ORIGINAL RESEARCH

Examination of Resource Use and Clinical Interventions Associated With Chronic Kidney Disease in a Managed Care Population

ROGER LONDON, MD, MBA; AMY SOLIS, BS; GEORGE A. GOLDBERG, MD, FACP; SALLY WADE, MPH; and WING W. CHAN, MS

ABSTRACT

BACKGROUND: The management of chronic kidney disease (CKD) is multifaceted, including monitoring, early diagnosis, and treatment of comorbidities such as diabetes, hypoalbuminemia, and anemia, and initiating timely procedures in preparation for dialysis such as vascular access placement. Presumably, optimal care provided to patients during the predialysis phase will produce a significant impact on morbidity and mortality outcomes.

OBJECTIVE: A retrospective analysis was conducted to assess specific factors that may be associated with optimal quality of care for CKD patients during the predialysis phase.

METHODS: Health care resource utilization and the occurrence of interventions associated with optimal predialysis care were evaluated with claims data. Predialysis erythropoietin (EPO) therapy, nephrology referrals, and nutritional supplement administration were all examined during the 12 months prior to dialysis.

RESULTS: Medical and pharmacy claims from a managed care database were analyzed for 1,936 incident dialysis patients. Of these, 48.7% did not have any interventions associated with optimal care. Only a minority of patients received prescription iron preparations (6.8%), vitamin D (4.0%), and phosphate binders (7.7%). A total of 20.8% patients had a vascular access placement, and 29.8% were in the care of a nephrologist during this same time period. Only 10.5% received predialysis EPO, yet more than 40% were diagnosed with anemia. Of the EPO users, however, 72.4% were also receiving other interventions to appropriately manage CKD.

CONCLUSION: These claims-documented results suggest that the lack of EPO use in predialysis patients in a managed care plan may predict overall suboptimal treatment of these patients. There is an apparent need for the proactive management of CKD in a managed care plan to potentially redistribute or reduce health care resource utilization while improving patient outcomes.

KEYWORDS: CKD, Erythropoietin alpha, Predialysis care

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Authors

ROGER LONDON, MD, MBA, Pound Ridge, New York (At the time of this research, London was Vice President, Quality Management, Medical Affairs, Oxford Health Plans, White Plains, New York.); AMY SOLIS, BS, is a Project Manager, Health Care Information Group, and GEORGE A. GOLDBERG, MD, FACP, is Vice President, Clinical Development, Protocare Sciences, Herndon, Virginia; SALLY WADE, MPH, is Director of Research, Zynx Health, Beverly Hills, California (At the time this study was performed Wade was Director, Health Care Information Group, Protocare Sciences, Santa Monica, California.); WING W. CHAN, MS, is a Manager, Pharmacoeconomics, Amgen Inc., Thousand Oaks, California.

AUTHOR CORRESPONDENCE: Roger London, MD, MBA, 82 Pound Ridge Rd., Pound Ridge, NY 10576-1631. Tel: (914) 764-5105; Fax: (914) 764-4713; E-mail: Rlondon@optonline.net

A number of underlying diseases, such as diabetes mellitus and hypertension, can contribute to the incidence of chronic kidney disease (CKD), which in 1996 accounted for 43% and 23% of incident cases of end-stage renal disease (ESRD), respectively (Table 1).[1,2] Simultaneous with the proactive management of these underlying diseases, these patients should also undergo comprehensive preparatory treatment for entry into ESRD. According to The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative Guidelines (NKF–K/DOQI) recently released for CKD,[3] the evaluation and treatment of patients with CKD requires understanding of separate but related concepts of diagnosis, comorbid conditions, severity of disease, complications of disease, and risks for loss of kidney function and cardiovascular disease. Among CKD patients, the disease stages are defined based on the level of kidney function, thus the rate at which patients approach ESRD varies. Defining the stages of CKD is crucial to the effective management of these patients and requires "categorization" of continuous measures of kidney function. Presumably, the staging of CKD will facilitate application of clinical practice guidelines, clinical performance measures, and quality improvement efforts to the evaluation and management of CKD.[3]

Optimal standards of predialysis care should encompass early interventions focused on delaying the progression of chronic renal failure, implementation of educational programs targeted at maximum rehabilitation, timely initiation of kidney function replacement, and judicious management and correction of anemia.[4] Severe anemia of chronic renal failure is associated with left ventricular dilation, left ventricular hypertrophy, and high output cardiac failure, all of which are important predictors of mortality and cardiac complications in patients with renal failure.[5-8] Several studies have shown that the correction of anemia with erythropoietin (EPO) therapy in patients with renal failure is associated with significant improvements in quality of life, immune function, and energy level.[9-12] For this reason, EPO use was selected as an index of optimal quality of predialysis care.

Optimal predialysis care should also include the timely placement of dialysis access.[13,14] This is the site where blood will be removed and returned during dialysis, allowing for easier and more efficient removal of blood with fewer complications.[15] The presence of a functioning vascular access site represents a critical factor in the well-being of these patients. Ideally, vascular access should be placed at least 6 months prior to the start of dialysis. The well-timed administration of nutritional supplements such as iron, vitamin D, and phosphate binders[16,17] is also crucial in ongoing predialysis treatment because previous

TABLE 1	Causes of ESRD	
	Incidence Count	
Patient Characteristics	**N**	**%**
Diabetes	36,904	43.2
Hypertension	19,659	23.0
Glomerulonephritis	10,528	12.3
Cystic kidney disease	2,507	2.9
Urologic disease	4,118	4.8
Other known cause	3,408	4.0
Unknown cause	6,734	7.9
Missing cause	1,662	1.9
Total	85,520	100

Includes new patients, residing in the 50 states and Washington, D.C. (with valid birthdates), who began End-Stage Renal Disease therapy in 1998.[1,2]

studies have shown a strong association between increased risk of death in dialysis patients and malnutrition and nonrenal comorbidity.[18-20]

Referral to a nephrologist is another expected intervention that should occur during the time between the diagnosis of CKD and dialysis initiation. Data from multiple international studies have shown that delayed referral to a nephrologist is a significant problem and is associated with a higher prevalence of uremic complications at the initiation of dialysis, with increased hospitalization and higher cost of care.[21-24] In addition, Arora and colleagues demonstrated that incident dialysis patients who were referred late (defined as the first encounter with a nephrologist occurring within 4 months of dialysis initiation) were significantly more likely to have hypoalbuminemia and hypocalcemia and less likely to have received EPO and a permanent vascular access before the first hemodialysis. Late referrals to a nephrologist were also associated with lower levels of renal function at dialysis initiation, as documented by higher serum creatinine and a higher proportion of patients with predicted glomerular filtration rate <5 mL/min per 1.73 m^2.[25]

As soon as a diagnosis of CKD has been established, screening for complications of CKD and disease management planning should commence. There is a growing consensus that the timing and quality of predialysis care may be pivotal to improved patient outcomes. Optimal predialysis care in CKD patients begins early and, as documented above, should include an aggressive treatment strategy that incorporates interventions that protect existing renal function, delay disease progression, prevent or attenuate comorbid conditions, correct anemia, and prepare patients for kidney function replacement so that it can be initiated in a timely manner.[26-29] The lack of interventions during the predialysis period may have an enormous effect on the outcomes of mortality, cost of care, illness, and disability at the time of dialysis,[30] and improved treatment for ESRD could have a substantial impact on national resource expenditures for ESRD, estimated at $14.55 billion across all payers in 1996.[31]

The primary aim of this study was to examine factors that may be associated with optimal quality of care for CKD patients during the predialysis phase in order to determine if opportunities exist in a managed care population to improve management of these patients by initiating clinically important interventions during the year prior to initiation of dialysis.

■ Methods

Data Source

This study consisted of a retrospective administrative claims-based analysis using a large, proprietary managed care database with annual membership of 3 million enrollees. The integrated claims database contains facility, professional, and outpatient pharmacy services and associated billed amounts for each service, as well as demographic and enrollment records.

Representing a wide geographic distribution, members reside in 22 states, with concentration in the South, Southwest, and Midwest. Approximately 72% of the managed care database members belong to health maintenance organization (HMO) or preferred provider organization (PPO) plans. Over the past decade, the database has been used by researchers as a data resource for a variety of analyses, including cost of illness and postmarketing drug surveillance studies.[32-34]

The database contains all diagnosis and procedure codes submitted with each professional and facility claim. Coding schemes used in the database include the International Classification of Diseases (ICD-9-CM) diagnosis and procedure codes, Common Procedural Technology (CPT-4) procedure codes, and Health Care Financing Administration Common Procedure Coding System (HCPCS) procedure codes.

Within health plans, managed care capitation arrangements and provider contractual agreements produce different billed charges for the same services. Although complete utilization data are available in this database, cost data for patients receiving services under these specific arrangements may not be reflected in the actual billed amounts. To adjust for the differences in charge data, a proprietary resource-based relative value scale fee schedule based on the standard Medicare RBRVS fee schedule was applied for all study patients. Costs were then standardized to 1999 health care Consumer Price Index (CPI) levels. Total pharmacy charges were the drug ingredient cost plus dispensing fee plus sales tax (i.e., including the member cost-share) for each claim.

Study Selection and Data Extraction

During the study time period, the prevalence of chronic renal disease in the entire managed care database was 60,475 patients (3.3%) and incidence was 52,333 patients (2.9%). Patients were enrolled in the study population if they had at least one ICD-9-CM diagnosis code (V45.1, V56, V56.0, V56.1, V56.2, V56.8), CPT-4 code (90935, 90937, 90945, 90947), HCPCS code (A4690, A4820, A4900, A4901, A4905, E1510, E1590, E1592, E1594, E1632, E1635), or ICD-9-CM procedure code (39.95,

TABLE 2 Demographics of Study Population (N=1,936)

Age Group	Total Population			EPO* Population			Non-EPO Population		
	% Total	% Female	% Male	% Total	% Female	% Male	% Total	% Female	% Male
1-44	7.9	4.7	3.4	8.4	5.4	3.0	7.8	4.4	3.3
45-64	26.5	13.7	12.9	38.9	22.7	16.2	25.0	12.6	12.5
65-74	31.9	14.4	17.6	28.0	12.3	15.7	32.4	14.5	17.8
75-99	33.7	13.5	20.1	24.7	11.9	12.8	34.7	13.7	21.1
Total patients	**1,936**	**46**	**54**	**203 (10.5%)**	**52.3**	**47.7**	**1,733 (89.5%)**	**45.2**	**54.7**
Mean age	66.8			64.2			67.1		
Minimum age	1.0			27.0			1.0		
Maximum age	99.0			88.0			99.0		
SD	14.7			12.7			14.9		
Peritoneal dialysis	2.5								
Hemodialysis	89.9								
Both types of dialysis	7.6								

* EPO= erythropoietin.

54.98) indicating renal dialysis at any time during the 24-month time period of January 1, 1998, through December 31, 1999 (n=7,049). Patients receiving dialysis prior to their first dialysis date during the defined time period (index date) were excluded (n=4,833). In addition to evidence of initial renal dialysis, all patients were aged 99 years or younger, had continuous medical eligibility and pharmacy benefits for at least 12 months prior to their index date, had at least one claim of any type in the 12 months prior to their index date, and were not enrolled in a Medicare supplement plan (n=2,359). All patients received dialysis in response to chronic renal failure. Patients receiving dialysis in response to an acute catastrophic event only, e.g., an accident, were also excluded (n=1,936).

According to federal regulations, if ESRD patients have any insurance (i.e., HMO, PPO, or fee-for-service [FFS]) through their employer, then Medicare coordination of benefits becomes primary at 33 months for hemodialysis and 30 months for peritoneal dialysis. Medicare+Choice plans will accept patients already receiving dialysis if the patient has existing coverage through an HMO, PPO, or FFS plan. Uninsured hemodialysis patients are eligible for Medicare 3 months after initiating dialysis, and uninsured peritoneal dialysis patients are eligible immediately upon dialysis initiation. Since all patients included in this analysis were covered under a commercial health plan and the claims for these patients were analyzed prior to dialysis initiation, the regulations outlined above did not directly apply in this study.
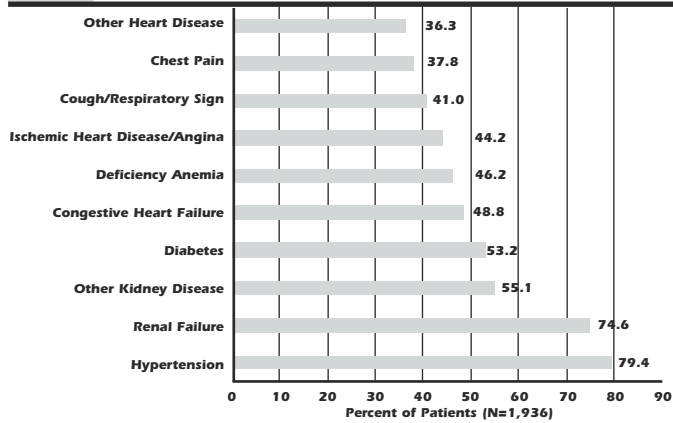
Data Synthesis

Aggregated comorbidities were defined by the 18 fundamental categories of ICD-9-CM diagnosis coding. In order to accurately define each condition explicitly analyzed, a comprehensive evaluation was performed to select all diagnosis codes that correctly describe each condition. Diagnoses recorded during the entire predialysis year were assessed, and an overall aggregated comorbidity score was calculated for each patient. The Charlson Comorbidity Index (CCI) was also used to quantify the comorbidity level of each study patient.[35,36] The CCI used is consistent with published versions, with necessary modifications to account for the use of administrative claims instead of medical records as the data source. CCI was chosen to adjust for comorbidities because it focuses on chronic conditions, typically the principal drivers for health care resources consumed among this population.

Resource use and total costs were calculated for facility, professional, and outpatient pharmacy services during the 12 months prior to initiating dialysis. Facility resource use was further classified as inpatient hospital, outpatient hospital, and emergency room (ER) visits.

Clinically important interventions associated with the optimal care of CKD patients and preparation for dialysis initiation, such as predialysis EPO therapy, nephrology visits, vascular access placement, and nutritional supplement administration, were quantified. The number of patients who sought services from a nephrologist and the number of patients who underwent a vascular access placement during the 12 months prior to initiating dialysis were examined. Also examined was the administration of specific prescription nutritional supplements and other medications during the year prior to initiating dialysis. The number of patients administered vitamin D and iron preparations (injectable and oral) as well as the administration of phosphate binders over the course of the year prior to dialysis

FIGURE 1 Top 10 Documented Comorbid Conditions During the Year Prior to Dialysis

Percent of Patients (N=1,936)

Condition	Percent
Other Heart Disease	36.3
Chest Pain	37.8
Cough/Respiratory Sign	41.0
Ischemic Heart Disease/Angina	44.2
Deficiency Anemia	46.2
Congestive Heart Failure	48.8
Diabetes	53.2
Other Kidney Disease	55.1
Renal Failure	74.6
Hypertension	79.4

TABLE 3 Overall Resource Utilization

Claim or Service Type	Utilizing Patients	Total Annual Charges (% of total)	Mean Charge per Utilizing Patient
Facility	91.2%	$50,730,701 (70.2)	$26,204
Professional	97.6%	$18,630,114 (25.8)	$9,623
Pharmacy	95.7%	$2,910,105 (4.0)	$1,503
Total		$72,270,920	$37,330

initiation was quantified. The number of patients who received more than one type of intervention during the 12 months prior to initiating dialysis was quantified as well.

Because EPO use was selected as an indicator for optimal predialysis care (see introduction), all interventions described above were further stratified by whether or not patients were also receiving EPO therapy to determine if patients receiving predialysis EPO were more likely to receive optimal care than patients not receiving EPO.

Statistical Analysis

Baseline characteristics such as age, gender, and comorbid conditions as well as clinically important interventions (i.e., vascular access placement) were described using descriptive statistics. Whenever comparisons were made between EPO and non-EPO events, the groups were assessed and compared using chi-square and *t* tests.

■ Results

Demographics

The average age of the 1,936 patients was 66.8 years and 54.0% were male (Table 2). Prior to dialysis initiation, 203 (10.5%) patients received supportive EPO therapy and 1,733 (89.5%)

were not receiving EPO. The average age of the EPO treatment group was 64.2 years, younger than the untreated group (67.1 years). The gender mix of the 2 comparison groups differed as well, although this difference did not achieve statistical significance. For the purposes of this analysis, the pediatric population (i.e., patients under the age of 18 years) was retained; it represented less than 2% of the overall population.

Comorbid Conditions

Patients, overall, had an average of 8±3 aggregated comorbidities during the 12 months prior to initiating dialysis. EPO patients had 9±3 comorbidities, and non-EPO patients had 8±3 aggregated comorbidities during the 12 months prior to dialysis. The average CCI was 4.9 for the EPO group compared to 4.1 for the untreated group (*P*=0.0001). Hypertension (79.4%), renal failure (74.6%), other forms of kidney disease (55.1%), and diabetes (53.2%) were the most common comorbidities (Figure 1). When stratified by EPO use, 60.1% of all EPO patients and 52.3% of all nonusers had a diabetes diagnosis during the year prior to dialysis (*P*=0.0360).

Cost and Resource Utilization
Economic Burden

Total annual charges for the entire CKD population were $72,270,920, with a mean overall charge per utilizing patient of $37,330. Total annual facility charges were $50,730,701, accounting for 70.2% of the total annual charges. Total annual professional charges were $18,630,114, which was 25.8% of the total annual charges. Total annual pharmacy charges were $2,910,105, or 4% of the total annual charges (Table 3). The detailed financial profile of health care service use (total and average charges per utilizing member per month) were previously reported by London et al.[37]; this paper focuses on patterns of care from the clinical perspective.

Inpatient Hospitalization and Emergency Room Visits

Of all patients, 62.6% were hospitalized at least once during the year prior to dialysis, with an average length of stay of 7.82 days. Congestive heart failure was the most frequently occurring discharge diagnosis, followed by hypertensive renal disease with renal failure and acute renal failure. A total of 60.3% of all patients visited the ER at least once during the 12 months prior to initiating dialysis. The average number of ER visits per patient was 2.

Professional Services

Of all patients, 92.8% had at least one office visit in the year prior to initiating dialysis, which was the most frequently occurring service during the predialysis period (Figure 2). The average number of office visits per patient was 12.
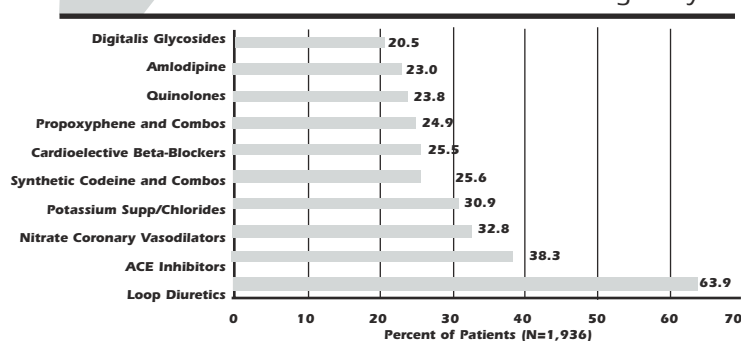
Medication Use

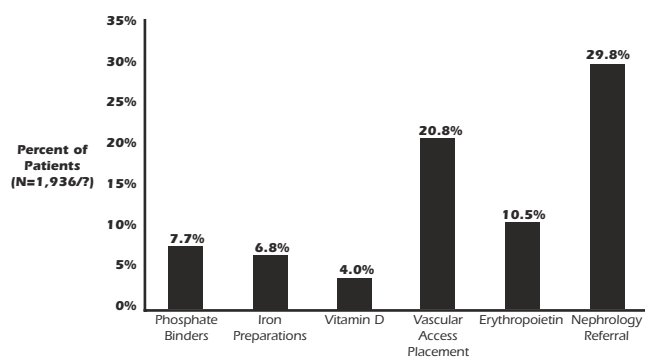In the predialysis period, loop diuretics, angiotensin-converting

FIGURE 2 Ten Most Frequently Occurring Services During the Year Prior to the Index Date
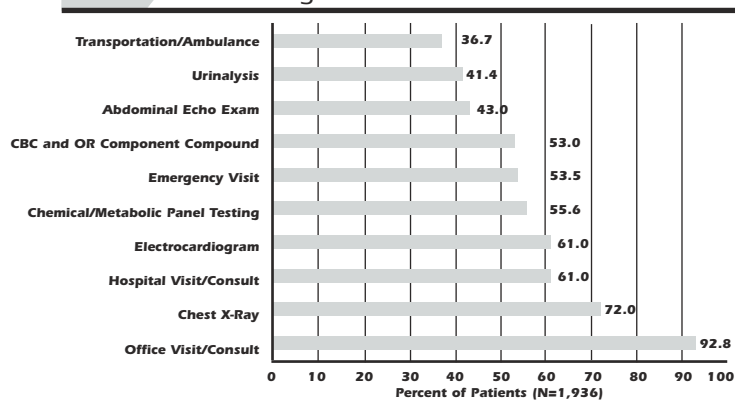
FIGURE 3 Ten Most Frequently Occurring Drugs Within the Year Prior to Initiating Dialysis

FIGURE 4 Interventions Within One Year Prior to Initiating Dialysis

enzyme inhibitors, and nitrate coronary vasodilators were the most commonly prescribed medications (Figure 3).

Clinically Important Interventions

Clinical interventions, defined as vascular access placement,

nephrology visits, the administration of vitamin D, iron preparations, phosphate binders, and EPO therapy, were examined during the year prior to initiating dialysis (Figure 4). Of the total population, 942 patients (48.7%) did not have any of these expected interventions within 12 months of initiating dialysis.

Vascular Access Placement

There were 403 patients (20.8%) who established access during the 12 months before initiating dialysis. Of these patients, 260 (64.5%) received at least one other intervention in the predialysis period in addition to vascular access placement.

Patients who were also on EPO therapy were almost twice as likely as patients who did not receive EPO to have an access procedure performed in the predialysis period (35.5% and 19%, respectively, *P*<0.01) and also more likely to have the access placed more than 60 days before initiating dialysis than patients not receiving EPO (15.76% and 6.12%, respectively).

Nephrology Visits

A total of 576 patients (29.8%) had at least one outpatient nephrology visit during the 12 months prior to dialysis. Of these patients, 151 (26.2%) were seen by a nephrologist for the first time within 30 days preceding dialysis initiation. Of the 576 patients, 267 (46.4%) also received at least one other intervention in the predialysis period. Further examination of nephrology practice patterns revealed that, of the 576 patients, 282 (49.0%, which is 14.6% of all predialysis CKD patients) were actually "in the care" of a nephrologist, as defined by the occurrence of ≥3 nephrology visits, with at least 30 days between the first and last visit. EPO patients (n=50, 24.6%) were significantly more likely to be in the care of a nephrologist than non-EPO patients (n=232, 13.4%; *P*<0.0001).

Nutritional Supplement Administration

Iron preparations. A total of 131 (6.8%) patients received iron preparations. Of the 131, 85 (64.9%) received iron preparations in combination with at least one other intervention during the year prior to dialysis. For those patients who also received EPO, 17.2% were administered iron preparations, while only 5.9% of patients non-EPO users received iron preparations during the year prior to dialysis (*P*<.00005).

Vitamin D. Of the 78 (4.0%) total patients on vitamin D therapy, 65 patients (83.3%) were administered vitamin D in combination with at least one other intervention during the year prior to dialysis. For those patients who were also on EPO therapy, 10.1% filled at least one prescription for vitamin D, and 3.5% of patients who were not on EPO therapy received vitamin D during the year prior to dialysis (*P*<0.00005).

Phosphate binders. A total of 149 (7.7%) patients were administered phosphate binders during the year prior to initiating dialysis. Of these patients, 118 (79.2%) were administered phosphate binders in combination with at least one other

TABLE 4 Predialysis EPO as an Indicator of Optimal Care During the Year Prior to Initiating Dialysis

Intervention	EPO Users (n = 203) %	Non-EPO users (n = 1,733) %	P Value*
Vascular access placement	35.5	19.0	<0.01
Nephrology visit	24.6	13.4	<0.0001
Iron preparations	17.2	5.9	<0.00005
Vitamin D	10.1	3.5	<0.00005
Phosphate binders	14.1	7.3	0.0008

Chi-square and t tests were employed.

intervention during the year prior to dialysis. For those patients who were also on EPO therapy, 14.1% filled at least one prescription for phosphate binders, and 7.3% of those who were not on EPO therapy (P=0.0008) received phosphate binders during the year prior to dialysis.

Erythropoietin Therapy

Although 46% of all patients were diagnosed with deficiency anemia, only 10.5% (n=203) received EPO therapy during the 12 months prior to dialysis. Of the 203 patients, 147 (72.4%) received EPO in combination with at least one other intervention. That is, the majority of patients receiving EPO also received additional predialysis interventions to manage CKD, such as a vascular access placement (Table 4). In contrast, of the 1,733 non-EPO patients, 794 (45.8%) received at least one intervention to manage CKD.

Management of Clinical Interventions

A small percentage of the study population (0.05%) received all interventions concurrently within the year prior to initiating dialysis. When interventions were examined one by one, of those patients who underwent vascular access placement, 143 (35.5%) did not have any other interventions; 31 (20.8%) who received phosphate binders, 13 (16.7%) who received vitamin D, and 46 (35.1%) who received iron preparations did not receive any other interventions during the predialysis period; and 56 patients (27.6%) who received EPO therapy did not receive any other interventions. Of the 576 patients who saw a nephrologist, 306 (53.1%) did not have any other of the interventions during the year prior to dialysis.

Patients were more likely to receive their first intervention in the months closer to dialysis initiation. Specifically, of those who underwent a vascular access procedure, 73.7% did so within the 90 days preceding dialysis initiation; 39.4% seen by a nephrologist had their first nephrology consultation within 90 days preceding dialysis; and 29.0% who filled their first prescription for iron preparations, 32.0% who filled their first pre-

scription for vitamin D, and 45.6% who filled their first prescription for phosphate binders did so within 90 days of initiating dialysis. Of those patients who were receiving EPO, 35.5% began treatment within 90 days of initiating dialysis.

■ Discussion

Clinically Important Interventions

Optimal standards of care for progressive renal disease include identification and treatment of renal disease progression, adequate blood pressure control, proper nutritional support, good glycemic control, and anemia correction with EPO as well as administration of vitamin D, phosphate binders, and calcium.[4] If dialysis is chosen for renal replacement therapy, vascular access needs to be placed prior to dialysis.

In the current study, nearly half of all study patients from a managed care population did not receive any of the interventions associated with the proactive management of CKD and preparation for renal dialysis. Results also suggested suboptimal use of EPO among patients entering dialysis in a managed care plan.

A minority of the study population received nutritional supplements such as iron preparations, vitamin D, and phosphate binders, all of which are associated with appropriate management of CKD. Interestingly, even though 92.8% of all patients had at least one office visit, only one third of the eligible population was actually seen by a nephrologist during the year prior to initiating dialysis, with many of the initial consultations occurring within 90 days of dialysis.

Although it is recognized that not all patients are appropriate candidates for all of the interventions studied, results revealed evidence of underutilization and delayed utilization of expected resources and interventions associated with CKD during the critical period prior to initiating dialysis, when CKD should be diagnosed and suitable management should begin. When interventions occurred, they were typically first introduced during the late predialysis stages of the disease (as defined by the number of months prior to initiating dialysis), suggesting opportunities to employ clinical strategies for early detection and diagnosis, followed by treatment and management of CKD and underlying conditions.

Factors Associated With Optimal Predialysis Care

In a recent study, Revicki and colleagues concluded that the correction of anemia using EPO therapy in renal failure patients produced improvements with health-related quality of life, significant cardiovascular benefits, and improved renal function.[12] Despite these documented strong clinical advantages, only 10.5% of the eligible population in the current study received EPO, even though nearly half of the study population was diagnosed with deficiency anemia, thus underscoring the need to maintain specific programs to facilitate the management of CKD and comorbidities.

It is remarkable that of the subpopulation that received supportive predialysis EPO therapy, the majority of these patients

were also receiving other interventions associated with the management of CKD. For example, only 1 in 5 study patients underwent a vascular access placement to prepare for dialysis. However, receiving EPO raised the likelihood of this procedure, as EPO patients in the current study were almost twice as likely to have the access procedure performed and even more likely to have the access placed greater than 60 days before initiating dialysis. In another illustration, patients on supportive EPO therapy were statistically significantly more likely to receive nutritional supplements such as iron preparations, vitamin D, and phosphate binders than those patients not receiving EPO.

The results from the current study suggest both triumph and challenge for the managed care pharmacist. Results stress that aggressively approaching the management of CKD and comorbidities with pharmacologic therapies in the earlier stages of their disease may redistribute health care resources, while improving patient outcomes. This provides support and validation to the managed care pharmacist that the concept of a well-designed, appropriate drug-use program or disease management program to focus on correction through pharmacologic therapies to ultimately reduce health care costs and improve outcomes is crucial. The challenge for the managed care pharmacist is complex and begins with designing a benefit and managing a formulary that will provide the patient with the most effective treatments to manage CKD at the most appropriate time, while controlling cost. Managing compliance of these patients will be a great hurdle, yet key to the success of their outcomes, requiring careful monitoring of disease progression, early detection and diagnosis, followed by the treatment of CKD and underlying conditions.

Limitations

The financial profile presented in this analysis is not a reflection of managed care organization financial statistics, allowed charges, or net health plan costs after subtraction of member cost-sharing responsibilities from the allowed charges. Rather, estimated charges reported in this analysis were calculated from a Medicare-based fee schedule. Although the occurrence of a procedure or laboratory or other test was evident via the CPT-4 and HCPCS code(s) identified on claims, the results of these services (e.g., laboratory values) were not available. Prescription medications and supplements were quantified in this analysis. Utilization of these products may be underestimated because data for the over-the-counter medications and supplements (e.g., iron preparations) were not available.

■ Conclusion

In this managed care plan, nearly half of all study patients were not receiving interventions for the management of CKD or preparation for dialysis initiation despite published standards of care and the complexity of these patients, as evidenced by the number of comorbidities per patient.

Noteworthy is the fact that predialysis EPO use indicated a significantly higher quality of care, as measured by the presence of other appropriate services received by EPO patients in comparison to patients not receiving EPO. These results underscore the suitability of implementing specific guidelines to effectively manage the care of these patients. Guidelines should specify early detection based on disease staging, appropriate and timely utilization of pharmacologic therapies, and the employment of a multidisciplinary approach to managing these patients,[38] including timely specialist referrals, administration of nutritional supplements, and vascular access placement. Many opportunities exist to further explore the timing of each of the interventions and whether the implementation of guidelines, earlier detection, and aggressive treatment can reduce the total health care resource utilization and cost burden in the CKD managed care population as well as improve the clinical outcomes.

REFERENCES

1. *U.S. Renal Data Set (USRDS).* 1999 ADR. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); April 1999. Appendix, Table A-1.

2. *U.S. Renal Data Set (USRDS).* 1999 ADR. Bethesda, MD: NIH, NIDDK; April 1999. Appendix, Table A-15.

3. National Kidney Foundation. *NKF–K/DOQI Clinical Practice Guidelines*; update 2002.

4. Evans R, Manninen D, Garrison L, Hart L, Blagg C, et al. The quality of life and patients with end stage renal disease. *N Eng J Med.* 1985;213:553-59.

5. Eschbach J. The anemia of chronic renal failure. Pathophysiology and the effects of recombinant erythropoietin. *Kidney Int.* 1989;35:134-38.

6. London G, Parfrey P. Cardiac disease in chronic uremia: pathogenesis. *Adv Renal Replace Ther.* 1997;4:194-211.

7. Silberberg J, Barre P, Prichard S, Sniderman A. Impact of left ventricular hypertrophy on survival in end-stage renal disease. *Kidney Int.* 1989;36:286-90.

8. Foley R, Parfrey P, Harnett J. Left ventricular hypertrophy in dialysis patients. *Semin Dial.* 1992;5:31-41.

9. Ecshbach J, Egrie J, Downing M, Browne J, Adamson J. Correction of anemia of end-stage renal disease with recombinant human erythropoietin. *N Engl J Med.* 1987;316:73-78.

10. Levin N. Maximizing health benefits with epoetin alfa therapy: national cooperative rHu erythropoietin study in patients with chronic renal failure—an interim report. *Am J Kidney Dis.* 1993;22:3-12.

11. Marsh J, Brown W, Wolcott D, et al. rHuEPO treatment improves brain and cognitive function in anemic dialysis patients. *Kidney Int.* 1991;39:155-63.

12. Revicki D, Brown R, Feeny D, et al. Health-related quality of life associated with recombinant human erythropoietin therapy orpredialysis chronic renal disease patients. *Am J Kidney Dis.* 1995;25:548-54.

13. Eadington D. Delayed referral for dialysis: higher morbidity and higher costs. *Semin Dial.* 1995;8:258-60.

14. Levin A, Lewis M, Mortiboy P, et al. Multidisciplinary predialysis programs: quantification and limitations of their impact on patient outcomes in two Canadian settings. *Am J Kidney Dis.* 1997;29:533-40.

15. National Institutes of Health/NIDDK. Healthy *People 2010 Objectives: Chronic Kidney Disease* [proposed chapter].

16. Ifudu O, Dawood M, Homel P, Friedman E. Excess morbidity in patients starting uremia therapy without prior care by a nephrologist. *Am J Kidney Dis.* 1996;28:841-45.

17. Pereira B. Optimization of pre-ESRD care: the key to improved dialysis outcomes. *Kidney Int.* 2000;57:351-65.

18. Held P, Port F, Wolfe R, et al. The dose of hemodialysis and patient mortality. *Kidney Int.* 1996;50:550-56.

19. Owen W, Lew N, Liu Y, Lowrie E, Lazarus J. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. *N Engl J Med.* 1993;329:1001-06.

20. Keane W, Collins A. Influence of comorbidity on mortality and morbidity in patients treated with hemodialysis. *Am J Kidney Dis.* 1994;24:1010-18.

21. Innes A, Rowe P, Burden R, Morgan A. Early deaths on renal replacement therapy. The need for early nephrological referral. *Nephrol Dial Transplant.* 1992;7:467-71.

22. Jungers P, Zingraff J, Page B, Albouze G, Hannedouche T, Man N. Detrimental effects of late referral in patients with chronic renal failure: a case-control study. *Kidney Int.* 1993;43(suppl 41):S170-S173.

23. Khan I, Catto G, Edward N, MacLeod A. Chronic renal failure: factors influencing nephrology referral. *Q J Med.* 1994;87:559-64.

24. Sesso R, Belasco A. Late diagnosis of chronic renal failure and mortality in maintenance dialysis. *Nephrol Dial Transplant.* 1996;11:2417-20.

25. Arora P, Obrador GT, Ruthazer R, et al. Prevalence, predictors, and consequences of late nephrology referral at a tertiary care center. *J Am Soc Nephrol.* 1999;10:1281-86.

26. Zabetakis PM, Nissenson AR. Complications of chronic renal insufficiency: beyond cardiovascular disease. *Am J Kidney Dis.* 2000;36(suppl 3):S31-S38.

27. Obrador GT, Arora P, Kausz AT, Pereira BJG. Pre-end-stage renal disease care in the United States: a state of disrepair. *J Am Soc Nephrol.* 1998;9(suppl 12):S44-S54.

28. Pereira BJG, Burkart JM, Parker TF III. Strategies for influencing outcomes in pre-ESRD and ESRD patients. *Am J Kidney Dis.* 1998;32(suppl 4):S2-S4.

29. Obrador GT, Ruthazer R, Arora P, Kausz AT, Pereira BJG. Prevalence of and factors associated with suboptimal care before initiation of dialysis in the United States. *J Am Soc Nephrol.* 1999;10:1793-1800.

30. *USRDS.* 1999 ADR. Bethesda, MD: NIH, NIDDK; April 1999. Appendix, Table A-6.

31. www.healthypeople.gov/Document/pdf/volume1/04CKD.pdf

32. Dubois R, Chawla A, Neslusan C, Smith M, Wade S. Explaining drug spending trends: does perception match reality? *Health Aff.* 2000:19:231-39.

33. Lim D, Farup C, Lawrence B, Sorell L, Dubois R, Zeldis J. Gastrointestinal illness in managed care health care utilization and costs. *Am J Managed Care.* 1997:3:1859-72.

34. Freedman K, Kaplan F, Bilker W, Strom B, Lowe R. Treatment of osteoporosis: are physicians missing an opportunity? *J Bone Joint Surg.* 2000; 82-A:1063-70.

35. Beddhu S, Bruns F, Saul M, Seddon P, Zeidel M. A simple comorbidity scale predicts clinical outcomes and costs in dialysis patients. *Am J Med.* 2000;108:609-13.

36. Charlson M, Pompei P, Ales K, MacKenzie C. A new method of classifying prognostic comorbidity in longitudinal studies, development and validation. *J Chronic Dis.* 1987;40:373-83.

37. London R, Solis A, Goldberg G, Wade S, Ryu S. Health care resource utilization and the impact of anemia management in patients with chronic kidney disease. *Am J Kidney Dis.* 2002;40(3):539-48.

38. National Kidney Disease Education Program Strategic Development and Planning Meeting, June 28 and 29, 2001 [meeting summary].