

FULL-LENGTH ORIGINAL RESEARCH

The economic burden of caregiving in epilepsy: An estimate based on a survey of US caregivers

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Abstract

Objective: The burden of caregiving for persons with epilepsy (PWEs) has not been examined previously in the United States. We assessed the clinical impact and direct and indirect economic costs for caregivers of PWEs.

Methods: An internet survey of 500 caregivers of PWEs was conducted from May to July 2015 using a combination of validated instruments and questions designed specifically for this survey. Caregivers were stratified by PWE age (adult/child) and disease severity (low: 0 vs high: 1 + seizures in the prior month). Annual self-reported direct and indirect costs were reported per caregiver and extrapolated to all US caregivers. The economic burden of caregiving for PWEs was defined as the difference between costs for caregivers and the general population.

Results: Caregivers reported that PWEs averaged 11.4 seizures in the prior month. Eighty percent of respondents were female and the average age was 44.3. Since becoming a caregiver, many reported anxiety (52.8%), depression (41.0%), and insomnia (30.8%). Annual mean direct medical costs for caregivers of children with low vs high seizure frequency were \$4344 and \$10 162, respectively. Costs for caregivers of adult PWEs were \$4936 and \$8518. Mean indirect costs associated with caregiving for a child with low vs high seizure frequency were \$20 529 and \$40 137; those for caregivers of an adult were \$13 981 and \$28 410. The cost estimates are higher vs the general US population; annual per-person healthcare utilization costs were \$2740 and productivity loss costs were \$5015. When extrapolating to the US population of PWE caregivers, annual costs exceeded \$62 billion vs \$14 billion for the general population, resulting in a caregiver burden of nearly \$48 billion.

Significance: The clinical and economic burden of caregivers for PWE were substantial, and greatest for those caring for children with frequent seizures. The impact on caregivers should be considered when estimating the value of interventions that control epilepsy.

KEYWORDS

costs, health economics, health-related quality of life, indirect costs, productivity

1 | INTRODUCTION

According to the Centers of Disease Control and Prevention (CDC), 5.1 million children and adults in the United States have epilepsy.¹ Incidence is highest in children and older adults, and prevalence is higher in older ages given the relatively low mortality rate.² The burden of seizures varies tremendously, with some persons with epilepsy (PWEs) experiencing seizures only at initial diagnosis and others having daily seizures throughout their lives. Because epilepsy can be a life-long, disabling condition, care for PWEs is often provided by a family member, such as a parent, spouse, or sibling. Caregiver responsibilities may include ensuring safety during seizures, calling for medical help, administering medication, providing transportation, and attending medical appointments.^{2,3}

Health care for PWEs is burdensome and expensive, with recent estimates of annual direct epilepsy-specific healthcare costs ranging from \$8412 to \$11 354 in 2013 dollars.⁴ Many studies have examined healthcare costs to PWE themselves, both in terms of direct (eg, medication, physician visits, hospitalization) and indirect costs (ie, sick days, productivity losses).⁴⁻⁶ The clinical and economic burden on caregivers is much more sparsely researched. A review of all published literature using PubMed found only two studies examining the economic impact of epilepsy on caregivers, neither of which were performed in the United States.^{7,8}

To develop a comprehensive understanding of the impact of epilepsy in the United States, estimates of the burden of caregiving are needed. We undertook this multi-method study to measure this burden, determine whether the burden differed depending on PWE characteristics, and to translate the findings into an estimate of the excess costs associated with caregiving for PWEs across the US population.

2 | METHODS

2.1 | Overview

In this study, we surveyed caregivers of PWE in 2015 to estimate the economic burden of caregiving and identify sub-populations with higher burden. Respondents gave information about their own demographics, health, health service use, and caregiver burden (using several validated instruments). Respondents were then divided into subgroups based on characteristics of the PWE (ie, age and disease severity). Caregiving was monetized using survey responses and publicly available data, and costs were calculated for each subgroup and for the population as a whole (Figure 1). Using these results, we estimated the incremental costs of caregiving for PWEs relative to the general population, and the differences in costs based on the characteristics of the PWE.

Key Points

- Although the clinical and economic burden on people with epilepsy in the United States has been studied frequently, there is little research on the burden to caregivers.
- To fill the gap in the literature, a survey was administered to 500 caregivers of persons with epilepsy (PWEs) to assess the clinical and economic burden of caregiving.
- Nearly one-third of caregivers reported depression symptoms; symptoms were reported more often by those caring for children with epilepsy.
- Costs of caregiving exceeded those for the general population and increased significantly with increasing seizure frequency.
- Results highlighted the high burden for caregivers, with costs exceeding previously estimated direct costs to the patients themselves.

2.2 | Caregiver survey

A survey was administered to assess the caregiver experience and quantify the time and health burden of providing care to PWEs. Survey respondents were recruited through the Epilepsy Foundation (n = 247) using direct email, social media, and the Foundation website,⁹ and through Lightspeed Research (n = 253), an organization that recruits participants for online surveys via email. Eligible participants were at least 18-years-old, based in the United States, able to read and write in English, provided informed consent, and self-identified as being caregivers of PWEs. Institutional review board approval was obtained through the Sterling Institutional Review (Atlanta, GA).

The survey comprised multiple domains and consisted of both items developed for this project and items from previously validated surveys. Caregiver characteristics collected were age, gender, education, annual household income, insurance status, marital status, and relationship to the PWEs. The survey also asked length of time providing care, the number of hours per week providing care, and whether respondent was paid for providing care. Caregiver health characteristics included body mass index (BMI), smoking status, exercise behavior, alcohol consumption, and current health conditions. Caregivers were asked, over the past 6 months, whether and how often they had visited a doctor's office (for both psychiatric and medical care), the emergency room (ER), or been admitted to the hospital for their own (and not the PWE's) health. The accuracy of self-reported information on major healthcare use by PWEs over a relatively brief recall period has been validated in a previous study.¹⁰ In addition,

the Charlson Comorbidity Index (CCI)¹¹ was used to calculate a comorbidity burden score. Caregivers also reported the following characteristics of the PWEs: age, gender, race/ethnicity, insurance status, and type, years diagnosed with epilepsy, diagnosing physician specialty, type of epilepsy, seizure frequency within the past month, and use of prescription medications.

Six survey instruments were used to examine various aspects of caregiver burden: the Patient Health Questionnaire-9 (PHQ-9);¹² the Zarit Burden Interview (ZBI);¹³ the Bakas Caregiving Outcomes Scale (BCOS);¹⁴ the 12-Item Short Form Survey Instrument version 2 (SF-12v2);¹⁵ a measure of stress-related comorbidity (designed specifically for this study); and the Work Productivity and Activity Impairment (WPAI) questionnaire. Other than the stress measure, these instruments have been validated and used extensively, both in the United States and internationally, in a variety of different populations.¹²⁻¹⁶

The nine-item PHQ-9 was used to assess depression severity: minimal (0-4), mild (5-9), moderate (10-14), moderately severe (15-19), and severe (20-27).¹² The ZBI¹³ is a 22-item questionnaire that evaluates the caregiver's health condition, psychological well-being, finances, and social life. The total score is additive and categorized as: little or no burden (0-20 points), mild-to-moderate burden (21-40 points), moderate-to-severe burden (41-60 points), and severe burden (61-88 points). Change in the caregivers' circumstances was assessed via the BCOS,¹⁴ a 15-item measure of life changes each rated from -3 ("Changed for the Worst") to +3 ("Changed for the Best"). For the SF-12v2, we calculated the physical component summary (PCS) and the mental component summary (MCS), which are normed to a mean of 50 and a standard deviation of 10. Higher scores indicate better health status. In addition, potentially stress-related comorbidities were identified by asking respondents: "Since becoming a caregiver for the person with epilepsy have you experienced the following" and then listing as possible conditions: anxiety, chronic constipation, depression, diarrhea, gastroesophageal reflux disease (GERD), headache/migraine, heartburn, high blood pressure (hypertension), insomnia, irritable bowel syndrome, and sleep disorder. Respondents were not asked whether it was the first experience with these conditions, but rather if they had occurred since becoming a caregiver. The WPAI is a six-item validated instrument,¹⁶ which consists of four metrics quantified as the percentage of the work week impacted over the past 7 days: absenteeism, defined as time missed because of one's health; presenteeism, defined as time in which the worker is on the job but, because of illness or other medical conditions, not fully functioning; overall work productivity loss, an overall impairment estimate that is a combination of absenteeism and presenteeism; and activity impairment, the percentage of impairment in daily

activities because of one's health. Only respondents who reported being employed full- or part-time provided data for absenteeism, presenteeism, and overall work impairment, whereas all respondents provided data for activity impairment.

2.3 | Cost calculations

Using a subset of data from the survey described above, we monetized the responses to estimate both indirect and direct costs to caregivers. To estimate the indirect costs, we converted the individual respondent estimates of productivity losses, reported as a proportion of the workweek, to dollar terms. From the WPAI, we estimated the productivity losses associated with providing care as the sum of absenteeism and presenteeism times. We converted the estimates of the proportion of time missed among employed respondents to annual hours missed, assuming a 40-hour workweek and 50 weeks worked per year, the latter to reflect holidays and vacation. To calculate annual costs due to presenteeism and absenteeism, annual hours missed were multiplied by hourly wage rates, which were estimated from survey respondents based on the household income level selected. Income level choices included <\$25 000, \$25 000-\$49 000, \$50 000-\$75 000, and >\$75 000. It was assumed that respondents within the middle groupings earned the midpoint of the ranges, those selecting <\$25 000 were assigned an income of \$12 500, and those selecting >\$75 000 were assigned an income of \$100 000. Because WPAI responses were not provided by those not employed, they were excluded from the calculation of productivity losses.

Direct costs (eg, healthcare utilization of PWE caregivers) were estimated from the survey based on number of doctor visits, psychiatrist visits, emergency department visits, and hospitalizations for each respondent over the prior 6 months. Doctor visits and psychiatrist visits were combined into a single, composite measure, "physician visits," to better allow comparison of results with those from the general population. Six-month estimates of utilization from survey respondents were doubled to calculate annual medical encounters. The cost of each type of utilization was based on estimates reported in the 2015 Medical Expenditures Panel Survey (MEPS) responses.¹⁷ Costs from the 2015 MEPS were used to match the timeframe the survey was conducted.

To put the PWE caregiver costs in perspective, we calculated productivity losses and healthcare utilization for the general population. Because the necessary information regarding productivity losses for the general population was not available from MEPS, we required data from another source. The ideal population would match our epilepsy caregivers in all aspects except being a caregiver. To identify such a group, we explored other analyses that

estimated productivity losses for caregivers and included a comparator group of noncaregivers of approximately the same age as epilepsy caregivers. Although no other analyses estimated the impact of epilepsy caregiving, we did find a study that estimated absenteeism and presenteeism in caregivers of schizophrenia patients.¹⁸ Because patients with schizophrenia are more similar in age to PWEs than those with other conditions who had available data, we selected that study for inclusion. In that study, schizophrenia caregivers were matched with nonschizophrenia caregivers, and the values for noncaregivers were used in our analysis as reported. Wage rates for the general population were assumed to be equal to the average wage for a caregiver of PWEs. The possibility that caregivers of PWEs could have lower average wages than the general population, due to self-selecting different occupations that would enable them to be caregivers, was not considered. However, other socioeconomic indicators for caregivers and noncaregivers were explored and reported in Table 1. Resource utilization for the general population was based

on data from the 2015 MEPS, and per-visit costs were assumed equivalent to those used for caregivers of PWEs.¹⁷ The MEPS healthcare resources included were physician office visits, inpatient stays, emergency room visits, and physician hospital visits. Nonphysician visits were excluded to match the focus of the questionnaires used in the caregiver survey.

Costs to epilepsy caregivers were estimated on a per-respondent basis and for four predefined subgroups: adult PWEs, child PWEs, low seizure frequency (0 seizures in the prior month), high seizure frequency (≥ 1 seizure in the prior month). Costs for caregivers of PWEs were also compared to results from the general population, although statistical testing was not possible given a lack of information regarding the variation in the data for the comparator group. Outcomes were calculated both for the average PWE caregiver and then extrapolated to model the total US burden in a hypothetical US population of PWE caregivers. The latter metric was based on the US census for demographic information, the CDC for estimates of epilepsy

TABLE 1 Demographic information of caregivers of patients with epilepsy responding to the survey and MEPS respondents

	All caregivers of persons with epilepsy (n = 488)	Caregiver of child with low seizure frequency (n = 53)	Caregiver of child with high seizure frequency (n = 109)	Caregiver of adult with low seizure frequency (n = 124)	Caregiver of adult with high seizure frequency (n = 202)	MEPS survey respondents
Age (years), mean \pm SD	44.5 \pm 12.9	39.9 \pm 9.5	39.0 \pm 8.1	48.4 \pm 13.9	46.4 \pm 13.7	38.5
Sex, n (%)						
Male	97 (19.9%)	3 (5.7%)	15 (13.8%)	39 (31.5%)	40 (19.8%)	48.0%
Female	391 (80.1%)	50 (94.3%)	94 (86.2%)	85 (68.5%)	162 (80.2%)	52.0%
Marital Status, n (%)						
Single	71 (14.6%)	5 (9.4%)	12 (11.0%)	20 (16.1%)	34 (16.8%)	26.5%
Married	308 (63.1%)	41 (77.4%)	73 (67.0%)	76 (61.3%)	118 (58.4%)	34.5%
Other	109 (22.3%)	7 (13.2%)	24 (22.0%)	28 (22.6%)	50 (24.8%)	39.0%
Education Level, n (%)						
Less than college degree	291 (59.6%)	28 (52.8%)	56 (51.4%)	81 (65.3%)	126 (62.4%)	73.9%
College degree	191 (39.1%)	25 (47.2%)	52 (47.7%)	42 (33.9%)	72 (35.6%)	16.9%
No Response	6 (1.3%)	0 (0%)	1 (0.9%)	1 (0.8%)	4 (2.0%)	9.2%
Employment status, n (%)						
Currently employed	276 (56.6%)	31 (58.5%)	56 (51.4%)	70 (56.5%)	119 (58.9%)	44.5%
Not currently employed	212 (43.4%)	22 (41.5%)	53 (48.6%)	54 (43.6%)	83 (41.1%)	55.5%
Annual household income, n (%)						
<\$50 000	240 (49.2%)	18 (34.0%)	55 (50.5%)	62 (50.0%)	105 (52.0%)	-
>\$50 000	248 (50.8%)	35 (66.0%)	54 (49.5%)	62 (50.0%)	97 (48.0%)	-

prevalence, and published literature for the proportion of PWEs with a caregiver.^{1,19,20} Data reporting the number of adult PWEs with caregivers are limited; however, an observational study found 60% of adult PWEs admitted to an elective epilepsy monitoring unit were accompanied by a caregiver.²⁰ We used this 60% estimate in the base case, and conducted scenario analyses in which we varied the proportion of adults with caregivers from 40% to 80%. We assumed all children have one caregiver.

2.4 | Statistical methods

Descriptive statistics for the survey included means and standard deviations (SD) for continuous variables, and percentages and frequencies for categorical variables. Differences in burden between caregivers of children and adults were assessed using *t* tests for continuous variables and chi-square tests for categorical variables. Multivariable generalized linear regression models were used to estimate the effect of seizure frequency on caregiver burden, controlling for caregiver gender, age, marital status, and comorbidity (CCI scores), relationship to the PWEs, age of PWEs, months providing care, type of health insurance for the PWEs, and recruitment panel (Epilepsy Foundation vs Light Speed Research). Mean imputation was used for missing values. A normal distribution was specified for the SF-12v2, the ZBI, and the BCOS scores, and a negative binomial distribution with log-link function was specified for the PHQ-9 (due to skewness). Continuous cost data were reported as medians and interquartile range (IQR). Caregiver cost medians for less- vs more-severe PWEs were compared using the Wilcoxon rank-sum test. Comparisons between all four groups were performed using the Kruskal-Wallis test for medians. Comparisons of mean direct and indirect costs between caregivers and non-caregivers were conducted using Student's *t* test. Because the sample size and standard deviation for the noncaregiver group were unknown for these composite measures, they were made equal to the values for caregivers. Mean values were used to extrapolate to the hypothetical US population of epilepsy caregivers. Estimates with *P*-values < .05 were considered statistically significant. Analyses were performed using Statistical Analysis System software 9.3 (SAS Institute).

3 | RESULTS

3.1 | Survey

There were 500 caregivers of PWEs who responded to the survey, 80.0% were female, the average age was 44.3 years

(SD = 13.0), 70.8% were married, and 60.2% reported having less than a college degree. Caregivers had been providing care for an average of 11.4 (SD = 10.6) years and spent 57.4 hours per week (SD = 51.8) providing such care. Mean duration of epilepsy was 13.0 (SD = 12.3) years, 33.2% of PWE were <18 years of age, 46.0% were female, and 65.4% had generalized seizures. Compared to the caregiver population, the average MEPS respondent was 6 years younger, more likely to be male (48.0% vs 19.9%), less likely to be employed (44.5% vs 56.6%), and less likely to have a college degree (35.6% vs 39.1%; Table 1).

Stress-related caregiver comorbidities included anxiety (52.8%), depression (41.0%), headache (31.4%), and insomnia (30.8%). Caregivers of children were significantly more likely to report anxiety, headaches/migraines, insomnia, and irritable bowel syndrome than caregivers of adults (*P* < .05 for all). Caregiver mental health status measured by SF12v2 mental component summary was worse for those caring for a child with epilepsy (mean = 40.3, SD = 11.6) than those caring for an adult (mean = 43.6, SD = 10.9; *P* = .002). Overall, 31.4% of caregivers reported experiencing moderate-to-severe depression symptoms, and caregivers of children with epilepsy reported greater depression severity (mean = 8.4, SD = 6.6) than caregivers of adults (mean = 7.1, SD = 6.2; *P* < .05; Table 2).

Caregiver burden as assessed by the Zarit Burden Interview was mild-to-moderate (mean = 27.1, SD = 17.9), although 25.6% of caregivers reported moderate-to-severe burden. Caregivers of children were significantly more likely to report severe burden (6.2% vs 2.5%, respectively; *P* < .05; Table 2). On the BCOS, the mean score was 53.8 (SD = 15.8). No differences were found between caregivers of children or adults.

In regression models, greater seizure frequency was statistically significantly associated with increased burden on the ZBI (*P* = .002) and the BCOS (*P* = .007). A borderline significant relationship was found between seizure frequency and mental component summary scores from the SF-12v2 (*P* = .06). Higher seizure frequency was not associated with SF-12v2 physical component summary (*P* = .91) or PHQ-9 (*P* = .48).

3.2 | Costs

Mean per-person direct medical cost for caregivers of PWEs was \$7522 (± \$27 152). The median cost was \$1256 with an interquartile range (IQR) of \$0-\$3140. The mean direct medical cost among the general, non-caregiving US population was \$2740 per person based on 2015 MEPS data,¹⁷ and statistically significantly lower than the corresponding cost for caregivers (*P* = .006). Caregivers of PWEs missed approximately 5 hours weekly due to absenteeism and 13 hours due to presenteeism, resulting in a mean annual cost of \$26 188

TABLE 2 Caregiver health outcomes by age of person with epilepsy

	Total (n = 500)	Caregiver of Child (n = 162)	Caregiver of Adult (n = 326)	P-value
Stress-related comorbidities experienced since becoming a caregiver				
Anxiety (%)	264 (52.80%)	104 (64.20%)	156 (47.85%)	<.001
Chronic constipation (%)	45 (9.00%)	16 (9.88%)	28 (8.59%)	.640
Depression (%)	205 (41.00%)	76 (46.91%)	126 (38.65%)	.081
Diarrhea (%)	59 (11.80%)	22 (13.58%)	37 (11.35%)	.477
Gastroesophageal reflux disease (%)	62 (12.40%)	17 (10.49%)	45 (13.80%)	.301
Headache/migraine (%)	157 (31.40%)	64 (39.51%)	92 (28.22%)	.012
Heartburn (%)	105 (21.00%)	42 (25.93%)	63 (19.33%)	.095
Hypertension (%)	82 (16.40%)	20 (12.35%)	61 (18.71%)	.075
Insomnia (%)	154 (30.80%)	65 (40.12%)	88 (26.99%)	.003
Irritable bowel syndrome (%)	44 (8.80%)	21 (12.96%)	23 (7.06%)	.032
Sleep disorder (%)	85 (17.00%)	24 (14.81%)	60 (18.40%)	.322
PHQ-9, Mean ± SD	7.52 ± 6.43	8.36 ± 6.62	7.07 ± 6.21	.035
PHQ-9 severity categories				
Minimal (%)	208 (41.60%)	59 (36.42%)	143 (43.87%)	.116
Mild (%)	135 (27.00%)	45 (27.78%)	89 (27.30%)	.911
Moderate (%)	71 (14.20%)	23 (14.20%)	46 (14.11%)	.979
Moderately severe (%)	52 (10.40%)	22 (13.58%)	29 (8.90%)	.111
Severe (%)	34 (6.80%)	13 (8.02%)	19 (5.83%)	.356
Bakas Caregiving Outcomes Scale, mean ± SD	53.79 ± 15.84	52.43 ± 16.45	54.29 ± 15.22	.218
Zarit Burden Interview, mean ± SD	27.07 ± 17.87	29.02 ± 18.98	26.49 ± 17.27	.142
Zarit Burden Interview categories				
Little or no burden (%)	207 (41.40%)	63 (38.89%)	135 (41.41%)	.593
Mild-to-moderate burden (%)	165 (33.00%)	54 (33.33%)	109 (33.44%)	.982
Moderate-to-severe burden (%)	110 (22.00%)	35 (21.60%)	74 (22.70%)	.785
Severe burden (%)	18 (3.60%)	10 (6.17%)	8 (2.45%)	.040
Mental component summary, mean ± SD	42.54 ± 11.30	40.30 ± 11.62	43.63 ± 10.90	.002
Physical component summary, mean ± SD	50.82 ± 10.41	54.052 ± 8.52	49.27 ± 10.91	<.001

Note: Age was not provided for 12 respondents; PHQ-9, Patient Health Questionnaire-9.

(± \$29 385) and median \$17 788 (\$3582-\$38 462). For the non-caregiving population, indirect costs related to absenteeism and presenteeism were significantly lower and estimated to be \$5015 ($P < .001$) based on a published estimate from 2015.¹⁸

Caregivers of children with high seizure frequency numerically had the highest (though not statistically significant) median cost of hospitalization and ER visits (hospitalization, $P = .65$; ER visits, $P = .14$). Median costs for outpatient office visits were similar across the four subgroups (ie,

caregivers of adult PWE with low seizure frequency [0 seizures in the prior month], caregivers of adult PWE with high seizure frequency [≥ 1 seizure in the prior month], caregivers of children with epilepsy with low seizure frequency, caregivers of children with epilepsy with high seizure frequency) ($P = .83$). Mean direct medical costs are shown in Figure 2. Median productivity losses were higher in caregivers of children than caregivers of adults, as well as caregivers of those with high seizure frequency (Figure 3, $P < .001$). In pairwise comparisons by seizure frequency within each age group, differences were statistically significant ($P < .001$). Mean indirect costs for each subgroup, as well as for all caregivers and the general population, are shown in Figure 3 stratified by absenteeism and presenteeism.

We estimated that there are approximately 1.8 million caregivers of PWEs in the United States, of which about 75% were caregivers for adults. Given the average costs per caregiver and the population estimates, we estimated that the national, annual direct medical cost to epilepsy caregivers was \$13.9 billion, and annual indirect cost was \$48.3 billion. Similar estimates for the general population were \$4.9 billion and \$9.3 billion for direct medical costs and indirect costs, respectively, leading to an incremental direct medical cost of \$9.0 billion, and an incremental indirect cost of \$39.0 billion. We consider the total incremental cost of \$47.8 billion to be the economic burden of caregiving. When varying the proportion of caregiving to adults from 60% (the default assumption) across the range 40%-80%, caregiver burden ranged from \$37 billion to \$58 billion.

4 | DISCUSSION

Providing care for PWEs adversely affects caregiver's psychological health, with half of respondents reporting experiencing anxiety, more than 40% experiencing depression, and nearly a third having insomnia after becoming caregivers. Physical symptoms, such as headaches, were also quite common. Caregiving for a PWE who has more frequent seizures was associated with higher burden, in both the adult and child PWE population. The burden on caregivers of children is also likely to extend for a longer period, given the chronic nature of the disease. These adverse effects lead to dramatically higher direct and indirect costs for caregivers of PWEs than for the general population. Furthermore, costs were higher for caregivers of children and of patients of any age with high seizure frequency.

The Twelve-Item Short Form Survey Instrument scores were consistent with those for caregivers of PWEs observed in prior research²⁰ and for caregivers of patients with traumatic brain injury,²¹ multiple sclerosis,²² and Parkinson disease.²³ ZBI scores were in the mild-to-moderate burden range, consistent with the range seen in those conditions.²¹⁻²³

Prior research has found similarly that being a caregiver increases worry, stress, anxiety, and depression symptoms, and that utilization of mental health services was the primary driver of higher direct medical costs for caregivers.^{2,24-27} Our study supports these findings. We did not include mental health service costs beyond medical encounters (eg, medication, group therapy) and therefore may have underestimated true mental health costs.

We estimated the total incremental cost of caregiving for PWEs to be \$47.8 billion annually in the United States. In a PubMed search, we found no prior studies using US caregiver samples. In a German population-based, cross-sectional study of children with epilepsy and their parents, caring for a child with epilepsy was found to result in total indirect costs of \$1367-\$3144 per year in mothers and \$92-\$658 per year in fathers.⁸ In a study from China, it was estimated that costs of productivity losses to caregivers were \$103.77 per PWE per year.⁷ Some previous analyses have reported direct and indirect costs for PWEs. A 2000 study found that the annual costs for all diagnosed PWEs in the United States were \$12.5 billion in 1995 US\$²⁸ (\$19.4 billion in 2015 US\$).²⁹ The magnitude of the current results, \$62 billion in total costs, of which \$48 billion is incremental (eg, above the expected for a similar, noncaregiver population), suggests that the burden suffered by caregivers is quite high in economic terms.

Results of this analysis should be considered in light of its limitations. First, we based the analysis on a survey of those who self-identified as caregivers, through online research panels and the Epilepsy Foundation, and there is no way to be certain that respondents are truly caregivers of epilepsy patients and representative of the caregiver population. It is possible that those caring for individuals with more severe epilepsy would be more motivated to participate. If it were the case that those caring for individuals with more severe disease were sampled, our estimates of the caregiver burden could be an overestimate. In addition, those with more education or better access to the internet could be oversampled, and to the extent that those with higher socioeconomic status have better health outcomes, our estimates of the caregiver burden could be an underestimate if the education level of the sample was not representative. Second, all answers were self-reported and could not be corroborated. Third, a similar study of 151 caregivers reported that their PWEs had an average of 8.3 ± 16.4 seizures per month, which is less than our observed 11.4 seizures in the last month and raises further questions about the generalizability of our findings.³⁰ If the seizure burden in the PWEs that our respondents care for is higher than what is typically seen, our findings would be an overestimate of the disease burden. Fourth, when estimating indirect costs for the caregiver population, we assumed that all of those who were unemployed did not have any productivity losses, when in reality some likely left

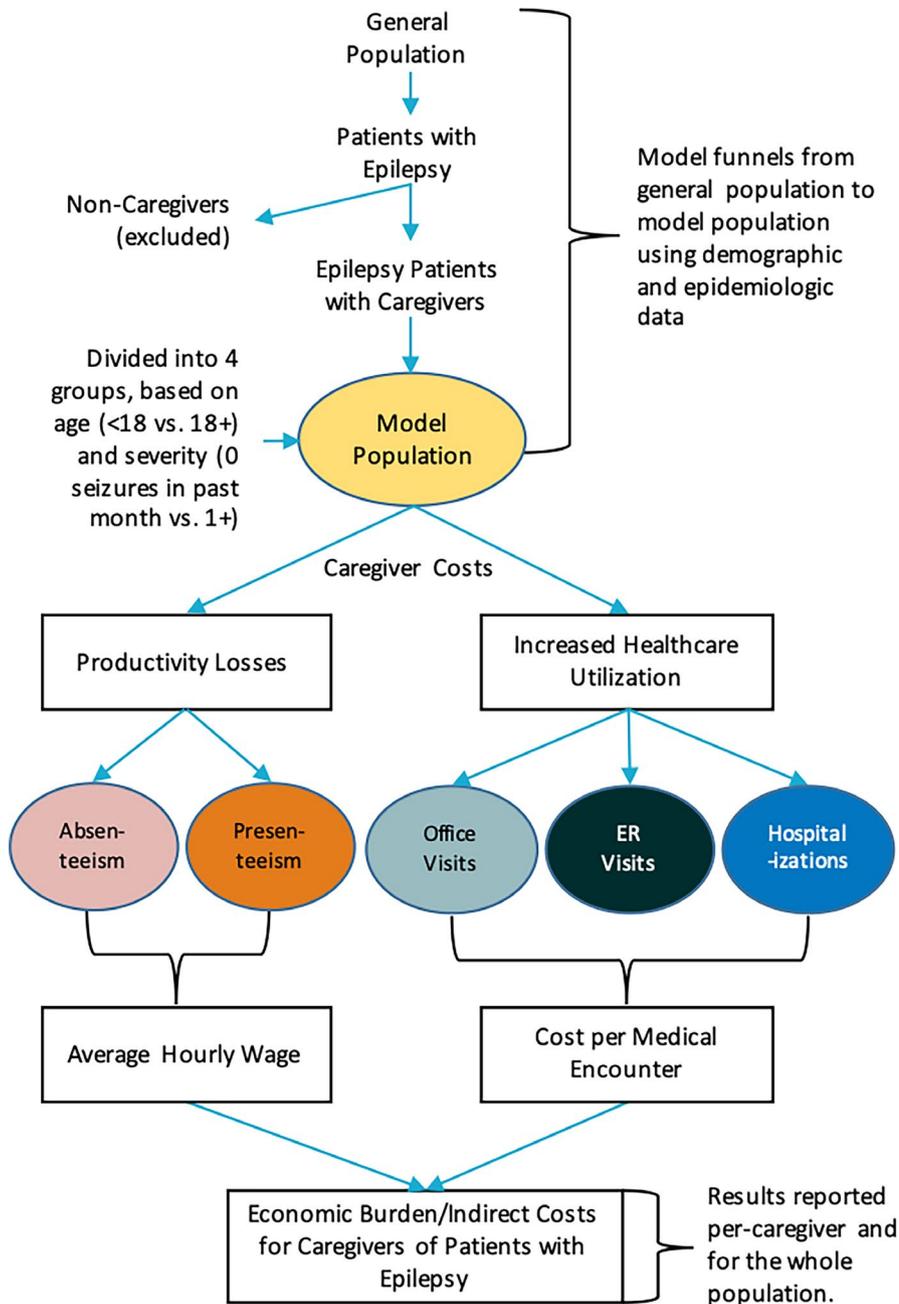


FIGURE 1 Analysis schematic, depicting the starting patient population, costs included in the analysis, and outcomes measured

employment to serve as a caregiver. This assumption could lead to an underestimate of the caregiver burden. Fifth, the comparator group in this analysis was the general population, which was necessary due to data limitations; however, this group likely includes a small proportion of caregivers. We calculated direct medical costs that arise as a result of caregiving using general population estimates from MEPS; however, for productivity losses we used estimates from those not caring for individuals with schizophrenia as a proxy for those not caring for PWEs. To the extent that schizophrenia caregivers differ from epilepsy caregivers, those matched with either group might differ. Sixth, there were also substantial differences between the caregiver respondents and the comparator group, as the caregivers

surveyed were more likely to be female, older, married, highly educated, and employed. It should be noted that the same wage was used to estimate the productivity losses for both caregivers and the comparator group; therefore the estimates that could be biased by these differences are strictly the losses in productivity. To the extent that older individuals are more likely to have other health issues, the estimate of caregiver burden could be an overestimate. However, those highly educated typically have better health outcomes such that one would expect lower utilization, and the impact of sex and marital status on resource utilization is less clear. When considering the impact of all of these differences, it is difficult to hypothesize how differences in demographics, socioeconomic status, and comorbidities

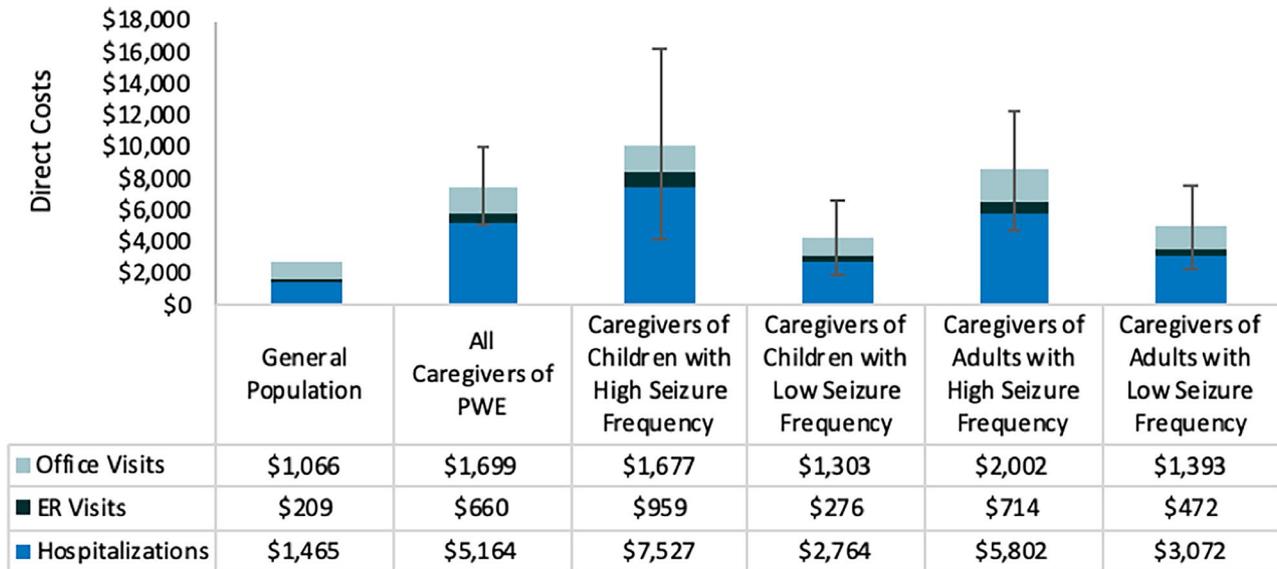


FIGURE 2 Mean direct medical costs by visit type for the general population, all caregivers, and by subgroup of caregivers. Mean values were presented, as they are more informative than medians due to the skewed nature of the distributions. Error bars represent 95% confidence interval around total mean direct medical costs. Findings were not significant at $P = .05$ when comparing between median costs within subgroups of caregivers of like-aged PWEs

between the general population and caregivers may impact economic outcomes; however, it was determined to be the most reasonable comparison group. Finally, the estimate of the proportion of epilepsy patients with a caregiver was based on a small study and assumptions were required in using this value in our analysis. As shown in scenario analyses, the total nationwide burden is sensitive to the estimate of the number of caregivers. More research into the total number of caregivers could better inform the inputs used in our analyses, and without knowing the directional

bias in our assumption, we are unable to estimate the impact on results.

Despite these limitations, this is the first study to obtain standardized, comprehensive, epilepsy-specific clinical and cost estimates of caregiving. The magnitude of the preliminary estimates suggests the importance of considering this component when understanding the full consequences of the burden of epilepsy. Identification of subgroups that face the highest economic burden can better allow researchers to target interventions for populations who could benefit the most.

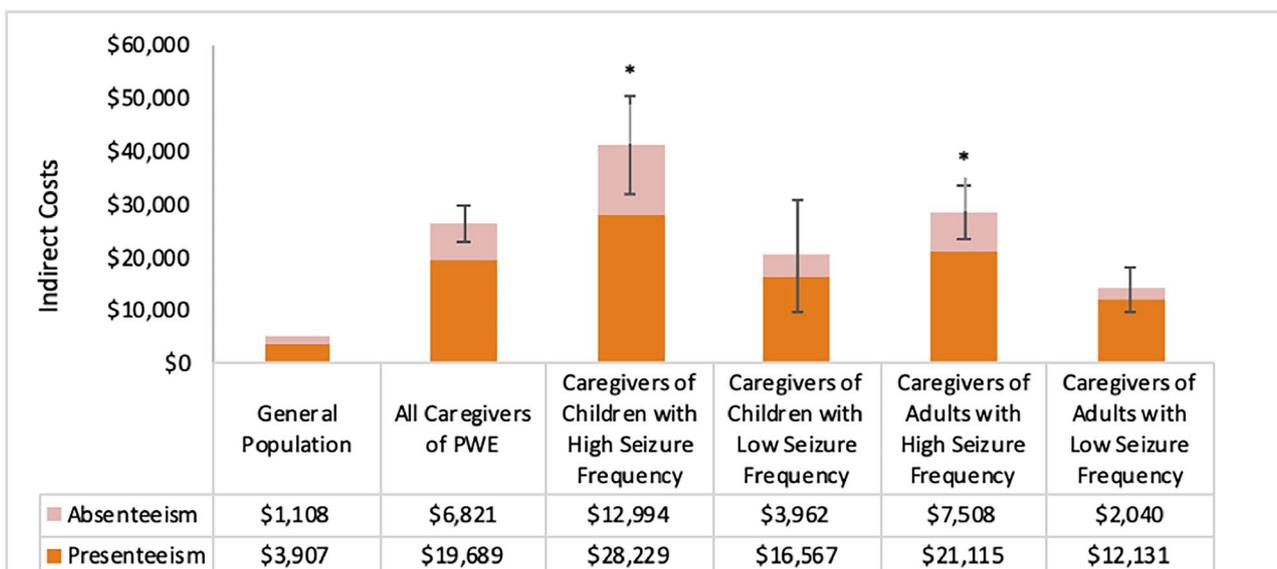


FIGURE 3 Productivity losses, by presenteeism and absenteeism, for the general population, all caregivers, and by subgroup of caregivers. Error bars represent 95% confidence interval around total mean indirect medical costs. Asterisks (*) denote subgroups in which median costs are statistically significant ($P < .001$) compared to caregivers of persons with low seizure frequency in the same age group

Although more research into this important topic would be beneficial, these preliminary findings could allow policy-makers to better weigh the costs and benefits of interventions reducing the burden of epilepsy and to allocate resources more efficiently.

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CONFLICT OF INTEREST

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ETHICAL APPROVAL

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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REFERENCES

- Centers for Disease Control and Prevention. Epilepsy fast facts [Internet]. 2016 [cited 2016 Oct 14]. Available from <http://www.cdc.gov/epilepsy/basics/fast-facts.htm>
- England MJ, Liverman CT, Schultz AM, Strawbridge LM. Epilepsy across the spectrum: promoting health and understanding: a summary of the institute of medicine report. *Epilepsy Behav.* 2012;25:266–76.
- The National Society for Epilepsy. Caring for someone with epilepsy [Internet]. Epilepsy Society. 2016 [cited 2016 Oct 14]. Available from <https://www.epilepsysociety.org.uk/caring-someone-epilepsy>
- Begley CE, Durgin TL. The direct cost of epilepsy in the United States: a systematic review of estimates. *Epilepsia.* 2015;56:1376–87.
- Jennum P, Christensen J, Ibsen R, Kjellberg J. Long-term socioeconomic consequences and health care costs of childhood and adolescent-onset epilepsy. *Epilepsia.* 2016;57:1078–85.
- Ryan JL, McGrady ME, Guilfoyle SM, Junger K, Arnett AD, Modi AC. Health care charges for youth with newly diagnosed epilepsy. *Neurology.* 2015;85:490–7.
- Gao L, Xia L, Pan S-Q, Xiong T, Li S-C. Burden of epilepsy: a prevalence-based cost of illness study of direct, indirect and intangible costs for epilepsy. *Epilepsy Res.* 2015;110:146–56.
- Riechmann J, Strzelczyk A, Reese JP, et al. Costs of epilepsy and cost-driving factors in children, adolescents, and their caregivers in Germany. *Epilepsia.* 2015;56:1388–97.
- Epilepsy Foundation [Internet]. Epilepsy Foundation. [cited 2018 Jan 17]. Available from <https://www.epilepsy.com/>
- Lairson DR, Basu R, Begley CE, Reynolds T. Concordance of survey and billing data in a study of outpatient healthcare cost and utilization among epilepsy patients. *Epilepsy Res.* 2009;87:59–69.
- Goren A, Gilloteau I, Lees M, DaCosta DiBonaventura M. Quantifying the burden of informal caregiving for patients with cancer in Europe. *Support Care Cancer.* 2014;22:1637–46.
- Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatr Ann.* 2002;32:509–15.
- Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist.* 1980;20:649–55.
- Bakas T, Champion V, Perkins SM, Farran CJ, Williams LS. Psychometric testing of the revised 15-item bakas caregiving outcomes scale. *Nurs Res.* 2006;55:346.
- Ware JJ, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care.* 1996;34:220–33.
- Reilly M, Zbrozek A, Dukes E. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics.* 1993;4:353–65.
- Medical Expenditure Panel Survey Home [Internet]. [cited 2016 Oct 14]. Available from <https://mepsahr.gov/mepsweb/>
- Csoboth C, Witt EA, Villa KF, O'Gorman C. The humanistic and economic burden of providing care for a patient with schizophrenia. *Int J Soc Psychiatry.* 2015;61:754–61.
- U.S. Census Bureau. 2010 census demographic profile: table DP-1 - profile of general population and housing characteristics: 2010 [Internet]. American FactFinder. 2011 [cited 2016 Oct 18]. Available from http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pxmlid=DEC_10_DP_DPDP1&src=pt
- Karakis I, Cole AJ, Montouris GD, San Luciano M, Meador KJ, Piperidou C. Caregiver burden in epilepsy: determinants and impact. *Epilepsy Res Treat.* 2014;2014:e808421.
- Bayen E, Pradat-Diehl P, Jourdan C, Ghout I, Bosserelle V, Azerad S, et al. Predictors of informal care burden 1 Year after a severe traumatic brain injury: results from the Paris-TBI study. *J Head Trauma Rehabil.* 2013;28:408–418.
- Bayen E, Papeix C, Pradat-Diehl P, Lubetzki C, Joël ME. Patterns of objective and subjective burden of informal caregivers in multiple

- sclerosis. *Behav Neurol*. 2015 [cited 2018 Jan 12]. Available from <https://www.hindawi.com/journals/bn/2015/648415/>
23. Martínez-Martín P, Forjaz MJ, Frades-Payo B, Rusiñol AB, Fernández-García JM, Benito-León J, et al. Caregiver burden in Parkinson's disease. *Mov Disord*. 2007;22:924–31.
 24. Camfield C, Breau L, Camfield P. Impact of pediatric epilepsy on the family: a new scale for clinical and research use. *Epilepsia*. 2001;42:104–12.
 25. Cousino MK, Hazen RA. Parenting stress among caregivers of children with chronic illness: a systematic review. *J Pediatr Psychol*. 2013;38:809–28.
 26. Duffy LV. Parental coping and childhood epilepsy: the need for future research. *J Neurosci Nurs*. 2011;43:29–35.
 27. Lv R, Wu L, Jin L, Lu Q, Wang M, Qu Y, et al. Depression, anxiety and quality of life in parents of children with epilepsy. *Acta Neurol Scand*. 2009;120:335–41.
 28. Begley CE, Famulari M, Annegers JF, Lairson DR, Reynolds TF, Coan S, et al. The cost of epilepsy in the United States: an estimate from population-based clinical and survey data. *Epilepsia*. 2000;41:342–51.
 29. United States Department of Labor, Bureau of Labor Statistics. CPI (Consumer Price Index) Inflation Calculator [Internet]. 2017 [cited 2018 Jan 2]. Available from http://www.bls.gov/data/inflation_calculator.htm
 30. Gutierrez-Angel AM, Martinez-Juarez IE, Hernandez-Vanegas LE, Crail-Melendez D. Quality of life and level of burden in primary caregivers of patients with epilepsy: effect of neuropsychiatric comorbidity. *Epilepsy Behav*. 2018;81:12–7.

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