

# Annual Healthcare Costs and Utilization in Adults Taking Long or Short Acting Antiepileptic Monotherapy

Cramer JA<sup>1</sup>, Wang Z<sup>2</sup>, Chang E<sup>3</sup>, Copher R<sup>2</sup>, Cherepanov D<sup>3</sup>, Broder M<sup>3</sup>

<sup>1</sup>Yale School of Medicine, <sup>2</sup>Eisai Inc., <sup>3</sup>Partnership for Health Analytic Research, LLC

## BACKGROUND

- Epilepsy, the 4<sup>th</sup> most common neurological disorder, affects about 2.2 million people in the United States and accounts for \$9.6 billion/year in direct medical costs.<sup>1</sup>
- A variety of AEDs and other therapies are available to treat epilepsy. However, adherence to antiepileptic drugs (AEDs) is imperfect; lack of adherence which has been linked to increased healthcare utilization and cost.<sup>2,3</sup>
- It has been hypothesized that patients who are not adherent to therapy may experience breakthrough seizures. It is important to assess whether AEDs with long duration of action might mitigate the impact of poor adherence on healthcare costs.

## OBJECTIVE

- To compare the healthcare costs and utilization between patients treated with long-acting (LA) and short-acting (SA) AED monotherapy.

## METHODS

- This was a cross-sectional retrospective cohort study using data from a commercial HIPAA-compliant administrative claims database.
- Study population included adults (≥18 years old), diagnosed with epilepsy, and treated with LA<sup>a</sup> or SA<sup>b</sup> AED monotherapy during calendar year 2011 (study period).
- AEDs were grouped into those with increased half-life or longer duration of action<sup>4</sup> (extended or controlled release) and short-acting AEDs:
- LA AEDs:** dilantin, phynitek, phenytoin (PHT ER); carbamazepine ER, carbazol, tegretol ER (CBZ ER); topiramate, topamaz, topiragen (TPM); divalproex ER, depakote ER (DVP ER); divalproex DR, depakote DR (DVP DR); phenobarbital, luminal (PB); levetiracetam ER, keppra ER (LEV ER); zonisamide, zonegran (ZNS).
- SA AEDs:** levetiracetam, keppra (LEV); lamotrigine, lamictal (LTG); carbamazepine, epital, tegretol (CBZ); oxcarbazepine, trileptal (OXC).

### Inclusion Criteria:

- ≥2 medical claims (≥30 days apart) with epilepsy diagnosis (ICD-9-CM 345.xx or 780.39) in any diagnosis field, with 1 claim occurring in the study period and 1 in the prior year;
- ≥2 pharmacy claims or AEDs<sup>a-b</sup> in the study period;
- AND ≥18 years at the end of the study period.

### Exclusion Criteria:

- >1 type of AED filled in the study period;
- not continuously enrolled during the study period and for 3 months prior; OR
- <9 months treatment duration or a treatment gap >60 days.

**Study Cohorts:** the study sample was stratified into two cohorts:

- LA users<sup>a</sup>** – PHT ER, CBZ ER, TPM, DVP ER, DVP DR, PB, LEV ER, or ZNS.
- SA users<sup>b</sup>** – LEV, LTG, CBZ, or OXC.

**Measures:** All claims in study period were used to determine study measures

• Outcomes: overall costs and utilization, epilepsy-related costs (claims with an epilepsy diagnosis or epilepsy-related tests) and utilization (AED fills and services with an epilepsy diagnosis).

• Other measures:

• AED adherence: Medication Possession Ratio (MPR) defined as total days of therapy available in the study period divided by 365.

• demographics, usual care physician specialty (specialty seen at the most visits),<sup>5</sup> number of chronic conditions, Charlson comorbidity index (CCI),<sup>6</sup> and epilepsy-specific comorbidities.

**Statistical Analyses:** SAS® version 9.3 was used for all analyses.

• Chi-square test or t-test were used for descriptive comparisons and regression and logistic regression models were used to adjust for cohort differences. All tests were 2-sided with significance level of 0.05.

### Cohort Identification

- 8,180 adult AED users met the study selection criteria, of which
  - 4,058 (49.6%) used LA AEDs and 4,122 (50.4%) used SA AEDs.

### Patient Characteristics

- Mean age was 47.7 years for LA users and 45.1 years for SA users (p<.001).
- 47.6% of LA users and 57.0% of SA users were female (p<.001).
- The cohorts did not differ in geographic distribution: 45.8% were from the South, 29.6% were from the Midwest, 14.1% were from the West, and 10.4% were from the Northeast (p=.829).
- LA and SA users most frequently received their usual care from primary care physicians (52.4% vs. 39.6%), followed by neurologists (28.9 vs. 39.5%), and other specialists (18.7% vs. 20.9%; p<.001).
- LA and SA users were not significantly different (p=0.125) in AED adherence, with a mean MPR of 0.899 (SD: 0.13; median: 0.953) in LA users versus MPR of 0.903 (SD: 0.13; median: 0.959) in SA users.

### Comorbidity

- LA users had a lower mean number of chronic conditions (2.9 vs. 3.1) and mean CCI (0.7 vs. 0.8) (all p<.001).
- A lower proportion of LA users had any epilepsy-specific comorbidity (19.0% vs. 25.0%; p<.001).
- Compared with SA users, fewer LA users had head injury (0.4% vs. 0.8%), brain tumor (2.3% vs. 5.7%), cerebrovascular disease (7.1% vs. 9.7%), and depression and other mood disorders (10.6% vs. 12.0%) (all p<.05).

### Annual Overall and Epilepsy-Related Healthcare Costs

	LA Users n=4,058	SA Users n=4,122	P Value
<b>Mean (SD)</b>			
<b>Overall cost, \$</b>	9,757 (21,634)	12,689 (25,358)	<.001
Non-pharmacy cost, \$	6,745 (19,984)	8,331 (23,557)	0.001
Pharmacy cost, \$	3,012 (4,891)	4,358 (6,042)	<.001
<b>Epilepsy-related cost, \$</b>	3,539 (11,077)	5,279 (17,157)	<.001
Non-AED cost, <sup>a</sup> \$	2,355 (10,896)	3,197 (17,002)	0.008
AED cost, \$	1,184 (1,733)	2,082 (2,412)	<.001

AED, antiepileptic drug; LA, long-acting; SA, short-acting; SD, standard deviation.  
<sup>a</sup> Medical claims with epilepsy diagnosis in any diagnosis field or epilepsy-related tests.

- Compared with SA users, LA users' costs were lower by:

- \$2,932 for overall costs, including \$1,586 less in non-pharmacy costs and \$1,346 less in pharmacy costs (all p≤.001); and
- \$1,740 for epilepsy-related costs, including \$842 less in non-AED costs and \$898 less in AED costs (all p≤.008).

## RESULTS

### Annual Overall and Epilepsy-Related Healthcare Utilization

	LA Users n=4,058	SA Users n=4,122	P Value
<b>Annual Overall Healthcare Utilization</b>			
<b>Inpatient hospitalizations, n (%)</b>			0.003
0	3,704 (91.3)	3,676 (89.2)	
1	295 (7.3)	357 (8.7)	
2+	59 (1.5)	89 (2.2)	
<b>ED visits, n (%)</b>			0.009
0	3,735 (92.0)	3,724 (90.3)	
1	156 (3.8)	184 (4.5)	
2	35 (0.9)	64 (1.6)	
3+	132 (3.3)	150 (3.6)	
<b>Office visits, mean (SD)</b>	8.8 (9.4)	9.9 (10.0)	<.001
<b>Annual Epilepsy-Related<sup>b</sup> Healthcare Utilization</b>			
<b>Inpatient hospitalizations, n (%)</b>			0.005
0	3,826 (94.3)	3,812 (92.5)	
1	208 (5.1)	279 (6.8)	
2+	24 (0.6)	31 (0.8)	
<b>ED visits, n (%)</b>			0.343
0	4,037 (99.5)	4,094 (99.3)	
1+	21 (0.5)	28 (0.7)	
<b>Office visits, mean (SD)</b>	1.8 (1.5)	2.0 (1.6)	<.001

AED, antiepileptic drug; ED, emergency department; EEG, electroencephalograph; LA, long-acting; SA, short-acting; SD, standard deviation.  
<sup>b</sup> Medical services with claims with epilepsy diagnosis in any diagnosis field or epilepsy-related tests.

- Compared with SA users, LA users had a:

- lower rate of overall and epilepsy-related hospitalization,
- fewer overall ED visits,
- fewer mean number of overall and epilepsy-related office visits,
- and higher rate of testing for AED levels,
- but a lower rate EEGs and brain imaging studies (all p<.01).

### Adjusted Estimates for LA Users vs. SA Users

Outcome Variable	Coefficient	SE	P Value
<b>Mean overall healthcare costs, \$</b>	-686	460	0.137
<b>Mean epilepsy-related<sup>c</sup> healthcare costs, \$</b>	-894	319	0.005
	<b>OR</b>	<b>95% CI</b>	<b>P Value</b>
<b>Risk of inpatient hospitalization</b>	1.02	0.87 – 1.21	0.772
<b>Risk of epilepsy-related<sup>d</sup> inpatient hospitalization</b>	0.94	0.78 – 1.13	0.497

CI, confidence interval; OR, odds ratio; SE, standard error.  
<sup>c</sup> Medical claims with epilepsy diagnosis in any diagnosis field or epilepsy-related tests.  
<sup>d</sup> Inpatient hospitalizations with epilepsy diagnosis in any diagnosis field.

- After adjusting for demographics, usual care physician specialty, and comorbidities:
  - Mean overall costs were lower by \$686 (p=.137) and mean epilepsy-related costs were lower by \$894 (p=.005) in LA users than in SA users; and
  - Odds of overall and epilepsy-related inpatient hospitalization were the same for both cohorts.

## LIMITATIONS

- MPR captures the rate of AED fills only. Missing individual doses and other non-adherence behaviors are not captured by MPR, but may affect outcomes.
- Claims data are collected for payment and do not capture disease severity.
- The study may not be generalizable to a non-managed care population.
- Epilepsy-related costs account for less than 50% of total observed costs which suggests that comorbid conditions may be costly and/or that epilepsy-related utilization was under-identified.

## CONCLUSIONS

- Although MPR was similar in LA and SA groups, patients treated with LA AED monotherapy incur a lower economic burden than those treated with SA AED monotherapy.
- Adherence may also be impacted by convenience as LA AEDs have fewer doses per day relative to the SA AEDs.
- Use of AEDs with extended duration of action may decrease healthcare use and lower costs.
- Future studies should assess the impact of duration of action on outcomes in combination therapy and in adolescents, and also examine reasons for the observed cohort differences in the current study.

## REFERENCES

- IOM (Institute of Medicine). Epilepsy across the spectrum: Promoting health and understanding. Washington, DC: The National Academies Press, 2012.
- Davis KL, Cadrillili SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. *Epilepsia*. 2008; 49:446-454.
- Ettinger AB, Manjunath R, Cadrillili SD, Davis KL. Prevalence and cost of nonadherence to antiepileptic drugs in elderly patients with epilepsy. *Epilepsy Behav* 2009; 14:324-329.
- Patsalos PN, Berry DJ, Bourgeois BF, et al. Antiepileptic drugs—best practice guidelines for therapeutic drug monitoring: a position paper by the subcommission on therapeutic drug monitoring, ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2008;49(7):1239-76.
- O'Malley AS, Pham HH, Schrag D, Wu B, Bach PB. Potentially avoidable hospitalizations for COPD and pneumonia: the role of physician and practice characteristics. *Med Care*. 2007;45(6):562-70.
- Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613-619.