07 on-line at www.Kidney.org.

Ware J, Kosinski M. (2001) Interpreting SF–36 Summary Health Measures: A response. Quality of Life Research (is. 10: pp 405–413). Retrieved June 4, 2007 online http://www.sf-36.org/.

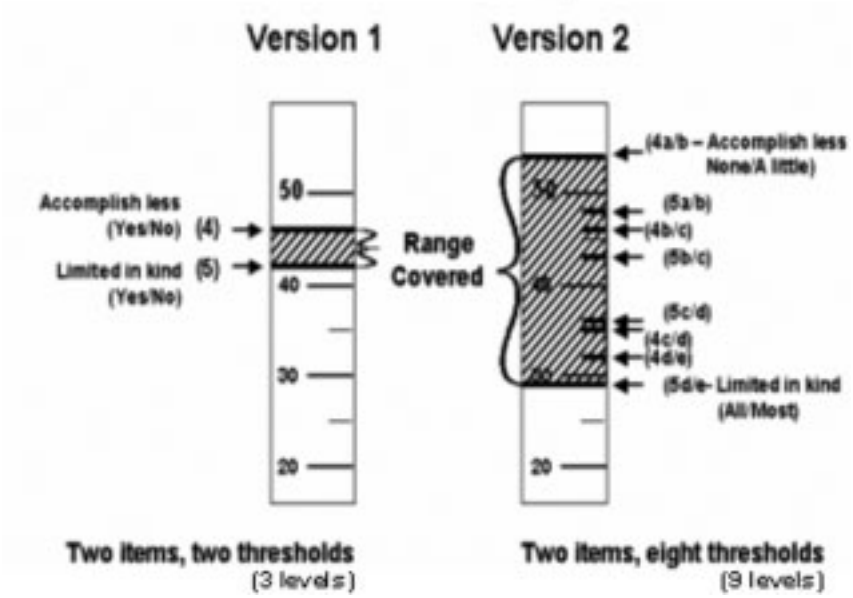
Appendix A

SF–36v2™ and SF–12v2™ Health Surveys Offer Substantial Improvements)

New versions of the SF–36® (SF–36v2™) and SF–12® (SF–12v2™) Health Surveys, developed by scientists at Quality Metric Incorporated and collaborators, have been shown to produce substantial improvements over the originals. Improvements in item wording and format and a 6-fold increase in the ranges of scores covered were achieved for both surveys without increasing respondent burden. Survey developers, with over 10 years of experience in health outcomes measurement, recommend adoption of the SF–36v2™ or SF–12v2™ for clinical trials, disease management, risk prediction, population monitoring, and other studies where scientific validity and precise measurement are required. New up-to-date norms and guidelines are available for maintaining backward comparability with studies published to date, providing complete standardization between the surveys and allowing for comparison of data sets for trend analyses.

Used successfully in more than 600 randomized clinical trials reported in over 240 scientific and medical journals, the SF–36®, SF–36v2™, SF–12®, SF–12v2™, and SF–8™ are proven responsive in 44 disease conditions and are accepted by the FDA as proof of benefit for improved functioning and other patient-reported outcomes. Additionally, the SF–36v2 and the SF–12v2 have been adopted as the standard of measurement by key government agencies, including the Agency for Healthcare Research and Quality (AHRQ), which has adopted use of the SF–12v2 for the nationally significant Medical Expenditure Panel Study (MEPS).

Figure 1 SF-12v2 Role Physical Items Achieve 6-Fold Increase in Range Measured



Improvements Include:

After more than 10 years of testing, new versions of the SF–® (SF–36v2™) and SF–12® (SF–12v2™) Health Surveys were published to correct deficiencies that had been identified in the original versions. Improvements, which are documented in the SF–36v2 user's manual (Ware, Kosinski and Dewey, 2000) and in the SF–12v2 user's manual (Ware, Kosinski, Turner-Bowker and Gandek, 2002) were implemented after careful study using both qualitative and quantitative methods in the US and other countries.

Briefly, the SF–36v2 and SF–12v2 improvements include:

- better instructions and questionnaire items to shorten and simplify the wording and make them more familiar and less ambiguous;
- an improved layout for questions and answers in the self-administered forms that makes it easier to read and complete, and that reduces missing responses;
- greater comparability with translations and cultural adaptations widely-used in the U.S. and in other countries;
- five-level responses in place of dichotomous response choices to greatly increase the range and precision of scores.

As shown in the figure, a 6-fold increase in the range covered by the SF–12v2 Role-physical functioning scale was achieved. As documented in the new SF–12v2 and SF–36v2 user's manuals, comparable improvements were achieved for both role scales in both v2 forms. Specifically, the adoption of 5-choice (over dichotomous) response categories for items measuring both physical and emotional role functioning led to substantial increases in precision as indicated by the number of levels measured as well as the internal-consistency reliability of those scales for both SF–36 and SF–12 forms. Among the practical implications are virtual eliminations of the "floor" effects and substantial reductions in the ceiling effects for both SF–36v2 and SF–12v2 role functioning scales, in comparison with the original v1.

In the figure, norm-based scoring (NBS) algorithms are used to achieve a mean and SD that are 50 and 10, respectively, for both v2 measures to be comparable with SF–36v1 and SF–12v1. As explained in the user's manuals, item response theory (IRT) thresholds are used in the figure to show the differences in ranges covered

by v1 and v2 items in a large representative sample of the general US population in 1999 (see the SF–12 user's manual for more information).

Quality Metric's SF™ Generic Health Surveys (SF–36®, SF–36v2™, SF–12®, SF–12v2™, and SF–8™ Health Surveys) can be scored online accurately, securely, and reliably now, with exclusive new desktop scoring software set for launch in early 2004.

http://www.sf-36.org/community/SF36v2andSF12v2.shtml

Appendix B

The SF–36v2™ HEALTH SURVEY

Instructions for Completing the

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by filling in the bubble that best represents your response.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor

2. Compared to one year ago, how would you rate your health in general now?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a) Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports			
b) Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing			
c) Lifting or carrying groceries			
d) Climbing several flights of stairs			
e) Climbing one flight of stairs			
f) Bending, kneeling, or stooping			
g) Walking more than a mile			
h) Walking several hundred yards			
i) Walking one hundred yards			
j) Bathing or dressing yourself			

SF–36v2™ © 1999 QualityMetric, Inc. All Rights Reserved.

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the amount of time you spent on work or other activities					
b) Accomplished less than you would like					
c) Were limited in the kind of work or other activities					
d) Had difficulty performing the work or other activities (for example, it took extra effort)					

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the amount of time you spent on work or other activities					
b) Accomplished less than you would like					
c) Did work or other activities less carefully than usual					

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors,

Not at all	**Slightly**	**Moderately**	**Quite a bit**	**Extremely**

Friday, June 22, 2007 **Page 2 of 4**

SF–36v2™ © 1999 QualityMetric, Inc. All Rights Reserved.

7. How much *bodily* pain have you had during the *past 4 weeks*?

None	**Very mild**	**Mild**	**Moderate Severe**	**Very severe**

8. During the *past 4 weeks*, how much did *pain* interfere with your normal work (including both work outside the home and housework)?

Not at all	**A little bit**	**Moderately**	**Quite a bit**	**Extremely**

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks . . .

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
a) did you feel full of life?					
b) have you been very nervous?					
c) have you felt so down in the dumps nothing could cheer you					
d) have you felt calm and peaceful?					
e) did you have a lot of energy?					
f) have you felt downhearted and depressed?					
g) did you feel worn out?					
h) have you been happy?					
i) or groups? did you feel tired?					

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visting friends, relatives, etc.)?

All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**

Friday, June 22, 2007 **Page 3 of 4**

SF–36v2™ © 1999 QualityMetric, Inc. All Rights Reserved.

11. How TRUE or FALSE is *each* of the following statements for you?

Definitely	**Mostly true**	**Don't know**	**Mostly false**	**Definitely**

a) I seem to get sick a little easier than other people
b) I am as healthy as anybody I know
c) I expect my health to get worse
d) My health is excellent

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE!

Friday, June 22, 2007 **Page 4 of 4**

SF–36v2™ © 1999 QualityMetric, Inc. All Rights Reserved.

Appendix C **Quality of Life Outcomes Related to Anemia Management of Patients with Chronic Renal Failure**

RETAHAMILTON MSN, RN, CNS, APRN, BC

SHEILA HAWLEY MSN, RN, CNS, APRN, BC, CRNI **Clinical Nurse Specialist: The Journal for Advanced Nursing Practice**

May/June 2006

Volume 20Number 3

Pages139–14

Purpose: The purpose of this study was to evaluate the impact of a clinical nurse specialist-managed outpatient anemia management program on quality of life for patients with anemia related to chronic kidney disease.

Description of the study: A retrospective study was conducted using information from the Medical Outcomes Short Form 36 Item Health Survey, which is completed by patients with anemia at their initial, 3-month, 6-month, and 12-month visits, and annually thereafter. Thirty-four patients completed the 3-month survey, 19 completed the 6-month survey, and 10 completed the 12-month survey.

Outcomes: There was a statistically significant increase in quality of life indicators at the 3 and 6 months' interval. The increase in physical and decrease in mental indicators were not substantiated through the 12-month interval.

Conclusion: Quality of life was significantly improved for patients in a clinical nurse specialist-managed outpatient anemia management program. The National Anemia Action Council and Healthy People 2010 have identified anemia as a significant public health concern. At least 3.4 million Americans have been diagnosed with anemia, and millions more may be undiagnosed or at increased risk of developing anemia.[1,2] Anemia is associated with lower functional ability, self-care deficits, and depression. Even though the body tries to compensate for the effects of anemia, almost every organ system is eventually affected. Even mild anemia adversely affects the patient's quality of life.[3]

Many studies have been conducted which consider the impact of anemia on patients' quality of life. Decline in physical functioning because of anemia has an adverse effect on the patient's quality of life. Several clinical trials in young patients with renal disease or undergoing chemotherapy for various malignancies have reported a strong positive correlation between quality of life score and hemoglobin concentrations. Available data have also shown that overall prognosis is improved by successfully managing and correcting anemia in patients with chronic diseases such as congestive heart failure and end-stage renal disease.[3]

The purpose of this retrospective study was to determine the impact of a clinical nurse specialist (CNS)-managed anemia management program (AMP) on patient quality of life. Patients treated in the AMP have anemia related to chronic kidney disease (CKD). 'As kidney function declines, the likelihood of anemia associated with erythropoietin deficiency increases because the diseased kidneys are unable to produce sufficient quantities of EPO. Frequently, anemia manifests early in the spectrum of CKD and worsens over time.[5] Effective treatment of the anemia of CKD improves survival, decreases morbidity, and increases quality of life.[4] Quality of life can be difficult to define because it means different things to different people. For the purpose of this study, we will be looking at health-related quality of life because it impacts every aspect of a person's life. Health-related quality of life usually refers to aspects of our lives that are dominated or significantly influenced by our mental or physical well-being.[6] The specific aim of this study was to test the following research question: Do patients treated in a CNS-managed AMP for patients with anemia related to CKD experience a significant increase in quality of life?

The CNS who manages the AMP also wanted to test her hypothesis that patients treated in the AMP for anemia related to CKD experience the greatest improvement in quality of life during the first 3 months of treatment. The CNS speculates that after 3 months, the patients maintain this improved level of functioning, but she expects that the findings from the study will show that patients maintain or show a slight decrease in functioning. The CNS attributes this to patients with anemia being so weak when they first begin treatment and improve so drastically that, after a few months, they do not remember how physically and mentally weak they were when starting treatment.

Evidence-based treatment protocols for patients with anemia treated in the AMP include intravenous iron sucrose and subcutaneous injections of erythropoietin. Individual dosages are adjusted with each visit based on the patient's hemoglobin level and iron studies. Patients are seen in the AMP every 1 to 2 weeks, depending on their hemoglobin and iron levels. If patients are severely anemic and symptomatic, they may receive a transfusion of packed red blood cells. These treatment protocols are consistent with recommendations from multiple sources including the National Anemia Action Council and the National Kidney Foundation.[1,4]

As the CNS developed the AMP, attention was given to nonpharmacological interventions, such as patient education regarding their disease process, symptom management, nutrition, and exercise. Patients receive written and verbal education on their initial visit. During each follow-up visit, ongoing education is provided. Patients are given a thorough physical assessment at each visit, including weight, vital signs, and hemoglobin monitoring. Patients identified point of care testing for hemoglobin levels as one of the most popular interventions initiated by the CNS. Hemoglobin levels are measured by the AMP staff in the clinic, which saves the patient the time and inconvenience of going to the laboratory for a blood draw. The CNS and staff of the AMP are also a source of support and encouragement for the patients and the family members who accompany them to the clinic.

DESIGN

This retrospective study was conducted in an outpatient AMP. The program is actively managed by a CNS who treats patients with anemia related to CKD. The average age of patients treated in the AMP is 71 years. Patients in the AMP are asked to complete version 2.0 of the Medical Outcomes Short Form 36 Item Health Survey (SF–36) to monitor quality of life indicators. The SF–36 is given to the patient by the AMP staff during the patient's initial visit with a brief explanation of its purpose and directions for completing it. The SF–36 is self-administered and is completed by the patients with anemia at their initial, 3-month, 6-month, and 12-month visits, and annually thereafter. Thirty-four patients completed the 3-month survey, 19 completed the 6-month survey, and 10 completed the 12-month survey.

Sample

Tracking the quality of life outcomes of patients at various stages of the AMP provides greater insight into the effectiveness of the treatment program. The patients' pretreatment results were compared with their post treatment results. For a patient's results to be included, they must have completed each required survey. Those patients who had completed a12-month survey have also completed the initial, the 3-month, and the 6-month surveys before being included in the study. Patients included in the 6-month evaluation group have completed the initial, the 3-month, and the 6-month surveys. Patients included in the 3-month evaluation have completed both the initial and the 3-month surveys. Information from the SF–36 surveys is put into a software program called the Orion Outcomes Database which stores and analyzes the data. There were 73 patients in the Orion Outcomes Database, who had completed the initial survey. Of these 73 patients, 34 had completed both the initial and the 3-month surveys, 19 had completed the initial, the 3-month, and the 6-month surveys, and 10 had completed all the required surveys up to 12-months.

The SF–36 is the assessment tool used for monitoring health-related quality of life issues for patients in the AMP because it is a useful and reliable instrument for assessing quality of life in patients with many chronic conditions including chronic renal disease.[8] The SF–36 is self-administered and takes approximately 5 minutes to complete and is divided into 8 dimensions which include Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health. There are 36 outcomes assessed under these 8 dimensions. The dimensions of the SF–36 are scored on a range from 0 (the worst score) to 100 (the best score).[8]

Version 2.0 of the SF–36 is an updated version that includes 2 summary measures. These summary measures are the Physical Component Score, which is a summary score of all the physical components, and the Mental Component Score, which is a summary of all the mental component scores of the SF–36. Using these 2 summary components makes interpreting outcomes easier because it reduces the number of statistical comparisons necessary to capture differences in health status, offers greater precision for measuring general physical and mental health outcomes, and has more straightforward interpretation of physical and mental health scores.[6]

The SF–36 has been used in multiple studies to evaluate quality of life issues for patients with chronic diseases, including anemia. One such study was conducted by a group of nephrologists in Spain using the SF–36 to evaluate health-related quality of life in chronic allograft nephropathy patients with anemia. The chronic allograft nephropathy patients' anemia was treated with recombinant human erythropoietin.[9] Findings related to quality of life for the chronic allograft nephropathy patients with anemia were similar to those for other patients with anemia treated with erythropoietin. The poor health-related quality of life of patients with chronic allograft nephropathy and anemia improved with erythropoietin treatment. This improvement varied from moderate to large for various components on the SF–36.[9]

The construct validity of the SF–36 has been tested by factor analysis using both psychometric and clinical tests of validity. The SF–36 has been tested for internal

consistency reliability by Cronbach coefficient alpha and has been translated for use in more than 50 countries. The SF–36 continues to be a valuable tool which is widely used to compare health-related quality of life outcomes for general and specific populations. One limitation of the SF–36 is that the patient must be able to read in order to self-administer the survey. For patients who are unable to read, the tool could be administered orally by a staff member if necessary.[10] Staff members in the AMP have not orally administered the SF–36 to their patients with anemia. Orally administering the SF–36 to patients in the AMP who need assistance should be considered as a means of increasing survey completion.

Information from the completed SF–36 forms is entered into the Orion Outcomes Database by a staff member in the AMP. The Orion Outcomes Database not only stores the data from the SF–36 surveys but also provides an analysis of the data. The Orion Outcomes analyzes the data, and statistical significance is calculated using the counts, means, and SDs of the 2 different samples.[11] A P value is identified for each dimension of the SF–36 survey and for the 2 summary measures with a P value of the SF–36 survey and for the 2 summary measures with a P value of <.05 which is considered statistically significant.[11]

RESULTS

The results of the study are summarized in *Table 1.* The Physical and Mental Component Scores for the 3-month, 6-month, and 12-month follow-up periods were compared with the patients' initial Physical and Mental Component Scores. For the 3-month period, 34 patients (n = 34) completed both the initial and the 3-month surveys. For the 6-month period, 19 patients (n = 19) had completed the initial and the 6-month surveys. For the 12-month period, 10 patients (n = 10) had completed all the required surveys.

SF-36 Dimensions Measured	Evaluates	3-Month Score (n = 34)	6-Month Score (n = 19)	12-Month Score (n = 10)
Physical Component Score	Summary of physical component scores	2.42 (P = .048)*	3.35 (P = .024)*	0.59 (P = .402)
Role Physical	Problems with work and other daily activities	5.82 (P = .002)*	3.77 (P = .041)*	1.94 (P = .231)
Bodily Pain	The severity of pain and its effect on physical functioning	5.31 (P = .006)*	6.75 (P = .002)*	1.72 (P = .330)
Physical Functioning	Limitations on physical functioning (eg, bathing, dressing)	2.44 (P = .067)	1.45 (P = .248)	−0.04 (P = .495)
General Health	Perception of their personal health	1.13 (P = .195)	0.91 (P = .335)	−2.98 (P = .094)
Mental Component Score	Summary of mental component scores	4.28 (P = .019)*	6.04 (P = .024)*	−0.58 (P = .435)
Vitality	Feeling tired, worn-out, or full of pep and energy	7.10 (P = <.001)*	4.74 (P = .032)*	0.51 (P = .434)
Role Emotional	Problems with work or other daily activities as a result of emotional problems	5.03 (P = .022)*	7.24 (P = .017)*	2.47 (P = .294)
Social Functioning	The level of interference with normal social activities	4.87 (P = .013)*	7.70 (P = .009)*	2.64 (P = .239)
Mental Health	Feeling of nervousness and depression versus peaceful, happy, and calm	3.48 (P = .024)*	2.85 (P = .111)	−2.72 (P = .160)

*Indicates Statistical Significance

Table 1. Summary of SF–36

Scores For the Physical Component Score, the Role Physical dimension had the greatest increase between the initial and the 3-month periods, with an mean increase of 5.82 (P =.002). The Role Physical dimension relates to problems with work or other daily activities as a result of physical health issues.[6] The greatest increase in physical functioning for the 6-month surveys was in the Bodily Pain dimension with a mean of 6.75 (P =.002). Bodily pain evaluates the severity of pain and its effect on physical functioning.[6] The greatest increase in physical functioning at 12 months was in the Role Physical dimension with a mean of 1.94 (P =.231). During the 12-month survey, there was a decrease in the mean of 2 physical dimensions, General Health and Physical Functioning. Physical Functioning evaluates the patient's ability to perform basic activities such as bathing or dressing to the ability to perform the most vigorous activities without limitations. General Health evaluates the patients' perceptions of their personal health.[6] The mean for all physical components for the 12-month survey were not statistically significant.

For the Mental Component Scores, the Vitality dimension had the greatest increase between the initial and the 3-month periods, with a mean of 7.10 (P >= .001). The Vitality dimension relates to feeling tired and worn-out or full of pep and energy.[6] The greatest increase in mental functioning from the initial to the 6-month surveys was in the Social Functioning dimension with a mean of 7.70 (P = .009).

Social Functioning evaluates the level of interference with normal social activities due to physical or emotional problems.[6] The Mental Health dimension was the only mental health component which did not show a statistically significant change for the 6-month follow-up, with a mean of 2.85 (P = .111). The greatest increase in mental functioning for the 12-month survey group was also in the Social Functioning imension with a mean of 2.64 (P = .239). Again, the findings for the 12-month period were not statistically significant.

CONCLUSION

Analysis of data from this retrospective study supports the hypothesis that patients treated in a CNS-managed AMP for anemia related to CKD experience the greatest improvement in quality of life during the first 3 months of treatment. The most rapid increase in functioning was during the first 3 months in both the Physical and the Mental Component Scores. During the next 3 months, however, the patients' quality of life did continue to improve but not as dramatically as during the first 3 months. The findings for the 12-month survey showed a slight decrease in the Mental Component Score, which was not statistically significant, but due to the small sample size, these findings are inconclusive. The Physical Component Score components continued to show a slight increase even with the small sample size, although this increase was not statistically significant. Patients may have had difficulty with recall after several months of treatment; there may be progression of underlying disease and the influence of multiple chronic health problems and comorbidities. These factors may have accounted for lower scores at 12 months.

LIMITATIONS

One limitation which may have impacted this study was lack of a power analysis. A power analysis would have determined the number of patients needed to detect if an increase in quality of life was due to anemia treatment. Information regarding a power analysis was not provided by the analysis database. Another limitation of the study relates to administration of the SF–36. There were incidents when the staff failed to make the SF–36 available to the patients for self-administration at the designated intervals. There were also surveys that were excluded from the study due to missing data.

RECOMMENDATIONS

Repeating this study with a larger sample may show a greater increase in the mean scores for both the Physical and the Mental Component Scores in each of the posttreatment time frames, especially the 12-month survey. A more consistent, orderly approach in the administration of the SF–36 would be beneficial in tracking the progress of patients in the AMP and increasing sample size for future studies. Continued education and encouragement should be provided to the AMP staff concerning the importance of making the SF–36 available to the patients at the appropriate times and checking the surveys for completeness of information. It may be beneficial for the staff to assist patients with limited reading ability by reading questions to the patient and by reviewing all surveys for completeness of information when collected from the patients. Repeating the study with a larger sample size and including longer treatment intervals could be very informative regarding the ongoing effectiveness of an AMP.

IMPLICATIONS FOR CNS PRACTICE

Data have shown that overall prognosis is improved by successfully managing and correcting anemia of chronic disease whether it is related to CKD, cardiovascular disease, or cancer.[3] This study shows that patients treated in a CNS-directed AMP for anemia related to CKD do experience improved quality of life. The knowledge, clinical expertise, and versatility of a CNS put the CNS in the ideal position to care for patients with anemia from various causes, not just those related to CKD. With the growing number of patient with anemia and the devastating effects that anemia has on patients' quality of life, the positive effects of the AMP are worthwhile to the patients and the healthcare community.

The CNS who manages the AMP identified earlier referrals by primary care providers as the intervention with the greatest potential to positively impact quality of life for patients with anemia. Research supports the CNS's view. Symptoms of chronic renal failure appear late in the course of the disease, and earlier referral to a nephrologists can lead to better quality of life for patients with renal disease.[12] The CNS has an opportunity to make a positive impact on patient outcomes by educating other members of the healthcare team, such as physicians, case managers, and diabetes educators, regarding the advantages of identifying and screening high-risk patients. Earlier screening can lead to earlier referral. With the continued increase in CKD and the anemia that accompanies it, organizations may find CNSs

to be a valuable resource for managing this patient population. A CNS is well prepared and qualified to manage patients with chronic health problems, and the positive impact of a CNS-managed program need not be limited to anemia.

References:

1. National Anemia Action Council. Anemia: hidden epidemic. 2002. Available at: http://www.anemia.org/. Accessed June 4, 2005.
2. National Institutes of Health. Healthy people 2010. Available at: http://www.healthypeople.gov/. Accessed June 13, 2005.
3. Lipschitz D. Medical and functional consequences of anemia in the elderly. J Am Geriatr Soc. 2003;51(3):s10–s13.
4. National Kidney Foundation, Inc. Kidney disease outcomes quality initiative: guidelines for anemia of chronic kidney disease. 2001. Available from http://www.kidney.org/. Accessed June 26, 2005.
5. Sowers J, McClellan W, Schoolwerth A. An Educational Monograph. Timing is everything; a proactive approach to CKD management. AdvancMed, LLC. 2005;1–44. Available from http://www.advancmed.org/edu.php. Accessed September 5, 2005.
6. Ware J. SF–36 Health Survey Manual and Interpretation Guide. Boston: Nimrod Press; 1997.
7. National Association of Clinical Nurse Specialists. Statement on Clinical Nurse Specialist Practice and Education. Harrisburg, Pa: National Association of Clinical Nurse Specialists; 2004.
8. Loos C, Briancon S, Frimat L, Hanesse B, Kessler M. Effect of end-stage renal disease on the quality of life of older patients. J Am Geriatr Soc. 2003;51:229–233.
9. Rebollo P, Baltar J, Campistol J, Ortega T, Ortega F. Quality of life of patients with chronic renal allograft rejection and anemia. J Nephrol. 2004;17:531–536. Available at http://www.sin-italy.org//jnonline/vol17n4/531.html. Accessed June 13, 2005.
10. Ware J, Kosinski M. Interpreting SF–36 summary health measures: a response. Quality of Life Research. 2001;10:405–413. Available at http://www.sf–36.org/. Accessed June 14, 2005.
11. Orion Software Development Outcomes Data Management System: Users Manual. Longmont, Co: Orion Software Development; 2001.
12. Frimat L, Loos-Ayav C, Panescu V, Cordebar N, Briancon S, Kessler M. Early referral to a nephrologist is associated with better outcomes in type 2 diabetes patients with end-stage renal disease. Diabetes Metab. 2004;30:67–74.

Appendix D

CNS AMP Projected Budget

Quality of Life Outcomes Related to Anemia Management of Patients with Chronic						
. Resources Needed for Solution Implementation						
	Start up	monthly	annual			
CNS Salary	76209	76209	914508			
SF-36	405					
Orion Outcome Database License	500	500	6000			
Survey Cost						
Printing	350	350	4200			
Resource Share						
10% of department budget	10000	10000	120000			
Re-imbursement bonuses quarterly	-7500	2125	30000			
equipment and supplies	325	325	3900			
least cost for office	650	650	7800			
Phone	35	35	420			
Printer	25	25	300			
Fax	15	15	180			
Computer	1500	110	1320			
Internet/intranet	29	29	348			
Expenses	165	165	1980			
Uniforms	200	33.33	399.96			
Total	82908	90571.33	1091356			

Proposal CNS managed AMP /07