The Cost of Treating Seizure Patients in a Managed Care Organization

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OBJECTIVE: To identify direct costs, principal cost drivers, treatments, comorbidities, and resource utilization for patients with epilepsy.

DESIGN: Records of patients with epilepsy or seizure ICD-9 codes of 345.00 to 345.90 and 780.0 in any of eight diagnostic fields were extracted for a 12-month period from September 1, 1995–August 31, 1996, from a managed care database. From these data, a relational database was constructed, all pharmacy claims for these patients were extracted, and costs were stratified by patients' sex, age, and cost. The medication combinations used to treat seizures were identified and their costs calculated. Comorbid conditions associated with seizures in these patients were determined.

RESULTS: 2,446 seizure patients consumed \$5,950,000 in direct costs to the MCO. The age groups with the highest cost were patients aged 0–4 and 40–74 years. Patients aged 40–74 years accounted for almost 45% of the total costs.

The 80 patients in the highest cost group (> \$12,500) accounted for 46% of the total direct cost. Inpatient services comprised 57% of the total direct seizure or seizure-epilepsy treatment-related costs. Most of the \$368,108 in pharmacy costs for these patients were for phenytoin, carbamazepine, and valproate (19%, 30%, and 23%, respectively). Alteration in consciousness was the most frequent comorbid medical condition.

CONCLUSIONS: Age groups that are most costly to treat are the very young (0–4 years) and those aged 40–74 years. The most commonly used drugs consume the largest prescription resources. Because inpatient services comprised 57% of total costs, improvements in seizure control that result in decreased hospitalizations could have a large impact on reducing disease-related costs.

KEYWORDS: Epilepsy, Seizure, Cost

J Managed Care Pharm 1999; 351-56

More than 50 million people worldwide and 2 million in the United States have epilepsy.^{1,2} As many as 50 in 100,000 people are diagnosed with epilepsy each year.² Epilepsy is a general term that encompasses several different types of seizures that may manifest as a change in sensory perception or in subjective/objective behavior, disturbance in consciousness, or tonic-clonic convulsions.

Drug therapy is the cornerstone of epilepsy treatment. Because as many as 80% of patients can be controlled with one drug, monotherapy is preferred;³ however, adjunctive use of additional drugs may improve seizure control in some patients. Appropriate therapy is dictated by the patient's seizure type.^{1, 4-6}

Limited comparative pharmacoeconomic data are available to help select the most cost-effective agent. A cost minimization analysis of monotherapy with phenytoin, carbamazepine, and divalproex sodium was published in 1995.⁷ The study evaluated data collected from an expert panel of three neurologists and determined that phenytoin is least costly, followed by carbamazepine and divalproex sodium. Although this analysis did not include different efficacy rates, consider therapeutic failures, or include a range of common doses, it did consider costs to manage adverse drug reactions as well as costs of drug therapy, laboratory tests, and physician visits.

To date, the most thorough estimate of the cost of epilepsy was published by Begley and colleagues.⁸ This study, based on persons with a diagnosis of epilepsy in 1990, estimated the total lifetime costs of epilepsy in the United States to be \$3 billion. The lifetime cost per patient ranged from \$4,272 for persons with remission following initial diagnosis to \$138,602 for persons with intractable epilepsy. Antiepileptic drugs were estimated to be the largest of the direct costs. Indirect costs, such

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as days lost for work, accounted for 62% of the total cost of epilepsy. The authors estimated that patients with newly diagnosed epilepsy would have two to four times the national rate of unemployment and that employed individuals would have increased rates of absenteeism. In addition, such patients often are unable to drive a car until they are seizure-free for one year. The authors estimated that if seizures were recurrent over a period of three years or more, then the patient would have a higher mortality rate (1.2–4 times the national age/sex rate) for the 10 years following diagnosis.⁸

Data from the United Kingdom estimated that direct costs of epilepsy averaged \$917 for the first year.⁹ After eight years, the direct costs fell to \$254 per patient per year (pp/py). When both direct and indirect costs of epilepsy were included, it was estimated that 69% of the total cost was due to indirect costs.

A cohort of Pennsylvania Medicaid patients (N=13,473) was used to study direct costs of epilepsy.¹⁰ This study included rates and costs of outpatient services, pharmaceuticals, nursing home services, emergency room, ambulance, hospitalization room and board, laboratory tests, surgical procedures, and diagnostic procedures. The Medicaid cost was \$2,011 pp/py in 1992 dollars. The normative cost, defined as the estimated fee-for-service cost to an insurer, would be \$5,047 pp/py.

More recently, the cost of refractory epilepsy in adults has been estimated.¹¹ Using the previously cited literature in addition to an expert panel of physicians, Murray and associates¹¹ estimated a prevalence of 335,167 patients with refractory epilepsy. Their model predicts that the total yearly medical costs for these patients would be \$3,905,183,463, one-third of which are direct medical costs.

Two studies in the United Kingdom have evaluated the cost-effectiveness of individual drug regimens. The first study estimated that the costs of one year of treatment with vigabatrin or lamotrigine were 50% higher than with clobazam.¹² The second study found that for the first year, gabapentin treatment resulted in a lower total treatment cost than either lamotrigine or vigabatrin, largely as a result of fewer adverse events.¹³

To date, no information has been published that estimates the costs of seizures or epilepsy within a U.S. managed care population. The objectives of this study were to: 1) determine the direct costs of epilepsy within a managed care organization (MCO); 2) identify the principal cost drivers of epilepsy treatment; 3) determine the principal treatment options and combinations being used in therapy; 4) quantify the resource units utilized in patients with seizures or epilepsy; 5) determine the direct cost to the health care system to manage seizures or epilepsy; and 6) identify the most common comorbidities observed in patients with seizures or epilepsy.

METHODS

Data Collection

This study was conducted using a managed care database. Up to eight diagnostic fields per claim were captured in the

database. International Classification of Diseases ninth edition (ICD-9) codes are maintained in the database for all medical claims. Patients with epilepsy or seizure ICD-9 codes of 345.00 to 345.90 and 780.0 in any of the eight fields were extracted for a 12-month period from September 1, 1995, to August 31, 1996. A relational database was constructed using the member numbers of the patients with these ICD-9 codes, and all pharmacy claims for these patients were extracted. Costs (not charges) to the managed care system are included in the analysis. Standard query language (SQL) was used to search the database. The current procedure terminology (CPT) codes were reviewed, determined to be either related or unrelated to epilepsy or seizure treatment, and categorized into resource unit groups (outpatient services, laboratory, clinic services).

The results were summarized in tables describing the patient groups and resource unit categories. Descriptive statistics were used to summarize these resource units and their respective costs. Overall costs to manage epilepsy or seizures were determined and a mean was used to calculate the cost of treatment per seizure patient per year. A mean was calculated for drug costs and medical treatment costs and these means were stratified by age, sex, and cost groups. The number of patients with epilepsy or seizures using single or combination drug therapy also was determined. Each drug was stratified by dose and route of administration.

For each CPT category, the cost, member count, and claim count was calculated. In addition, the frequency of comorbidities was extracted from the database.

RESULTS

Overall, 2,446 patients with epilepsy were identified. They consumed \$5,950,000 in resources related to epilepsy or seizure care.

Costs by Age Group

Medical Costs—Seizure-related costs by age group are shown in Table 1. The medical cost category describes items in the medical claims and is composed of physician visits, hospital visits, laboratory tests, radiology tests, emergency services, skilled medical services, nursing, and supplies. The highest cost age group comprised children 0–4 years old. This group had the most members (N=243, 9%) and required \$627,509 for care (11% of the total medical costs).

Patients 50–54 years of age had the highest average medical costs (\$3,758 pp/py), followed by the 0–4-year-old age group (\$2,582 pp/py), and the 40–44-year-old age group (\$1,693 pp/py).

Pharmacy Costs—The highest pharmacy costs were found in the 45–49-year-old group (\$47,216 or \$262 pp/py). Patients aged 40–74 years comprised only one-third of all patients but accounted for almost 45% of the total costs associated with therapy.

Total Costs—The total costs to treat seizure patients for not only seizures but all comorbid conditions are shown in

Table 1. Seizure-Related Costs by Age Group

Age Group	Members	Total Medical Cost (\$)	Medical Cost Avg (\$)	Total Pharmacy Cost (\$)	Pharmacy Cost Avg (\$)	Total Cost (\$)	Total Cost Avg (\$)
0-4	243	627,509	2,582	4,579	19	632,088	2,601
5-9	153	296,564	1,938	25,316	165	321,880	2,104
10-14	147	221,458	1,507	21,297	145	242,755	1,651
15-19	145	352,308	2,430	18,077	125	370,385	2,554
20-24	103	93,458	907	15,979	155	109,437	1,063
25-29	125	167,618	1,341	26,696	216	194,587	1,557
30-34	171	278,136	1,627	34,314	201	312,450	1,827
35-39	181	254,648	1,407	39,656	219	294,304	1,626
40-44	184	311,536	1,693	44,089	240	355,625	1,933
45-49	180	488,088	2,712	47,216	262	535,304	2,974
50-54	129	484,901	3,759	17,081	132	501,982	3,891
55-59	119	347,841	2,923	24,586	207	372,427	3,130
60-64	110	380,771	3,462	19,278	175	400,049	3,637
65-69	132	365,931	2,772	19,012	144	384,943	2,916
70-74	122	392,158	3,214	13,111	107	405,269	3,322
75-79	104	276,418	2,658	10,068	97	286,486	2,755
80-84	59	150,722	2,555	2,799	47	153,521	2,602
85-89	27	48,904	1,811	1,928	71	50,832	1,883
90-94	11	24,687	2,244	744	68	25,431	2,312
95-99	1	496	496	7	7	503	503
Totals	2,246	5,564,152		386,108		5,950,260	

Table 2. In terms of the total costs to treat patients with epilepsy for seizures and other diseases, patients from 0-4 years old remained the most costly age group overall (\$1,508,766). However, the per-person expenditure was greatest for patients 60-64 years old (\$11,948 pp/py), followed by patients 50-54 (\$10,488 pp/py) and 75-79 (\$10,373 pp/py). Patients 45-49 years old utilized the most prescription resources overall (\$116,809), but 55-59-year-olds incurred the highest average pharmacy costs (\$919 per person per year). One interesting result that emerged from this study is that the highest medical cost group (0-4 years old) had the second lowest pharmacy costs, which raises the question of whether increasing the pharmacy costs could possibly lower the medical costs for this group.

Cost Groups—The 80 patients who incurred costs greater than \$12,000 make up only 3.2% of the population, but account for more than 46% of the total cost of treatment.

Costs by Age and Gender—Among women, those 50-54 years old had the highest medical costs (\$345,999 or \$4,943

pp/py) and total costs (\$353,371 or \$5,048 pp/py); and those 20-24 years of age had the lowest medical costs (\$747 pp/py) and total costs (\$889 pp/py). Women 45-49 years old had the highest prescription costs (\$27,657; \$282 pp/py).

Among men, those aged 45-49 had the highest medical costs (\$315,745) and they also utilized the most resources overall (\$335,303 per year). The 25-29-year-old group had the highest prescription average (\$295 pp/py).

Current Procedure Terminology (CPT) Group

Costs unrelated to the patients' seizure disorder (unrelated claims) plus the seizure costs describe total health care costs to manage patients with epilepsy or seizures, as shown in Table 2 and mentioned above. Inpatient services accounted for 22% of total resources; however, when unrelated claims were excluded, inpatient services accounted for 57% of the total resources consumed. This category was followed by radiology (3.6%), outpatient services (3.5%), emergency services (3.0%), pharmacy (2.7%), and laboratory (2.4%).

Table 2. Total Costs to Treat Patients with Seizures for All Conditions, Including Comorbidities

Age Group	Members	Total Medical Cost (\$)	Medical Cost Avg (\$)	Total Pharmacy Cost (\$)	Pharmacy Cost Avg (\$)	Total Cost (\$)	Total Cost Avg (\$)
0-4	243	1,486,958	6,119	21,808	90	1,508,766	6,209
5-9	153	737,183	4,818	54,147	354	791,330	5,172
10-14	147	328,345	2,234	43,455	296	371,800	2,529
15-19	145	752,758	5,191	54,006	372	806,764	5,564
20-24	103	264,967	2,572	34,977	340	299,944	2,912
25-29	125	443,218	3,546	55,727	446	498,945	3,992
30-34	171	774,972	4,532	94,505	553	869,477	5,085
35-39	181	608,358	3,361	105,422	582	713,780	3,944
40-44	184	719,647	3,911	116,214	632	835,861	4,543
45-49	180	1,144,236	6,357	116,809	649	1,261,045	7,006
50-54	129	1,252,401	9,709	100,213	777	1,352,614	10,485
55-59	119	943,690	7,930	109,384	919	1,053,074	8,849
60-64	110	1,221,480	11,104	92,844	844	1,314,324	11,948
65-69	132	969,375	7,344	88,215	668	1,057,590	8,012
70-74	122	1,140,914	9,352	78,284	642	1,219,198	9,993
75-79	104	1,025,838	9,864	52,934	509	1,078,772	10,373
80-84	59	419,003	7,102	25,889	439	444,892	7,541
85-89	27	143,884	5,329	6,791	252	150,675	5,581
90-94	11	70,193	6,381	6,730	612	76,923	6,993
95-99	1	1,646	1,646	7	7	1,653	1,653

Therapeutic Combinations

The three most prescribed drugs were phenytoin (17%), carbamazepine (9.9%), and valproate (6.4%). The most commonly prescribed drug combinations were valproate and carbamazepine (1.6%), phenytoin and carbamazepine (1.6%), and phenytoin and phenobarbital (<1%). Other therapeutic combinations account for 4.6% of drug combinations. Gabapentin was used as either monotherapy or combination therapy by 45 patients. Lamotrigine was used alone or in combination therapy by six patients. A result worthy of careful attention is that 1,069 patients (44%) with a seizure- or epilepsy-related claim received no drug therapy within the pharmacy claims system.

Drug Costs and Route of Administration

The five most expensive medications were valproate (\$114,541; 30% of drug costs), carbamazepine (\$87,319; 23%), phenytoin (\$74,249; 19%), gabapentin (\$60,230; 16%), and lamotrigine (\$17,373; 4.5%). Of the 46 different drugs used in treatment, only two were administered by injection; the remaining 44 were all oral medications.

Comorbid Medical Conditions

Table 3 lists the most frequently documented comorbid medical conditions by the first three digits of ICD-9 codes that are associated with an epilepsy or seizure diagnosis. The ICD-9 codes 780.1-780.9, described as alteration in consciousness, were most frequent. The second most common ICD-9 code was generalized nonconvulsive epilepsy.

DISCUSSION

This study identified 2,446 patients with an epilepsy or seizure diagnosis who used a total of \$5,950,260 in seizure-related health care resources. In general, as patients with epilepsy aged, they utilized more resources from the MCO. Eighty patients with epilepsy (3.2% of the seizure population) accounted for more than 46% of the total resources used. For patients with epilepsy or seizures, 57% of expenditures was spent on inpatient services. These data are quite distinct from the estimates in the Begley model⁸ in which the cost of antiepileptic drugs was predicted to be the principal cost driver.

Table 3 Seizure Comorbidities

ICD-9-CM (First 3 digits)	ICD-9 Description	Frequency
780	Alteration in consciousness	2,262
345	Generalized nonconvulsive epilepsy	1,091
V72	Special investigations and examinations	1,016
799	Other ill-defined causes of morbidity and mortality	939
786	Symptoms involving respiratory and other chest symptoms	827
784	Symptoms involving head and neck	608
789	Other symptoms involving abdomen and pelvis	558
401	Essential hypertension	496
465	Acute URI of multiple or unspecified sites	487
719	Other unspecified disorders of the joint	465
V70	General medical examination	432
599	Other disorders of the urethra and urinary tract	419
462	Acute pharyngitis	394
729	Other disorders of the soft tissue	373
724	Other unspecified disorders of the back	358
382	Suppurative and unspecified otitis media	341
466	Acute bronchitis and bronchiolitis	341
782	Symptoms involving skin and integumentary tissue	290
787	Symptoms involving the digestive system	285
V20	Health supervision of an infant or child	278
276	Disorders of the fluid, electrolyte, and acid-base	277
473	Chronic sinusitis	264
477	Allergic rhinitis	264
486	Pneumonia, organism unspecified	262
959	Injury other and unspecified	261
V04	Need for prophylactic vaccination	261
493	Asthma	249
427	Cardiac dysrhythmias	244
558	Other noninfectious gastroenteritis and colitis	244
79	Viral and chlamydial infection	241
518	Other diseases of the lung	235
414	Other forms of chronic ischemic heart disease	228
715	Osteoarthritis and allied disorders	217
311	Depressive disorders, not otherwise specified	215
300	Neurotic disorders	214
INV	Invalid diagnosis	213
436	Acute but ill-defined cerebrovascular disorders	209
381	Nonsuppurative otitis media/Eustachian tube disorder	208
796	Other unspecified abnormal findings	203
785	Symptoms involving the cardiovascular system	199
272	Disorders of the lipid metabolism	197
250	Diabetes mellitus	187
692	Contact dermatitis and other eczema	181
V76	Special screening for malignant neoplasms	180
346	Migraine	178
723	Other disorders of the cervical region	177
847	Sprains/strains other and unspecified of the back	176
285	Other and unspecified anemias	175
490	Bronchitis, not specified as acute or chronic	175

In this managed care study, although the antiepileptic drugs account for \$391,273 per year, the principal cost driver was inpatient services, which accounted for \$3,141,981 per year.

Several assumptions were made regarding data collection: 1) ICD-9 codes recorded were correct; 2) physicians' diagnoses were correct; 3) patients' identification numbers remained constant throughout the database (numbers entered correctly); 4) CPT codes were accurate representations of what actually occurred

when the patients received health care services; and 5) the process of categorizing related and unrelated CPT codes was accurate.

This study has several important limitations. First, data concerning clinical outcomes, such as the number of patients with complete seizure control, severity of seizures, or presence or absence of any adverse effects, were unavailable. Second, generalizing the results of this study to other health systems or geographic areas with different health systems, different cost

structures, or different patient populations may not be appropriate. Third, the pharmacy claims may have under-counted the use of newer antiepileptic agents, because any drug samples that patients receive would not appear in the pharmacy claims. Fourth, this study measured only the direct costs to an MCO; no indirect costs are included.

The Pennsylvania Medicaid patients study¹⁰ measured direct costs, which included outpatient services, pharmaceuticals, nursing home services, emergency room services, ambulance services, hospitalization room and board, laboratory tests, surgery, and diagnostic procedures. Similar categories were used in this managed care study for direct costs. The Medicaid study derived a cost of \$2,011 pp/py (1992 dollars) for a total of 13,473 Medicaid patients. The normative cost, defined as the estimated fee-for-service cost to an insurer, was \$5,047 pp/py.¹⁰ In comparison, this managed care study determined that an average of \$2,400 pp/py was spent to treat patients with epilepsy.

Reports in the literature suggest that up to 80% of patients with epilepsy can be controlled with one drug.³ In this study, of the patients taking medications, 70% received monotherapy and 30% were treated with multidrug therapy. The most commonly used antiepileptic drugs were phenytoin, carbamazepine, and valproate. Because these are among the oldest of the available drugs for the treatment of epilepsy, this is not an unexpected finding. However, growth in use of newer agents such as gabapentin and lamotrigine is important. The greater number of patients treated with gabapentin as compared with lamotrigine in this study could be attributed to a lower reported rate of adverse effects and drug interactions.

A cost minimization analysis of monotherapy with three agents published in 1995⁷ determined that phenytoin was least costly, followed by carbamazepine, and divalproex sodium. Based on pharmacy costs alone, the same rank order of drug costs is found in the present study.

This study raises several important disease management issues.¹⁴ Based on the literature, the high proportion of costs for inpatient care was unexpected. Disease management efforts to improve seizure control in patients with epilepsy may be able to prevent some of these admissions. The availability of new antiepileptic agents also may be effective in reducing some of these hospitalizations. In addition, the fact that 44% of the patients with a diagnosis of epilepsy or seizure received no antiepileptic drug prescriptions is an important point to note. For patients who have had an isolated seizure, no medication may be required; further, some patients may be able to successfully taper off their antiepileptic drugs. However, the group of patients without antiepileptic prescriptions also may include non-compliant patients. This database could be used to identify patients who may be noncompliant with their prescribed regimens.

Evaluating the "total patient" with a disease may raise useful disease management questions. Considering associated

comorbidities may be wise when planning a disease management program. Commonly occurring comorbid disease states may impact how the diseases are managed and monitored. For example, because approximately 500 patients in this study had essential hypertension as well as a seizure disorder, blood pressure measurement may be a useful component in monitoring epilepsy in this health system.

CONCLUSION

This study was designed to identify the direct costs incurred by an MCO in the treatment of epilepsy or seizures. In general, the age groups that are the most costly to treat are the very young (0–4 years) and the middle to upper ages (40–74 years) in both sexes. The most commonly used drugs also consume the largest prescription resources. Inpatient services account for 57% of the total resources used to manage epilepsy or acute seizures. Reductions in hospitalizations could result in substantial cost savings.

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