Health Care Resource Utilization and Medical Costs Before and After Initiation of Epidiolex® in Commercially Insured Patients in the US

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Background

- EPIDIOLEX® oral solution is a plant-derived pharmaceutical formulation of highly purified cannabidiol (CBD) approved by the US Food and Drug Administration for the treatment of seizures associated with Lennox-Gastaut syndrome (LGS), Dravet syndrome (DS), and tuberous sclerosis complex (TSC) in individuals aged ≥1 year.[1]
- There is a growing body of real-world evidence on the effectiveness of CBD treatment based on caregiver-reported seizure and nonseizure outcomes.[2,3]
- However, there is still a limited understanding of how CBD may be associated with health care resource utilization (HCRU) and medical costs in the real-world setting.

Objective

- To assess the difference in HCRU and medical costs before and after initiation of CBD, among commercially insured patients with DS, LGS, TSC, and other refractory epilepsies.

Methods

- This was a retrospective pre–post claims study using the US MarketScan® administrative claims database (**Figure 1**).
- HCRU and medical costs included visits to the physician's office, hospital outpatient, and emergency department (ED), home health, inpatient admissions, and intensive care unit admissions.
- Within-person differences between outcomes in the 6-month baseline versus 6-month follow-up were analyzed.
- Interrupted time series (ITS) model (SAS proc autoreg) estimates and plots (**Figure 2**) were used to explore trends in HCRU, medical costs, and the impact of COVID-19.

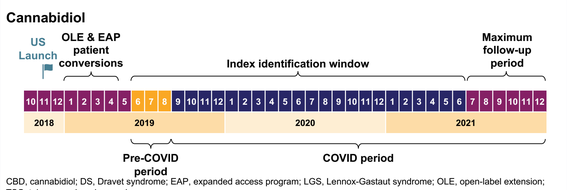
Results

- Of 506 patients included in the analysis, 271 had LGS, 15 had DS, 15 had TSC, and 205 had other refractory epilepsies.
  - Patient characteristics are shown in **Table 1.**

Analysis of within-person differences

- Difference between 6 months pre- and post-CBD initiation was analyzed.
- The mean ± standard deviation (SD) difference in the number of visits per patient after CBD initiation was −0.07 ± 1.02 (*P*=0.042) for ED and −0.14 ± 3.65 (*P*=0.009) for the physician's office visits with epilepsy as the first or second diagnosis.
- For patients with epilepsy as the first diagnosis, mean ± SD difference in the number of visits per patient after CBD initiation was −0.05 ± 0.89 (*P*=0.098) for ED and −0.13 ± 3.02 (*P*=0.001) for physician's office visits.
- The mean cost of ED and physician's office visits per patient was 47% and 14% lower (*both P*=0.002) for patients with epilepsy as the first or second diagnosis after CBD initiation.
- The mean cost of ED and physician's office visits was reduced by 39% (*P*=0.014) and 17% (*P*<0.0005) per patient, respectively, after CBD initiation for patients with epilepsy as the first diagnosis.

Figure 1. Study design and sample selection



CBD, cannabidiol; DS, Dravet syndrome; EAP, expanded access program; LGS, Lennox-Gastaut syndrome; OLE, open-label extension; TSC, tuberous sclerosis complex.

CBD prescription during index identification (n=4803)
↓
New users of CBD (n=3039)
↓
LGS, DS, TSC, or other refractory epilepsy diagnosis at baseline (n=2697)
↓
New CBD users in commercial health plans (n=812)
↓
180 days continuous enrollment at baseline (n=648)
↓
180 days of continuous enrollment at follow-up (n=506)

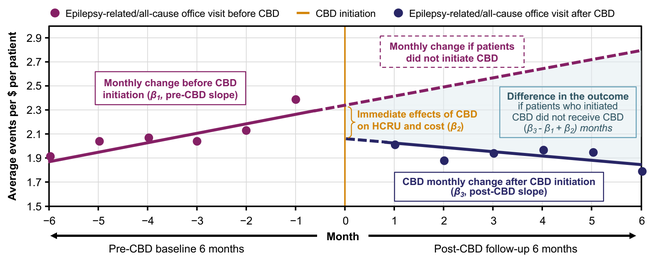
Table 1. Patient characteristics

Characteristic	All[a] (n=506)	LGS (n=271)	DS (n=15)	TSC (n=15)	Other refractory epilepsy (n=205)
Age, mean (SD)	15.7 (10.9)	15.0 (9.4)	11.9 (9.2)	12.8 (8.2)	17.2 (12.7)
Female gender, n (%)	249 (49)	121 (45)	6 (40)	11 (73)	111 (54)
Comorbidities, n (%)					
CCI[b]					
0	10 (2)	0	0	1 (7)	9 (4)
1–2	272 (54)	133 (49)	9 (60)	10 (67)	120 (59)
3–4	186 (37)	117 (43)	4 (27)	3 (20)	62 (30)
5+	38 (8)	21 (8)	2 (13)	1 (7)	14 (7)
Asthma	33 (7)	21 (8)	2 (13)	0	10 (5)
Diabetes	0	0	0	0	0
Cancer	8 (2)	0	0	1 (7)	7 (3)
Anxiety	62 (12)	27 (10)	2 (13)	3 (20)	30 (15)
Attention deficit hyperactivity disorder	7 (1)	1 (0.4)	0	2 (13)	4 (2)
Autism spectrum disorder	96 (19)	69 (25)	7 (47)	5 (33)	15 (7)
Bipolar disorder	5 (1)	2 (1)	1 (7)	0	2 (1)
Depression	34 (7)	3 (1)	1 (7)	2 (13)	28 (14)
Intellectual disorder(s)	259 (51)	187 (69)	14 (93)	6 (40)	52 (25)
Learning disabilities	28 (6)	20 (7)	0	0	8 (4)
Schizophrenia	1 (0.2)	1 (0.4)	0	0	0

[a]The epilepsy categories are mutually exclusive. Three patients with both LGS and TSC diagnosis at baseline were assigned to TSC only. [b]CCI includes myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, dementia, paraplegia and hemiplegia, diabetes, diabetes with complications, renal disease, mild liver disease, moderate/severe liver disease, peptic ulcers, rheumatic disease, human immunodeficiency virus/acquired immunodeficiency syndrome, cancer, and metastatic solid tumor.
CCI, Charlson Comorbidity Index; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; SD, standard deviation; TSC, tuberous sclerosis complex.

Interrupted time series (ITS) analysis[4,5]

Figure 2. ITS analysis to demonstrate trends in HCRU before and after CBD initiation

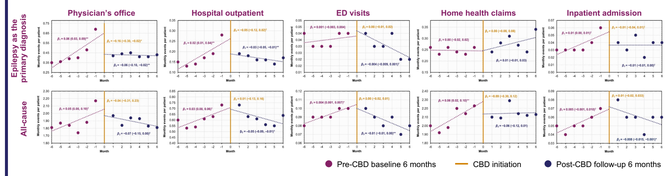


CBD, cannabidiol; HCRU, health care resource utilization.

- ITS analysis is a quasi-experimental observational study that involves analyzing the time-series data or an outcome that is measured over time in a population and comparing the outcome before versus after an intervention.
- ITS segmented regression-based techniques are used to estimate linear trends.

Figure 3. ITS analysis of HCRU (mean number of events per month per patient)

View via QR code

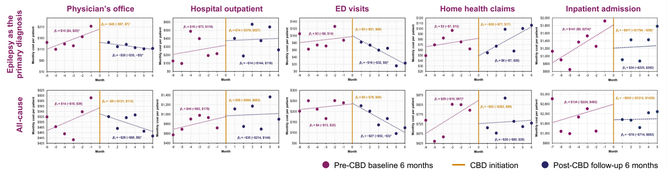


95% confidence intervals. *P<0.05; **P<0.01; †underpowered analysis results.
CBD, cannabidiol; ED, emergency department; HCRU, health care resource utilization; ITS, interrupted time series.

- Epilepsy-related HCRU is defined as HCRU with epilepsy as the first diagnosis.
- ITS analysis of change in epilepsy-related HCRU shows increasing trends pre-CBD initiation and clear decreasing/flat trends post-CBD for all categories, except in home health care use (**Figure 3** and **Table 2**).
- Changes in all-cause HCRU show increasing trends pre-CBD and clear decreasing/flat trends post-CBD initiation for all categories (**Figure 3** and **Table 2**).

Figure 4. ITS analysis of medical costs (mean $ per month per patient)

View via QR code



95% confidence intervals. *P<0.05; †underpowered analysis results.
CBD, cannabidiol; ED, emergency department; ITS, interrupted time series.

Table 2. Estimated changes in HCRU pre- and post-CBD initiation

	Epilepsy as primary diagnosis		All-cause	
Based on pre- and post-changes estimated from ITS analysis	**Average change in number of events**	**Average % change in number of events**	**Average change in number of events**	**Average % change in number of events**
	Per patient across 12 months		**Per patient across 12 months**	
Physician's office	−3.35	−94	NS	NS
Hospital outpatient	−0.67	−48	−0.60	−10
Emergency department	NS	NS	−0.14	−14
Home health	0	0	−0.70	−3
Inpatient admission	NS	NS	−0.10	−21
ICU admission	NS	NS	−0.07	−34

CBD, cannabidiol; ICU, intensive care unit; NS, not statistically significant (underpowered due to sample size and event rates).

Effect of COVID-19 and lockdown (details available via QR code)

- The impact of COVID-19 is limited to the utilization of inpatient admissions and hospital outpatient visits during the lockdown period. Further analysis may exclude patients with an index date in the COVID-19 lockdown period.

Limitations of the study

- No causality can be inferred based on the study design.
- Generalizability of the findings is limited beyond the population in the MarketScan database.
- Potential misclassification is possible because of reliance on the accuracy of diagnostic codes and the patient identification algorithm.
- Follow-up time was short, restricted to 6 months. A longer follow-up period may be more informative in evaluating changes in HCRU and costs post-CBD initiation.

Conclusions

- After the initiation of CBD, the average physician's office and ED visits and their costs were lower in the study period among the commercially insured patients in the US.
- Patients had significant trends toward lower epilepsy-related physician's office and outpatient office visits. There was also a significantly lower trend of epilepsy-related physician's office medical costs. Other epilepsy-related HCRUs and their associated medical costs had flat (non-increasing) trends of post-CBD initiation versus pre-CBD initiation.
- Patients had significant trends toward lower all-cause HCRU, except for physician's office visits (underpowered), and a significant trend toward lower all-cause associated medical costs for ED visits and flat (non-increasing) trends for other HCRU categories post-CBD initiation versus pre-CBD initiation.

References: 1. EPIDIOLEX® [prescribing information]. Jazz Pharmaceuticals, Inc. 2023. **2.** Dixon-Salazar T, et al. Presented at the AES Annual Meeting; December 3–7, 2021; Chicago, IL, USA. Abstract 3.3. **3.** Berg AT, et al. Presented at the AES Annual Meeting; December 3–7, 2021; Chicago, IL, USA. Abstract 3.304. **4.** Kontopantelis E, et al. *BMJ.* 2015;350:h2750. **5.** Wagner AK, et al. *J Clin Pharm Ther.* 2002;27(4):299-309.

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