

Direct medical costs for patients seeking emergency care for losses of epilepsy control in a U.S. managed care setting

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ABSTRACT

The objective of this retrospective claims database study was to compare the costs of care from a U.S. payer perspective before and after epilepsy treatment in emergent care settings and, secondarily, to describe the frequency of toxic effects and physical injuries occurring on the date of the emergent care. Nine and four-tenths percent of patients receiving emergent care for epilepsy (114/1213) had an injury or adverse antiepileptic drug effect on the same date. The majority of incidents were superficial injuries and contusions (28%), fractures (21%), open wounds or injury to blood vessels (19%), intracranial injury (10%), and/or medication toxicity (10%). Both non-epilepsy-related (US\$12,745.56) and epilepsy-related (US\$2013.62) direct medical costs of care pre-index were significantly different from those post-index (US\$15,274.95 and US\$7087.53, respectively). The cost of care for possible reestablishment of epilepsy control and treatment of co-occurring injuries is significant when compared with that for the period prior to seizure.

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1. Introduction

Epilepsy is a potentially life-threatening neurological condition that affects approximately 2.5 million individuals of all ages in the United States, with 200,000 new cases being diagnosed each year [1]. In 2000, the annualized burden of epilepsy in the United States was estimated at \$12.5 billion (1995 U.S. dollars), which was driven primarily by individuals with intractable epilepsy, thus emphasizing the importance of seizure control [2]. Numerous studies have found that an increase in seizure frequency increases cost [3–5], with a significant portion of direct costs in the United States driven by emergency room visits and inpatient admissions [6,7]. The direct costs associated with managing epilepsy are generally the highest following the initial diagnosis because of diagnostic evaluation and initial treatment [2]. Over time, there is a downward trend that is reflective of decreased service use by those whose seizures continue and a large number of patients who achieve remission and, in some cases, subsequently discontinue antiepileptic medication.

The literature suggests a link between epilepsy and increased morbidity, some of which may be related to a higher risk of accidents, fractures, head injuries, and burns as compared with the general population. A large prospective European cohort study found a 5% higher 12-month incidence of injuries in patients with epilepsy when compared with the general population [8]. In addition, several retrospective, survey-based studies suggest that 30 to 35% of patients with epilepsy, depending on the time horizon examined, have experienced an injury coincident with a seizure [9,10]. The rates of specific injury types have also been evaluated [8,11–15]. A U.S. survey of patients who had a seizure within the prior year reported that 24% of patients sustained at least one head injury, 16% a burn or scald, 10% a dental injury, and 6% a fracture [10]. Data also suggest that injury-related intensive care is up to three times more prevalent in patients with epilepsy than in controls [15].

Although there is extensive literature describing the burden of epilepsy in general, there is only limited information describing the injury prevalence and direct cost of care when a patient with epilepsy requires emergent care after an extended period of disease control. Many patients with controlled epilepsy are no longer under the typical seizure restrictions (e.g., operating a motor vehicle, navigating heights, operating heavy or electrical machinery) and, subsequently, might be engaged in activities that are potentially

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harmful if a seizure were to occur. These circumstances have gained greater scientific attention with the introduction of generic anti-epileptic drugs (AEDs). Recent studies have suggested a relationship between AED formulation changes and loss of disease stability [16–19]. As payers discuss population-based care policies, it is critical to understand the clinical and financial impact of interruptions in condition stability, including reestablishment of epilepsy control. The purpose of this study was to describe the direct medical cost of an interruption in epilepsy control requiring emergent care from a U.S. payer perspective. Additionally, the frequency and types of injuries and AED toxicity were evaluated in addition to the cost of the initial event and subsequent follow-up care.

2. Methods

A retrospective claims database analysis was conducted using health claims data from the PharMetrics® database (IMS Health, Watertown MA, USA). The PharMetrics Patient-Centric Database® comprises fully adjudicated medical and pharmaceutical claims for more than 50 million unique patients and 90 regional health plans across the United States. The individuals covered by these plans are geographically diverse across the United States. The plans provide fully insured coverage for physician, hospital, and prescription drug services, and the providers of these services submit their claims for payment directly to the health plans. The data source and study methods were compliant with the Health Insurance Portability and Accountability Act. Institutional review board approval was not required for this study.

This study assumes that patients experiencing unexpected interruptions in epilepsy control (e.g., seizures, AED toxicity) following a prolonged period of relative stability are likely to seek care in emergency or inpatient settings. The acute and follow-up care associated with the unexpected event may significantly impact the overall direct medical cost from the payer perspective. Therefore, the outcome of interest was the direct medical cost of care for both epilepsy-related and non-epilepsy-related claims in the pre-emergent care period (pre-event) compared with cost of the event including follow-up.

The time frame for this study was January 2005 through December 2006. This time frame was chosen because it represented the most recent fully adjudicated claims data set available at the time of analysis. Patients were identified in the period July 2005 to June 2006 to allow 6 months of data before and after the emergent epilepsy care for analyses. The population consisted of commercial health plan members who had a diagnosis of epilepsy as evidenced by at least one claim during the study period for ICD-9 code 345.xx (i.e., epilepsy and recurrent seizure codes), excluding 345.6x (infantile spasms). [*The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*] The population of patients with epilepsy were required to have at least one instance of emergent care defined as an inpatient admission, emergency room visit or an ambulance ride with a primary or secondary ICD-9 code of 345.xx (excluding 345.6x), 780.39 (i.e., other convulsions), and/or an Episode Treatment Group (ETG) code of 152 (i.e., epilepsy without surgery). The and/or criterion was used to increase the sensitivity of the sample to capture patients who experienced AED toxicity or other epilepsy-related conditions that may not have been coded as seizure related (i.e., 345.xx or 780.39). The index date was the earliest date of emergent epilepsy care during the study period. All patients were continuously enrolled in their health plan for 6 months before and after the index date. Patients included were between 12 and 64 years of age and were dispensed a 145-day or longer supply of an AED in the pre-index period as determined by First Data Bank® therapeutic code classifications. This 145-day supply criterion was used to strengthen the

assumption that patients were being treated for epilepsy in the pre-index period and had received at least 80% of medication days supply to meet conventional medication adherence standards. Finally, patients were excluded from the study if there was evidence of an epilepsy-related emergent care visit in the 6 months prior to the index date. This exclusion was used to strengthen the assumption that patients with epilepsy were sufficiently stable and did not require ambulance, emergency room, or inpatient medical attention during the time frame immediately prior to the index event.

The ETG is an illness classification and episode building system originally developed for case mix adjustment [20]. A brief description of the methods associated with ETG is provided here, with more complex descriptions, case studies, tutorials, and diagnosis reference tables referred to in this description provided elsewhere [21]. ETG codes are assigned using tables of coding systems used for reimbursement including ICD-9-CM, Current Procedural Terminology (CPT-4), National Drug Code (NDC), and the Healthcare Common Procedure Coding System (HCPCS). Each ICD-9-CM primary diagnosis code is mapped to only one ETG, which is the basis of initial assignment to a claim. Primary diagnosis is the principal means of assignment. Secondary diagnoses of comorbid conditions or procedure codes of a more advanced condition (e.g., surgery) may shift an ETG to a more complicated ETG. However, epilepsy in ETG Version 6 has only two ETG classifications (“151” with surgery and “152” without surgery) unaffected by comorbidities. Medication (NDCs) and procedure (HCPCS, CPT-4, ICD-9-CM) codes are also mapped to ETGs for assigning episodes of care for ambulatory, inpatient, and pharmacy claims. Episodes are assigned a unique number originating from an anchor record. Anchor records represent a service by a clinician engaging in the direct evaluation, management, or treatment of a patient. In this study, the anchor is a claim submitted for clinician-directed hospital or emergency services. Nonanchor records representing ancillary care or medications (e.g., lab test, medication, X-ray) are assigned episode numbers from anchor records based on a best-fit algorithm evaluating all active episodes of care for a patient. For example: “if both a chest X-ray and blood glucose test were provided to a patient during the same encounter and further, if the patient had active episodes of both chronic bronchitis and diabetes; the chest X-ray will be assigned to the chronic bronchitis episode while the blood glucose test is assigned to the diabetes episode. In other words, the blood glucose test is not eligible for assignment to the chronic bronchitis ETG” [20]. ETGs, along with unique identifiers for episodes of care, allow researchers to follow a complete treatment episode until there is a significant absence of claims (i.e., clean period) for treatment (in the case of epilepsy, it is 180 days). The presence of a subsequent anchor record of the same ETG class within a clean period causes the clean period to extend further. As implied in the example above, this system can track treatment of multiple conditions that may occur during the same patient encounter.

Total direct medical costs were calculated from the amounts reimbursed to the provider for all services performed that resulted in a medical or pharmacy claim. These claims encompassed inpatient and outpatient care, prescriptions, lab work, and all other services used in the direct care of the patient. The total direct medical cost occurring on the day of the index date was calculated for all patients. Follow-up care costs were also calculated by following all health claims for the ETG episode numbers present on the index date for a maximum of 6 months post-index. Total direct medical costs were also calculated for the 6 months prior to the index date and for the following 6 months including the index date. All cost information for each analysis was further categorized as being “epilepsy-related” or “non-epilepsy-related.” This was determined by evaluating if a claim had an ETG of 151–152 or if antiepileptic medications were identified through First Data Bank therapeutic code classifications suggesting that the treatment was related to

epilepsy. All other claims were classified as not being related to the epilepsy. By definition all patients had epilepsy-related costs in both the pre- and post-index periods due to selection criteria. Patients who had no claims for non-epilepsy-related services were imputed as having \$0.00 costs in each respective category for pre/post analyses. Zero costs were not imputed for descriptions of non-epilepsy-related per-patient costs on the day of the index event and for follow-up care related to episode codes assigned on the index date.

Epilepsy-related ICD-9-CM codes used on the day of the index event were grouped into four categories: three reflecting epilepsy or a convulsive diagnosis and one representing all other diagnoses on the day of the index event. The three epilepsy or convulsive diagnostic categories were “generalized” (345.0x–345.3x), “partial” (345.4x, 345.5x, 345.7x), and “other” (345.8x, 345.9x, 780.39). The frequency and types of injuries and AED toxicity were also reported by evaluating ICD-9 codes occurring on the index date. The ICD-9 code classification system was used to classify the various types of injuries into groups. For example, tibial fracture (823.xx) was grouped under ICD-9 group “fractures” (800–829). Paired sample *t* tests were used along with the Wilcoxon signed rank test to compare total direct medical costs before and after the index date. Sensitivity analyses were conducted on direct medical costs excluding patients who represented the top and bottom 5% of total costs for the entire 12-month study period. Sensitivity analyses were also conducted excluding patients with an ETG for epilepsy without a diagnostic code of 345.xx.

3. Results

3.1. Patient and emergent care characteristics

There were 1213 patients who met all inclusion and exclusion criteria. The average patient age was 38.6 (SD 15.3) years, and 55.3% were female ($n = 671$). The majority of patients resided in the Midwestern United States (40.1%), followed by South (27.5%), East (25.1%), and West (7.3%). Most patients were covered under an employer-sponsored commercial plan ($n = 1101$), followed by managed Medicaid ($n = 52$), self-insured ($n = 41$), and unknown ($n = 8$). Although patients over the age of 64 were excluded, 11 patients were enrolled in a Medicare at-risk plan where a commercial entity administers all of the benefits for the enrollee. These 11 Medicare patients were included in the sample as the payer under this plan was financially responsible for all medical claims.

With respect to the index emergent care epilepsy event and claims occurring on the same day, 15.1% of all the events involved an ambulance, with one instance involving an air or water rescue. A little over a third (35.2%) of the emergent care for epilepsy involved emergency room utilization, and more than half (55.4%) involved an inpatient hospitalization. Patients were most commonly diagnosed with multiple epilepsy ICD-9-CM codes on the day of the index event. A diagnosis of generalized epilepsy ($n = 318$) was more common than partial epilepsy ($n = 230$), and a small number had both general and partial diagnoses coded ($n = 37$). The most common diagnosis, however, was for nonspecific forms of epilepsy ($n = 469$). Finally, 159 patients had another condition coded related to epilepsy, but not 345.xx.

Overall, 9.4% ($n = 114$) of patients experienced a physical injury or toxic effect on the day of the index event. The types and frequency, as a percentage of injuries, for the 146 injuries or AED effects that occurred in 114 patients are illustrated in Fig. 1. More than half (57.5%) of the injuries were considered serious (fracture, intracranial injury, open wound, internal injury, dislocation, or burn). Superficial or contusion injuries were the most frequent injuries (28.1%). Fractures were the second most prevalent injury

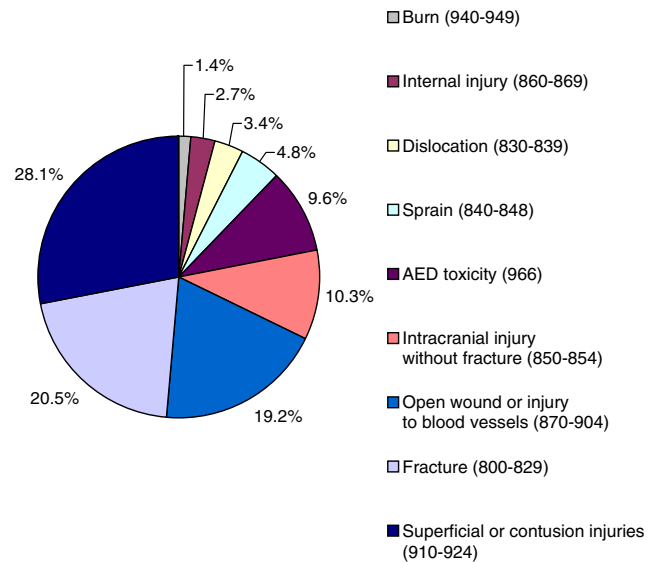


Fig. 1. Percentage of injuries by injury type or toxicity (ICD-9-CM) for patients experiencing epilepsy care in an emergent care setting ($n = 146$ injuries).

(20.5%), followed by open wounds or injury to blood vessels (19.2%).

3.2. Direct medical costs

Complete descriptions of direct medical costs by category are provided in Table 1. The mean epilepsy-related direct cost per patient ($n = 1213$) was \$3385.71 (SD = \$8937.23, median = \$462.79) for claims occurring on the day of the index event. Epilepsy-related costs appeared to triple in the post-index period relative to the pre-index period. The mean epilepsy-related direct cost per patient for 6 months post-index and including index ($n = 1213$) was significantly higher by \$5793.91 when compared with that for the 6 months before the index date (t test $P < 0.001$, Wilcoxon $P < 0.001$). The majority of epilepsy-related direct medical costs per patient for the post-index period appeared to be accounted for by follow-up care for episodes coded on the index event day (epilepsy-related: $n = 1213$, mean = \$7213.21, SD = \$13,025.93, median = \$2556.37).

A majority of patients ($n = 986$) had non-epilepsy-related costs on the day of the index event (mean = \$4375.24, SD = \$17,410.56, median = \$707.72). Mean non-epilepsy-related direct costs per patient were also significantly higher (mean difference = \$2529.39) in the post-index period when compared with the pre-index period (t test $P = 0.047$, Wilcoxon = $P < 0.001$). Similar to epilepsy-related post-index period costs, a large portion of non-epilepsy-related costs also appeared to be accounted for by follow-up care for the 974 patients who had episodes of care coded on and extending from the index date ($n = 974$, mean = \$10,757.82, SD = \$27,568.15, median = \$2289.27).

Sensitivity analyses eliminating the top and bottom 5% of patients by total direct medical costs over the 12-month study period were also conducted. The total direct medical costs (epilepsy and non-epilepsy) per patient ($n = 1213$) over the 12-month study period ranged from \$568.36 to \$730,872.73, and from \$3665.60 to \$132,604.21 after sensitivity analyses sample reductions ($n = 1093$). The mean epilepsy-related and non-epilepsy-related direct medical costs changed marginally from whole-sample estimates, though significant increases were enduring for both categories of cost from the pre-index period to the post-index period. Sensitivity analyses eliminating the 159 patients with an ETG for epilepsy, but no diagnostic code for 345.xx on the index date,

Table 1

Direct medical costs for the study period for the entire sample and for samples excluding patients for sensitivity analyses.

	Mean [median] [SD] (n)					
	Entire sample		Sample excluding patients representing top and bottom 5% of total costs for study period		Sample excluding patients with an epilepsy episode treatment grouper who had another condition coded related to epilepsy, but not 345.xx on index date	
	Epilepsy related	Non-epilepsy related	Epilepsy related	Non-epilepsy related	Epilepsy related	Non-epilepsy related
6 months prior to index date ^a	\$2,013.62 {\$1,415.95} [\$2,354.56] (1,213)	\$12,745.56 {\$2,329.12} [\$39,874.37] (1,213)	\$2,101.85 {\$1,574.29} [\$2,355.92] (1,093)	\$7,695.34 {\$2,396.12} [\$13,445.34] (1,093)	\$2,074.64 {\$1,529.96} [\$2,375.99] (1,054)	\$13,445.32 {\$2,383.05} [\$42,237.55] (1,054)
6 months post-index, including index day	\$7,807.53 {\$2,955.06} [\$13,627.82] (1,213)	\$15,274.95 {\$4,678.39} [\$31,962.92] (1,213)	\$7,765.64 {\$3,219.35} [\$11,623.14] (1,093)	\$11,305.99 {\$4,816.29} [\$16,638.13] (1,093)	\$8,477.71 {\$3,166.48} [\$14,407.57] (1,054)	\$14,997.48 {\$4,823.83} [\$30,529.28] (1,054)
P value comparing pre with post-index period <i>t</i> test; Wilcoxon	<0.001; <0.001	0.047; 0.001	0.001; 0.001	0.001; 0.001	0.001; 0.001	0.270; 0.001
Claims occurring on index day ^b	\$3,385.71 {\$462.79} [\$8,937.23] (1,213)	\$4,375.24 [\$707.72] [\$17,410.56] (986)	\$3,414.81 {\$500.49} [\$7,518.58] (1,093)	\$3,366.42 [\$748.05] [\$8,327.81] (884)	\$3,781.51 {\$479.44} [\$9,496.68] (1,054)	\$4,410.99 [\$741.95] [\$16,887.28] (856)
Claims in post-index period related by episode coding to care on index date ^c	\$7,213.21 {\$2,556.37} [\$13,025.93] (1,213)	\$10,757.82 {\$2,289.27} [\$27,568.15] (974)	\$7,175.67 {\$2,848.68} [\$11,065.35] (1,093)	\$7,539.02 {\$2,232.47} [\$14,099.36] (872)	\$7,876.57 {\$2,780.56} [\$13,784.95] (1,054)	\$11,239.81 {\$2,608.36} [\$28,197.51] (844)

^a For pre- and post-index comparisons, zero values were imputed for patients who did not have non-epilepsy-related care.

^b For descriptions of claims occurring on the index day, zeros were not imputed for patients who did not have non-epilepsy-related care, resulting in a lower sample size.

^c For descriptions of claims in the post-index period related by episode coding to care on the index date, zeros were not imputed for patients without identifiable episodes of care extending beyond the index date, resulting in a lower sample size.

did not change the significant findings with regard to epilepsy-related cost changes pre- to post-index. Though the nonparametric findings remained significant, the parametric significance estimate for the comparison of pre- to post-index non-epilepsy-related costs did change. Sensitivity analyses are provided in Table 1.

4. Discussion

This study has shown that emergent care utilization for epilepsy after a prolonged period of epilepsy stability (seizure control and adverse event profile not requiring emergent care) represents a significant escalation in direct medical costs for both epilepsy-related and non-epilepsy-related services when compared with the period prior to the emergent care event. Specifically, the follow-up care associated with a single epilepsy-related emergent care episode dominates total costs in the 6 months following the acute event, suggesting that the majority of costs may be related to reestablishment of condition stability and/or treatment of injuries. In our study, 9.4% of patients also experienced a toxic effect or injury, more than half of which were considered serious (i.e., a fracture, intracranial injury, open wound, internal injury, dislocation, or burn). This represents a significant cost to the payer, but also may significantly impact the life of the patient through additional medical disability including long-term morbidity and/or neurological sequelae and seizure restrictions (e.g., operating motor vehicles, navigating heights, operating heavy or electrical machinery). Overall these results demonstrate there is a significant financial impact from loss of epilepsy condition stability from a payer perspective that should be considered when making population-based intervention and care decisions.

Other studies have described the annual total medical costs of persons with epilepsy with estimates ranging from \$5424 to \$9617 per annum for the years 1992–1996 [6,7]. Caution must be applied to a direct comparison as the results presented here

are in 2006 U.S. dollars (i.e., no medical consumer price index adjustment), and represent specific situations where a loss of epilepsy control was coded. The estimates in the current study may be higher as situations where epilepsy control was maintained throughout the year are not included in the direct medical cost estimates. Previous studies have indicated that the direct costs associated with managing epilepsy are generally the highest immediately following a seizure diagnosis because of diagnostic evaluation and initial treatment [2]. In the years following the initial diagnosis, there is a downward trend in direct costs that is reflective of decreased service use by those whose seizures continue and a large number of patients who achieve remission and subsequently discontinue antiepileptic medications. Our study adds to previous findings by highlighting the economic impact from a payer perspective that a single epilepsy-related event requiring emergent care in a previously controlled patient may have. We found that patients experienced significant increases in both epilepsy-related (\$5793.91) and non-epilepsy-related (\$2529.39) direct medical costs after and including the breakthrough event. This escalation in costs from the pre- to the post-index period represents a 288% increase for epilepsy-related, and a 20% increase for non-epilepsy-related, direct medical costs. The total costs in the post-index period appear to be dominated by episodes of care identified on the day of the index event, with approximately 92% of epilepsy-related and 70% of non-epilepsy-related costs in the post-index period related to the index event by episode identifiers. Furthermore, these changes in cost from the pre- to the post-index period remained significant even after eliminating potential outliers.

To our knowledge there are no other studies that specifically report the frequency and types of injuries occurring in previously stable patients with epilepsy. However, the rate and types of co-occurring injuries in our study were similar to those in previous studies examining the overall population with epilepsy. Injuries and deaths were reported in as many as 15% of seizure episodes

evaluated in an emergency department, of which head contusions and lacerations were the most common types of injuries [12]. In addition, a retrospective chart review in Rochester, Minnesota, found that 16% of patients with epilepsy had an injury related to a seizure and sought medical treatment either for the injury or for improvement in seizure control [14]. The investigators also reported that 32% of these injuries were considered major. The slightly higher rate of injuries found in both of these studies in comparison to our study may be explained by the inclusion of patients that may not have been well controlled (e.g., newly diagnosed patients or those without a prolonged period of seizure freedom). Also, in the current study, we were able to quantify only injuries and toxic effects, and were unable to determine from claims data if death was an outcome. Further, our work examined patients with a diagnosis for epilepsy or other seizures and/or an ETG of epilepsy without surgery. This method was chosen to more accurately capture incidences of other epilepsy-related conditions that may not have been coded as a seizure. This method of inclusion may have lowered the estimates of patients experiencing an injury by including patients who were at lower risk of injury. Though a differential relative risk of injury between patients having a seizure, patients experiencing an AED effect, and those experiencing other types of interruptions in control has not been confirmed in the literature, increased seizure frequency and severity are associated with greater risk [10,14]. Finally, our study relied on medical claims that typically have a limited number of fields from which to code all that occurs during an emergent care visit. With a limited number of fields, more intense and highly reimbursed care may dominate these limited code spaces. Effectively this may represent a bias where fewer injuries are reported, but a higher proportion of serious injuries (i.e., resource intensive) are reported relative to minor injuries.

In our study, we did not evaluate potential risk factors of the patients with epilepsy presenting with a physical injury; however, this has been reported in the literature. Seizure type has been a risk factor in most studies, with an increased risk of injury in patients with generalized onset seizures such as tonic-clonic, atonic, and myoclonic because they lead to falls or a loss of consciousness [22]. However, it should be noted that injuries have also been reported to occur in patients with absence seizures [23]. An increase in seizure frequency can also increase the risk of injury [14]. In addition, it is possible that the potential risks for the patient and the general public from a seizure may be magnified when seizures occur after a prolonged period of seizure freedom. Recently, new literature is available suggesting that the automatic substitution of generic antiepileptic drugs may increase the likelihood of an interruption in condition stability in a subset of patients with epilepsy who were previously controlled [16–19,24,25]. Automatic generic substitution is often used as a cost savings measure, and in most states prior notification or approval by the prescriber or patient is not required. A recent retrospective, case-control database analysis found that there was an 81% greater odds of requiring emergent care for a seizure in patients who had an A-rated antiepileptic formulation switch relative to controls [16]. Without notification of possible risk associated with a change in formulation, previously stable patients may be unaware or less vigilant in monitoring their condition or limiting risky activities. Clinicians (including author B.J.S.) have reported their personal accounts of patients experiencing a seizure while driving a motor vehicle shortly after generic substitution, despite being seizure free for years. The ramifications and personal cost to the patient and other drivers/passengers involved in this type of incident cannot be calculated [19]. Thus, cost savings derived by generic substitution should be critically examined as there may be cost shifting because of the need for emergent medical care and/or other services in a subset of patients.

Careful consideration to the study design and limitations should be noted when interpreting the results of this study. Two main assumptions must be considered when interpreting the results: the index event was not the initial epilepsy diagnosis for a patient and represented an interruption in condition stability, and the 6 months prior to the index event represented a period during which the disease seizure control and AED adverse event profile was stable enough not to require emergent care. With regard to the first assumption, it is unlikely that the index event was an initial diagnosis, as all patients in this study were receiving antiepileptic medication prior to the index event. With regard to the second, epilepsy events are commonly treated in an ambulatory setting; therefore, it is possible that patients may have experienced less severe interruptions in condition stability prior to index with none rising to the level of inpatient care. The results of this study should be applied only to instances where the epilepsy event required emergent care as there may be selection bias for patients with a more severe injury to seek medical attention in an emergency setting versus an ambulatory setting. Though these results cannot be extrapolated to all interruptions in condition stability, they do represent the significant economic burden from a payer perspective for hospital-based emergent epilepsy care. Additionally, this study relied on Episode Treatment Grouper and Episode classification variables provided by PharMetrics®. The use of ETGs is common in the literature, but more needs to be published to support the validity of this classification system [14–29]. Lastly, this study relies on coded, administration data sets that are susceptible to bias due to misclassification if an incorrect diagnosis code was filed on a claim. Administrative claims may be biased toward more severe classifications of admissions due to the potential for a higher reimbursement. The costs reported in this study may also be an underestimation of the magnitude of the loss of epilepsy control, as follow-up costs were truncated at 6 months post-index date. Finally, the costs reported here represent only direct medical costs from a payer perspective. Arguably, a societal perspective would more accurately represent the true burden of the disease as it would include the patient's out-of-pocket direct medical expenses, lost wages, caretaker expenses, reductions in quality of life, and other medical and nonmedical costs precipitated by a loss of epilepsy control.

Our study approach, in the context of the limitations, is helpful in understanding the impact of emergent epilepsy care after a prolonged period of epilepsy stability. Approximately 9.4% of patients receiving care for epilepsy in an emergent setting presented with AED toxicity and/or secondary injuries according to medical claims. The cost of care for possible reestablishment of epilepsy condition stability and treatment of these complications is significant when compared with that for the period prior to seizure. These findings reinforce previously published information and suggest that long-term seizure control is essential in managing the economic burden and morbidity associated with epilepsy and even a single breakthrough event can have significant consequences.

Conflict of interest statement

Three authors (W.M.Z., Q.D.D., J.D.C., J.M.G.) are employees of Abbott Laboratories. B.J.S. has received funding independent of this research (speaker fees, educational grants, research funding) from Abbott Laboratories, GlaxoSmithKline, OrthoMcNeil Neurologics, Pfizer, UCB, and Valeant Pharmaceuticals International. B.J.S. does not hold stock or financial interest in any pharmaceutical company.

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References

- [1] United States Centers for Disease Control and Prevention, Department of Health and Human Services. Targeting epilepsy: improving the lives of people with one of the nation's most common neurological conditions [Internet]; 2009 [cited 2009 March 10]. Available from: <http://cdc.gov/nccdphp/publications/aag/pdf/epilepsy.pdf>.
- [2] Begley CE, Famulari M, Annegers JF, et al. The cost of epilepsy in the United States: an estimate from population-based clinical and survey data. *Epilepsia* 2000;41:342–51.
- [3] Van Hout B, Gagnon D, Souetre E, et al. Relationship between seizure frequency and costs and quality of life of outpatients with partial epilepsy in France, Germany, and the United Kingdom. *Epilepsia* 1997;38:1221–6.
- [4] Baker GA, Nashef L, van Hout BA. Current issues in the management of epilepsy: the impact of frequent seizures on cost of illness, quality of life, and mortality. *Epilepsia* 1997;38(Suppl. 1):1–8.
- [5] Jacoby A, Buck D, Baker G, McNamee P, Graham-Jones S, Chadwick D. Uptake and costs of care for epilepsy: findings from a U.K. regional study. *Epilepsia* 1998;39:776–86.
- [6] Frost FJ, Hurley JS, Petersen HV, Gunter MJ, Gause D. A comparison of two methods for estimating the health care costs of epilepsy. *Epilepsia* 2000;41:1020–6.
- [7] Griffiths RI, Schrammel PN, Morris GL, Wills SH, Labiner DM, Strauss MJ. Payer costs of patients diagnosed with epilepsy. *Epilepsia* 1999;40:351–8.
- [8] Beghi E, Cornaggia C, The RESt-1 Group. Morbidity and accidents in patients with epilepsy: results of a European cohort study. *Epilepsia* 2002;43:1076–83.
- [9] Neufeld MY, Vishne T, Chistik V, Korczyn AD. Life-long history of injuries related to seizures. *Epilepsy Res* 1999;34:123–7.
- [10] Buck D, Baker GA, Jacoby A, Smith DF, Chadwick DW. Patients' experiences of injury as a result of epilepsy. *Epilepsia* 1997;38:439–44.
- [11] Neufeld MY, Chistik V, Kogan E, Korczyn AD. Physically traumatic events in patients with epilepsy compared with non-epileptic subjects. *Seizure* 2000;9:595–7.
- [12] Kirby S, Sadler RM. Injury and death as a result of seizures. *Epilepsia* 1995;36:25–8.
- [13] Van den Broek M, Beghi E, the RESt-1 Group. Accidents in patients with epilepsy: types, circumstances, and complications: a European cohort study. *Epilepsia* 2004;45:667–72.
- [14] Lawn ND, Bamlet WR, Radhakrishnan K, O'Brien PC, So EL. Injuries due to seizures in persons with epilepsy: a population-based study. *Neurology* 2004;63:1565–70.
- [15] Tellez-Zenteno JF, Hunter G, Wiebe S. Injuries in people with self-reported epilepsy: a population-based study. *Epilepsia* 2008;49:954–61.
- [16] Zachry III WM, Doan QD, Clewell JD, Smith BJ. Case-control analysis of ambulance, emergency room, or inpatient hospital events for epilepsy and antiepileptic drug formulation changes. *Epilepsia* 2009;50:493–500.
- [17] LeLorier J, Duh MS, Paradis PE, et al. Clinical consequences of generic substitution of lamotrigine for patients with epilepsy. *Neurology* 2008;70:2179–86.
- [18] Andermann F, Duh MS, Gosselin A, Paradis PE. Compulsory generic switching of antiepileptic drugs: high switchback rates to branded compounds compared with other drug classes. *Epilepsia* 2007;48:464–9.
- [19] Berg MJ, Gross RA, Tomaszewski KJ, Zingaro WM, Haskins LS. Generic substitution in the treatment of epilepsy: case evidence of breakthrough seizures. *Neurology* 2008;71:525–30.
- [20] Ingenix[®]. Symmetry Episode Treatment Groups[®] (ETGs[®]) White Paper [Internet]; 2007 [cited 2009 March 10]. Available from: http://www.symmetry-health.com/downloads/ETG_WhitePaper.pdf.
- [21] Ingenix[®]. Measuring and improving the quality & efficiency of health care. [Internet]; 2007 [cited 2009 July 10]. Available from: <http://www.ingenix.com/transparency>.
- [22] Wirrell EC. Epilepsy-related injuries. *Epilepsia* 2006;47(Suppl. 1):79–86.
- [23] Wirrell EC, Camfield PR, Camfield CS, Dooley JM, Gordon KE. Accidental injury is a serious risk in children with typical absence epilepsy. *Arch Neurol* 1996;53:929–32.
- [24] Rascati KL, Richards KM, Johnsrud MT, Mann TA. Effects of antiepileptic drug substitutions on epileptic events requiring acute care. *Pharmacotherapy* 2009;29:769–74.
- [25] Hansen RN, Campbell JD, Sullivan SD. Association between antiepileptic drug switching and epilepsy-related events. *Epilepsy & Behavior* 2009;15(4):481–5.
- [26] Prescott JD, Factor S, Pill M, Levi GW. Descriptive analysis of the direct medical costs of multiple sclerosis in 2004 using administrative claims in a large nationwide database. *J Manag Care Pharm* 2007;13:44–52.
- [27] Greene RA, Beckman H, Chamberlain J, et al. Increasing adherence to a community-based guideline for acute sinusitis through education, physician profiling, and financial incentives. *Am J Manag Care* 2004;10:670–8.
- [28] Garrett N, Martini ME. The boomers are coming: a total cost of care model of the impact of population aging on the cost of chronic conditions in the United States. *Dis Manag* 2007;10:51–60.
- [29] Thomas JW. Should episode-based economic profiles be risk adjusted to account for differences in patients' health risks? *Health Serv Res* 2006;41:581–98.