Hemodialysis International 2008; **12**:441–449

Costs of managing anemia with erythropoiesis-stimulating agents during hemodialysis: A time and motion study

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Abstract

Use of erythropoiesis-stimulating agents (ESAs) presents a significant time and cost burden in the management of anemia of chronic kidney disease (CKD). We conducted a prospective, observational, activity-based costing study to estimate the health care personnel time and resulting direct medical costs associated with administering epoetin 3 times weekly to patients with end-stage renal disease on dialysis. The study was conducted at 5 US hemodialysis centers. The personnel time and costs were derived from time and motion observations. Predicted time and cost savings were modeled for switching patients to once-monthly ESA therapy. Patients also completed a survey questionnaire to assess their level of CKD knowledge and information needs. Total per-patient-per-year (PPPY) time expended on anemia management with epoetin averaged 608 minutes (range 512–915 minutes), with an average PPPY cost of $548 (range $342–$651). Use of a once-monthly ESA, compared with epoetin, could decrease average PPPY time expenditure by 79% (127 minutes [range 96–173 minutes]) and reduce PPPY costs by 81% ($104 [range $79–$136]). The patient questionnaire reported insufficient education on CKD. Use of a once-monthly ESA to correct anemia in dialysis patients may provide substantial time, resource, and cost savings compared with current treatment practices.

Key words: Personnel time, costs, resource utilization, drug administration, erythropoiesis-stimulating agent (ESAs)

INTRODUCTION

Anemia due to erythropoietin deficiency is a common complication of chronic kidney disease (CKD).[1] As CKD progresses to end-stage renal disease (ESRD), the incidence of anemia increases.[2] The presence of anemia has been associated with worsening cardiovascular morbidity[3] and accelerated rate of kidney damage in CKD patients.[4,5] Further, anemia in both predialysis and dialysis CKD patients has been shown to impair quality of life, causing fatigue[6] and cognitive deficits.[7] As such, effective anemia management is an important part of patient care,[8] which may improve clinical outcomes.[9]

Two erythropoiesis-stimulating agents (ESAs), epoetin and darbepoetin, are currently approved for anemia treatment in ESRD patients requiring dialysis. The approved dosing intervals for these agents are 2 to 3 times weekly for epoetin,[10] and once-weekly or once every 2 weeks for darbepoetin.[11] The use of ESAs in anemia management has been shown to be effective in reducing the need for regular red blood cell transfusions in dialysis patients.[12,13] This avoids the risk of infectious complications and sensitization following blood transfusion that would make kidney transplantation difficult. These benefits significantly reduce overall health care expenditures, and more than offset the additional drug cost of ESA use.[14,15] However, ESA admin-

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istration during hemodialysis is labor intensive and adds to the already significant workload in dialysis centers.

Because of the growing number of ESRD patients, driven in part by an aging population and the longer life expectancy of patients treated for advanced CKD, Medicare expenditures alone are projected to increase from \$10.8 billion in 1997 to \$28.3 billion by 2010.[16] A clear understanding of the costs involved in anemia management is important to manage the anticipated large numbers of ESRD patients effectively.

Typically, only drug acquisition expenses are considered in cost analysis studies. However, the true cost of ESA therapy, as assessed for patients with cancer, has been shown to include those costs associated with preparation of ESA doses, medication administration, record keeping, supplies, drug ordering, and personnel expense for these services.[17] In addition to the monetary costs required to treat anemia, there are "opportunity costs," which are the lost opportunities for personnel time and expenditure spent on anemia management to be used in other activities such as direct patient care and education.[18]

To better understand the actual costs involved in managing anemia of CKD in dialysis patients, we undertook an activity-based costing study. The primary objective of this study was to estimate the health care personnel time and resulting direct medical costs associated with administering epoetin 3 times weekly in ESRD patients visiting hemodialysis centers. Only epoetin, rather than darbepoetin, was assessed in this study, as epoetin was the standard of care in all 5 dialysis centers involved in this investigation. A secondary objective was to model the potential time and cost savings if patients converted to a once-monthly ESA treatment such as continuous erythropoietin receptor activator (CERA). Continuous erythropoietin receptor activator has been shown to maintain stable hemoglobin levels within the target range with a once-monthly dosing[19,20] and has been approved in Europe for the treatment of anemia associated with CKD. Another secondary objective was to assess the level of patient knowledge of CKD, as well as self-perceived patient educational needs.

MATERIALS AND METHODS

Study design

This was a prospective, observational, activity-based costing study of anemia management at 5 dialysis centers in the United States. No medical interventions, tests, or procedures, other than standard practice, were introduced in the study population. In addition, patients were asked to complete a survey questionnaire regarding their knowledge of CKD and the importance of educational activities.

Time and motion methods

The time and motion methodology was used to quantify time and nondrug supplies utilized in ESA-related tasks and activities. The study focused on epoetin administered 3 times weekly, as this was the regimen received by the majority of dialysis patients at the 5 centers. In each center, health care personnel were asked to identify and map all anemia management tasks in chronologic sequence. Four different case report forms (CRFs) were devised based on these interviews, which included (1) beginning-of-day group tasks (including preparation of epoetin and daily inventory); (2) end-of-day group tasks (including record keeping, preparation for the next day, and daily inventory); (3) individual injections of epoetin; and (4) inventory and ordering of epoetin. All centers used the same 4 CRFs, except for Center 2, which used a modified CRF for assessing beginning-of-day group tasks. This was necessary due to small variations in the beginning-of-day procedures at this center.

Staff members were also interviewed to estimate time spent on nonobserved and/or infrequent tasks, and nondrug supplies used. Personnel were also asked to identify tasks they thought might change if patients were switched from epoetin 3 times weekly to a once-monthly treatment.

Time and motion observations were randomly collected during hemodialysis shifts by trained observers using chronometers to determine minutes and seconds spent performing each activity. The observations of timed activities and supplies utilized, excluding epoetin drug usage, were then recorded on the appropriate CRFs. The staff collected 15 observations for the beginning-of-day and end-of-day CRFs (tasks performed once per day for all patients receiving epoetin that day) and 30 observations for tasks performed per individual patient administration. The time and cost savings assessed in this study were based on the opportunity cost principle and do not represent actual health care costs. All costs were calculated based on the perspective of a dialysis center.

Tasks observed and recorded on CRFs were preparation, injection and record keeping, and daily inventory. Nonobserved tasks reported by staff were day before administration (review of flow sheets, printing of epoetin labels, and collection of supplies); inventory, ordering and storage; scheduled blood sampling; physician visits; and review of laboratory results and epoetin prescription changes. Record keeping (end of day) was observed at 1 center but was nonobserved at the other 4 centers. Average observed and total (observed plus nonobserved) time was calculated per patient per epoetin session, per patient per year (PPPY), and for all patients per year at each center.

Activity-based costing method

Labor costs associated with the time and motion records were computed from personnel time, using wage and benefit rates. Cost per minute by type of personnel was calculated from national salary averages as reported by the United States Department of Labor, Bureau of Labor and Statistics (2005 and 2006 level).[21]

Nondrug supply costs were calculated based on the types and numbers of supplies used (excluding the quantity of epoetin). Unit cost data were derived from national sources to ensure comparability in costs across all centers. Supply costs were obtained from a current medical supply price list agreed upon between New York State and a leading vendor in that state.

Costs for overheads, waste management, blood sampling supplies, and laboratory tests were not included in the study analysis. It was not possible to determine the proportion of overheads and waste management attributable to anemia management.

Modeling time and costs of once-monthly ESA

The impact on observed and nonobserved time and costs of the hypothetical use of a once-monthly ESA was modeled. For the development of this simulation, it was assumed that (1) staff time associated with injection activities (preparation, injection, and record keeping) was the same for patients receiving once-monthly ESA or epoetin and (2) costs per minute, the number of supplies used, and unit cost for supplies did not change irrespective of the patient number per center or the absolute number or proportion of patients receiving a once-monthly ESA. This study assessed the associated costs of different dosing regimens only and did not consider ESA drug acquisition costs.

Cost calculations

The following calculations were used to estimate the wage costs, supply costs, and the average cost per patient per ESA administration:

$$\text{Wage costs} = T_1W_1 + T_2W_2 + \cdots + T_nW_n$$

where T is the total time in minutes, W is the average wage per minute through n staff categories, and "wage costs" is the total cost for multiple staff time for ESA management activities.

The supply costs were calculated by multiplying the estimated resource use by unit cost, as follows:

$$\text{Supply costs} = X_1Y_1 + X_2Y_2 + \cdots + X_nY_n$$

where X is the number of a specific supply used and Y is the unit cost of that supply through n supplies. For nonobserved time, the time estimates were obtained through interview.

Finally, the average cost per patient per ESA administration was calculated as

$$\begin{aligned}\text{Average cost} &= \text{preparation costs} + \text{inventory costs} \\ &\quad (\text{beginning of day}) + \text{record-keeping costs (end of day)} \\ &\quad + \text{inventory costs (end of day)} + \text{distribution/ESA} \\ &\quad \text{administration costs} + \text{record-keeping costs} \\ &\quad + \text{inventory/ordering costs} + \text{total nonobserved} \\ &\quad \text{activity costs} + \text{supply costs}.\end{aligned}$$

Patient survey

In addition to the time and motion observations, a patient questionnaire survey was conducted to assess the level of CKD knowledge and self-perceived information needs. Patients at each of the 5 dialysis centers were asked to complete a survey questionnaire. Those patients who responded to the questionnaire were required to submit written informed consent. Patients were asked 2 questions aimed to (1) assess how informed they felt on aspects of CKD management and (2) identify the tasks that they felt were important for staff to spend extra time on, if available:

Question 1—"Please think about what you have been told regarding your chronic kidney disease by the doctors and nurses who are looking after you." Patients were required to rate 6 topics from 1 ("no information received") to 3 ("all information I need").

Question 2—"Imagine that more time were available to health care professionals, doctors, and nurses at the dialysis unit. How important is it for you that staff would spend additional time for each of the activities listed below"? Patients were required to rate 8 activities from 1 ("not important") to 3 ("very important").

Statistical analysis

Descriptive statistics were used to describe personnel time, supplies, and cost for anemia management with epoetin. Time and costs of either ESA administration, and potential time and cost savings for switching administration, were expressed per ESA administration session, PPPY, and per center per year.

Two sets of analyses were undertaken: (1) time and costs obtained from observed tasks only and (2) combined time and costs from direct observations together with estimates of time spent on nonobserved tasks. All time estimates were adjusted to a time per patient per epoetin session by dividing the time of each task by the number of epoetin sessions per frequency of each task.

Because fewer than 30 observations were taken per center, bootstrap simulation was used to calculate the nonparametric mean and 95% confidence intervals (CI) for observed time. Confidence intervals were constructed for endpoints based on observed time only but could not be calculated for nonobserved time because only point estimates were available from interview. Therefore, minimum and maximum ranges across all the centers are reported for total (observed and nonobserved) time and costs.

Average scores for the topics in the questionnaire were calculated based on the responses of patients from all centers. Subgroup analyses of the average scores based on age and gender were not performed as no a priori differences were expected.

RESULTS

Observed time and costs associated with epoetin

Across the 5 centers, patients received epoetin, on average, 3 times weekly or 13 times monthly (Table 1). The average time per patient per epoetin session was 2.35 minutes (95% CI: 2.04 minutes, 2.67 minutes), with the majority of time (54%) being spent on tasks involved with administering the injection and record keeping (Figure 1a). This would result in 364 minutes (95% CI: 316 minutes, 414 minutes) PPPY. If this were extrapolated to a hypothetical dialysis center of 100 patients, the time spent per year on anemia management would average 606 hours. The average cost per patient per epoetin session (i.e., cost associated with time and supplies expended on all tasks related to administration of epoetin during a single visit) was \$2.56 (95% CI: \$2.38, \$2.75) (Figure 1b). Nondrug supplies accounted for 44% of average expenditure, with the labor costs associated with personnel

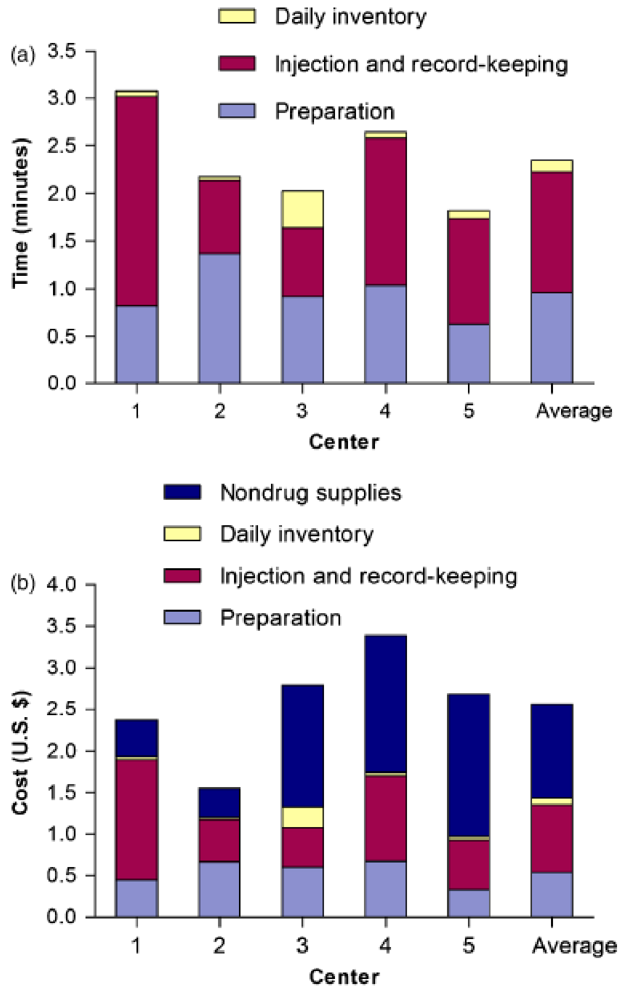

Figure 1 (a) Average observed time and (b) observed costs per patient per epoetin session, by center.

Table 1 Average patient epoetin sessions

	Center 1	Center 2	Center 3	Center 4	Center 5	Average
Number of dialysis patients per center	47	157	60	81	113	92
Number receiving epoetin per center	47	143	60	81	113	89
Epoetin sessions per patient per week	3.0	2.9	2.9	2.9	3.0	3.0
Epoetin sessions per patient per month	12.9	12.7	12.7	12.7	13.0	13.0
Epoetin sessions per patient per year	155.0	153.0	152.0	153.0	156.0	154.0

time accounting for the remaining 56%. This resulted in an annual cost of $395 (95% CI: $368, $424) PPPY. The hypothetical annual cost for 100 patients was $39,546.

Total time and costs associated with epoetin

When nonobserved tasks reported by staff were included in the analyses, the average time per patient per epoetin session was 4.09 minutes (range: 3.30 minutes in Center 2 to 6.19 minutes in Center 1), and the average cost per patient per epoetin session was $3.63 (range: $2.16 in Center 2 to $4.37 in Center 1). Annualized time and costs per patient were 608 minutes (range: 512 minutes in Center 2 to 915 minutes in Center 1) and $548 (range: $342 in Center 2 to $651 in Center 1). When all patients in each center were considered, the overall time ranged from 532 hours in Center 3 to 1242 hours in Center 2, with overall costs ranging from $30,576 in Center 1 to $64,770 in Center 5. The hypothetical time and cost for 100 patients per year were calculated to be 1013 hours and $54,799, respectively.

Modeled total time and costs associated with once-monthly ESA

Modeling analysis based on observed and nonobserved tasks predicted that an average reduction of 481 minutes (79% of total time spent on epoetin use) PPPY would be achieved if a patient were converted for a year from epoetin 3 times weekly to a once-monthly ESA (Figure 2a). This would result in an accompanying 81% saving of $444 PPPY (Figure 2b).

Figure 3 shows the distribution of time and cost savings with 100% of patients receiving a once-monthly ESA. Time savings would be driven by avoiding observed tasks per ESA administration (70%). The additional 30% of time savings would be obtained through expected reduction in the frequency of several tasks to once monthly: inventory, ordering, and storage; scheduled blood testing; and review of lab results and ESA dosage changes. Thirty-six percent of the time saved would be due to a reduction in time spent on tasks related to injection and record keeping, 32% in preparation tasks, and 17% in scheduled blood sampling. However, supplies (mostly saline infusion) constitute the main component of cost savings (36%), followed by time for injection and record keeping (25%), and time for preparation (20%).

Using the data for average savings per patient, potential savings were extrapolated to centers with varying proportions of patients receiving a once-monthly ESA. If 50%

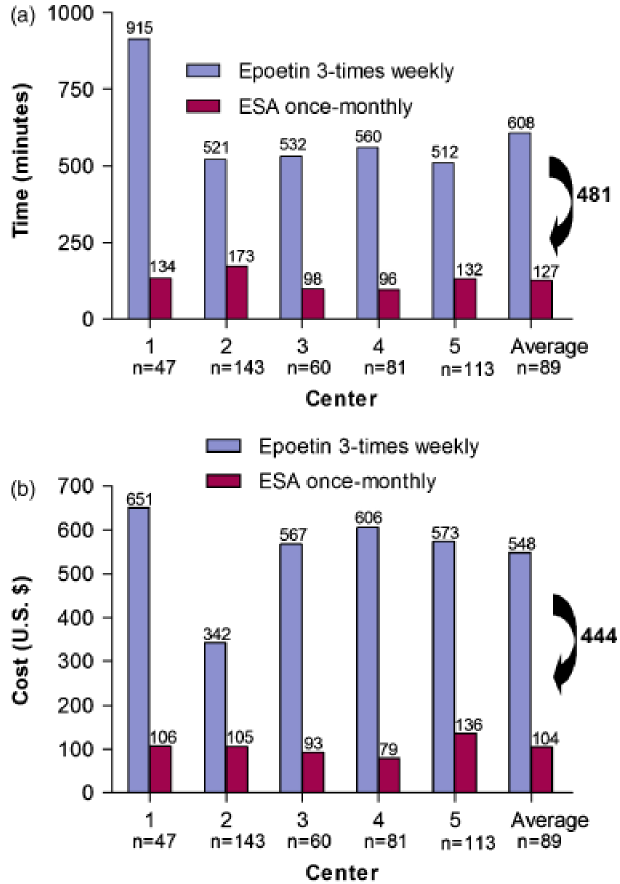

Figure 2 (a) Total time and (b) total costs per patient per year for epoetin 3 times weekly vs. erythropoiesis-stimulating agents (ESA) modeled at once-monthly use in 100% of patients, by center.

of patients were to use a once-monthly ESA, average time savings PPPY would be 241 minutes with a cost saving of $222 PPPY. Average savings were also modeled for varying center size. A hypothetical center with 100 patients all receiving epoetin 3 times weekly would potentially save 802 hours and $44,415 per year by converting to a once-monthly ESA. Greater savings could be achieved with larger centers, for example, a hypothetical center with 180 patients requiring ESA therapy could realize savings of 1444 hours and $79,950 per year.

Patient survey

A total of 91 completed surveys were received out of 150 requested at the participating centers: 56% of respondents were male, and the average age was 60 years. Information on CKD-related causes of anemia was

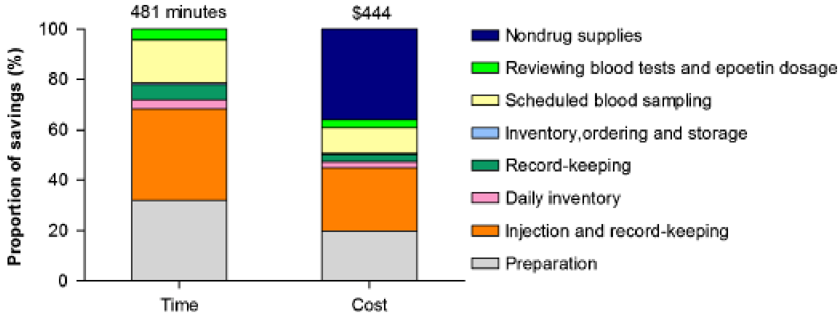

Figure 3 Distribution of predicted total time and cost savings, by task.

considered by most patients to be limited; 77% of respondents had no or insufficient information on this topic (Table 2). Participants felt most informed about home dialysis, with only 47% feeling that they received no or insufficient information on this topic (Table 2). With respect to tasks that health care professionals could be performing if more time were available, all topics proposed were considered to be fairly very important by the majority of patients. In particular, guidance on dealing with fatigue and easing symptoms of CKD were considered priorities, while advice on self-care and/or home dialysis was rated as least important (Table 3).

DISCUSSION

The findings of this study demonstrate that anemia management is associated with substantial time and costs, and show that major savings could potentially be achieved with the use of an ESA that can be administered once monthly. Using activity-based costing and modeling once-monthly administration, we found that an average time savings of 79% could be achieved per center per year by converting patients from current anemia treatment using epoetin 3 times weekly to utilization of a long-acting ESA. This would also result in an 81% reduction in corresponding costs associated with anemia management per center per year. It is important to note that these estimated time and related-cost savings represent "opportunity costs" associated with current ESA use and as such should not be considered to reflect actual savings that might be realized by dialysis centers. These "opportunity costs" represent the potential benefits if the time and expenditure was alternatively used. As such, the monetary

Table 2 Results from patient survey: knowledge of anemia

	Average (1–3)[a]	Respondents who received no or insufficient information (%)
How CKD causes anemia	1.80	77
Symptoms of anemia	1.85	76
Treatments for anemia	1.87	74
Complications associated with CKD	1.93	77
Information about kidney transplant	2.12	62
Information about home dialysis	2.33	47

[a]1: "I don't recall having received information"; 2: "I received information but would like to receive more"; 3: "I have all the information that I need."
CKD = chronic kidney disease.

Table 3 Results from patient survey: importance of health care staff tasks

Staff Task	Average (1–3)[a]	Respondents who considered task as "very important" (%)
Providing advice on how to deal with fatigue	2.66	70
Providing information about easing symptoms of kidney disease	2.63	69
Talking about health problems	2.59	62
Providing more information about CKD in general	2.51	60
Providing dietary advice	2.50	59
Providing more information about anemia	2.47	53
Providing information on kidney transplantation	2.36	61
Providing advice on self-care and/or home dialysis	2.04	37

[a]1: "Not important"; 2: "Fairly important"; 3: "Very important."
CKD = chronic kidney disease.

value of these cost savings is in the opportunity to reinvest such time in other valuable activities.

A published analysis of comparable design in 5 European dialysis centers found average times for tasks related to epoetin administration similar to those assessed in the current study.[22] The European study estimated that 3.9 minutes per patient per epoetin session—equivalent to 503 hours for 50 patients per year—was spent administering epoetin 3 times weekly (including nurses' and physicians' time combined). It also concluded that administration of darbepoetin once weekly instead of epoetin 3 times weekly would save 350 h/y for 50 patients.

The present study also estimated costs associated with the time spent on epoetin 3 times weekly compared with once-monthly ESA administration. In a previous study of CKD patients not on dialysis, ESA drug costs exclusive of administration costs were significantly greater for darbepoetin compared with epoetin ($190 vs. $155 per week; $P=0.028$).[23] However, another study showed that among a cohort of ESA-treated inpatients, those receiving epoetin for renal anemia had far higher median daily administration costs than those receiving darbepoetin ($2.69 vs. $0.99, $P<0.001$).[24] These studies suggest that in addition to acquisition costs, administration costs may account for a large part of overall costs of ESA treatment. Therefore, it is important for pharmacoeconomic analyses of anemia management to focus on direct costs associated with preparation, administration, and other ESA-related activities, as these can be major cost drivers. Indeed, the most labor-intensive anemia management tasks identified in the current study were drug administration and record keeping, with supplies (excluding drug costs) being the largest expense.

This analysis used activity-based costing to determine the time and costs associated with each task.[25,26] This approach identifies the relationship between the consumption of resources and the process or service by disassembling a health care process into discrete tasks. It is a more complex method than traditional cost accounting, which does not assign costs to specific services. Activity-based costing allows centers to compare the costs of anemia management between different ESAs. Analysis of activity-based costs allows evaluation of the economic impact of real-world practice patterns, including all components of nondrug costs. This analysis complements randomized clinical trials, which evaluate efficacy and safety under highly standardized conditions and seldom address economic factors.

Apart from reducing the costs of anemia management in dialysis patients, a once-monthly anemia treatment has the potential to improve dialysis care in several ways. First, in-center dialysis is very labor intensive; reducing the workload could help personnel at dialysis centers to provide more timely care. Second, a reduced workload could provide physicians and nurses with the opportunity to spend more time on clinical assessment and disease management. Finally, the time savings could also be used toward improving patient education efforts. Our patient survey results showed that $>75\%$ of patients at the dialysis centers felt that they received no information or insufficient information on various aspects of their disease, including the symptoms of anemia, anemia treatment, the association between anemia and CKD, as well as complications associated with CKD. Reducing the time spent on recurrent tasks may be used for individualized patient care and education, which can help improve overall disease management and patient satisfaction in dialysis centers.

Some limitations of this study should be noted. First, the relatively small number of sites and the small number of observations collected at each site may limit the generalizability of the results to different geographic areas of the United States. Three of these 5 centers were from a large dialysis organization, which has protocols in place that might have impacted estimated time. Also, only 2 ESA protocols were studied, which may differ from protocols applied in other dialysis organizations or hospital-based dialysis units. The cost calculations used national average salaries, which may not adequately take into account salary variations in private and public dialysis centers.

Second, estimates of nonobserved time were based on point estimates derived from staff interview and, hence, have a lower predictive value than directly observed time. Nonobserved tasks take up a significant amount of time spent on anemia management (30%, according to this study), but were difficult to measure accurately and were, therefore, not always included in these analyses. In addition, it is difficult to assign some nonobserved tasks exclusively to anemia management as they may also relate to other disease management (e.g., physician rounds, blood sampling).

Finally, our model for a once-monthly ESA use is hypothetical; as such, it was necessary to make several assumptions. We assumed that the number of supplies used per ESA administration, unit costs for supplies, and labor costs were the same for either administration. However, we believe it is unlikely that the change in frequency of ESA administration would impact supplies and labor costs. In addition, we assumed a reduction in time and costs only for those nonobserved activities that the center personnel were certain would be reduced by the conversion to once-monthly ESA. This was the case only for scheduled blood sampling and the subsequent review of laboratory results and ESA dosage. Hence, our model may underestimate savings associated with once-monthly ESA use compared with current epoetin 3 times weekly administration. Additionally, we assumed that the tasks and costs associated with each administration session would be similar between epoetin and a once-monthly treatment such as CERA, and would not be affected by the proportion of patients switching ESA. As with any new treatment, models for use will need to be refined further as details of impact on practice become available.

With regard to the patient questionnaire, patients generally felt that they were not provided with sufficient information about CKD or methods to manage the symptoms of the disease. Patients reported being well informed about self-care and home dialysis but had a low perceived need for this information. There may be a discrepancy between what practitioners emphasize in patient education (e.g., self-care and home dialysis) and what patients perceive as important educational needs (advice on dealing with fatigue and easing CKD symptoms, or on causes and symptoms of anemia).

In summary, this study evaluated the direct medical costs of current anemia management (excluding ESA acquisition costs) and highlights the importance of taking these factors into account when considering the actual costs involved in the administration of ESAs. Although total time per patient ESA session is relatively small (4.1 minutes), the time burden of anemia management for health care professionals across a whole dialysis center over 1 year is significant. A once-monthly administration of an ESA would reduce this time burden and may make time available for other important care activities, such as patient education, that may contribute substantially to patients' well-being and overall care satisfaction.

ACKNOWLEDGMENTS

The authors thank the principal investigators, study coordinators, staff members, and patients of the 5 participating centers. Principal investigators: Harry Alcorn Jr, PharmD; Paul Chidester, MD; Elias Ghafary, MD; Kenneth Rappaport, MD; Brigitte Schiller, MD. Coordinators: Bianca Bianco, RN, BSN; Sharon Brandl, RD; Connie Cook, RN; Deb Pilon, LPN; and Jeanne Rogers, RN. This study was conducted by United BioSource Corporation and was supported by Roche. The authors also gratefully acknowledge Nick Brown, PhD, of Envision Pharma for editorial assistance.

Manuscript received March 2008; revised May 2008.

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