Assessment of Time and Practice Resources Required to Provide Weekly or Monthly Erythropoiesis-Stimulating Protein Therapy to Chronic Kidney Disease Patients in the Physician Office Setting

MARIALIZA BERNARDO, MD; PAUL CRAWFORD, MD; JOACHIM HERTEL, MD; CHRIS SHOLER, MD; XIAO XU, PhD; THOMAS GOSS, PharmD; RESHMA KEWALRAMANI, MD; and DENISE GLOBE, PhD

ABSTRACT

BACKGROUND: There is an epidemic of chronic kidney disease (CKD) and a high prevalence of anemia (47%) observed in CKD patients. Little is known about the cost in physician office resources of routine erythropoiesis-stimulating protein (ESP) administration to treat patients with nondialysis CKD.

OBJECTIVES: The objectives of this research were (1) to explore the patterns of care in physician offices where nondialysis CKD patients receive routine ESP injections, (2) to examine differences in the monthly resources and related costs incurred by physician offices in treating patients receiving either weekly (QW) or monthly (QM) ESP regimens, and (3) to identify opportunities to minimize the burden of CKD treatment on physician offices.

METHODS: An observational, cross-sectional time and motion assessment was performed in 10 community-based outpatient nephrology practices (5 QW and 5 QM practices); each practice had ≥40 patients on routine ESP therapy for nondialysis CKD. Three observers trained in health care research documented injection-related tasks and time associated with 91 ESP injection procedures (47 QW and 44 QM) from patients’ arrival to and departure from the physician office, office personnel follow-up on billing and documentation, and injection-related staff time. Monthly injection times for QM were calculated by summing the time required to perform the tasks associated with administering a single injection of ESP to subjects, as documented by observers. Total monthly per-patient medical practice costs for providing QM ESP injections were calculated, including labor costs (calculated by applying average wage rates of practice staff to time observed for the specific activities performed) and supply costs (based on average list prices found in medical supply catalogs). Monthly injection times and costs for the QW regimen were calculated by summing the same list of activities as for the QM regimen and multiplying by 4.3 (4.3 weeks per month). Nephrology practice personnel completed a questionnaire summarizing practice characteristics and estimated the time required for some of the injection-related activities. The time and cost associated with each task were analyzed using descriptive and comparative statistics (i.e., Fisher’s exact test and t-test).

RESULTS: On average, patients spent 21 minutes in the clinic for a routine injection visit (QW: 17 minutes, QM: 25 minutes; P = 0.053), during which 11 minutes (52%) were spent interacting with clinic staff (QW: 8.9 minutes, QM: 13.4 minutes; P = 0.005). In the time spent interacting with staff, 3 minutes (QW: 2.9 minutes, QM: 3.6 minutes; P = 0.065) were for dose administration and 8 minutes (QW: 5.3 minutes, QM: 9.8 minutes; P = 0.011) were for staff providing various services to the patients, including registering patients on arrival, examining patients (vital signs, weight, blood work), consulting with patients, and scheduling patients’ next visits. Each month, clinic staff spent a total visit average of 38 minutes providing anemia-related treatment for each QW injection patient, compared with 13 minutes for each QM injection patient (P <0.001). After patients’ departure, clinic staff spent additional time (not quantified) on billing, filing claims, and other administrative responsibilities most of which could not be observed during our 1-day observation. The average total monthly practice cost of providing ESP therapy to a QW patient ($17.00 [95% confidence interval (CI), 13.00-27.13]) was more than double that for a QM patient ($6.78 [95% CI, 5.34-9.12]; P = 0.004). Differences in visit-related labor costs (QW: $8.34, QM: $3.43; P = 0.108) and injection supply costs (QW: $4.39, QM: $1.67; P <0.001) accounted for the largest portions of the total monthly cost differential between the treatment regimens. QM dosing would require, on average, 83 hours less staff time and $2,044 less estimated cost treating 200 patients per month compared with weekly administration per clinic.

CONCLUSIONS: Administering routine ESP injections to nondialysis CKD patients for anemia using a QM regimen results in substantial time and cost savings compared with a QW therapy regimen. Managing patients on less-frequent ESP dosing schedules may alleviate medical practice burden by reducing the staff time and supplies related to providing injections in the office.

KEYWORDS: Nondialysis chronic kidney disease, Anemia, Routine ESP administration, Patterns of nephrology care, Resource requirement

J Manag Care Pharm. 2006;12(9):714-25

It is estimated that chronic kidney disease (CKD) affects approximately 20 million Americans, with 80,000 newly diagnosed per year.1,2 The incidence and prevalence of the disease doubled in the past decade, and the rates reportedly increased in all 50 states over the same time period. Much of the observed increase in CKD stems from epidemic increases in obesity, type 2 diabetes, and hypertension among the U.S. population, with diabetes and hypertension estimated to account for 70% of new cases.1 Improved treatments for hypertension, diabetes mellitus, and coronary disease have increased longevity in affected patients and, therefore, their likelihood of developing CKD.1,2 Regardless of the type of kidney disease, the major

Authors

MARIALIZA BERNARDO, MD, is a principal investigator, Southwest Houston Research, Houston, Texas; PAUL CRAWFORD, MD, is a principal investigator, Associates in Nephrology, Evergreen Park, Illinois; JOACHIM HERTEL, MD, is a principal investigator, Nephrology Associates, PC, Augusta, Georgia; CHRIS SHOLER, MD, is a principal investigator, Plaza Medical Group, Oklahoma City, Oklahoma; XIAO XU, PhD, is a principal investigator and THOMAS GOSS, PharmD, is a vice president, Outcome Services, Covance, Inc., Gaithersburg, Maryland; RESHMA KEWALRAMANI, MD, is a medical director and DENISE GLOBE, PhD, is director of global health economics, Nephrology Team, Amgen, Inc., Thousand Oaks, California.

AUTHOR CORRESPONDENCE: Marializa Bernardo, MD, Principal Investigator, Southwest Houston Research, 8323 Southwest Fwy, Houston, TX 77074. Tel: (713) 484-8123, Fax: (713) 484-7859; E-mail: abernard0@houston.rr.com

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outcomes of CKD include progression to kidney failure, complications from decreased kidney function, and development of cardiovascular disease. For instance, approximately 20% of patients with severe CKD progress to dialysis.

Although it is well recognized from the third National Health and Nutrition Examination Survey (NHANES) that there is an increasing prevalence of early-stage kidney disease and an increasing incidence of end-stage renal failure, which leads to poor outcomes, CKD is still underdiagnosed and undertreated. To address this issue, the National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) Advisory Board was tasked to develop clinical practice guidelines to define CKD and to classify stages in the progression of CKD in 2000. The classification and clinical practice guidelines disseminated in 2002 were based on evaluation of the severity of kidney disease, association of level of kidney function with complications, and stratification of risks for loss of kidney function and development of cardiovascular disease. The system classifies individuals into 5 categories, based on glomerular filtration rate (GFR) levels from less severe (Stage I) to most severe (Stage V) (Table 1). GFR may be estimated from serum creatinine and patient characteristics using algorithms including the MDRD (modification of diet in renal disease) or the Cockcroft-Gault formula. The 2006 K/DOQI guidelines defines anemia in CKD patients by a hemoglobin level of <13.5 g/dL in men and 12 g/dL in women. Anemia prevalence rises with the worsening of kidney function, from 26.7% of patients in the early stages of CKD to 53.6% in the latest stage of CKD before dialysis.

Anemia is a common complication in CKD patients due to the kidneys’ inability to produce sufficient endogenous erythropoietin, a hormone essential for stimulating the bone marrow to produce new red blood cells and prevent anemia. Approximately half of CKD patients with GFR <60 cc/min/1.73 m² have CKD-related anemia, and anemia has been associated with decreased quality of life (QOL) and increased morbidity, health care costs, and mortality. CKD and anemia combined are thought to be synergistic for adverse health outcomes, particularly for cardiovascular morbidity and mortality.

Importantly, higher hemoglobin levels in CKD patients, both those dependent on dialysis and those not yet on dialysis, have consistently been associated with improved QOL and lower hospitalization and mortality rates. While this association is understood, CKD patients routinely present to dialysis with anemia. Data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) indicated that 27% of patients new to end-stage renal disease treatment received erythropoietin prior to initiation of dialysis, while 66% had a hemoglobin level of <11 g/dL.

The advent of erythropoiesis-stimulating proteins (ESPs) dramatically reduced the use of red blood cell transfusions as the mainstay of therapy for CKD anemia. Epoetin alfa (EpoGen), was approved by the U.S. Food and Drug Administration (FDA) for the treatment of anemia in dialysis patients, followed by the approval of ESPs for the treatment of anemia in June 1989 in CKD patients (I–IV) not on dialysis (epoetin alfa, Procrit in December 1990) and darbepoetin alfa, Aranesp, in September 2001). However, despite the efficacy of ESPs and Medicare’s willingness to pay for ESPs in patients with hematocrit <33% (after ruling out other treatable causes of anemia), it has been speculated that the low proportion of CKD patients receiving anemia treatment may have to do with the cumbersome frequency of physician visits that is required.

ESP regimens are commonly administered in the outpatient setting, including physician offices and nephrology clinics. Common ESP regimens include dosing frequencies ranging from 3 times per week (TIW) to monthly (QM), depending on patient and physician preference as well as choice of ESP administered. Four recent studies have established the safety and efficacy of QM dosing for darbepoetin alfa and epoetin alfa in the treatment of anemia in CKD patients. The Ling et al. study showed that, for patients initiated on weight-based, every-2-week dosing of darbepoetin alfa, the interval could be extended to QM and the dose was doubled. One of the 4 studies, Disney et al., was an open-label study of darbepoetin alfa. Studies have shown that different ESP dosing regimens routinely achieve comparable clinical results based on achieving targeted hemoglobin levels. Since clinicians perceive different ESP regimens to achieve comparable clinical results, economic and operational factors could influence the therapy and dosing regimen most commonly adopted by nephrology practices and the protocols implemented in these practices.

Currently, little is known about the quantity of medical clinic resources (including time and disposables [e.g., syringes, needles],

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Stages of Chronic Kidney Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Stage of Chronic Kidney Disease</td>
</tr>
<tr>
<td>eGFR range</td>
<td>290 ml per minute per 1.73m² of body surface area with evidence of kidney damage</td>
</tr>
<tr>
<td>II</td>
<td>60-89 ml with evidence of kidney damage</td>
</tr>
<tr>
<td>III</td>
<td>30-59 ml</td>
</tr>
<tr>
<td>IV</td>
<td>15-29 ml</td>
</tr>
<tr>
<td>V</td>
<td>&lt;15 ml or dialysis</td>
</tr>
</tbody>
</table>

*eGFR* = estimated glomerular filtration rate.
but excluding ESP product costs) consumed by administering routine ESP injections to nondialysis anemic CKD patients and whether there is an impact of dosing regimens, particularly dosing frequency, on medical clinic processes and/or burden. According to Crémieux et al., extended dosing intervals could translate into favorable clinical and economic outcomes for patients and caregivers; however, the study did not address the impact of extended dosing on medical clinics. In-office ESP administration to nondialysis CKD patients for anemia correction consumes a significant amount of time and medical practice resources. With the epidemic of CKD, managing patients on less-frequent ESP dosing schedules may alleviate practice burden by reducing the staff time and supplies related to providing injections in the office. Less-frequent dosing could facilitate redirection of medical practice resources to administration of other services and thus could increase capacity in the nephrologist’s office and improve the quality of CKD care for a greater number of patients. Therefore, knowing this type of information should be helpful to any medical practice with potentially constrained resources, including but not limited to pharmacy-based injection clinics, managed care clinics, and clinics accepting government reimbursement (e.g., Medicaid and Medicare).

The purpose of the Anemia Management Office Resource Evaluation Study was to examine patient-flow characteristics and assess patterns of care in clinics where nondialysis CKD patients receive ESP therapies. The study is intended to identify the overall impact of routine ESP administration on practice burden and to assess the impact of ESP injection administration dosing frequency on the practice burden in terms of monthly injection administration time and monthly injection-related supply costs, excluding ESP costs.

### Methods

#### Study Design

An observational, cross-sectional time and motion study was conducted to assess practice resources related to ESP injection. A convenience sample of 10 nephrology practices that treated at least 40 CKD patients (a relatively high volume) with a standard QM or QW (weekly) ESP regimen was included in the assessment. Five sites routinely administering ESP QM and 5 sites routinely administering ESP QW were selected for comparability of patient volume for the 2 regimens according to the following site selection criteria:

- Outpatient CKD clinic administering ESP QM or QW in the office with ≥40 patients receiving one or both regimens
- Willingness to allow time and motion observation of ESP-related practice activities
- Willingness to complete a brief practice survey

Selection of sites with comparable volumes of patients receiving ESP therapy was required to reduce the risk of bias associated with scale economies. Time and motion observation data were collected from June through September 2005. The study protocol was approved by an accredited central human institutional review board (IRB).

QM and QW regimens were defined by the dosing interval only, not by the product. The ESP injection could be any type of ESP drug. The observations that we recorded at each site were either QM or QW at a particular site even though some of the sites administered ESPs at both dosing intervals. Given that only 1 regimen was observed at each site, we thus classified the sites as QM or QW in this study.

#### Data Collection

Three researchers (observers), each with 2 to 4 years of health services research background, received standardized training on observing and recording times associated with various standard activities associated with ESP injection administration. The standardized 6-hour training included reviewing the study protocol, observation process, and practice flow; practicing time recording by watching injection videos; comparing documented times across observers and trainers; and analyzing the differences. The trained observers went to each site in pairs for a 1-day observation and observed all the injections throughout the entirety of the injection clinic schedule for the day on which the office observation was scheduled. Activities and time were recorded from each patient’s arrival in the clinic/office until the patient’s departure. After the patient’s departure, activities related to the injection, such as billing, were followed and recorded. To control for possible observer bias by treatment regimen, reasonable efforts were made to ensure that observers were “blinded” to regimen. Specifically, the trained observers were not provided a priori information concerning the type of ESP used or the frequency of patient dosing in the practice while they were on site to conduct the time and motion assessment. The study coordinators and staff working with the observers were trained not to inform the observers; the intent was for these observers to be unbiased with regard to the treatment regimen. A total of 44 QM injections were observed in the QM sites, and 47 QW injections were observed in the QW sites. To assess interrater reliability, the extent of the consensus among the observers, 2 trained observers at each site observed 10% of the injections (1 injection per site) concurrently. The injection to be observed concurrently was selected based on random number lists generated a priori (assuming an average of 8 injections to be observed per site).

#### Time and Motion Task List

A standardized task list was developed and used to record times in minutes and seconds. Data collected during the time and motion assessment included the number of injections scheduled for the same time slot, time of day the injection was administered, patient sign-in and sign-out time, injection-related clinical activities, injection-related administrative activities, clinical supplies used, providers seen during visit, and reimbursement-related activities.
The injection-related clinical and administrative activities were grouped into 5 main categories:

1. **Visit-related activities.** Greeting patient and taking him/her to the exam room, taking vital signs/blood pressure, weighing patient, taking blood sample, consulting by physician, dismissing patient

2. **Dose administration-related activities.** Reviewing patient chart and confirming dose, obtaining product from central storage area, preparing injection, administering injection, disposing waste, and documenting ESP injection

3. **Front office-related activities.** Scheduling appointments, rescheduling appointments, appointment reminder calls/cards, arranging travel for ESP patient, registering patient on arrival, pulling patient chart, filing labs into patient chart, filing ESP records into patient chart, and refile patient chart

4. **ESP-related financial activities.** Preparing bills, recording payments, filing claim, making calls to payers, preparing supporting documentation

5. **Other ESP-related activities.** Counting and ordering ESP inventory, stocking ESP inventory, making holiday arrangements for patient, recording and delivering iron prescriptions

Any activities observed that were not on the standard checklist were recorded under “other” where room was provided for a brief description. Patients’ waiting time also was documented. In addition, supplies used in the ESP administration, such as gloves, alcohol swabs, needle, and syringe, were documented in the task list.

**Practice Questionnaire**

Each investigator also completed a questionnaire assessing specific nephrology practice characteristics, including practice size,
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Methods of Analysis

Monthly injection times for QM were calculated by summing the observed time required to perform the tasks associated with administering a single injection of ESP to nondialysis CKD subjects, which included injection-related clinical activities (visit-related activities and dose administration-related activities) and injection-related administrative activities (front office-related activities, ESP-related financial activities, and other ESP-related activities). We were only able to observe ESP-related financial activities (e.g., filing claim, making calls to payers) for 2 injections and to observe counting and ordering ESP inventory at 1 site. Most of these activities occurred at different locations and/or times other than the days when we conducted on-site observations. Given the limited observations, we did not include time associated with these tasks in our total ESP-related time calculation. Monthly injection times for the QW regimen were calculated by summing the same list of activities as for QM regimen and multiplying by 4.3 (4.3 weeks per month). To compare perceived time with actual time spent on various activities, we compared the practice-reported injection time as estimated by the study coordinator at each study site to the actual injection time measured by the observer.

Total monthly per-patient practice costs for providing ESP injections were calculated using labor costs and supply costs. The labor costs were calculated by applying average wage rates of practice staff to time observed for the specific activities.

### Table 3: Nephrology Practice Characteristics for the Sites for Time and Motion Study

<table>
<thead>
<tr>
<th>Practice Characteristic</th>
<th>QW (n = 5)</th>
<th>QM (n = 5)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of practice, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private office</td>
<td>3 (60.0)</td>
<td>3 (60.0)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Nephrology clinic</td>
<td>2 (40.0)</td>
<td>2 (40.0)</td>
<td></td>
</tr>
<tr>
<td>Number of ancillary personnel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>15.2 [9.63]</td>
<td>8.8 [5.31]</td>
<td>0.229†</td>
</tr>
<tr>
<td>Median (range)</td>
<td>13 (4-29)</td>
<td>7 (4-17)</td>
<td>0.370‡</td>
</tr>
<tr>
<td>Average number of patients seen per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>56.0 [39.8]</td>
<td>44.4 [26.7]</td>
<td>0.603†</td>
</tr>
<tr>
<td>Median (range)</td>
<td>37 (15-110)</td>
<td>35 (25-90)</td>
<td>0.839‡</td>
</tr>
<tr>
<td>Number of nondialysis CKD patients currently seen in the office, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100-124</td>
<td>0 (0.0)</td>
<td>1 (20.0)</td>
<td>0.444*</td>
</tr>
<tr>
<td>250-274</td>
<td>0 (0.0)</td>
<td>1 (20.0)</td>
<td></td>
</tr>
<tr>
<td>&gt;300</td>
<td>5 (100.0)</td>
<td>3 (60.0)</td>
<td></td>
</tr>
<tr>
<td>Number of patients currently on ESP therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>217.6 [160.9]</td>
<td>292.0 [243.6]</td>
<td>0.584†</td>
</tr>
<tr>
<td>Median (range)</td>
<td>291 (27-400)</td>
<td>200 (60-600)</td>
<td>0.686‡</td>
</tr>
<tr>
<td>Practice organizes a specific injection day/time, yes, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>4 (80.0)</td>
<td>4 (80.0)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Median (range)</td>
<td>10.3 [8.1]</td>
<td>24.3 [10.7]</td>
<td>0.081†</td>
</tr>
<tr>
<td>Number of ESP injection patients treated on a typical day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>23.8 [14.6]</td>
<td>20.2 [8.3]</td>
<td>0.643†</td>
</tr>
<tr>
<td>Median (range)</td>
<td>18 (9-43)</td>
<td>20 (8-30)</td>
<td>0.919‡</td>
</tr>
<tr>
<td>Percentage of office hours spent doing injections</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean [SD]</td>
<td>42.9 [40.5]</td>
<td>67.6 [25.7]</td>
<td>0.283†</td>
</tr>
<tr>
<td>Median (range)</td>
<td>26.7 (8.9-100.0)</td>
<td>62.2 (43.8-100)</td>
<td>0.368‡</td>
</tr>
</tbody>
</table>

* P value from Fisher’s exact test.
† P value from student t test.
‡ P value from Wilcoxon test.
CKD = chronic kidney disease; ESP = erythropoiesis-stimulating protein; QM = each month; QW = each week.
performed. We used standardized national wage rates from the 2005 U.S. Department of Labor/Bureau of Labor Statistics, National Compensation Survey, and salary.com to assign practice staff wage rates. The supply costs were based on average list prices found in medical supply catalogs. The costs of resources used as determined by the activities and supplies listed above were summed to calculate QM costs, while the monthly costs for QW were calculated by summing the costs of the resources observed (reported) per injection and multiplying by 4.3 (52 weeks per year/12 months per year). This method of calculation has been widely used in other studies, including studies reported by Foster et al. in the Journal of the American Medical Association.39

Summary statistics (n, mean, standard deviation [SD], median, and range) were calculated for the continuous variables (e.g., monthly practice-level injection administration time, monthly practice-level billing time, and monthly cost of practice resources used). Frequency distributions were reported for the categorical outcomes (e.g., sex, employment status preference for ESP regimen). Differences between treatment groups were compared using Fisher’s exact test for categorical variables and the t test or Wilcoxon test for continuous variables.

The interrater reliability among the observers was calculated using 2 methods. First, for all the tasks, we established consensus (measured as the number of agreements [observed/not observed] divided by the total number of observations) and reported as a Kappa statistic. By convention, a Kappa of 0.40 to 0.59 is considered moderate interrater reliability, 0.60 to 0.79 is considered substantial interrater reliability, and 0.80 is considered outstanding interrater reliability.40 To assess how similar the observed times were between observers for each activity and to what extent the observers agreed on the length of time taken for each observed activity, we calculated the intraclass correlation (ICC).41 The interpretation of ICC is similar to Kappa.

**Results**

We screened 232 nephrology practices to identify 15 sites that
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were interested and able to participate in the study and could use a central IRB. Among these 15 sites, we selected 10 large sites that met study inclusion criteria. Table 3 summarizes the participating study site characteristics by treatment regimen (QW vs. QM). These practice demographics provide several important insights on nephrology practices treating CKD patients with anemia. On average, 254 patients were receiving ESP therapy at each site (218 at QW sites and 292 at QM sites). Among the practices, 80% (4/5 QW and 4/5 QM) reported using a specific “injection clinic” day or time to manage routine ESP injections. The QW sites reported designating an average of 10 hours per week, while QM practices reported designating an average of 24 hours per week for injection clinics. On a typical day, QW sites provided 24 injections and QM sites provided 20 ESP injections. All the sites participating in this study were accepting new patients. None of the differences between QW and QM sites reached statistical significance.

Time Assessments

We observed 91 ESP injections—47 in the QW practices and 44 in the QM practices—and when we assessed consensus in activities observed and time recorded between the observers, we observed a high degree of interrater reliability (Kappa = 0.81, ICC = 0.79) among the observers. There were differences between QW and QM sites in the relative frequency in which routine activities were performed as part of a visit in which an ESP injection was administered, including weighing the patient, taking blood pressure/vital signs, taking blood for laboratory analysis, and providing physician consultation (Figure 1 A-D). For example, taking blood pressure/vital signs was not routinely performed in 23% of QW observations compared with only 2% of the QM observations (P = 0.004). Physician consultation was only observed in 4% of QW patients but in 21% of QM patients (P = 0.024). There also was a substantial variation in the time spent on injection-related activities between QM and QW injection sites on a per-injection basis (data not presented). For example, the time spent administering an injection took only half a minute for the QW regimen but 1 minute for the QM regimen (P < 0.001). Among patients who received physician consultation, the average consultation time was 7.8 minutes per QM patient but 5.2 minutes per QW patient (P = 0.684).

Figure 2 summarizes the observed time per patient per month spent on injection-related activities. Each month, nephrology practices spent a mean (SD) of 38.2 (33.1) minutes with each QW patient (8.9 minutes at injection level) compared with 13.4 (7.3) minutes with each QM patient (P < 0.001 for comparison at monthly level; P = 0.0048 for comparison at injection level). Further, QW and QM sites reported 150 and 87.5 (median) additional minutes per patient per month, respectively, for administrative tasks related to ESP injections, which were not observed directly by the trained observers. We note that the relationship between QM and QW injections is not linear (i.e., QW injections do not require 4 times the time observed for 1 QM injection on a per-patient per-month basis).

Per month, patients on QW regimen spent 74.8 minutes in nephrology clinics receiving their ESP injections, while patients on QM regimen only spent a total time of 24.8 minutes (P < 0.001, Figure 2). Patients receiving ESP injections spent a substantial amount of time waiting and on activities other than receiving the injection. Overall, patients spent a mean (median) time of 21 (19) minutes in the clinic for a routine injection visit (mean: QW: 17 minutes, QM: 25 minutes; P = 0.053). During this time, 3 minutes (QW: 2.9 minutes, QM: 3.6 minutes;
were spent interacting with clinic staff for dose administration (reviewing chart, confirming dose, preparing and administering injection, disposing of waste, and documenting injection) and 8 minutes (QW: 5.3 minutes, QM: 9.8 minutes; P = 0.011) were spent on staff providing various services to the patients, including registering patients on arrival, examining patients (vital signs, weight, blood work), consulting with patients, and scheduling patients’ next visits. The other 10 minutes were spent on waiting (QW: 8.8 minutes, QM: 11.6 minutes; P = 0.319).

Observer-Questionnaire Agreement
Some ESP-related activities, such as rescheduling appointments, front-office preparation for injection for patient, and actual ESP injection, were both observed and estimated by practices. The sites consistently overestimated the time spent on routine injection-related activities by a substantial amount (Figure 3). For example, the practices estimated spending 7 minutes preparing medication to completing administration and waste disposal for QW injection and 15 minutes for QM injection per injection, but only 2.7 minutes for QW injection and 3.4 minutes for QM injection were observed.

Practice Costs
One of the main objectives of this study was to estimate the monthly costs of administering ESP regimens from the nephrology practice perspective. The mean (SD) total monthly nephrology practice cost of providing ESP therapy to a QW patient ($17.00 [21.80]) was more than double that for a QM patient ($6.78 [6.20]), respectively, for activities observed in this study. A summary of the components of the monthly cost of providing an ESP regimen is provided in Figure 4. Mean costs were different between the QM and QW groups for total monthly injection-related practice costs (P = 0.004), labor costs of visit-related (P = 0.108), dose administration-related (P < 0.001), and front office-related activities (P = 0.005), and injection-related supplies costs (P < 0.001). As mentioned earlier, since most of the other ESP-related activities (i.e., ordering and counting ESP inventory) and financial activities (i.e., filing claims, making calls to payers) occurred at different locations and/or times other than the days when we conducted on-site observations, the labor costs estimates associated with practice staff time did not include time of these 2 categories of activities.

Discussion
This is one of very few studies to collect empirical data on activities and resource utilization associated with routine ESP administration from nephrology practices (outpatient clinics and physician offices) administering in-office ESP therapy and the only study to our knowledge to report these data from nephrology offices on nondialysis CKD patients. Our study observed that the average number of ancillary personnel at the QW sites was almost 100% higher than at the QM sites, while the average number of patients seen per day was only about 26% higher. Further, the number of patients on ESP therapy at QM sites was about 34% higher compared with QW sites.

Management of CKD patients generally includes monitoring patients’ vital signs, weight, and lab results and adjusting therapy accordingly. Although we observed that these activities were not necessarily performed routinely at each injection visit, they were performed in a larger proportion of observed QM injections compared with QM injections. In this study, there was no evidence that more frequent office visits for injection resulted in more comprehensive care. While this study provides an overview of the activities and staff resources used during routine ESP injection visits, there was a notable variation in the average time spent per injection: staff spent an average of 13 minutes interacting with QM patients while only 8.9 minutes with QW patients per injection. The relationship between QM and QW injections is not linear (i.e., QW injections do not require 4 times the time observed of 1 QM injection on a per-patient-per-month basis). Patients treated with a QM regimen spent more time with their physicians, nurse practitioners, and nurses for their consultation compared with patients on a QW regimen (4% of QW [equivalent to 17% QM] and 21% of QM patients had a physician consultation observed, with the mean observed time being 5.2 minutes for QW patients and 7.8 minutes for QM patients).

The average number of patients receiving injections in the observed nephrology practices each month was more than 200. Each month, nephrology practices spent a mean of 38.2 minutes with each QW patient and 13.4 minutes with each QM patient.
Considering the number of patients receiving injections, the nephrology practices spent 82.7 more hours per month performing observed injection-related activities to treat 200 QW patients compared with 200 QM patients. Stated another way, the observed staff time required to administer QW injections to 200 patients each month is equivalent to the observed staff time required to administer QM injections to 570 patients, which suggests that switching from a QW to a QM injection schedule could increase nephrology practice capacity by 185% in a practice treating 200 patients per month. Also, at a monthly level, the total monthly nephrology practice cost was twice as high for providing QW regimen compared with QM regimen (mean cost: QW $17.00, QM $6.78). To put the estimates in the context of the number of patients receiving injections in a busy nephrology practice treating 200 patients per month, the medical practice would have incurred an estimated $2,044 more in total monthly practice costs when providing QW ESP therapy compared with a QM regimen.

On the basis of the findings from the present study, in estimating time savings for providing ESP injections to a hypothetical clinic size of 200 patients on a cumulative monthly basis, QM dosing would require, on average, 83 fewer hours of staff time and $2,044 less cost per month compared with QW. It is possible that the time saved could be used to see other CKD patients or to provide other components of CKD care. CKD clinics that provide comprehensive care for anemia management provided by nurse practitioners have reported positive outcomes of slowed progression of CKD among patients, and improved blood pressure control, medication compliance, and diabetes self-management skills.44-45 With the practices having more time, more comprehensive and quality care could be provided to patients to improve their overall health and well-being.

Given that some of the activities (such as billing and inventory) were not observed, the actual medical practice burden is likely greater than the time and costs presented in this study. The unobserved time (e.g., practice preparation time, retrieval of laboratory results) could not be included because this information could not be collected accurately at the patient level. In addition, our estimate of medical practice costs (based on time, labor, and disposables) clearly excludes the costs associated with practice overhead and malpractice insurance expenses. The overall weighting of the relative value unit (RVU) for typical physician services comprises 3 factors: a work component (approximately 30%-35%), practice expense component (approximately 63%-68%), and physician liability insurance component (2%-3%) for common injection and level 1 evaluation and management codes. The payment rate for a routine administration (Current Procedural Terminology [CPT] code 90772) is approximately $18.57 per injection, and CPT code 99211 is approximately $21.60, according to the 2006 Medicare Physician Fee Schedule from the Centers for Medicare and Medicaid Services (CMS). Using the RVU proportion of the work component, medical practices are reimbursed from $5.57 to $7.56 per injection for injection-related work. The time observed in the practices represented only a proportion of the staff work time per injection. Thus, the current reimbursement rate may be insufficient for the amount of work associated with administration practices for injections.

An important observation from the current study is the apparent discrepancy between practice-reported estimates of time spent on activities, which were both observed directly by the trained observers and self-reported by the medical practices. For the ESP injection-related activities that were both recorded by observers and reported by practice staff, sites overwhelmingly and consistently overestimated the time sent on routine injection-related activities, possibly because practice staff had a difficult time separating out time for discrete tasks. This finding is consistent with the finding from another time and observation study reporting physician activities during time out of the examination room.46 Given that the nephrology practice personnel overestimated the resources required for routine ESP administration, they might underestimate their capacity to treat nondialysis CKD patients, which validates the need for studies like this.

Limitations

While the sample size studied was sufficient to observe some of these important differences between QM and QW regimens, it is possible that other important differences may not have been observed and that the results cannot be generalized to all sites providing ESP therapy to CKD patients. First, this study focused on sampling large nephrology practices to ensure its timely completion. A broad sample of sites was contacted to assess interest in participation; however, the participation rate was quite low due to the criterion of selecting large nephrology practices that currently had, on average, at least 40 CKD patients with anemia requiring ESP injections. The time observed might underestimate the actual activity time, given that the participation sites might be more efficient in injection-related activities because of high patient volume.

Second, this is a convenience sample because the clinics volunteered to participate. It is possible that these sites may differ in some unknown ways from other CKD practices that routinely provide ESP therapy. On one hand, we are aware that our trained study observers were in the nephrology practices for only 1 day per practice site, and it is possible that the injections we observed are not able to be completely generalized to the nephrology practices on other days. On the other hand, convenience samples have been frequently used in published research. According to Kalton,47 most behavioral and social science studies use convenience samples consisting of students, paid volunteers, and patients. Studies with such samples are useful primarily for documenting that a particular characteristic or phenomenon occurs within a given group or,
It alternatively, for demonstrating that not all members of that
group manifest a particular trait. Such studies are also very
useful for detecting relationships between different phenomena.
As this study was based on a convenience sample, P values from
inferential statistics should be interpreted carefully.

A third potential limitation to this study includes the fact
that we preselected the injection intervals to study. We know
that other common regimen frequencies, such as Q2W, Q3W,
and Q5W (every 2, 3, and 5 weeks, respectively), would be of
interest and relevant to the practicing nephrology community,
but these dose regimens were beyond the scope of the current
study and would have added complexity and cost to study design
and execution. We also note with interest that this study provided
sufficient data for us to conclude that the time and costs associ-
ated with these other regimens wouldn’t simply be linear relative
to the QW regimen (i.e., 2, 3, or 5 times the time and costs
associated with the QW regimen). Fourth, where the injection-
related activities were not observed, practice-reported data may
overestimate the time (and therefore the costs) associated with
some injection-related activities.

While we note these limitations, we believe that the overall
study results provide new and meaningful data to help CKD
practices inform the selection of ESP regimens to help improve
practice efficiency while ensuring high quality of care and the
effectiveness of the overall delivery of anemia management to
nondialysis CKD patients.

Conclusions

This study provides an overview of the activities and staff
resources required during routine QW and QM ESP injection
appointments. This study documents that CKD patients on ESP
therapy spend substantial amounts of their time in nephrology
practices, regardless of treatment regimen. The information
from this study may be used to identify clinic practices that
improve efficiency in managing nondialysis CKD patients, mini-
mizing both patient and clinic staff time while providing similar or
improved patient care.

Practices spent approximately two thirds less time per
month with patients on QM ESP therapy than with patients on
QW therapy. Extended ESP dosing reduces the time burden of
CKD clinic staff and can provide opportunities to perform
comprehensive patient care activities. Staff estimates of time
differed significantly from observed time, underscoring the
importance and the benefit of directly measuring the impact of
these common activities. Given the differences we observed
between routine QW and QM ESP administration in busy
nephrology practices, nephrology clinics could realize potential
benefits associated with more evidence-based resource planning.

ACKNOWLEDGMENTS

The authors thank the following Anemia Management Office Resource
Evaluation Study investigators and coordinators who assisted with data
collection for the current research: Felicia Chidolue, study coordinator,
Southwest Houston Research, Houston, Texas; Karen Roberts, study
coordinator, Associates in Nephrology, Evergreen Park, Illinois; Michael
Gemein, MD, principal investigator, and Jocie Thomas, study coordinator,
Western New England Renal and Transplant Associates, Springfield,
Massachusetts; Stephen Graham, MD, principal investigator, and Evonne
Daza, study coordinator, Tower Nephrology, Los Angeles, California; Mark
Gunning, MD, principal investigator, and Annette Borden, study coordinator,
Western Washington Medical Group–Nephrology, Everett, Washington; Samia
Khwaja, MD, principal investigator, Renal Medical Associates, Lynnwood,
Washington, California; Dan Legauld, MD, principal investigator, and Sue Saladin, study
coordinator, Renal Associates of Grand Rapids, PC, Grand Rapids, Michigan;
Della Dion, study coordinator, Plaza Medical Group, Oklahoma City,
Oklahoma; David Simon, MD, principal investigator, and Rosella McLean,
study coordinator, Metabolism Associates, New Haven, Connecticut; Mark
Smith, MD, principal investigator, and Lisa Futrelle, study coordinator,
Nephrology Associates, PC, Augusta, Georgia; Jacquelyn Swan, MD, principal
investigator, and Bianca Blanco, study coordinator, Nephrology Associates,
Palm Beach Gardens, Florida; Paul Turer, MD, principal investigator, and
Sheila Young, study coordinator, Mid-Atlantic Nephrology Associates, PA,
Baltimore, Maryland; Timothy Youell, MD, principal investigator, and Marilyn
Slater, study coordinator, Nephrology Associates of Central Florida, PA,
Orlando, Florida.
Assessment of Time and Practice Resources Required to Provide Weekly or Monthly Erythropoiesis-Stimulating Protein Therapy to Chronic Kidney Disease Patients in the Physician Office Setting


