Comparisons of the Health Benefit Costs Among Monotherapy and Adjunctive Therapy Patients with Epilepsy and Their Employed Spouses

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BACKGROUND

- Approximately 1/3 of patients with partial-onset seizures (POS) are drug resistant and frequently require adjunctive treatment.[1]

OBJECTIVE

- To compare direct care costs, health-benefit costs, and absenteeism among patients with POS receiving monotherapy vs. adjunctive therapy, and among their respective employed spouses, in a real-world setting.

METHODS

- Retrospective study using the Human Capital Management Systems (HCMS) database of commercially insured subjects.
  - Represents multiple geographically diverse, US-based employers in the retail, service, manufacturing, and financial industries and includes information on more than 2 million employees plus spouses and eligible dependents.
  - Extracted from claims between January 2001 to June 30, 2014.
  - The HCMS database has been used in prior research about epilepsy and employees.[2,3]
  - 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:
  - Spouses of employees (subjects) with partial onset seizures were identified by any primary, secondary or tertiary claims containing International Classification of Diseases 9th revision Clinical Modification (ICD-9) codes for localization-related (focal) (partial) epilepsy:
    - 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 anti-epilepsy drug (AED) use.
- Exclusion criteria:
  - Employee-partners of the spouses (employees) with partial onset seizures diagnosed with any form of epilepsy (ICD-9=345.x).

Cohort assignment and index dates:

- Subjects with concomitant use of a second AED for >90 days were classified as adjunctive therapy users and assigned an index date based on their second AED prescription.
- Subjects without concomitant use of a second AED were classified as monotherapy users and their initial AED prescription date was the index for monotherapy patients.
- All employee-spouse pairs had >365 days continuous eligibility post index.

Outcomes

- For the subjects:
  - Direct medical costs
  - Direct prescription costs for AEDs
  - Direct prescription costs for non-AEDs
- For the employees:
  - Health benefit costs, which include:
    - Direct medical costs
    - Direct prescription costs, and
    - Indirect costs due to payments for:
      - Sick Leave
      - Short-term Disability
      - Long-term Disability
      - Workers' Compensation (which also includes payments to providers under the workers' compensation benefit).

METHODS (Continued)

Outcomes (Continued)

- Lost time (in days) due to absences classified as:
  - Sick Leave
  - Short-term Disability
  - Long-term Disability, and
  - Workers' Compensation
- All costs were inflation-adjusted to September 2014 dollars
  - Medical costs used the medical cost component of the Consumer Price Index (CPI)
  - Prescription costs the prescription component
  - All other costs used the all other component of the CPI[4]

Comparisons were made for all outcomes between the adjunctive- and monotherapy cohorts.

- Descriptive components (demographic, job-related variables, and region) were compared between cohorts using:
  - T-tests for continuous variables
  - Chi-square (X^2) tests for binary variables
- Separate two-part regression models were used for each variable controlling for demographic, job-related, and other variables.
  - Part 1: Logistic
  - Part 2: Generalized Linear Models
- The employee models controlled for differences in: age, tenure (years with current employer), sex, marital status, race, exempt/non-exempt status (exempt employees are not paid on an hourly basis and are not paid for overtime work), full-time/part-time status, salary, employee's Charlson Comorbidity Index,[5] and geography (defined by the first digit of the employee's postal zip code).
  - Only employees eligible for each specific absence benefit were included in the regression models for that benefit. Indirect costs were summed over all absence claims begun at some point during the year following the index date.
- The subject models controlled for differences in age, sex, marital status, employee's job-related variables (i.e., exempt/non-exempt status, full-time/part-time status, and salary), subject's Charlson Comorbidity Index, and geography.
- Because different models were used for each component, the models were not additive.
- Differences were considered significant if $P<0.05$.
- All analyses conducted in SAS (version 9.3).

RESULTS

- The 367 employee-subject pairs were classified based on the subject's partial onset seizure therapy:
  - 129 (35.1%) were receiving adjunctive therapy
  - 238 (64.9%) were receiving monotherapy
  - Demographic comparisons between the two cohorts are in Table 1.
- The analysis of costs (Table 2) found:
  - Compared with those receiving monotherapy, subjects with epilepsy receiving adjunctive therapy had:
    - $12,293 higher direct medical costs ($30,315 vs. $18,022, $P=0.0010$)
    - $2,596 higher AED prescription costs ($4,500 vs. $1,904, $P<0.0001$)
    - $1714 higher non-AED prescription ($4,674 vs. $2,960, $P=0.0034$)
      $16,603 higher total costs ($39,489 vs. $22,885, $P<0.001$)
  - Compared with employees whose spouses were treated with monotherapy, employed spouses of adjunctively-treated subjects had:
    - $2294 higher medical costs ($4801 vs. $2507, $P=0.0002$)
    - $524 higher sick leave costs ($1086 vs. $563, $P<0.0001$)
    - $296 lower workers' compensation costs ($7 vs. $302, $P<0.05$)

RESULTS (Continued)

- The analysis of lost time due to absences (Figure 1), revealed:
  - Compared with employees whose spouses were treated with monotherapy, employed spouses of adjunctively-treated subjects had more:
    - Sick leave absence time (4.38 vs. 2.45 days, $P < 0.0001$)
    - Short-term disability absence time (0.69 vs. 0.26 days, $P > 0.05$)
  - No days were lost for either cohort under the long-term disability or workers' compensation benefit.

Table 1: Descriptive Statistics for Employees with Spouses* Diagnosed with Partial Onset Epilepsy

Variable	Monotherapy (N=238**) Mean	Monotherapy (N=238**) Standard Error	Adjunctive therapy (N=129***) Mean	Adjunctive therapy (N=129***) Standard Error	Comparison: Difference between cohorts	Comparison: *P*-value
Employee:						
Age, years (at index)	45.15	0.67	44.14	0.87	-1.01	0.3667
Tenure, in years (at index date)	9.86	0.59	10.24	0.80	0.38	0.7062
Gender=Female, percent	31.5%	3.0%	27.9%	4.0%	-3.6%	0.7693
Self-reported race:	38.2%	3.2%	37.2%	4.3%	-1.0%	0.9815
white, percent	38.2%	3.2%	37.2%	4.3%	-1.0%	0.9815
black, percent	5.5%	1.5%	5.4%	2.0%	0.0%	0.9999
Hispanic, percent	5.5%	1.5%	7.8%	2.4%	2.3%	0.7132
other race, percent	2.1%	0.9%	2.3%	1.3%	0.2%	0.9905
race missing, percent	48.7%	3.2%	47.3%	4.4%	-1.5%	0.9654
Exempt, percent	47.9%	3.2%	37.2%	4.3%	-10.7%	0.1369
Annual salary (in $US)	**$73,549**	**$2,871**	**$63,758**	**$3,283**	**-$9,792**	**0.0341**
Full-time status, Percent	98.7%	0.7%	98.4%	1.1%	-0.3%	0.9758
Charlson Comorbidity Index score	0.37	0.07	0.31	0.08	-0.06	0.6061
Subject						
Age, years (at index)	44.65	0.68	43.38	0.90	-1.27	0.2657
Gender=Female, percent	68.1%	3.0%	72.1%	4.0%	4.0%	0.7217
Charlson Comorbidity Index score	0.96	0.11	1.05	0.17	0.09	0.6408

*Information on this table based on HR data, existence of 'spouse' based on Benefits data.
** *N* for annual salary is 230 and N is 238 for other variables.
***N for Age and Tenure is 128, N for Annual Salary is 123, and N is 129 for other variables.

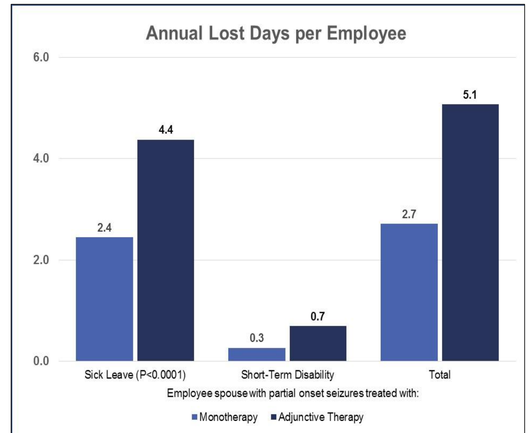
Table 2: Annual Direct Costs for Subjects with Partial Onset Seizures and Employees Health Benefit Costs[1] (per cohort)

Cost Category	Cohorts: Monotherapy (N = 238) Mean	Monotherapy (N = 238) S.E.	Adjunctive therapy (N = 129) Mean	Adjunctive therapy (N = 129) S.E.	Comparisons: Δ in means	Comparisons: *P*-value
Subjects:						
Medical	**$18,022**	**$1,498**	**$30,315**	**$3,418**	**$12,293**	**0.0010**
AED Drugs	**$1,904**	**$147**	**$4,500**	**$472**	**$2,596**	**<0.0001**
Non-AED Prescription Drugs	**$2,960**	**$247**	**$4,674**	**$530**	**$1,714**	**0.0034**
Total Subject Direct Costs (sum)	$22,885		$39,489		$16,603	
Employee Health Benefit Costs:						
Direct Components:						
Medical	**$2,507**	**$218**	**$4,801**	**$580**	**$2,294**	**0.0002**
Rx Drugs	$1,169	$107	$1,539	$191	$370	0.0907
Total Employee Direct Costs (sum)	$3,676		$6,340		$2,664	
Total Employee + Subject Direct costs	$26,561		$45,828		$19,267	
Indirect Components[2]						
Sick leave	**$563**	**$37**	**$1,086**	**$87**	**$524**	**<0.0001**
Short-term Disability	$17	$15	$60	$31	$43	0.2200
Long-term Disability[2]	---	---	---	---	---	---
Workers' Compensation	**$302**	**$151**	**$7**	**$7**	**-$296**	**0.0497**
Total Indirect Costs (sum of above)	$379		$848		$469	
Total Employee Costs (direct + indirect)	$4,055		$7,187		$3,133	
Total Employee Costs (direct + indirect) and Subject Direct Costs	$26,940		$46,676		$19,736	

[1] Costs were calculated using two-part (logistic-GLM) regression modeling by controlling for age, tenure, marital status, race, exempt status, full-time/part-time status, salary, location, Charlson Comorbidity Index Score (of the person being modeled), and other measures.
[2] Not modeled. No employees used Long-Term Disability benefits during the study period.
[3] The indirect benefit N's for the **Adjunctive therapy** cohort. Sick Leave: 78, Short-Term Disability: 112, Long-Term Disability: 100, Workers' Compensation: 122
[3] The indirect benefit N's for the **Monotherapy** cohort. Sick Leave: 118, Short-Term Disability: 202, Long-Term Disability: 185, Workers' Compensation: 221

RESULTS (Continued)

Figure 1: Annual Lost Days[1] per Employee Whose Spouses Have Partial Onset Epilepsy and Are Treated with Mono- or Adjunctive Therapy



[1] Days were calculated using two-part (logistic-GLM) regression modeling by controlling for age, tenure, marital status, race, exempt status, full-time/part-time status, salary, location, Charlson Comorbidity Index Score (of the employee), and other measures.

CONCLUSIONS

- In this retrospective study, adjunctively-treated subjects with epilepsy and their employed spouses had significantly higher medical and sick leave costs than monotherapy-treated subjects and their employed spouses.
- These differences were present in nearly all cost categories.
- The findings of this study suggest an increased burden of drug-resistant epilepsy on subjects and employees.

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Supported by funding from Sunovion Pharmaceuticals, Inc. RB, JES, and JWY are consultants that provide services to several pharmaceutical companies, including Sunovion Pharmaceuticals Inc. FV is an employee of Sunovion Pharmaceuticals Inc.

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