Cost Sharing for Antiepileptic Drugs: Medication Utilization and Health Plan Costs

Nina R. Joyce, PhD; Jesse Fishman, PharmD; Sarah Green, BA; David M. Labiner, MD; Imane Wild, PhD, MBA; and David C. Grabowski, PhD

ABSTRACT

OBJECTIVES: To examine the association between health plan out-of-pocket (OOP) costs for antiepileptic drugs and healthcare utilization (HCU) and overall plan spending among US-based commercial health plan beneficiaries with epilepsy.

STUDY DESIGN: Retrospective cohort.

METHODS: The Truven MarketScan Commercial Claims database for January 1, 2009, to June 30, 2015, was used. Patients 65 years or younger with epilepsy and at least 12 months of continuous enrollment before index (date meeting first epilepsy diagnostic criteria) were included. Analyses were adjusted for age group, gender, beneficiary relationship, insurance plan type, and Charlson Comorbidity Index score. Primary outcomes included proportion of days covered (PDC), HCU, and healthcare spending in 90-day postindex periods. Associations between OOP costs and mean PDC, HCU, and plan healthcare spending per 90-day period were estimated.

RESULTS: Across 5159 plans, 187,241 beneficiaries met eligibility criteria; 54.3% were female, 41.7% were aged 45 to 65 years, and 62.4% were in preferred provider organization plans. Across postindex 90-day periods, mean (SD) PDC, epilepsy-specific hospitalizations, outpatient visits, and emergency department visits were 0.85 (0.26), 0.02 (0.13), 0.34 (0.47), and 0.05 (0.22), respectively. Median (interquartile range) spending per 90-day period was $1488 ($459-$4705); median epilepsy-specific spending was $139 ($18-$623). Multivariable linear regression without health plan fixed effects revealed that higher OOP spending was associated with a decrease in PDC (coefficient, –0.008; 95% CI, –0.009 to –0.006; *P* <.001) and an increase in overall spending (218.6; 95% CI, 47.9-389.2; *P* = .012). Health plan fixed effects model estimates were similar, except for epilepsy-specific spending, which was significant (120.6; 95% CI, 29.2-211.9; *P* = .010).

CONCLUSIONS: Increases in beneficiaries' OOP costs led to higher overall spending and lower PDC.

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Over the past 15 years, many healthcare plans have increased beneficiary cost sharing for prescription drugs as a mechanism to contain healthcare spending, and literature suggests that less generous prescription drug coverage reduces drug expenditures for healthcare plans.[1-4] Some of this decrease simply shifts the drug acquisition costs, once paid by the plan, to the patients through higher out-of-pocket (OOP) costs in the form of increased deductibles, co-payments, or coinsurance. Similarly, individuals in high-deductible plans may have higher OOP spending. Higher cost sharing leads to lower medication utilization and adherence, especially among patients with chronic conditions.[5,6] Studies across a number of chronic diseases (eg, rheumatoid arthritis, multiple sclerosis, hypertension, and hypercholesterolemia) report an association between higher OOP costs and lower drug utilization.[7-10] Reduced utilization of prescription drugs with proven benefits could result in both worse health outcomes and higher overall costs.[6,11-13]

Epilepsy is a chronic brain disorder characterized by recurrent seizures. The Institute of Medicine (now the National Academy of Medicine) estimates that 1 in 26 individuals in the United States will have seizures during their lifetime and nearly 1% of the US population lives with active epilepsy.[14] Epidemiologically, epilepsy has a bimodal distribution of incident cases occurring early and later in a patient's life.[15] In the aging population, this increased incidence of epilepsy often results from stroke, trauma, and other etiologies.[16,17] Mortality associated with epilepsy is increased at all ages and is more common with poorly controlled seizures.[18]

Simply stated, the goal of epilepsy therapy is 2-fold: no seizures and no adverse effects (AEs). A wide range of antiepileptic drugs (AEDs) exist, and selecting the optimal treatment for an individual patient involves the consideration of many factors, including patient comorbidities and concomitant medications, risk of drug–drug interactions, and individual AED safety and efficacy profiles.[19] AEDs have been shown to be effective in controlling seizures in up to two-thirds of patients who receive them.[20,21] One-third of patients may not respond to initial AED monotherapy,[20] necessitating

TAKEAWAY POINTS

Health plans have increasingly shifted costs of medical care and medications to their beneficiaries, resulting in repercussions for the management of chronic disease.

- In beneficiaries with epilepsy, higher out-of-pocket (OOP) spending was associated with significant decreases in the proportion of days covered with an antiepileptic drug and in inpatient hospitalizations, and an increase in epilepsy-related outpatient visits.
- Higher OOP costs were associated with increased total healthcare spending.
- Greater formulary restriction has significant impact on beneficiaries and their management of epilepsy, with potentially severe consequences for patient outcomes.

modification of AED treatment. Breakthrough seizures may occur with suboptimal AED dosing due to intolerable AEs or titration or from inadequate efficacy. Patients who attain long-term (ie, ≥2 years) seizure freedom with medication may consider treatment cessation; however, this is a challenge,[22] with studies reporting seizure recurrence in more than one-fourth of patients after a median of 41 months.[23]

Higher cost sharing in the form of OOP costs may discourage or delay patients' access to the most appropriate medication that may control their seizures while minimizing AEs. As a consequence, treatment decisions driven by affordability rather than clinical appropriateness may lead to suboptimal treatment (from an efficacy or tolerability viewpoint). This may result in higher medical costs in both the short term (eg, due to injuries or hospitalizations) and the long term (eg, osteoporosis-related complications from long-term use of enzyme-inducing AEDs). To date, studies on the relationship between higher plan cost sharing for AEDs and the utilization of AEDs, overall healthcare utilization (HCU), and plan spending for enrollees with epilepsy have not been reported. The objective of this study was to examine how health plan cost sharing for AEDs relates to AED utilization, HCU, and overall plan spending among US-based commercial health plan beneficiaries with epilepsy.

METHODS

Data and Study Design

A retrospective cohort study of individuals with epilepsy was conducted using data from the Truven MarketScan Commercial Claims research database for January 1, 2009, through June 30, 2015, and reporting aligned with STROBE guidelines for cohort studies.[24] Individuals 65 years or younger were included in the analysis if they had at least 12 months of continuous enrollment prior to meeting 1 of the following diagnostic conditions: 2 or more inpatient or outpatient claims with an *International Classification of Diseases, Ninth Revision* (*ICD-9*) code of 345.xx; 1 or more claim with code 345.xx and 1 or more claim with code 780.39; 1 or more claim with code 345.xx and a pharmacy claim for an AED; and 2 or more claims with a code of 780.39 and a pharmacy claim for an AED. In cases requiring an *ICD-9* code and AED pharmacy claim, both had to occur within a 12-month period. The index date was defined as the date on which the first of the diagnostic criteria was met after a period of 12 months of continuous enrollment. Individuals in capitated health maintenance organization (HMO) plans were excluded because claims are not submitted for each service provided; thus, measurement of their HCU and spending was not captured. The follow-up period began at the index date and was divided into 90-day periods until the beneficiary was no longer enrolled or was administratively censored on December 31, 2015. All periods were required to have the full 90 days; any partial period due to censoring was excluded from the analysis. A 90-day period was chosen based on prior studies of the association between cost sharing and healthcare spending that found that outcomes assessed over quarters are sensitive enough to identify changes over time.[25,26] All patient characteristics, cost-sharing measures, and HCU and spending outcomes were assessed for each 90-day period.

Patient Characteristics

All analyses were adjusted for the individual's age group (0-18, 19-45, or 46-65 years), gender, relationship to beneficiary (employee, spouse, or child/other), insurance plan type (comprehensive, exclusive provider organization, HMO, point of service [POS], preferred provider organization [PPO], POS with capitation, consumer-driven health plan, or high-deductible health plan), and Charlson Comorbidity Index (CCI) score (0, 1, 2, or ≥3),[27] which was based on diagnoses in the year preceding the start of each 90-day period. In subgroup analyses, an epilepsy-specific comorbidity index[28] was included; however, estimates were unchanged and, thus, data reflect models adjusted for the CCI score.[28]

OOP Costs

The objective of the analysis was to estimate how OOP costs for AEDs related to the proportion of days covered (PDC) and health plan spending for individuals with epilepsy. Because drug prices are largely uniform across plans, we focused on price differences introduced by a plan's generosity. A commonly used method to construct a market-basket index of a set of representative AEDs was employed to calculate OOP costs.[5,29,30] To construct the market basket of AEDs, all dispensings in a calendar year for a random sample of 100 individuals with at least 1 dispensing for an AED in that year were aggregated. Each AED in this market basket was assigned a weight equal to the relative frequency of dispensings for that AED. For example, if in 2009, lacosamide made up 40% of all AED dispensing claims across the sample of 100 people and phenytoin made up the remaining 60%, then the weights for lacosamide and phenytoin would be 0.4 and 0.6, respectively. The

product of the weight and the average OOP cost, which included the patient's deductible, coinsurance, and co-payment, for the AED were then summed across all AEDs for each plan-year. Thus, if in health plan A, the average OOP cost was $5 for lacosamide and $10 for phenytoin, then the market-basket value would be the weighted average of the 2: ($5 × 0.4) + ($10 × 0.6) = $8. Because prescriptions could range from 30 to 90 days' supply, a standardized measure of the cost per day based on the days' supply of AEDs was created (instead of using the number of dispensings).

Outcomes

Primary outcomes were measures of PDC, HCU, and healthcare spending in each 90-day period; the mean and median across all postindex 90-day periods were calculated for each outcome measure. PDC was chosen, as opposed to other commonly used measures of adherence (eg, medication possession ratio), based on a study of AED adherence that found PDC to be a more stable measure.[31,32] PDC has also been used as a quality indicator for treatment of other chronic diseases.[33] An algorithm for calculating PDC across short time periods using claims data was employed.[34] The algorithm used shorter time periods as the denominator based on the pattern of drug dispensing to allow the PDC to vary, versus calculating the PDC over a set period of time, such as a year. For comparison with prior studies, the annual PDC was calculated according to standard methods.[31] Only individuals with at least 1 AED dispensing in each quarter were included in the PDC measure. HCU was calculated as the total number of inpatient admissions, outpatient visits, and emergency department (ED) visits; epilepsy-specific HCU required claims with a primary diagnosis of epilepsy (*ICD-9* code 345.xx or 780.39). Total outpatient, inpatient, and overall spending, as well as overall epilepsy-specific spending, were calculated as the sum of the deductible, co-pay, coinsurance, amount paid by insurance, and amount paid by coordination of benefits for each measure as identified from the adjudicated claims. Overall plan spending included total spending on all claims for patients with any primary diagnosis, whereas epilepsy-specific spending was defined as total spending on all claims for patients with a primary diagnosis of epilepsy.

Statistical Analysis

Multivariate linear models were used, first with and then without health plan fixed effects, to estimate the association between OOP spending for each plan and PDC and health plan spending in each 90-day period. For each 90-day period, a market-basket measure was used for the year in which the period began. Thus, the period beginning April 1, 2011, was assigned to the market-basket measure calculated for the calendar year 2011. Conducting the analysis over 90-day intervals is consistent with prior studies.[26] A stable measure of the market basket was calculated over a 1-year time frame to avoid spikes in the prescribing of a single drug. Consequently, the market-basket distribution of AEDs was more likely to reflect a representative distribution of AEDs. Each model was adjusted for the patient's age at the start of the period, gender, relationship to beneficiary, plan type, and calendar year. In sensitivity analyses, a categorical measure of OOP costs was used to further examine the linear relationship between healthcare spending and OOP costs. Categories were defined as low, medium, and high according to the tertile of OOP costs in that year.

Subgroup Analyses

To test model and study design assumptions, subgroup analyses were conducted. First, the cohort was limited to only those who were newly diagnosed with epilepsy, defined as beneficiaries with no AED dispensing or epilepsy diagnosis for at least 3 years. Second, the top and bottom 1% of spending values were excluded to limit the effect of spending outliers. In both cases, models were fit without health plan fixed effects. Last, 2-part models were used to account for skewed spending. However, because of the low prevalence of some of the outcomes (eg, inpatient hospitalizations), models failed to converge and are not included in the results.

RESULTS

Study Cohort

A total of 187,241 beneficiaries across 5159 health plans met the study's eligibility criteria (**Figure**). The mean number of 90-day periods per beneficiary was 10.4, and median OOP costs as measured by the market-basket index were $0.30 per day. There was a slightly higher percentage of females (54.3%), and 41.7% of beneficiaries were between the ages of 45 and 65 years. Most individuals were the primary beneficiary (42.6%), had a CCI score of 0 (72.4%), and were enrolled in a PPO plan (62.4%) (**Table 1**).

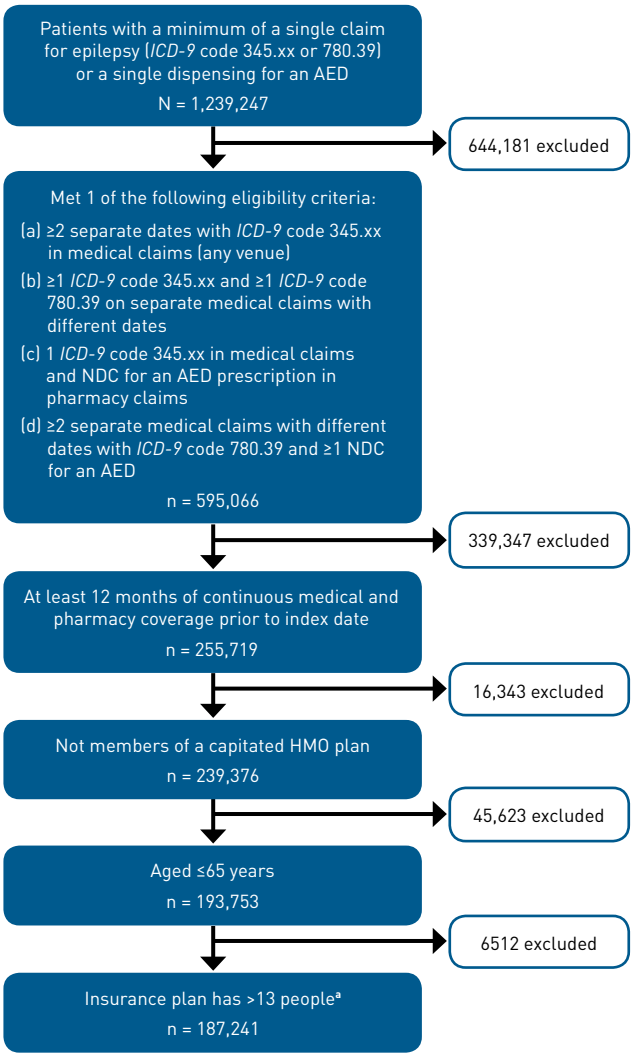
Outcomes

The mean (SD) PDC over 90-day periods was 0.85 (0.26), and 71.3% of individuals had a 90-day PDC greater than 0.80. The annual PDC was 0.79 (0.23). Analysis of HCU showed that overall and epilepsy-specific inpatient hospitalizations, as well as ED visits, across 90-day periods were infrequent, whereas the number of outpatient visits overall was higher (**Table 2**). Mean outpatient spending in a 90-day period made up the largest proportion of overall spending (45.0%). Epilepsy-specific healthcare spending was much lower, accounting for 15.8% of overall health plan spending in a 90-day period (Table 2).

Multivariable Regression

In multivariable linear regression models without health plan fixed effects, higher OOP spending was associated with statistically significant decreases in PDC and inpatient hospitalizations, but an

FIGURE. Flow Chart of Patient Inclusion Criteria



AED indicates antiepileptic drug; HMO, health maintenance organization; *ICD-9*, *International Classification of Diseases, Ninth Revision*; NDC, National Drug Code.
[a]Screening based on health plan identifier number.

TABLE 1. Demographics for Study Cohort at Baseline

	n	%
Health plans	5159	–
Total individuals	187,241	–
Female	101,680	54.3
Age group, years		
0-18	42,760	22.8
19-45	66,364	35.4
46-65	78,117	41.7
Relationship to beneficiary		
Employee	79,713	42.6
Spouse	44,272	23.6
Child/other	63,256	33.8
Health plan type		
Comprehensive	8236	4.4
EPO	2905	1.6
HMO	14,841	7.9
POS	15,019	8.0
PPO	116,893	62.4
POS with capitation	1087	0.6
CDHP	11,181	6.0
HDHP	5805	3.1
Missing plan type	11,274	6.0
CCI score		
0	135,520	72.4
1	20,908	11.2
2	17,872	9.5
≥3	12,941	6.9

CCI indicates Charlson Comorbidity Index; CDHP, consumer-driven health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization.

increase in epilepsy-related outpatient visits (**Table 3**). Similarly, higher OOP spending was associated with an increase in overall spending, both inpatient and outpatient, but not overall epilepsy-specific spending (Table 3). When health plan fixed effects were included in the model, overall plan spending had similar trends and higher coefficients, with the exception of overall epilepsy-specific and total epilepsy-specific outpatient spending. Point estimates for PDC were slightly attenuated from models without health plan fixed effects and were not statistically significant ($P = .057$) (Table 3). In sensitivity analyses, the direction of results was generally consistent with linear specifications of OOP costs, with the exception of total outpatient costs, which were negatively associated with OOP spending (**eAppendix A** [eAppendices available at **ajmc.com**]).

Subgroup Analyses

Several subgroup analyses were conducted to test the robustness of the estimates. All subgroup analyses were fit models without fixed effects. First, when the cohort was limited to newly diagnosed beneficiaries (n = 15,990), no significant associations were found between OOP spending and PDC or healthcare spending, with the exception of total outpatient spending, which was positively associated with OOP spending (**eAppendix B**). Second, when the top and bottom 1% were trimmed from the total spending values, overall plan spending (coefficient, 169.9; 95% CI, 98.6-241.2; $P < .001$) was positively associated with OOP costs, whereas total inpatient spending (coefficient, –72.6; 95% CI, –108.5 to –36.7; $P < .001$), overall epilepsy-specific spending (coefficient, –28.7; 95% CI, –39.3 to –18.2;

P <.001), and total epilepsy-specific outpatient spending (coefficient, –7.9; 95% CI, –13.1 to –2.7; P = .003) were negatively associated with OOP costs (**eAppendix C**).

TABLE 2. HCU and Spending

HCU Outcome Across 90-Day Periods	Mean	SD	Median	IQR
PDC	0.85	0.26	1	0.78-1.00
Inpatient hospitalizations	0.08	0.26	0	0-0
Epilepsy-specific inpatient hospitalizations	0.02	0.13	0	0-0
Outpatient visits	0.87	0.34	1	1.00-1.00
Epilepsy-specific outpatient visits	0.34	0.47	0	0-1.00
ED visits	0.17	0.37	0	0-0
Epilepsy-specific ED visits	0.05	0.22	0	0-0
Healthcare Spending (OOP costs) Per 90-Day Period	**Mean ($)**	**SD ($)**	**Median ($)**	**IQR ($)**
Overall plan spending	7109	26,738	1488	459-4705
Total inpatient spending	2698	22,007	0	0-0
Total outpatient spending	3201	10,898	564	138-2444
Overall epilepsy-specific plan spending	1123	5807	139	18-623
Total epilepsy-specific inpatient spending	297	4947	0	0-0
Total epilepsy-specific outpatient spending	448	2324	0	0-116

ED indicates emergency department; HCU, healthcare utilization; IQR, interquartile range; OOP, out-of-pocket; PDC, proportion of days covered.

DISCUSSION

In this study of more than 180,000 privately insured individuals with epilepsy, higher OOP cost sharing for AEDs was associated with a decrease in PDC and an increase in overall and epilepsy-related healthcare spending. These findings were consistent across several subgroup analyses, including variable definitions and model specification. Shifting costs to patients is one way that insurers can try to reduce spending. However, our results suggest that the unintended consequences of this approach may actually increase health plan spending in the long run. Thus, policies (eg, requirements to fail 1 treatment first) that penalize patients via higher OOP costs for not responding to a particular treatment financially disincentivize patients from taking a prescribed medicine that may be their best treatment. Additionally, they may detour physicians from their initial treatment selection, which was in the best interest of the patient.

The association among OOP costs, HCU, and spending has been previously examined.[25,26] Although higher OOP costs are generally associated with lower utilization and higher spending, these associations are often weaker in patients with a chronic condition receiving ongoing care, reflecting a lower price sensitivity than in patients receiving intermittent medications, such as nonsteroidal anti-inflammatory drugs or antihistamines.[5] Thus, although we found a negative association between OOP spending and HCU, the magnitude of those associations may reflect this trade-off. In addition, our estimates reflect the association over a 90-day period, in which small estimates may translate into substantial changes over longer periods of time. For example, these results indicate that a $10 increase in OOP spending is associated with a decrease in PDC of 0.16 per year. Furthermore, although the magnitude of our estimates may appear small relative to previous studies, the high costs associated with the treatment of epilepsy suggest that

TABLE 3. Adjusted[a] Multivariable Linear Regression of OOP Costs for AEDs on PDC and Health Plan Spending

	Without Health Plan Fixed Effects			With Health Plan Fixed Effects		
Outcome	**Coefficient**	**95% CI**	***P***	**Coefficient**	**95% CI**	***P***
PDC	–0.008	–0.009 to –0.006	<.001	–0.004	–0.009 to 0.000	.057
Hospitalization	–0.006	–0.007 to –0.004	<.001	0.006	0.001-0.010	.010
Outpatient visit	–0.003	–0.005 to –0.001	.018	0.006	0.001-0.011	.031
Epilepsy-specific hospitalization	0.000	–0.001 to 0.000	.345	0.001	–0.001 to 0.003	.224
Epilepsy-specific outpatient visit	0.009	0.006-0.012	<.001	0.009	0.001-0.016	.022
Overall plan spending	218.6	47.9-389.2	.012	702.9	288.9-1116.9	.001
Total inpatient spending	211.0	67.3-354.7	.004	378.9	29.4-728.5	.034
Total outpatient spending	140.4	72.2-208.6	<.001	232.4	67.6-397.3	.006
Overall epilepsy-specific plan spending	–0.4	–37.9 to 37.2	.985	120.6	29.2-211.9	.010
Total epilepsy-specific inpatient spending	11.4	–21.1 to 43.9	.492	13.5	–65.6 to 92.5	.738
Total epilepsy-specific outpatient spending	2.0	–12.5 to 16.5	.790	43.7	8.5-79.0	.015

AED indicates antiepileptic drug; OOP, out-of-pocket; PDC, proportion of days covered.
[a]All models are adjusted for female gender, age group, relationship to beneficiary, plan type, Charlson Comorbidity Index score (0, 1, 2, or ≥3), and calendar year.

the impact in absolute terms may still be very high. The Institute of Medicine has estimated the total direct and indirect annual costs associated with epilepsy to be $15.5 billion.[35] Thus, if all health plans capped their OOP spending at the median value of $0.30 per day, one would expect to save $140 per person per year among privately insured individuals, translating to an estimated savings of $121 million per year, or 0.8% of the total costs associated with epilepsy (**eAppendix D**).

To our knowledge, this study is the first to examine the association among OOP costs, HCU, and spending in a population of privately insured individuals with epilepsy. Several strengths are worth mentioning. First, the use of a market-basket index to measure OOP spending[5] allowed us to standardize the comparisons across plans, thereby avoiding the potential for one plan's benefit design to bias the comparison. A second strength of the study is the large sample size. Although epilepsy is the fourth most common neurological condition in the United States,[36] it is still rare enough that large cohorts of individuals with epilepsy can be difficult to find and expensive to follow.[14] The Truven MarketScan database has more than 40 million covered lives, which provided a large enough sampling to identify and follow more than 180,000 individuals with epilepsy, providing the statistical power to test hypotheses related to rare outcomes, such as inpatient hospitalization. A third study strength is the use of a newly published validated algorithm for calculating PDC over shorter time periods, such as the 90-day periods used in the current analysis.[34] PDC measured over this shorter period provided a granularity in the measures that would not be possible over the more commonly used longer periods of time (eg, 1 year).

Limitations

Although this is the first study to examine the effect of OOP costs on HCU and spending for individuals with epilepsy, there were several limitations. First, this was a privately insured population 65 years and younger; therefore, our results may not be generalizable to uninsured individuals, those with Medicaid or Medicare, or individuals with a lower socioeconomic status, for whom the cost-sharing structures may differ greatly. Second, although the use of a 90-day period over which to measure outcomes provided the sensitivity to detect smaller changes over time, some outcomes, such as epilepsy-related hospitalizations, were rare and resulted in zero-inflated counts in each period, which limited the options for model specification. Third, patients varied with respect to the length of time since their initial epilepsy diagnosis, and individuals' experiences prior to inclusion in the study were not captured. Fourth, we did not look at treatment patterns, persistence, or rate of abandonment, which could also have been factored into our models as HCU measures or as outcomes. In subgroup analyses, the sample was limited to beneficiaries with new diagnoses, but because of the dramatic reduction in sample size and the highly skewed distribution of outcomes, estimates were not stable.

CONCLUSIONS

As healthcare costs continue to rise, payers may seek out alternative methods of limiting spending, including transferring some of the cost burden to patients. However, our findings suggest that, for patients with epilepsy, the long-term effect of this decision may be counterproductive, as patients reduce their use of preventive services and medications, which may translate into costlier care later on. Furthermore, given the potentially severe consequences of reducing medication adherence, such as greater seizure frequency that can lead to death, payers should carefully consider the unintended consequences of increased cost sharing for patients with epilepsy. ■

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Author Affiliations: Department of Health Care Policy, Harvard Medical School (NRJ, DCG), Boston, MA; Department of Health Services Research, Policy and Practice, Brown University (NRJ), Providence, RI; UCB Pharma (JF, IW), Smyrna, GA; Precision Health Economics (SG), Los Angeles, CA; Department of Neurology, The University of Arizona Health Sciences Center (DML), Tucson, AZ.

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Address Correspondence to: Nina R. Joyce, PhD, Brown University School of Public Health, Box G-S121-6, 121 South Main St, Providence, RI 02198. Email: nina_joyce@brown.edu.

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eAppendix A. Adjusted Multivariable Linear Regression of Tertile Measures of Out-of-pocket Costs for AEDs on PDC and Health Care Spending[a] (Reference category is tertile 1, lowest cost sharing)

	Without Health Plan Fixed Effects			With Health Plan Fixed Effects		
Outcome	**Coefficient**	**95% CI**	***P***	**Coefficient**	**95% CI**	***P***
PDC						
Medium cost share	0.004	0.002 to 0.007	.001	0.001	-0.003 to 0.005	.960
High cost share	0.004	0.001 to 0.006	.392	0.000	-0.004 to 0.004	.046
Hospitalization						
Medium cost share	0.001	-0.001 to 0.003	.203	0.001	-0.003 to 0.004	.769
High cost share	-0.001	-0.003 to 0.001	.266	0.005	0.001 to 0.009	.016
Outpatient visit						
Medium cost share	0.010	0.007 to 0.012	<.001	0.004	-0.001 to 0.008	.126
High cost share	0.006	0.003 to 0.008	<.001	0.003	-0.002 to 0.009	.187
Epilepsy-specific hospitalization						
Medium cost share	0.000	-0.001 to 0.001	.738	0.000	-0.002 to 0.002	.765
High cost share	0.000	-0.001 to 0.001	.429	0.002	0.000 to 0.004	.034
Epilepsy-specific outpatient visit						
Medium cost share	0.004	0.001 to 0.008	.020	0.003	-0.003 to 0.010	.299
High cost share	0.009	0.006 to 0.013	<.001	0.007	0.000 to 0.014	.052
Overall plan spending						
Medium cost share	-138.7	-339.4 to 62.1	.176	347.3	-13.5 to 708.0	.059
High cost share	205.2	10.8 to 399.6	.039	610.9	215.9 to 1005.9	.002
Total inpatient spending						
Medium cost share	73.8	-95.2 to 242.8	.392	310.3	5.7 to 614.9	.046
High cost share	271.8	108.1 to 435.5	.001	471.7	138.2 to 805.2	.006
Total outpatient spending						
Medium cost share	-210.3	-290.5 to -130.0	<.001	17.7	-126.0 to 161.3	.810
High cost share	-16.0	-93.8 to 61.7	.686	114.2	-43.1 to 271.5	.155
Overall-epilepsy specific plan spending						
Medium cost share	-9.2	-53.4 to 34.9	.682	-87.0	-166.6 to -7.4	.032

High cost share	19.9	-22.9 to 62.7	.361	-11.6	-98.8 to 75.5	.794
Total-epilepsy specific inpatient spending						
Medium cost share	-28.1	-66.3 to 10.1	.149	-106.5	-175.4 to -37.6	.002
High cost share	-9.0	-46.0 to 28.0	.633	-57.0	-132.4 to 18.4	.138
Total-epilepsy specific outpatient spending						
Medium cost share	-14.9	-32.0 to 2.1	.087	-11.3	-42.0 to 19.5	.472
High cost share	-7.0	-23.6 to 9.5	.404	-3.3	-36.9 to 30.4	.849

AED indicates antiepileptic drug; CI, confidence interval; PDC, proportion of days covered.

[a]All models are adjusted for female gender, age group, relationship to beneficiary, plan type, Charlson comorbidity score (0, 1, 2 or 3+) and calendar year.

eAppendix B. Subgroup Analysis:[a] Multivariable Linear Regression of Out-of-Pocket Costs for AEDs on PDC and Health Plan Spending Among Individuals Newly Diagnosed With Epilepsy

Outcome	**Coefficient**	**95% CI**	***P***
PDC	0.0008	-0.01 to 0.01	.900
Hospitalization	-0.0244	-0.04 to -0.01	<.001
Outpatient visit	0.0112	0.00 to 0.02	.009
Epilepsy specific hospitalization	-0.0066	-0.01 to 0.00	.071
Epilepsy specific outpatient visit	0.0202	0.00 to 0.04	.021
Overall plan spending	-493.3	-2170.9 to 1184.3	.564
Total inpatient spending	-1103.39	-2565.3 to 358.5	.139
Total outpatient spending	760.468	198.0 to 1322.9	.008
Overall epilepsy-specific plan spending	-187.076	-679.1 to 305.0	.456
Total epilepsy-specific inpatient spending	-182.447	-656.9 to 292.0	.451
Total epilepsy-specific outpatient spending	-13.278	-122.7 to 96.2	.812

AED indicates antiepileptic drug; CI, confidence interval; PDC, proportion of days covered.

[a]All models are adjusted for female gender, age group, relationship to beneficiary, plan type, Charlson comorbidity score (0, 1, 2 or 3+) and calendar year.

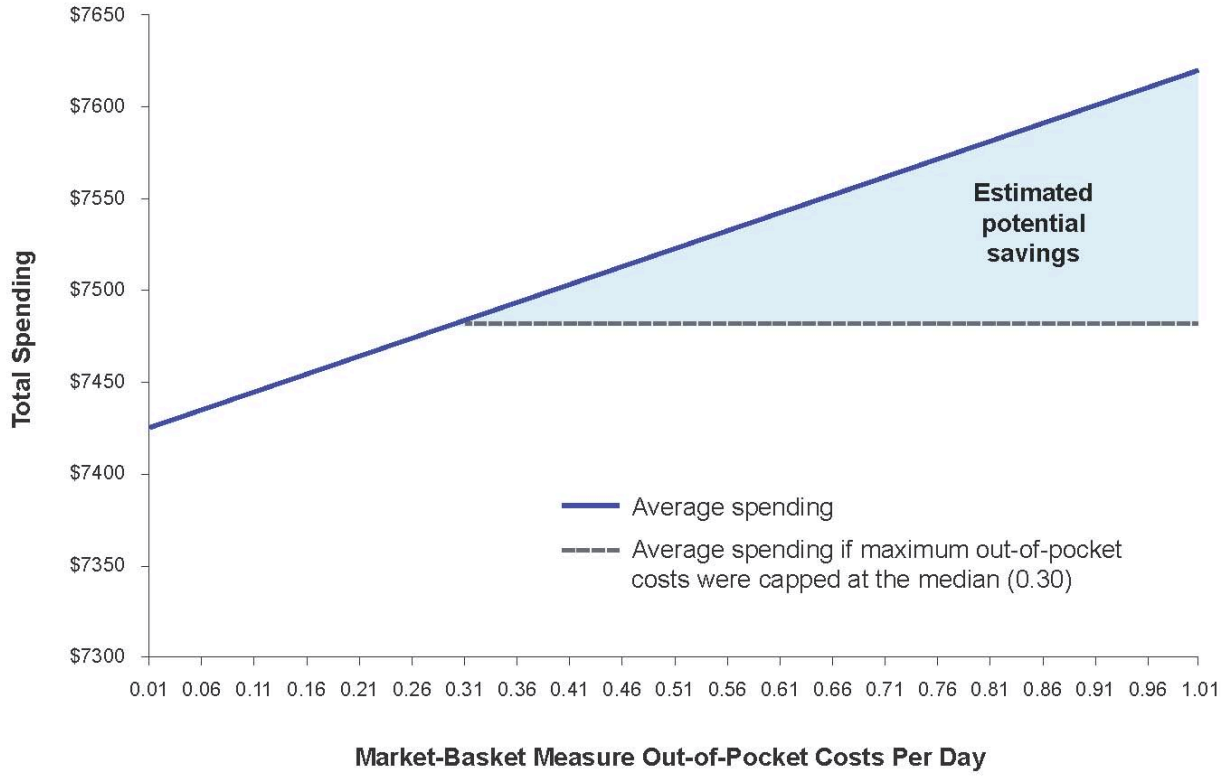
eAppendix C. Subgroup Analysis[a]: Multivariable Linear Regression of Out-of-pocket Costs for AEDs on Healthcare Spending (Top and Bottom 1% of Healthcare Spending Excluded)

Outcome	Coefficient	95% CI	*P* Value
Overall plan spending	169.9	98.6 to 241.2	<.001
Total inpatient spending	-72.6	-108.5 to -36.7	<.001
Total outpatient spending	-9.3	-38.6 to 20.0	.534
Overall epilepsy-specific plan spending	-28.7	-39.3 to -18.2	<.001
Total epilepsy-specific inpatient spending	0.2	-2.9 to 3.3	.907
Total epilepsy-specific outpatient spending	-7.9	-13.1 to -2.7	.003

AED indicates antiepileptic drug; CI, confidence interval; PDC, proportion of days covered.

[a]All models are adjusted for female gender, age group, relationship to beneficiary, plan type, Charlson comorbidity score (0, 1, 2, or 3+), and calendar year.

eAppendix D. Overall Spending[a] by Out-of-pocket Costs for AEDs per Day



[a]Based on an average savings of $140 per person per year according to our model; 2.4 million adults with active epilepsy,[1] of which 36% have private insurance;[2] and an estimated $15.5 billion a year in direct and indirect costs attributable to epilepsy.[1] Savings are estimated as the total predicted spending across all values of out-of-pocket costs minus the predicted spending if all values greater than the median (0.3) were capped at 0.3. Estimates were then multiplied by 4 to obtain the annual savings.

[1]National Center for Chronic Disease Prevention and Health Promotion. Epilepsy fast facts. 2016; https://www.cdc.gov/epilepsy/basics/fast-facts.htm. Accessed April 7, 2017.

[2]Thurman DJ, Kobau R, Luo YH, Helmers SL, Zack MM. Health-care access among adults with epilepsy: The U.S. National Health Interview Survey, 2010 and 2013. *Epilepsy and Behavior.* 2016;55:184-188. doi: 10.1016/j.yebeh.2015.10.028.