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Healthcare utilization and costs in adults with stable and uncontrolled epilepsy

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ABSTRACT

Despite the availability of numerous antiepileptic drugs (AEDs), some epilepsies remain resistant to treatment. We compared utilization and costs in patients with uncontrolled epilepsy to those with stable epilepsy. Claims data (2007–2009) were used to identify adults with epilepsy requiring additional AED therapy (having uncontrolled epilepsy) and those not requiring additional AED therapy (having stable epilepsy). The date in 2008 on which an additional AED was started was the index date for patients with uncontrolled epilepsy, and a randomly selected date was used for patients with stable epilepsy, whose AED use was unchanged in the preceding year. In the postindex year, all pharmacy and medical claims were used to estimate overall utilization and costs; claims with epilepsy in any diagnosis field were used to estimate epilepsy-related outcomes. Outcomes were adjusted using multivariate analyses. We identified 1536 patients with uncontrolled epilepsy and 8571 patients with stable epilepsy (mean age: 42.8 years; female: 48%). Patients with uncontrolled epilepsy had higher comorbidity rates ($p < .02$). A greater proportion of patients with uncontrolled epilepsy had ≥1 hospitalization or emergency department visit ($p < .001$). Patients with uncontrolled epilepsy had a greater mean length of hospital stay and more physician office visits ($p < .034$). After adjustment, the odds of hospitalization (OR: 1.8, any diagnosis; 2.2, epilepsy-related) and emergency department visit (OR: 1.6, any diagnosis; 1.9, epilepsy-related) were greater for patients with uncontrolled epilepsy. Annual overall ($23,238 vs. $13,839) and epilepsy-related ($12,399 vs. $5511) costs were higher in patients with uncontrolled epilepsy and remained higher after adjustment ($p < .001$). Patients with uncontrolled epilepsy use more services and incur higher costs compared with those with stable epilepsy. Epilepsy-related costs accounted for <50% of the total costs, suggesting that comorbid conditions and/or underidentification of utilization may substantially contribute to costs.

1. Introduction

Epilepsy, the fourth most common neurological disorder in the United States after migraine, stroke, and Alzheimer's disease, is characterized by recurrent seizures and affects about 2.2 million people in the United States [1–3]. For people whose seizures are not fully controlled, the burden of epilepsy is immense both on an individual and a societal level. It adversely affects multiple aspects of life including physical and mental health, quality of life, and activities of daily living [3]. Although a variety of antiepileptic drugs (AEDs) and other therapies may be used to treat epilepsy, many patients continue to have seizures that may lead to a significant increase in healthcare resource use [3–8]. The estimated economic impact of epilepsy in the US includes $9.6 billion of direct medical care costs and additional indirect care costs [3,8,9]. Moreover, indirect costs associated with epilepsy, such as those resulting from productivity loss, can be considerably higher than direct medical costs associated with this disorder [3,9–11]. Although the economic burden of epilepsy has been studied, there are few studies comparing the burden of illness in patients with stable epilepsy to patients with uncontrolled epilepsy [12]. We compared overall and epilepsy-related healthcare utilization and costs between groups of adult patients (aged ≥18 years) identified as having stable or uncontrolled epilepsy.

2. Methods

2.1. Study design and data sources

We conducted a retrospective cohort study using data from the Thomson Reuters MarketScan Commercial database, a Health Insurance

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Portability and Accountability Act compliant administrative claims database of millions of covered lives, representing all major regions of the United States. The database contained de-identified adjudicated pharmacy and medical claims submitted for payment by providers, healthcare facilities, and pharmacies. The database contained information on physician visits, medical procedures, hospitalizations, drugs dispensed in the outpatient setting, dates of services/prescriptions, number of days of medications supplied, and tests performed. Paid amounts were recorded for medical, inpatient, and pharmacy claims. Member enrollment and limited patient demographic information were also available. Data used covered a study time period from 1/1/2007 to 12/31/2009. This was an analysis of a Health Insurance Portability and Accountability Act compliant secondary database; hence, no Institutional Review Board review was required for this study.

2.2. Study population

Study patients were ≥18 years old, diagnosed with epilepsy, and treated with at least one AED in the identification (ID) period (calendar year 2008). The included AEDs were carbamazepine, clonazepam, divalproex, valproate, ethosuximide, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, pregabalin, primidone, tiagabine, topiramate, vigabatrin, and zonisamide. To identify the patients, we first identified all patients with ≥2 medical claims, ≥30 days apart, with epilepsy (ICD-9-CM codes: 345.xx or 780.39) in any diagnosis field in the ID period, and who either 1) continued on the same AED (either monotherapy or combination) for ≥12 months or 2) added additional AED(s) in the ID period. Additional AED therapy was defined as ≥3 months of baseline therapy, followed by ≥3 months with both baseline and additional AED(s). We excluded patients if they were <18 years old in the baseline period, if they were not continuously enrolled in the baseline and follow-up periods, or if they had diagnoses of neuropathic or chronic pain or evidence of pregnancy, fibromyalgia, bipolar disorder, or migraines in the baseline or follow-up periods since the AEDs may have been used for these conditions rather than epilepsy [13–15].

Study patients were classified into two cohorts and labeled as either "having stable epilepsy" if they had no change in AED monotherapy or combination therapy for at least 1 year or as "having uncontrolled epilepsy" if they added AEDs to an existing regimen during the year of observation. An index date was selected for each group: the date on which an additional AED was started for patients with uncontrolled epilepsy and a randomly selected date during the ID period for patients with stable epilepsy, whose AED use (either single agent or combination) was unchanged in the preceding year.

The definition of "uncontrolled" reflected the lack of clinical detail in claims. Specifically, AEDs can be changed for different reasons. Changes from one drug (or regimen) to a different drug (or regimen) may represent either intolerance to treatment or uncontrolled seizure activity, but these cases cannot be reliably distinguished using claims and, therefore, were excluded from the study. In contrast, the addition of an AED to an existing regimen was felt to more likely represent a need for a greater intensity of treatment (e.g., lack of seizure control), since intolerance of the regimen would be expected to lead to a change in the offending agent.

2.3. Study measures

We used enrollment files, medical claims, and pharmacy claims to derive study measures. The claims database contains every claim for an individual's period of enrollment. No missing data are assumed since a payment is processed only if a claim exists. Baseline measures were determined by reviewing all pharmacy and medical claims in the 12-month preindex period and included patient demographics, physician specialty, and burden of illness. Patient demographics included age, gender, and US census region and were identified in enrollment records. Using a published algorithm, the physician specialty with the largest plurality of office visits that carried evaluation and management (E&M) service codes was assigned as the "usual care specialty" [16]. That is, if a patient had 6 E&M visits during the year, 4 of them with a neurologist, the patient would be assigned "neurology" as the usual care specialty. Three measures were used to describe burden of illness. First, we used the widely validated Healthcare Cost and Utilization Project Chronic Condition Indicator to calculate the number of chronic conditions experienced by each patient [17,18]. The indicator categorizes ICD-9-CM diagnosis codes as chronic or not chronic, defining a chronic condition as one that lasts ≥12 months and either (a) places limitations on self-care, independent living, and social interactions or (b) results in the need for ongoing intervention with medical products, services, and special equipment [18]. Second, we included the Charlson comorbidity index (CCI). Although initially developed as a predictor of in-hospital mortality, the CCI has been adapted and widely used to measure overall burden of illness in the general population [19,20]. Finally, to account for burden of illness due to central nervous system (CNS) specific comorbidities, we identified the presence of head injury (ICD-9-CM: 854.x), brain tumor (ICD-9-CM: 191.x, 198.3, 225.x, 237.5, or 239.6), cerebrovascular disease or stroke (ICD-9-CM: 430-438.xx, or 997.02), tuberous sclerosis (ICD-9-CM: 759.5), and depression and other mood disorders (ICD-9-CM: 296.xx, 298.0, 300.4, 309.1, or 311) in the preindex period.

Outcome measures included annual overall healthcare utilization and costs, estimated using pharmacy and medical claims in the postindex (follow-up) year. Other outcomes were epilepsy-related utilization, estimated using AED fills and services associated with claims with epilepsy (ICD-9-CM: 345.xx or 780.93) in any diagnosis field and epilepsy-related costs, estimated using claims with epilepsy in any diagnosis field or epilepsy-related tests. Measures of overall and epilepsy-related utilization included number of inpatient hospitalizations, number of days of stay among patients with inpatient hospitalizations, number of emergency department (ED) visits, and number of physician office visits. Measures of epilepsy-related utilization also included treatments (number of AEDs and number of vagus nerve stimulation devices implanted) and tests (electroencephalographic [EEG] or brain imaging). Measures of overall and epilepsy-related costs included medical costs (inpatient hospitalization cost, ED visit cost, and outpatient/non-ED service cost) and pharmacy costs. Indirect costs, including informal or out-of-pocket expenses such as patient transport and time off work, were not evaluated in this study.

2.4. Analysis

Descriptive statistics were reported for all study measures and were reported separately for patients with stable epilepsy and for patients with uncontrolled epilepsy. We compared differences between the two cohorts using Chi-square tests and t-tests, where applicable. Multivariate analyses were conducted to adjust for relevant baseline measures, including age, sex, US census region, usual care physician specialty, number of chronic conditions, CCI, and CNS comorbidities. Analysis of covariance (ANCOVA) was used to estimate the incremental increase in overall and epilepsy-related costs associated with uncontrolled epilepsy and logistic regression to estimate the incremental increase in risk of overall and epilepsy-related inpatient hospitalization and ED visits. All data transformations and statistical analyses were performed using SAS© version 9.2 (SAS Institute, Cary, NC).

3. Results

There were 243,484 patients with at least one medical claim for epilepsy (ICD-9-CM: 345.xx or 780.39) in the ID period. Of these, 99,438 patients had at least two claims ≥30 days apart, and 62,132 patients used AED therapy in the ID period. From the 25,033 patients who both had ≥2 claims with epilepsy diagnoses and used AEDs, we