

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: primarily 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 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 commonly used as part of an adjunctive therapy regimen 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 continuous eligibility following initial AED use and concomitant use of a second AED for >90 days.

Exclusion criteria

- Employees: diagnosed with any form of epilepsy (ICD-9 = 345.x).
- Subjects: managed by monotherapy

METHODS (Continued)

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

Table 1. Baseline demographic and clinical characteristics for the Adjunctive Therapy cohort (n = 129)

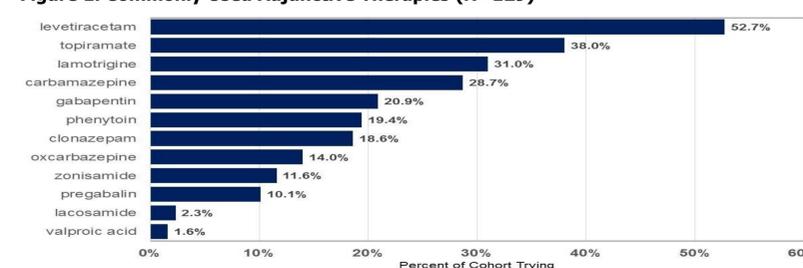
Variable	
Employees:	
Age at index date, years; mean (SE)	44.14 (0.87)
Tenure, ^a years; mean (SE)	10.24 (0.80)
Female, %	27.9%
Exempt (salaried), ^b %	37.2%
Annual salary, ^c \$; mean (SE)	\$63,758 (\$3,283)
Full-time Employment, %	98.4%
Charlson Comorbidity Index score; mean (SE)	0.31 (0.08)
Subjects^d:	
Age at index date, years; mean (SE)	43.38 (0.90)
Female, %	72.1%
Charlson Comorbidity Index score; mean (SE)	1.05 (0.17)

^a Duration of employment.
^b Denotes exempt status from certain time-tracking requirements.
^c N for Salary=123
^d Patients with POS treated with AED monotherapy.
 SE: standard error.

- The AEDs most commonly used as AT during 1 year of follow-up were levetiracetam (52.7% of subjects), topiramate (38.0%), lamotrigine (31.0%), carbamazepine (28.7%), and gabapentin (20.9%) (**Figure 1**).

RESULTS (Continued)

Figure 1. Commonly Used Adjunctive Therapies (N=129)



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

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

AED	Annual AED supply per subject (days)	
	N	Mean (SE)
phenytoin	23	308 (46)
carbamazepine	36	290 (26)
lamotrigine	40	282 (25)
levetiracetam	68	279 (17)
gabapentin	28	267 (30)
zonisamide	12	259 (49)
topiramate	48	255 (25)
pregabalin	15	253 (35)
Phenobarbital	8	237 (58)
valproic acid	2	197 (17)
oxcarbazepine	17	193 (38)
clonazepam	24	148 (28)
lacosamide	3	85 (48)

AED: antiepileptic drug; SE: standard error.

- For AEDs used as adjunctive therapy 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.
- Table 4** shows the mean cost per subject in the total adjunctive therapy cohort.

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

AED	N	Cost per patient (\$) Mean (SE)
lamotrigine	40	\$4,842.69 (\$1,579.98)
levetiracetam	68	\$2,539.39 (\$367.37)
topiramate	48	\$1,945.32 (\$372.24)
pregabalin	15	\$1,944.35 (\$318.31)
phenytoin	23	\$1,129.63 (\$738.21)
lacosamide	3	\$1,009.17 (\$399.59)
carbamazepine	36	\$977.55 (\$140.23)
zonisamide	12	\$909.58 (\$339.15)
oxcarbazepine	17	\$872.91 (\$230.19)
gabapentin	28	\$857.70 (\$193.57)
valproic acid	2	\$267.71 (\$19.92)
Phenobarbital	8	\$125.79 (\$91.42)
clonazepam	24	\$97.08 (\$45.67)

^aBased on all patients in the adjunctive therapy cohort (n = 129). AED: antiepileptic drug; SE: standard error.

RESULTS (Continued)

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

AED	Cost per patient (\$) Mean (SE)
lamotrigine	\$1,501.61 (\$524.44)
levetiracetam	\$1,338.60 (\$223.15)
topiramate	\$723.84 (\$160.75)
carbamazepine	\$272.80 (\$54.79)
pregabalin	\$226.09 (\$65.75)
phenytoin	\$201.41 (\$134.76)
gabapentin	\$186.17 (\$51.89)
oxcarbazepine	\$115.04 (\$39.42)
zonisamide	\$84.61 (\$38.27)
lacosamide	\$23.47 (\$15.45)
clonazepam	\$18.06 (\$8.99)
Phenobarbital	\$7.80 (\$5.96)
valproic acid	\$4.15 (\$2.93)

^a Based on all patients in the adjunctive therapy cohort (n = 129). AED: antiepileptic drug; SE: standard error.

CONCLUSIONS

- In this retrospective study, approximately one third of subjects with POS who initiated monotherapy with an AED progressed to adjunctive therapy within a year.
- Subjects who progressed to adjunctive therapy usually did so within 4–6 weeks.
- Levetiracetam, topiramate, lamotrigine, carbamazepine, and gabapentin were the AEDs most frequently used as adjunctive therapy.
 - These AEDs also had high days' supply.
 - Carbamazepine and gabapentin were the least costly of the top five on a per-patient basis.

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DISCLOSURES

FFV: employee of Sunovion Pharmaceuticals Inc. RAB: employee of The JeSTARx Group. JWY: former employee of HCMS Group. JES: employee of The JeSTARx Group.

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