Cost of epilepsy-related health care encounters in the United States

Simon Borghs, MSc; Silky Beaty, PharmD, MSPH; Witesh Parekh, BPharm(Hons), MSc, MRPharmS;
Linda Kalilani, MBBS, MPhil, PhD; Nada Boudiaf, MSc; and Andrea Loewendorf, MBA

What is already known about this subject

- Epilepsy is characterized by acute exacerbations in the form of seizures.
- The cost of epilepsy is typically reported as total expenditure over a defined time period.
- More granular cost information could be used to more accurately estimate the cost-benefit ratio of new acute treatments.

What this study adds

- This retrospective cohort study provides the first health plan-paid cost per epilepsy-related health care encounter.
- These data can be the basis for more granular cost-benefit analyses of not only chronic but also acute treatments of epilepsy.

Author affiliations

Simon Borghs, MSc; Witesh Parekh, BPharm(Hons), MSc, MRPharmS; and Nada Boudiaf, MSc, UCB Pharma, Slough, UK. Silky Beaty, PharmD, MSPH, and Andrea Loewendorf, MBA, UCB Pharma, Smyrna, GA. Linda Kalilani, MBBS, MPhil, PhD, UCB Pharma, Raleigh, NC.

AUTHOR CORRESPONDENCE:
Simon Borghs, +44 (0) 1753 534 655,
simon.borghs@ucb.com

ABSTRACT

BACKGROUND: The cost of epilepsy is usually reported as total expenditure over a certain period. However, with the increased availability of acute treatments for use in the community setting, intermittent, single-seizure treatment is now possible in addition to the chronic epilepsy drug treatment paradigm. Data on the cost of discrete health care encounters are needed to substantiate the cost-benefit of these new treatments.

OBJECTIVE: To estimate the health plan-paid costs of discrete epilepsy-related health care encounters in patients with epilepsy.

METHODS: This retrospective cohort study utilized IBM MarketScan Commercial Claims, Medicare Supplemental and Coordination of Benefits (Medicare patients with supplemental insurance), and Multi-State Medicaid research databases. The primary analysis determined health plan-paid cost (adjudicated claims) of discrete epilepsy-related health care encounters, defined as having a primary diagnosis code of epilepsy or convulsion, from 2013 to 2018, in patients with epilepsy aged ≥12 years. Costs were adjusted to 2018 prices. Epilepsy cases were defined using ICD-CM codes. We excluded patients on capitated insurance plans as their cost per health care encounter is unknown.

RESULTS: In total, 353,530 commercially insured, 378,051 Medicaid, and 69,176 Medicare plus supplemental insurance patients with epilepsy were included. More than 160,000 epilepsy-related emergency transportations, 225,000 emergency department (ED) visits, 49,000 hospitalizations, 700 urgent care visits, and ~2.5 million office visits were analyzed. 37.4% of epilepsy-related hospitalizations included care in the intensive care unit (ICU). In commercially insured patients, epilepsy-related health care encounters had median health plan-paid costs of $22,305 (Q1-Q3=$14,336-$36,096, hospitalization); $3,375 ($565-$9,095, ICU visit); $1,913 ($417-$4,163, ED visit); $687 ($415-$1,083, emergency transportation); $95 ($23-$232, office visit); and $57 ($0-$171, urgent care visit). The median length of stay for epilepsy-related hospitalizations in working age, commercially insured patients was 4 (Q1-Q3=2-5) days.

CONCLUSIONS: This is the first study to report health plan-paid cost per epilepsy-related health care encounter. These data can serve as a basis for more granular cost-benefit analyses of not only chronic but also acute treatments of epilepsy.

An estimated 3.4 million people have active epilepsy in the United States.[1] Among newly diagnosed patients who are starting antiepileptic drug (AED) treatment, the majority (63%) will either have persistent seizures despite repeated trials with different AEDs, fluctuate between periods of seizure freedom and recurrence, or enter remission after a period as short as 6 months or as long as 18 years.[2] In recent years, 2 acute treatments for use in the community setting have become available in the United States that are intended to stop seizure clusters, reduce seizure-related harm, and prevent progression to serious consequences, including emergency room visits and other health care encounters.[3-5]

In the literature, the cost to insurers[6,7] or insurer-borne cost plus patients' out-of-pocket expenses[8] of health care resource use in patients with epilepsy is usually calculated as total expenditure over a certain time period. However, because epilepsy is a disease characterized by acute exacerbations in the form of seizures, and with the increased availability of acute treatments, cost data on discrete epilepsy-related health care encounters can support more accurate cost-benefit analysis of epilepsy care.

A systematic review on the cost to the health care system of epilepsy in the United States, including insurer-borne cost and patients' out-of-pocket expenses, found annual epilepsy-specific cost estimates ranging from $1,022 to $19,749 per person, and costs were considerably higher for uncontrolled/treatment-resistant epilepsy versus controlled/treatment-responsive epilepsy.[8] Data sources for the cost estimates included commercial insurance and/or Medicaid and Medicare paid claims and encounter databases, provider billing and medical record data, and a combination of population survey and provider billing data.

The primary objective of the current analysis, therefore, was to estimate the health plan-paid cost per epilepsy-related health care encounter. As a secondary objective, the health plan-paid cost per all-cause health care encounter in patients with epilepsy was analyzed, in order to evaluate the excess cost of epilepsy-related encounters versus other encounters.

Methods

DATA SOURCE
This retrospective cohort study used IBM MarketScan Commercial Claims (CCMC [Commercial] 2008-2018 v0.1), Medicare Supplemental and Coordination of Benefits (Medicare patients with supplemental insurance; MDCR [Medicare] 2008-2018 v0.1), and Multi-State Medicaid (MDCD [Medicaid] 2008-2017 v1.0) research databases, which are compliant with the Health Insurance Portability and Accountability

Act. All patient data were deidentified before delivery to UCB Pharma. Therefore, institutional review board approval was not required for this research. The database contained information on medical (inpatient, outpatient, emergency care) and outpatient pharmacy claims, as well as enrollment history for over 150 million covered lives. The study followed the Guidelines for Good Epidemiologic Practice outlined in the 2005 Food and Drug Administration Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment and the 2008 International Society of Pharmacoepidemiology Guidelines for Good Pharmacoepidemiology Practices, in relation to protocol development, responsibilities, personnel, facilities, resource commitment, and contractors; study conduct; communication; and archiving.

PATIENT SELECTION AND FOLLOW-UP
The analysis included patients with epilepsy aged 12 years and older because this is the cutoff age for many antiepileptic treatments and we decided to focus on adults. Patients were defined as having epilepsy if they fulfilled any of the criteria listed in Supplementary Table 1 (available in online article). Patients on capitated insurance plans were excluded as their cost per health care encounter is unknown.

The index date was the date patients fulfilled the criteria of an epilepsy diagnosis; for definitions requiring ≥2 *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) or *International Classification of Diseases, 10th Revision, Clinical Modification* (ICD-10-CM) codes on any diagnosis position of a claim, the second code chronologically was selected as the index date. Follow-up started on the index date and continued until the patient was no longer enrolled or the end of the patient selection period (last data availability: January 1, 2014-December 31, 2018, for CCMC and MDCR; January 1, 2013-December 31, 2017, for MDCD). The last 5 years of available data were chosen to remain relatively current with regard to insurance plan design, while capturing a large sample.

MAIN OUTCOME MEASURES AND STATISTICAL ANALYSES
The primary analysis calculated the average health plan-paid cost per epilepsy-related health care encounter type, defined as having a primary diagnosis code of epilepsy or convulsion (based on position 1), using the adjudicated claim costs recorded in the data. The secondary analysis calculated the average health plan-paid cost per all-cause health care encounter type in patients with epilepsy. Health care encounter types of interest included emergency department (ED) visits that did not lead to inpatient hospitalization; ED visits that led to inpatient hospitalization; inpatient

hospitalizations (including the cost of intensive care unit [ICU], specialist attendants, from admission to discharge); emergency transportation services (ambulance services, including ground and air mileage); urgent care visits; ICU visits (cost billed as ICU only, including part cost of an inpatient hospitalization); and outpatient (office) visits attended by a physician or only by a nurse. This study did not assess treatment effects.

The mean cost for each type of health care encounter was calculated as the sum of the total insurer-borne cost (NETPAY) associated with all encounters of that type during follow-up divided by the total number of encounters of that type. NETPAY is the variable for Net Payment, which is the payment received by the provider excluding patient out-of-pocket and Coordination of Benefits (COB; i.e., employer or plan liability). For encounters in patients insured by Medicare with supplemental insurance, the variable used was NETPAY (the proportion of charge for a health care service the commercial insurer paid) plus COB (i.e., the Medicare-covered portion of payment). Costs were adjusted to 2018 U.S. dollars using the medical care component of the Consumer Price Index. Feasibility counts and sample size calculations were not performed for this analysis.

Results

BASELINE DEMOGRAPHICS
A total of 353,530 commercially insured, 378,051 Medicaid, and 69,176 Medicare plus supplemental insurance patients with epilepsy were selected for analysis (Table 1). The mean (SD) age of Medicare patients was 76 (9) years; for Medicaid and commercial insurance patients the mean age was 44 (19) and 40 (16) years, respectively. The proportion of females was 55.3% in commercially insured patients, 56.2% in Medicaid patients, and 53.7% in Medicare patients with supplemental insurance.

HEALTH PLAN-PAID COST OF EPILEPSY-RELATED HEALTH CARE ENCOUNTERS
This analysis included 161,995 epilepsy-related emergency transportations, 225,833 ED visits, 49,601 hospitalizations, 706 urgent care visits, and 2,495,547 office visits. The proportion of epilepsy-related health care encounters is shown in Supplementary Table 2 (available in online article). In the overall epilepsy cohort, the proportion of epilepsy-related hospitalizations that included care in the ICU was 37.4% (18,538/49,601) and the proportion of all-cause hospitalizations that included care in the ICU was 29.4% (116,508/396,748). In commercially insured patients and

TABLE 1	Baseline Demographics		
	Commercially Insured Patients (n = 353,530)	Medicaid Patients (n = 378,051)	Medicare Patients with Supplemental Insurance (n = 69,176)
Age, years			
Mean (SD)	40 (16)	44 (19)	76 (9)
12-18, n (%)	40,713 (11.5)	38,594 (10.2)	0
19-64, n (%)	308,690 (87.3)	288,804 (76.4)	2,525 (3.7)
≥65, n (%)	4,127 (1.2)	50,653 (13.4)	66,651 (96.3)
Female, n (%)	195,470 (55.3)	212,346 (56.2)	37,179 (53.7)
Region of residence, n (%)			
South	149,444 (42.3)	NA	20,698 (29.9)
North central	73,260 (20.7)	NA	22,260 (32.2)
Northeast	71,798 (20.3)	NA	16,076 (23.2)
West	53,583 (15.2)	NA	9,330 (13.5)
Unknown	5,445 (1.5)	NA	812 (1.2)
Missing	0	378,051 (100.0)	0

NA = not available.

Medicaid patients, 37.0% and 24.3% of emergency transportations, respectively, as well as 10.6%-22.5% of ED visits, hospitalizations, and ICU visits were epilepsy-related. In Medicare patients with supplemental insurance, 2.4%-11.4% of all-cause health care encounters were epilepsy-related.

In commercially insured patients, epilepsy-related health care encounters had a median health plan-paid cost of $22,305 (Q1-Q3 = $14,336-$36,096) for a hospitalization, $3,375 ($565-$9,095) for an ICU visit, $1,913 ($417-$4,163) for an ED visit, $687 ($415-$1,083) for an emergency transportation, $95 ($23-$232) for an office visit, and $57 ($0-$171) for an urgent care visit (Table 2 and Supplementary Figure 1, available in online article). In Medicaid patients, epilepsy-related health care encounters had a median health plan-paid cost of $9,837 ($5,092-$14,991) for a hospitalization, $1,955 ($0-$5,572) for an ICU visit, $646 ($186-$1,295) for an ED visit, $190 ($132-$333) for an emergency transportation, $73 ($39-$165) for an office visit, and $0 ($0-$37) for an urgent care visit (Table 2 and Supplementary Figure 1). In Medicare patients with supplemental insurance, epilepsy-related health care encounters had a median health plan-paid cost of $19,577 ($12,232-$36,543) for a hospitalization, $5,168 ($994-$10,262) for an ICU visit, $695 ($173-$2,105) for an ED visit, $485 ($401-$688) for an emergency transportation, $100 ($60-$208) for an office visit, and $81 ($0-$112) for an urgent care visit (Table 2 and Supplementary Figure 1).

In a subset of commercially insured patients of working age (19-64 years), the median length of stay of an epilepsy-related hospitalization was 4 (Q1-Q3=2-5) days (Table 2). The median length of stay was also 4 days in working age patients of the Medicaid and Medicare with supplemental insurance groups.

HEALTH PLAN-PAID COST OF ALL-CAUSE HEALTH CARE ENCOUNTERS IN PATIENTS WITH EPILEPSY

All-cause hospitalizations in patients with epilepsy had a 21%-30% higher median health plan-paid per-encounter cost compared with epilepsy-related hospitalizations, for all insurer types (Table 2 and Supplementary Table 3, available in online article).

Discussion

This retrospective cohort study estimated the health plan-paid cost per epilepsy-related health care encounter in the United States, using IBM MarketScan claims databases. In commercially insured patients, epilepsy-related encounters carried a median health plan-paid cost of $22,305 for a hospitalization, $3,375 for an ICU visit, $1,913 for an ED visit, $687 for an emergency transportation, $95 for an office visit, and $57 for an urgent care visit. For patients on Medicaid, these costs were $9,837, $1,955, $646, $190, $73, and $0, respectively. Although no statistical analysis was performed, our data suggest that Medicare patients with supplemental insurance paid the highest median per-encounter costs for office visits, ICU visits, and urgent care visits. This is possibly because of the age difference between the groups, as older age has been associated with increased epilepsy expenditures.[9]

To our knowledge, no previous study has reported data on the health plan-paid cost per epilepsy-related health care encounter. Although the median health plan-paid costs per epilepsy-related hospitalization reported here ($9,837-$22,305, in 2018 U.S. dollars) are generally consistent with previously published data as detailed below, they are not comparable because the costs in the other studies include patients' out-of-pocket expenses in addition to what was covered by the health plan. Previous studies include a retrospective U.S. database review that reported normalized hospital charges to the patient of $16,046 per admission in 2008 for patients with epilepsy.[10] Other U.S. studies found an annual mean medical expenditure for patients with epilepsy of $13,848 (in 2011/2014, adjusted to 2016 U.S. dollars)[9] and average charge of $30,952 for hospitalizations because of uncontrolled epilepsy (in 2012).[11] Wide variation in epilepsy-specific direct costs was found in a systematic review, with annual estimates ranging from $1,022 to $19,749 (in 2013 U.S. dollars).[8]

Although no statistical analysis was performed, in patients with epilepsy all-cause hospitalizations appeared to carry a higher health plan-paid per-encounter cost than epilepsy-related hospitalizations, regardless of insurer type. The higher cost may be because of the longer length of stay versus epilepsy-related hospitalizations (median, commercially insured patients 4 vs. 3, Medicaid patients 5 vs. 3, Medicare patients with supplemental insurance 5 vs. 4).

In commercially insured and Medicaid patients with epilepsy, a considerable proportion of all-cause emergency transportations (37.0% and 24.3%, respectively) were related to epilepsy, as well as 10.6%-22.5% of ED visits, hospitalizations, and ICU visits. This points to the urgency of epilepsy-related events. In Medicare patients with supplemental insurance, the proportion of epilepsy-related encounters seemed to be lower (2.4%-11.4%), although no statistical analysis was performed. This could be because of the likely higher number of comorbid conditions in these older patients, and/or the relatively better epilepsy prognosis in the elderly.[12,13] In our analysis, 37.4% of epilepsy-related hospitalizations included care in the ICU. To the best of our knowledge, this study is the first to report the inclusion of ICU care in epilepsy-related hospitalizations. For working age patients of all insurer types, the median length of stay of an epilepsy-related hospitalization was 4 days. This is consistent with previously reported means of 3.7-3.9 days.[10,11]

LIMITATIONS

The main strengths of the current study are the reliance on accurate data of actually paid claims as a proxy for health plan-paid costs and the large sample size. On the other hand, the analysis is limited by its retrospective and descriptive nature and by the inherent limitations of claims data including potential miscoding, missing information, and reporting errors. In addition, data for Medicare-only patients were not available, and the number of health care encounters per patient was not analyzed because we did not require equal follow-up for patients. Because the distribution of commercially insured, Medicaid, and Medicare patients with supplemental insurance in the MarketScan databases may not be representative of the United States as a whole, the overall costs only apply to the database population. Therefore, we have reported costs per insurer type. Nevertheless, we performed a weighted extrapolation analysis that showed that the cost of epilepsy-related encounters to each type of insurer was largely similar when weighted from MarketScan to the entire U.S. population (data not shown). This suggests that the sample is representative of the U.S. population for each insurer type.

TABLE 2 Health Plan-Paid Cost Per Epilepsy-Related Health Care Encounter and Length of Hospital Stay, by Insurer Type

Epilepsy-Related Encounters	Commercially Insured Patients (n = 353,530)		Medicaid Patients (n = 378,051)		Medicare Patients with Supplemental Insurance[a] (n = 69,176)	
Emergency transportation						
Events, n	54,372		94,326		13,297	
Cost, median (Q1-Q3), $	687	(415-1,083)	190	(132-333)	485	(401-688)
Mean (SD), $	1,020	(2,918)	256	(266)	705	(1,679)
Emergency department visit[b]						
Events, n	88,366		125,346		12,121	
Cost, median (Q1-Q3), $	1,913	(417-4,163)	646	(186-1,295)	695	(173-2,105)
Mean (SD), $	3,140	(4,775)	940	(1,136)	2,894	(7,515)
Hospitalization						
Events, n	23,747		20,477		5,377	
Cost, median (Q1-Q3), $	22,305	(14,336-36,096)	9,837	(5,092-14,991)	19,577	(12,232-36,543)
Mean (SD), $	38,085	(71,666)	13,298	(27,093)	38,464	(73,785)
Length of hospital stay (all ages)						
Days, median (Q1-Q3)	3	(2-5)	3	(2-5)	4	(3-6)
Mean (SD)	4	(5)	5	(7)	5	(5)
Length of hospital stay (19-64 years)						
Days, median (Q1-Q3)	4	(2-5)	4	(2-5)	4	(3-6)
Mean (SD)	5	(5)	5	(6)	5	(4)
n	19,516		16,933		329	
Office visit						
Events, n	911,689		1,460,896		122,962	
Cost, median (Q1-Q3), $	95	(23-232)	73	(39-165)	100	(60-208)
Mean (SD), $	488	(4,021)	236	(1,225)	508	(2,827)
Intensive care unit visit[c]						
Events, n	8,546		8,273		1,957	
Cost, median (Q1-Q3), $	3,375	(565-9,095)	1,955	(0-5,572)	5,168	(994-10,262)
Mean (SD), $	8,700	(23,663)	3,999	(14,177)	10,298	(23,773)
Urgent care visit						
Events, n	518		157		31	
Cost, median (Q1-Q3), $	57	(0-171)	0	(0-37)	81	(0-112)
Mean (SD), $	231	(728)	21	(38)	2,165	(8,474)

[a]Costs for Medicare patients with supplemental insurance are the sum of costs paid by the supplemental insurance and by Medicare.
[b]Only includes emergency department visits not leading to hospitalization.
[c]Intensive care unit costs are a component of, and included in, hospitalization costs.

Conclusions

Our results, the first estimates of the health plan–paid cost per epilepsy-related health care encounter, confirm the burden associated with the current, suboptimal treatment of epilepsy. These data can be the basis for more granular cost-benefit analyses of not only chronic but also acute treatments of epilepsy.

DATA SHARING STATEMENT

Data from noninterventional studies are outside of UCB's data sharing policy and are unavailable for sharing.

REFERENCES

1. Zack MM, Kobau R. National and state estimates of the numbers of adults and children with active epilepsy—United States, 2015. MMWR *Morb Mortal Wkly Rep.* 2017;66(31):821-25.

2. Brodie MJ, Barry SJE, Bamagous GA, Norrie JD, Kwan P. Patterns of treatment response in newly diagnosed epilepsy. *Neurology.* 2012;78(20):1548-54.

3. Nayzilam (midazolam) nasal spray, CIV. UCB, Inc. May 2019. Accessed October 8, 2020. https://www.ucb.com/_up/ucb_com_products/documents/Nayzilam%20COL%20Rev.%205-2019.pdf

4. Valtoco (diazepam nasal spray), CIV. Neurelis, Inc. January 2020. Accessed July 15, 2020. https://www.valtoco.com/sites/default/files/VALTOCO_Prescribing_Information.pdf

5. McKee HR, Abou-Khalil B. Outpatient pharmacotherapy and modes of administration for acute repetitive and prolonged seizures. CNS *Drugs.* 2015;29(1):55-70.

6. Cramer JA, Wang ZJ, Chang E, et al. Healthcare utilization and costs in adults with stable and uncontrolled epilepsy. *Epilepsy Behav.* 2014;31:356-62.

7. Divino V, Petrilla AA, Bollu V, Velez F, Ettinger A, Makin C. Clinical and economic burden of breakthrough seizures. *Epilepsy Behav.* 2015;51:40-47.

8. Begley CE, Durgin TL. The direct cost of epilepsy in the United States: a systematic review of estimates. *Epilepsia.* 2015;56(9):1376-87.

9. Lekoubou A, Bishu KG, Ovbiagele B. Nationwide trends in medical expenditures among adults with epilepsy: 2003-2014. J *Neurol Sci.* 2018;384:113-20.

10. Vivas AC, Baaj AA, Benbadis SR, Vale FL. The health care burden of patients with epilepsy in the United States: an analysis of a nationwide database over 15 years. *Neurosurg Focus.* 2012;32(3):E1.

11. Singh G, Lingala V, Mithal A. Hospitalizations for uncontrolled epilepsy in U.S.: a national perspective. Paper presented at: American Epilepsy Society 69th Annual Meeting 2015; December 4-8, 2015; Philadelphia, PA. Accessed October 8, 2020. https://www.aesnet.org/meetings_events/annual_meeting_abstracts/view/2326914

12. Stephen LJ, Kelly K, Mohanraj R, Brodie MJ. Pharmacological outcomes in older people with newly diagnosed epilepsy. *Epilepsy Behav.* 2006;8(2):434-37.

13. Brodie MJ, Stephen LJ. Outcomes in elderly patients with newly diagnosed and treated epilepsy. *Int Rev Neurobiol.* 2007;81:253-63.