

Reasons for treatment discontinuation and switch in patients with epilepsy: a retrospective observational study in a US population

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INTRODUCTION

- Epilepsy is the fourth most prevalent neurological disorder in the US.
- An important goal of treatment is to achieve seizure freedom, but this is frequently hampered by patients' inability to continue on to the prescribed regimen, due to either lack of efficacy or tolerability issues.
- The availability of real-world data from US outpatient visits provides an opportunity to elucidate the reasons for treatment discontinuations and switches among patients with epilepsy.

OBJECTIVE

- To evaluate patient characteristics associated with antiepileptic drug (AED) discontinuations and switches among patients with epilepsy.

STUDY DESIGN

- A retrospective analysis of the RealHealthData medical transcription database (www.RealHealthData.com) was conducted.
 - Data were collected between January, 2002, and April, 2014.
 - The database includes data derived from transcriptions of narrative medical records, providing a detailed list of diagnoses, based on patient interactions with physicians from different specialties across the US.
 - The database comprises more than five million records, and multiple records for each patient, which allows for retrospective longitudinal analysis.
- Inclusion criteria: adult patients (aged ≥18 years) with a diagnosis of epilepsy and ≥1 AED prescription.
- Patients were grouped into four cohorts based on their history of AED discontinuations and switches during the entire study period.

Definition of cohorts

Switch: at least one transcript record of a switch in AED treatment, and no record of a discontinuation.

Discontinuation: at least one transcript record of a discontinuation of AED treatment, and no record of an AED switch.

Discontinuation/switch: at least one record of discontinuation of AED treatment, and of at least one AED switch.

No discontinuation/switch: no records of either a discontinuation of AED treatment, or an AED switch.

- Patient demographics and medications for the four cohorts were compared.

Data analysis

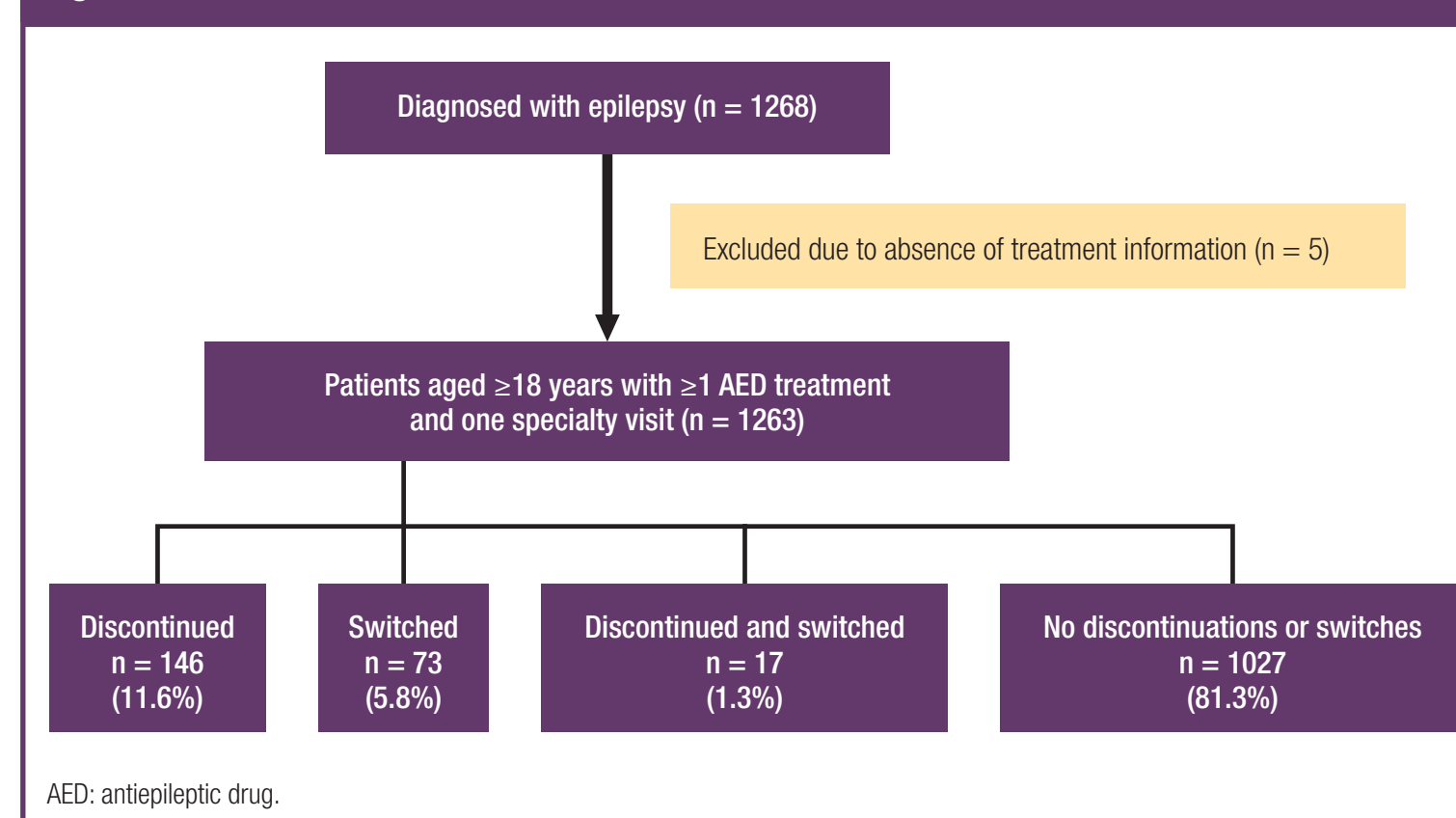
- Continuous data were expressed as mean, standard deviation (SD), and median.
- Comparisons between groups were conducted using either the Wilcoxon rank-sum test, the Kruskal-Wallis test for nominal/ordinal data, or the chi-square test for continuous data.
- Correlations were analyzed using Pearson's correlation analysis.
- The statistical analysis was conducted using Statistical Analysis System (SAS®) Version 9.3.

RESULTS

Patient selection

- Of the 1268 patients with epilepsy identified from the database, 1263 met the inclusion criteria and were eligible for the analysis (Figure 1).
- Overall, 146 patients (11.6%) discontinued AED treatment, 73 patients (5.8%) switched AEDs, 17 patients (1.3%) both discontinued and switched AEDs, and 1027 patients (81.3%) did not discontinue or switch AED treatment.

Figure 1. Patient selection from the RealHealthData database



Patient demographics and clinical characteristics

- The patients' median age was 42 years (range 18–90) (Table 1).
- The majority of patients were Caucasian and the gender proportions were similar between groups, with the exception of the discontinuation/switch group, in which the proportion of females (76.5%) was notably higher than the proportion of males (23.5%; not significant) (Table 1).
- A low proportion of patients had previously undergone epilepsy-related surgery (2.4%) or vagal nerve stimulation (5.5%) (Table 1).
- In all groups, depression was the most frequent comorbidity (13.6% of patients). Other comorbidities present in all groups were: hypertension, migraine, and mental retardation (Table 1).

Reasons for switch/discontinuation of AED treatment

- The most common reasons for AED switches and discontinuations (Table 2) were adverse events (AEs; side effects) (41% and 47% of patients, respectively) and lack of treatment efficacy (16% and 10% of patients, respectively).
- Switching treatment was partially correlated with the following: body weight (Pearson's correlation coefficient: $r = 0.36$), age ($r = 0.21$), physician specialty ($r = 0.22$), Charlson Comorbidity Index (CCI) score ($r = 0.19$) and seizures per year ($r = 0.12$) (Table 3).
- Discontinuation of treatment was correlated with the following: age ($r = -0.20$), drug/alcohol abuse ($r = -0.18$), weight gain ($r = -0.18$) and type of seizures ($r = -0.19$), all being statistically significant correlations (Table 3).

Table 1. Patient demographics and clinical characteristics

Variable	All patients n = 1263	Switched n = 73	Discontinued n = 146	Switched/ discontinued/ n = 17	No discontinuations/ switches n = 1027	p
Age, years						
Mean (SD)	42.3 (17.3)	36.8 (16.2)	39.5 (16.6)	40.0 (21.3)	43.1 (17.3)	0.2456
Median (range)	42 (18–90)	33 (18–79)	37 (18–84)	34 (18–86)	43 (18–90)	
Gender (%)						0.5521
Female	52.4	50.7	54.8	76.5	51.8	
Male	47.4	49.3	45.2	23.5	48.0	
Race, n (%)						0.9112
African-American*	29 (2.3)	1 (1.4)	2 (1.4)	1 (5.9)	25 (2.4)	
Caucasian	142 (11.2)	6 (8.2)	18 (12.3)	0 (0.0)	118 (11.5)	
Hispanic/Latino	32 (2.5)	1 (1.4)	3 (2.1)	1 (5.9)	27 (2.6)	
Body weight, lbs						0.6385
Mean (SD)	173.1 (48.7)	166.3 (53.0)	167.9 (41.6)	146.8 (50.8)	174.6 (49.4)	
Median (range)	165 (73–371)	151 (99–265)	161 (102–290)	138 (90–230)	168 (73–371)	
D/A abuse, n (%) [†]	189 (15.0)	14 (19.2)	22 (15.1)	2 (11.8)	151 (14.7)	0.2078
CCI, mean (SD)	0.2 (0.7)	0.1 (0.4)	0.2 (0.6)	0.1 (0.2)	0.2 (0.7)	0.5249
Range	0–7	0–2	0–4	0–1	0–7	
Surgery [‡] (%)	30 (2.4)	1 (1.4)	4 (2.7)	1 (5.9)	24 (2.3)	0.7267
VNS (%)	69 (5.5)	0 (0.0)	8 (5.5)	1 (5.9)	60 (5.8)	0.2114
Type of seizure, n (%)						<0.0001
Complex partial [§]	93 (7.4)	14 (19.2)	13 (8.9)	1 (5.9)	65 (6.3)	
Multiple	143 (11.3)	14 (19.2)	26 (17.8)	5 (29.4)	98 (9.5)	
Other	92 (7.3)	7 (9.6)	7 (4.8)	4 (23.5)	74 (7.2)	
Prim generalized [¶]	100 (7.9)	12 (16.4)	17 (11.6)	1 (5.9)	70 (6.8)	
Tonic-clonic	100 (7.9)	6 (8.2)	15 (10.3)	0 (0.0)	79 (7.7)	
Unspecified	598 (47.4)	15 (20.6)	57 (39.0)	4 (23.5)	522 (50.8)	
Comorbidities, n (%)						
Hypertension	169 (13.4)	7 (9.6)	16 (11.0)	2 (11.8)	144 (14.0)	0.5628
Migraine	76 (6.0)	5 (6.8)	13 (8.9)	2 (11.8)	56 (5.5)	0.2824
Depression	172 (13.6)	9 (12.3)	23 (15.8)	3 (17.6)	137 (13.3)	0.8082
Anxiety disorder	117 (9.3)	8 (11.0)	21 (14.4)	0 (0.0)	88 (8.6)	0.0679
Mental retardation	103 (8.2)	6 (8.2)	6 (4.1)	1 (5.9)	90 (8.8)	0.2821
Epilepsy-related injuries, n (%)						0.0848
Concussion	3 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.3)	
Crush injury	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	
Fall with injury	27 (2.1)	1 (1.4)	4 (2.7)	2 (11.8)	20 (1.9)	
Fall without injury	11 (0.9)	0 (0.0)	1 (0.7)	1 (5.9)	9 (0.9)	
Fracture	4 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)	3 (0.3)	
Unspecified injury	29 (2.3)	2 (2.7)	5 (3.4)	0 (0.0)	22 (2.1)	
Specialist clinic visit, n (%)						0.9514
General healthcare	67 (5.3)	0 (0.0)	10 (6.8)	0 (0.0)	57 (5.6)	
Internal medicine	67 (5.3)	2 (2.7)	10 (6.8)	0 (0.0)	55 (5.4)	
Neurology	706 (55.9)	62 (84.9)	93 (63.7)	15 (88.2)	536 (52.2)	
Psychiatry	101 (8.0)	6 (8.2)	10 (6.8)	2 (11.8)	83 (8.1)	
Psychology	42 (3.3)	1 (1.4)	6 (4.1)	0 (0.0)	35 (3.4)	

Categorical data are shown as numbers and percentages of patients.
*African American/Black.
†Drug/alcohol abuse, n (%).
‡Epilepsy-related.
§TL.
¶Primary generalized.
||Grand mal.
CCI: Charlson Comorbidity Index; SD: standard deviation, TL: temporal lobe, VNS: vagal nerve stimulation.

Table 2. Reasons for patients' first AED switch or discontinuation

Reason, n (%)	AEDs switched (n = 90)	AEDs discontinued (n = 163)
AE/side effects	37 (41.1)	77 (47.2)
Economic/insurance reasons	2 (2.2)	1 (0.6)
Lack of efficacy	14 (15.6)	16 (9.8)
Patient non-compliance	2 (2.2)	10 (6.1)
Seizure freedom	0	1 (0.61)
Other	13 (14.4)	23 (14.1)
Missing	22 (24.4)	35 (21.5)

AE: adverse event; AED: antiepileptic drug.

Table 3. Correlation between patient characteristics and switch or discontinuation of AED therapy

Variable	Switched (n = 68)*		Discontinued (n = 127)*	
	r	rank	r	rank
Age	-0.21	3	-0.20 [†]	1
Gender	-0.12	8	-0.12	6
Physician specialty	0.22	2	0.02	13
Seizures per year	0.12 [‡]	7	-0.05 [‡]	11
Body weight	-0.36	1	-0.11	7
Weight gain [§]	-0.04	14	0.18 [†]	3
Weight loss [¶]	-0.11	9	0.17	5
Drug/alcohol abuse	-0.04	13	-0.18 [†]	4
CCI per patient	-0.19	4	†	14
Injury: all causes	0.05	12	0.10	9
Injury: epilepsy-related	-0.18	5	0.04	12
Comorbidities	0.08	10	-0.10	8
Surgery: epilepsy-related	0.10	11	0.07	10
Type of seizure	-0.12	6	0.19 [†]	2

*Not all patients had available data for these analyses.
†Statistically significant, $p < 0.01$.
‡ $n = 43$; $n = 64$; [§]Calculated as the cumulative sum over the entire study period.
AED: antiepileptic drug, CCI: Charlson Comorbidity Index; r: Pearson's correlation coefficient.

CONCLUSIONS

- In this retrospective observational study based on transcripts of records for epilepsy outpatients, AED discontinuations were approximately twice as frequent as switches.
- Treatment switches and discontinuations were approximately twice as likely to be related to AEs as lack of efficacy.
- The reasons for switching or discontinuing therapy were correlated with age, body weight, physician specialty and alcohol/substance abuse.
- To better inform treatment selection, additional research is required to understand the interaction between patient characteristics and AED AE profile.

DISCLOSURES

FFV: employee of Sunovion Pharmaceuticals Inc. TP and MM: employees of PAREXEL.

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