

Progression to adjunctive therapy among commercially-insured patients with partial-onset epilepsy

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INTRODUCTION

- Epilepsy is a chronic neurologic disorder characterized by recurrent seizures. Approximately 2.2–3 million people in the United States (US) have epilepsy, and about 150,000 new cases are diagnosed each year.¹
- There are two main types of epilepsy: primary generalized epilepsy and localization-related epilepsy.
 - Localization-related epilepsy accounts for 60–75% of all epilepsy cases; patients have one or more of three types of partial-onset seizures (POS): simple partial, complex partial, or POS with secondary generalization.²
- Approximately two thirds of patients with previously untreated epilepsy achieve adequate seizure control with either the first or second trial of antiepileptic drug (AED) monotherapy.³
 - Patients with epilepsy who fail initial AED monotherapy may switch to a different AED or progress to adjunctive therapy (AT).
 - About 35% of patients have refractory epilepsy which does not respond to monotherapy.^{3,4}

OBJECTIVES

- Using a database of commercially insured subjects (i.e., employees), the present study sought to identify employee spouses with POS (i.e., patients), to determine:
 - the time from diagnosis with POS to initiation of monotherapy and AT
 - the supply of medicine (in days) for the different AEDs
 - the annual cost of each AED
 - which AEDs were successful as monotherapy for patients with POS.

METHODS

- This retrospective study was performed using the Human Capital Management Systems (HCMS) database of commercially insured subjects.
 - The database reflects multiple, geographically diverse, US-based employers in the retail, service, manufacturing, and financial industries, and includes information on more than 2 million employees, plus their spouses and eligible dependents.
 - Data were extracted from claims made between January 1, 2001 and June 30, 2014.
 - The HCMS database has previously been used to evaluate the costs of specific health conditions to employers.^{5,6}
 - The data were de-identified to comply with the Health Insurance Portability and Accountability Act, and the contractual obligations between HCMS and its employer-contributors.

Inclusion criteria

- Subjects with POS (patients) were identified by the occurrence of any primary, secondary or tertiary claims containing International Classification of Diseases, 9th Revision (ICD-9) codes for localization-related (focal/partial) epilepsy and epileptic syndromes with:
 - complex partial seizures (ICD-9 = 345.4x) or
 - simple partial seizures (ICD-9 = 345.5x).
- Subjects were required to have >365 days of continuous eligibility following initial AED use.

Exclusion criteria

- Employees: diagnosed with any form of epilepsy (ICD-9 = 345.x).
- Subjects: concomitant use of a second AED for >90 days.

Outcomes

- Days from diagnosis with POS to initiation of therapy.
- Based on adjudicated prescription claims in each subject's 12-month follow-up period:
 - the most commonly used AEDs
 - annual supply of medicine (days) per user for each AED
 - mean annual cost per user (total prescription costs divided by number of subjects using each AED)
 - mean annual cost for the cohort (total prescription costs per AED divided by the number of subjects in the cohort).
- All costs were adjusted for inflation to September 2014 US dollars (prescription costs, the prescription component) and all other costs were calculated using the 'all other' component of the Consumer Price Index.⁷

RESULTS

- 367 pairs were identified in which the subject had POS and the employee did not have epilepsy.
 - 238 subjects (64.9%) were using AED monotherapy.
 - These subjects began taking their first AED as monotherapy an average of 18 days after being diagnosed with POS.
 - Baseline characteristics of the 238 pairs (the 'monotherapy cohort') are shown in **Table 1**.
 - 129 subjects (35.1%) were excluded due to use of AED AT (concomitant use of more than one AED for >90 days).
 - These subjects began taking AT an average of 57 days after being diagnosed with POS.
 - Subjects who progressed from monotherapy to AT did so after an average of 41 days.

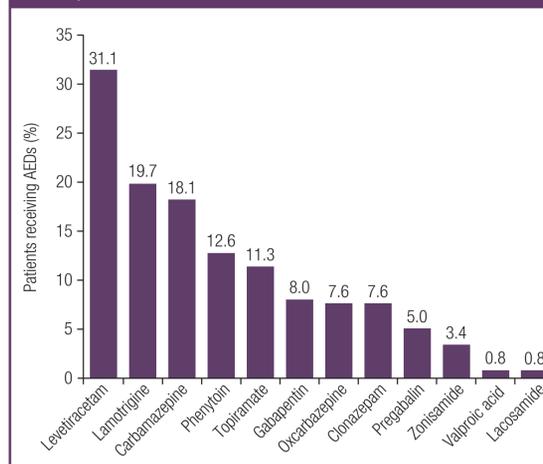
Table 1. Baseline demographic and clinical characteristics for the monotherapy cohort (n = 238)

Characteristic	Value
Employees	
Age, years; mean (SE)	45.15 (0.67)
Tenure, ^a years; mean (SE)	9.86 (0.59)
Female, %	31.5
Exempt (salaried), ^b %	47.9
Annual salary, \$; mean (SE)	73,549 (2871)
Full-time employment, %	98.7
Charlson Comorbidity Index score; mean (SE)	0.37 (0.07)
Subjects ^c	
Age at index date, years; mean (SE)	44.65 (0.68)
Female, %	68.1
Charlson Comorbidity Index score; mean (SE)	0.96 (0.11)

^aDuration of employment.
^bDenotes exempt status from certain time-tracking requirements.
^cPatients with POS treated with AED monotherapy.
 AED: antiepileptic drug; POS: partial-onset seizures; SE: standard error.

- The AEDs most commonly used as monotherapy during 1 year of follow-up were levetiracetam (31% of subjects), lamotrigine (20%), carbamazepine (18%), phenytoin (13%) and topiramate (11%; **Figure 1**).

Figure 1. AEDs commonly used as monotherapy during 1 year follow-up^a



^aIn the monotherapy cohort (238 patients with POS).
 AED: antiepileptic drug; POS: partial-onset seizures.

- The supply of medicine (days) per subject for each AED used as monotherapy during the follow-up year is shown in **Table 2**.

Table 2. Mean annual supply per subject, for AEDs used as monotherapy during 1 year of follow-up

AED	Annual AED supply per subject (days)	
	n	Mean (SE)
Carbamazepine	43	332 (28)
Phenobarbital	7	330 (59)
Phenytoin	29	312 (35)
Oxcarbazepine	18	288 (34)
Lamotrigine	45	284 (27)
Levetiracetam	74	278 (19)
Topiramate	27	239 (40)
Clonazepam	18	217 (31)
Valproic acid	2	180 (150)
Lacosamide	2	165 (105)
Gabapentin	18	164 (31)
Pregabalin	12	140 (40)
Zonisamide	7	70 (31)

AED: antiepileptic drug; SE: standard error.

- For AEDs used as monotherapy during the 1-year follow-up period, the annual costs are shown in **Tables 3** and **4**. **Table 3** shows the mean cost per subject for each AED group, and **Table 4** shows the mean cost per subject in the total monotherapy cohort.

Table 3. Costs per year for AEDs used as monotherapy (per AED group)

AED	n	Cost per patient (\$) Mean (SE)
Lamotrigine	45	3277.64 (932.61)
Topiramate	27	2564.71 (831.72)
Levetiracetam	74	2451.73 (434.29)
Lacosamide	2	2203.29 (1330.25)
Oxcarbazepine	18	1485.07 (341.64)
Carbamazepine	43	819.49 (122.30)
Pregabalin	12	769.20 (227.21)
Gabapentin	18	413.83 (104.98)
Phenytoin	29	364.51 (47.61)
Valproic acid	2	304.99 (259.65)
Zonisamide	7	292.35 (213.41)
Clonazepam	18	117.86 (50.64)
Phenobarbital	7	46.09 (13.35)

^aBased on number of patients taking each AED (n).
 AED: antiepileptic drug; SE: standard error.

Table 4. Costs per year for AEDs used as monotherapy (for the monotherapy cohort)

AED	Cost per patient (\$) Mean (SE)
Levetiracetam	762.30 (153.29)
Lamotrigine	619.72 (193.60)
Topiramate	290.95 (106.77)
Carbamazepine	148.06 (29.97)
Oxcarbazepine	112.32 (35.83)
Phenytoin	44.42 (9.62)
Pregabalin	38.78 (15.50)
Gabapentin	31.30 (10.50)
Lacosamide	18.52 (15.28)
Clonazepam	8.91 (4.24)
Zonisamide	8.60 (6.65)
Valproic acid	2.56 (2.38)
Phenobarbital	1.36 (0.62)

^aBased on all patients in the monotherapy cohort (n = 238).
 AED: antiepileptic drug; SE: standard error.

CONCLUSIONS

- In this retrospective study, approximately two thirds of subjects with POS who initiated monotherapy with an AED did not progress to AT within a year.
- Subjects who progressed to AT usually did so within 4–6 weeks.
- Levetiracetam, lamotrigine, carbamazepine, phenytoin, and topiramate were the AEDs most frequently used as monotherapy.
 - These AEDs also had the highest days' supply.
 - Among these frequently-used drugs, carbamazepine and phenytoin were the least costly of the top five, on a per-patient basis.

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DISCLOSURES

FV: employee of Sunovion Pharmaceuticals Inc. RB: employee of The JeSTARx Group. JY: employee of HCMS Group.

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