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A Population Health Study of Patients Prescribed Cannabidiol in the Epilepsy Learning Healthcare System (ELHS) Registry

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Introduction

- Despite recent advances in epilepsy management, 30% of people with epilepsy have treatment-resistant seizures; factors affecting patient outcomes include access to specialty care, diagnosis of comorbidities, and utilization of new treatments[1]
- The Epilepsy Learning Healthcare System (ELHS) is an Epilepsy Foundation–sponsored initiative to collect standardized data from outpatient visits across participating centers to drive quality improvement in epilepsy care[1]
  - As of February 2025, the ELHS network includes 11 pediatric and adult epilepsy care centers across the United States (US), and the ELHS registry includes data on >39,000 patients[2]
- In collaboration with Jazz Pharmaceuticals, Inc., the ELHS conducted a retrospective analysis on a de-identified subset of patients with documented use of FDA-approved cannabidiol (CBD; Epidiolex®, 100 mg/mL oral solution)[3]
  - CBD (Epidiolex®) is approved in the US for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients ≥1 year of age
- The collaboration aimed to describe demographic characteristics, epilepsy classifications, seizure patterns, and concomitant antiseizure medications (ASMs) in patients with epilepsy who were treated with CBD for >6 months

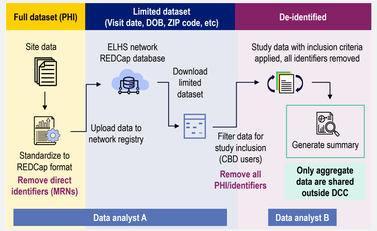
Objective

- To describe demographic and clinical characteristics of patients treated with CBD for >6 months using data from the ELHS registry contributed by participating epilepsy care centers

Methods

- Seven epilepsy care centers in the ELHS network contributed registry data collected using standardized case report forms (CRFs)
- We retrospectively analyzed characteristics of pediatric and adult patients with epilepsy who were prescribed CBD between January 2019 and February 2025
- Patients prescribed CBD for >6 months were identified in the registry on the basis of having at least 2 clinical visits with CBD prescription documentation in the ELHS CRFs
- A de-identified dashboard was developed to visualize demographic and clinical characteristics, including seizure types, syndromes, etiologies, and ASM patterns (**Figure 1**)
- CRFs or ICD-10 codes, when available, were used to assess diagnoses of epilepsy syndromes and etiologies
- This study was conducted with CRF documentation of Epidiolex®, and as such, the results do not apply to other CBD-containing products

Figure 1. De-identification process

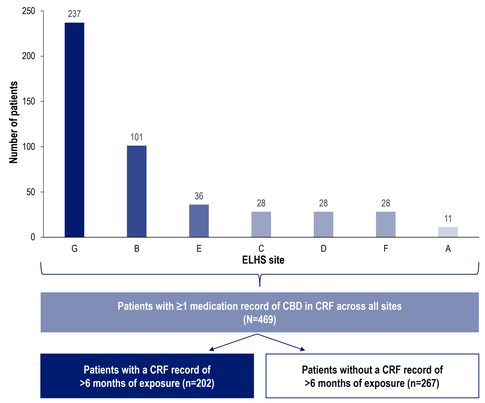


CBD, cannabidiol; DCC, data coordinating center; DOB, date of birth; ELHS, Epilepsy Learning Healthcare System; MRNs, medical record numbers; PHI, protected health information; REDCap, Research Electronic Data Capture.

Results

Baseline demographics

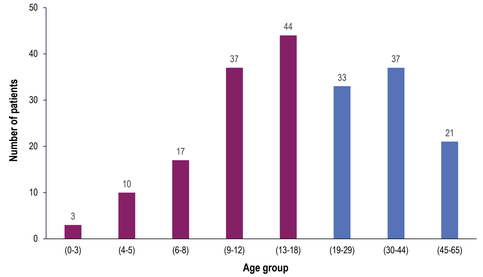
Figure 2. Number of unique patients by site and selection for analysis



CBD, cannabidiol; CRF, case report form; ELHS, Epilepsy Learning Healthcare System.

- A total of 202 patients had a record of using CBD for >6 months (**Figure 2**)
- Among those without a CRF record of >6 months of exposure, follow-up data were unavailable for 140 patients

Figure 3. Age groups of patients prescribed CBD for >6 months



CBD, cannabidiol.

- Among identified patients, 111 were children (aged ≤18 years) and 91 were adults (aged >18 years) (**Figure 3**)

Patient characteristics

Table 1. Characteristics of patients prescribed CBD for >6 months

	Pediatric (n=111)	Adult (n=91)
Median age (range), years	11 (0–18)	33 (19–65)
Sex assigned at birth, n (%)		
Female	46 (41)	41 (45)
Male	65 (59)	50 (55)
Race, n (%)		
White	1 (1)	21 (23)
Black or African American	1 (1)	1 (1)
Asian	–	1 (1)
Other	–	–
Missing	109 (98)	68 (75)
Ethnicity, n (%)		
Hispanic	47 (42)	12 (13)
Non-Hispanic	64 (58)	21 (23)
Other	–	54 (59)
Declined	–	4 (4)
Missing	–	–
Language, n (%)		
English	2 (2)	75 (82)
Spanish	–	5 (5)
Other	–	2 (2)
Missing	109 (98)	9 (10)
Education level, n (%)		
8th grade or less	–	8 (9)
Some high school	–	7 (8)
High school graduate/GED	–	35 (38)
Some college	–	3 (3)
Graduated college	–	5 (5)
Post grad	–	2 (2)
Others	–	12 (13)
Declined	–	2 (2)
Missing	111 (100)	17 (19)

CBD, cannabidiol; GED, Test of General Educational Development.

- Median age was 11 years in the pediatric group and 33 years in the adult group; sex distribution was similar between the groups (**Table 1**)

Epilepsy classification

Table 2. Epilepsy type/syndrome for patients prescribed CBD for >6 months

	Overall (N=202)	Pediatric (n=111)	Adult (n=91)
Epilepsy type, n (%)			
Focal	34 (17)	17 (15)	17 (19)
Generalized	19 (9)	7 (6)	12 (13)
Both	4 (2)	–	4 (4)
Data not documented	145 (72)	87 (78)	58 (64)
Current epilepsy syndrome, n (%)			
Yes, a syndrome	123 (61)	76 (68)	47 (52)
No	6 (3)	1 (1)	5 (5)
Data not documented	73 (36)	34 (31)	39 (43)
Epilepsy syndrome ILAE classification, n (%)[a]			
Neonatal/infantile[b]	2 (1)	1 (1)	1 (1)
Adolescent/adult[c]	1 (<1)	–	1 (1)

[a]Total may not sum to N, and data not documented for all patients; [b]Epilepsy of infancy with migrating focal seizures and West syndrome; [c]Epilepsy with generalized tonic-clonic seizures alone. CBD, cannabidiol; ILAE, International League Against Epilepsy.

- Epilepsy type was recorded on CRFs for 57 (28%) patients and not documented for 145 (72%) patients (**Table 2**)
- Five of 7 sites provided ICD-10 diagnostic codes (**Table S1**)

Seizure frequency

Table 3. Seizure frequency[a] for patients prescribed CBD for >6 months

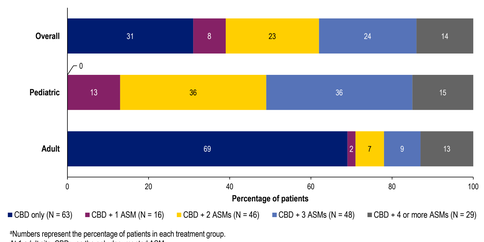
	Overall (N=202)	Pediatric (n=111)	Adult (n=91)
Seizure frequency, n (%)			
Daily or more	68 (34)	60 (54)	8 (9)
Weekly	21 (10)	17 (15)	4 (4)
Monthly	20 (10)	12 (11)	8 (9)
Yearly	7 (3)	6 (5)	1 (1)
Less than yearly	3 (1)	1 (1)	2 (2)
Unavailable	83 (41)	15 (14)	68 (75)
Timing of most recent seizure, n (%)			
≤6 months	122 (60)	103 (93)	19 (21)
>6 months	11 (5)	7 (6)	4 (4)
Unavailable	69 (34)	1 (1)	68 (75)
Date of most recent seizure, n (%)			
Today	57 (28)	49 (44)	8 (9)
>1 day to 6 days ago	37 (18)	34 (31)	3 (3)
>1 week to 4 weeks ago	12 (6)	7 (6)	5 (5)
>1 month to 3 months ago	13 (6)	10 (9)	3 (3)
>3 months to 6 months ago	3 (1)	3 (3)	–
>6 months to 12 months ago	3 (1)	3 (3)	–
>1 year to 2 years ago	4 (2)	2 (2)	2 (2)
>2 years ago	4 (2)	2 (2)	2 (2)
Unavailable	69 (34)	1 (1)	68 (75)

[a]Seizure frequency is provider-reported and taken from the last available visit. The duration of follow-up was variable.
CBD, cannabidiol.

- Overall, reported CRF data on seizure frequency suggest a high seizure burden in the population (**Table 3**)
  - Seizure frequency does not indicate seizure count or severity
- The seizure frequency records were mainly from the pediatric population; reporting was sparse in the adult population
- Despite absence of baseline data, a subset of patients reported monthly or less frequent seizures, including 5% seizure-free for >6 months, 1% for up to 1 year, and 2% for >2 years

Polypharmacy

Figure 4. Polypharmacy breakdown for patients prescribed CBD for >6 months[a]



[a]Numbers represent the percentage of patients in each treatment group.
At 1 adult site, CBD was the only documented ASM.
ASM, antiseizure medication; CBD, cannabidiol.

- Among those taking CBD >6 months, 63 (31%) patients had documentation of CBD alone (including 63 [69%] adults and 0 pediatric patients), 16 (8%) had documentation of CBD + 1 ASM, 46 (23%) had documentation of CBD + 2 ASMs, 48 (24%) had documentation of CBD + 3 ASMs, and 29 (14%) had documentation of CBD + ≥4 ASMs (**Figure 4**)

Concomitant ASMs

Table 4. Concomitant ASMs used by patients prescribed CBD for >6 months

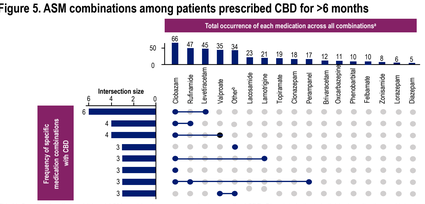
Other medications used with CBD, n (%)	Overall (N=202)	Pediatric (n=111)	Adult (n=91)
Clobazam	66 (33)	53 (48)	13 (14)
Rufinamide	47 (23)	39 (35)	8 (9)
Levetiracetam	45 (22)	37 (33)	8 (9)
Valproate	35 (17)	28 (25)	7 (8)
Lacosamide	23 (11)	17 (15)	6 (7)
Lamotrigine	21 (10)	12 (11)	9 (10)
Topiramate	19 (9)	15 (14)	4 (4)
Clonazepam	18 (9)	11 (10)	7 (8)
Perampanel	17 (8)	15 (14)	2 (2)
Brivaracetam	12 (6)	8 (7)	4 (4)
Oxcarbazepine	11 (5)	9 (8)	2 (2)
Felbamate	10 (5)	8 (7)	2 (2)
Phenobarbital	10 (5)	8 (7)	2 (2)
Zonisamide	8 (4)	6 (5)	2 (2)
Lorazepam	6 (3)	–	6 (7)
Diazepam	5 (2)	1 (1)	4 (4)
Other[a]	34 (17)	19 (17)	15 (16)

[a]Includes carbamazepine, cenobamate, clorazepate, eslicarbazepine, ethosuximide, gabapentin, phenytoin, pregabalin, vigabatrin, and others. ASMs, antiseizure medications; CBD, cannabidiol.

- Clobazam (33%), rufinamide (23%), levetiracetam (22%), and valproate (17%) were the most common concomitant ASMs with CBD (**Table 4**)

ASM combinations

Figure 5. ASM combinations among patients prescribed CBD for >6 months



This UpSet plot visualizes additional ASM combinations among patients prescribed CBD. Blue dots indicate individual medications, with horizontal connecting lines showing which medications are taken together. The bar graph on the left displays the frequency of specific medication combinations, while the top bar graph shows the total occurrence of each medication across all combinations. [a]All combinations also include CBD. *Includes carbamazepine, cenobamate, clorazepate, eslicarbazepine, ethosuximide, gabapentin, phenytoin, pregabalin, vigabatrin, and other. ASM, antiseizure medication; CBD, cannabidiol.

- Clobazam was included in 66 medication combinations with CBD, rufinamide in 47, and levetiracetam in 45 (**Figure 5**)
- Clobazam plus levetiracetam was the most frequently prescribed medication combination with CBD

Limitations

- Most data came from a single site; hence, the characteristics observed may not be generalizable
- Due to significant gaps in CRF documentation, the database does not yet support interpretable observations and the analyzed population may not have included all patients who continued CBD for >6 months
- The current CRF is not designed to capture dose and dosing information, and collection of baseline data on patients' seizure frequency and ASM use was not performed for this study

Conclusions

- This study highlights the potential of the ELHS to inform real-world treatment patterns and provides insights into the characteristics of pediatric and adult patients with epilepsy prescribed CBD
- With support for improved and consistent adoption, the structured CRFs used in the ELHS registry can provide real-world evidence on treatment outcomes at individual and population levels across clinical centers, as well as close gaps not addressed by data collected for clinical trials and administrative claims analyses

References: 1. Donahue MA, et al. *Epilepsy Behav*. 2021;117:107805. **2.** Epilepsy Foundation. The Epilepsy Learning Healthcare System. 2025. Available from: https://www.epilepsy.com/programs/epilepsy-learning-healthcare-system. (Accessed October 28, 2025.) **3.** US Food and Drug Administration. Epidiolex® Prescribing Information. 2025. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/210365s023lbl.pdf. (Accessed October 28, 2025.)

Acknowledgments: The authors would like to thank all of the study investigators, study staff, and patients for their participation in this research. Writing and editorial assistance was provided to the authors by Nirlep Chhiber, PhD, on behalf of Syneos Health, and funded by Jazz Pharmaceuticals, Inc., in accordance with Good Publication Practice (GPP) 2022 guidelines.

Support: This study was sponsored by Jazz Pharmaceuticals, Inc.

Disclosures: All authors met the ICMJE authorship criteria and had full access to relevant data and information. Neither honoraria nor payments were made for authorship. **TBS** and **KR** are employees of Jazz Pharmaceuticals, Inc., and hold stock and/or stock options in the company. **KMF**, **JAR**, **RBR**, **AE**, **LMVRM**, **PH**, and **BEF** have consulted for, conducted studies funded by, or received honoraria for services provided to Jazz Pharmaceuticals, Inc.

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Poster presented at American Epilepsy Society Annual Meeting, December 5–9, 2025; Atlanta, GA, USA

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Supplementary Material

Table S1. ICD-10 primary diagnosis in PWE prescribed CBD for >6 months as reported in the CRF

	Description	Overall	Pediatric	Adult
ICD codes,[a] n (%)				
G40.814	Lennox-Gastaut syndrome, intractable, without status epilepticus	39 (19)	24 (22)	15 (16)
G40.813	Lennox-Gastaut syndrome, intractable, with status epilepticus	26 (13)	22 (20)	4 (4)
G40.919	Epilepsy, unspecified, intractable, without status epilepticus	24 (12)	8 (7)	16 (18)
G40.219	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus	13 (6)	4 (4)	9 (10)
G40.909	Epilepsy, unspecified, intractable, without status epilepticus	9 (4)	5 (5)	–
G40.911	Epilepsy, unspecified, intractable, with status epilepticus	6 (3)	5 (5)	1 (1)
G40.319	Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus	6 (3)	2 (2)	4 (4)
G40.011	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus	5 (2)	5 (5)	–
G40.309	Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus	4 (2)	–	4 (4)
G40.109	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, without status epilepticus	4 (2)	1 (1)	3 (3)
G40.019	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus	4 (2)	2 (2)	2 (2)
G40.804	Other epilepsy, intractable, without status epilepticus	4 (2)	4 (4)	–
G40.419	Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus	4 (2)	3 (3)	1 (1)
G40.211	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus	4 (2)	3 (3)	1 (1)
G40.812	Lennox-Gastaut syndrome, not intractable, without status epilepticus	3 (1)	3 (3)	–
G40.834, Z15.1	Dravet syndrome, intractable, without status epilepticus/Genetic susceptibility to epilepsy and neurodevelopmental disorders	3 (1)	3 (3)	–

[a]ICD-10 code primary diagnoses recorded for ≤2 patients: G40.411, Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus, n=2; G40.802, Other epilepsy, not intractable, without status epilepticus, n=2; G11.6, Leukodystrophy with vanishing white matter diseases, n=1; G40.819, Juvenile myoclonic epilepsy, intractable, without status epilepticus, n=1; G40.833, Dravet syndrome, intractable, without status epilepticus, n=1; F84.2, Z15.1, Rett's syndrome, genetic susceptibility to epilepsy and neurodevelopmental disorders, n=1; G40.823, Epileptic spasms, intractable, with status epilepticus, n=1; G93.49, Other encephalopathy, n=1; G40.803, Other epilepsy, intractable, with status epilepticus, n=1; G40.A19, Absence epileptic syndrome, intractable, without status epilepticus, n=1; Q85.1, Tuberous sclerosis, n=1; G90.9, Disorder of the autonomic nervous system, unspecified, n=1; G40.209, Localization-related (focal) (partial) symptomatic epilepsy with complex partial seizures, not intractable, without status epilepticus, n=1.

CBD, cannabidiol; ICD-10, International Classification of Diseases, 10th Revision; PWE, people with epilepsy.

Acknowledgments: The authors would like to thank all of the study investigators, study staff, and patients for their participation in this research. Writing and editorial assistance was provided to the authors by Nirlep Chhiber, PhD, on behalf of Syneos Health, and funded by Jazz Pharmaceuticals, Inc., in accordance with Good Publication Practice (GPP) 2022 guidelines.

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