Epilepsy & Behavior 83 (2018) 28–35

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

# Trends in resource utilization and prescription of anticonvulsants for patients with active epilepsy in Germany from 2003 to 2013 — A ten-year overview

Laurent M. Willems [a], Saskia Richter [b], Nina Watermann [b], Sebastian Bauer [a,b], Karl Martin Klein [a,b], Jens-Peter Reese [c], Oliver Schöffski [d], Hajo M. Hamer [e], Susanne Knake [b], Felix Rosenow [a,b], Adam Strzelczyk [a,b,]*

[a] Epilepsy Center Frankfurt Rhine-Main, Department of Neurology, Goethe-University, Frankfurt am Main, Germany
[b] Epilepsy Center Hessen, Department of Neurology, Philipps-University, Marburg, Germany
[c] Coordinating Center for Clinical Trials, Philipps-University, Marburg, Germany
[d] Department of Health Management, Friedrich-Alexander-University, Nuremberg, Germany
[e] Epilepsy Center, Department of Neurology, Friedrich-Alexander-University, Erlangen, Germany

ARTICLE INFO

*Article history:*
Received 10 March 2018
Accepted 14 March 2018
Available online xxxx

*Keywords:*
Cost
Epilepsy
Seizure
Indirect cost
Work loss
Retirement
Economic burden
Resource use

ABSTRACT

This study evaluated trends in resource use and prescription patterns in patients with active epilepsy over a 10-year period at the same outpatient clinic of a German epilepsy center. We analyzed a cross-sectional patient sample of consecutive adults with active epilepsy over a 3-month period in 2013 and compared them with equally acquired data from the years 2003 and 2008. Using validated patient questionnaires, data on socioeconomic status, course of epilepsy, as well as direct and indirect costs were recorded.

A total of 198 patients (mean age: 39.6 ± 15.0 years, 49.5% male) were enrolled and compared with our previous assessments in 2003 (n = 101) and 2008 (n = 151). In the 2013 cohort, 75.8% of the patients had focal epilepsy, and the majority were taking antiepileptic drugs (AEDs) (39.9% monotherapy, 59.1% polytherapy). We calculated epilepsy-specific costs of €3674 per three months per patient. Direct medical costs were mainly due to anticonvulsants (20.9% of total direct costs) and to hospitalization (20.8% of total direct costs). The proportion of enzyme-inducing anticonvulsants and 'old' AEDs decreased between 2003 and 2013. Indirect costs of €1795 in 2013 were mainly due to early retirement (55.0% of total indirect costs), unemployment (26.5%), and days off due to seizures (18.2%).

In contrast to our previous findings from 2003 and 2008, our data show a stagnating cost increase with slightly reduced total costs and balanced direct and indirect costs in patients with active epilepsy. These findings are accompanied by an ongoing cost-neutral increase in the prescription of 'newer' and non-enzyme-inducing AEDs. However, the number and distribution of indirect cost components remained unchanged.



## 1. Introduction

Epilepsy is a common chronic neurological disorder characterized by sustained risk of recurrent seizures [1]. The vast majority of patients with epilepsy require an individually chosen anticonvulsant treatment for an extended period of time, and up to 30% of patients have epilepsy that remain refractory to antiepileptic drugs (AEDs) [2,3]. With about 39 million affected people in 2015, epilepsies represent a substantial burden for medical, social, and economic structures worldwide [4,5]. Economic evaluations are especially important in patients with active epilepsy as they account for a high proportion of total costs [6–10]. In consideration of the contrast between growing resource utilization and a limited amount of healthcare resources, collecting and analyzing costs have become more and more relevant to estimate and predict resource allocation on a scientific basis. In particular, the introduction of new AEDs, the increasing availability of generic medication, and the expanding fields of invasive and noninvasive brain stimulation and epilepsy surgery might lead to considerable changes in costs or to a shift in the distribution of direct cost components [11–16].

Increased indirect costs result from social and vocational stigmata still being strongly associated with epileptic seizures and epilepsy. As a consequence, patients have restricted access to the labor market and reduced employment opportunities. Moreover, quality of life is significantly reduced in patients and their caregivers [11,17–21].

* Corresponding author at: Epilepsy Center Frankfurt Rhine-Main, Department of Neurology, Goethe-University Frankfurt, Schleusenweg 2-16, 60528 Frankfurt am Main, Germany.
*E-mail address:* strzelczyk@med.uni-frankfurt.de (A. Strzelczyk).

https://doi.org/10.1016/j.yebeh.2018.03.025
1525-5050/

Comparing healthcare utilization between 2003 and 2008, we were able to show a significant shift in the distribution of direct cost components with increased hospital costs, which was accompanied by a cost-neutral increase in the prescription of 'newer' AEDs [22]. The objective of this study was to determine again direct and indirect costs in patients with active epilepsy in 2013 using a similar approach to both previous cohorts of 2003 and 2008 and, thus, to determine the trends in utilization of healthcare resources over a period of 10 years.

## 2. Patients and methods

### 2.1. Study settings and design

In line with the previous studies from 2003 [7] and 2008 [22], this study was performed at the epilepsy outpatient clinic of the University Hospital Marburg. The University Hospital Marburg is a large multispecialty tertiary care hospital in the center of Germany that provides healthcare to a population of over 1,000,000 patients. Marburg is located within the postal code area 35, which was used previously for a population-based estimation of the incidence of status epilepticus [23] and costs of epilepsy studies [24,25]. The study had the approval of the local ethics committee.

### 2.2. Patients

After receiving written informed consent, all adult patients aged 18 years or older with active epilepsy were eligible. The diagnosis was based on the definitions proposed by the International League Against Epilepsy and the International Bureau for Epilepsy [26]. Patients were excluded when a diagnosis of epilepsy could not be determined without doubt. The treating physician provided information on the epilepsy syndrome, concomitant diseases, and current AEDs taken. For this study, only people with active epilepsy (≥1 seizure during the last 12 months) were assessed.

### 2.3. Cost assessment

Costs of hospitalization, outpatient treatment and medication, and further direct as well as indirect costs were assessed based on a patient questionnaire examining a 3-month period. The questionnaire was validated in the 2003 cohort [7] and used for the 2008 cohort [22]. Direct costs, including inpatient and outpatient care, drug costs, ancillary therapy, special equipment, transportation, as well as indirect costs were evaluated according to German recommendations for performing health economic evaluations [27–29]. This study focuses on the genuine costs due to epilepsy and not on additional costs that may be triggered by other diseases not related to epilepsy. Therefore, patients and physicians were asked in detail whether or not the medication, service, or resource was used specifically for epilepsy. Costs attributed to other diagnoses were excluded from the analyses. The evaluation of costs was performed by means of a bottom-up approach from the perspective of the statutory health insurance (Gesetzliche Krankenversicherung, GKV). Drug costs were obtained from the official German price list of drugs, "Rote Liste" [30]. Costs for inpatient care (hospitalization and rehabilitation) were calculated based on the current issue of German Diagnosis Related Groups (G-DRG; www.g-drg.de). The charges for outpatient care, including specialists' consultations, ambulatory diagnostics, and physical therapy, were obtained from the official German doctors' fee scale (Einheitlicher Bewertungsmaßstab, EBM) [31]. Costs for home and special equipment, e.g., assistive or protective devices, were derived from providers' price lists. Indirect costs for lost productivity due to days off, unemployment, or early retirement were evaluated using the human capital approach for patients younger than 65 years. According to the Federal Statistical Office (www.destatis.de), the mean gross income was €32,609 in 2003, €34,209 in 2008, and €37,709 in 2013, i.e., €89.3 vs. €93.7 vs. €103.3 per calendar day. The productivity losses attributable to epilepsy were determined using calendar days of the remaining study period prior to the official retirement age (65 years). All costs were calculated for the 3-month evaluation periods and are provided in 2003, 2008, and 2013 Euro (€). To allow a comparison between the three cohorts, the costs of the first two cohorts (2003 and 2008) were adjusted for inflation and increase in mean gross income to 2013. Data on inflation of health expenditures and changes in the mean gross income were retrieved from the Federal Statistical Office (www.destatis.de), and calculations were performed according to previously described methods [22,24,32].

### 2.4. Data entry and statistical analysis

Data entry was performed using the File Maker Pro 8.5 database (Filemaker Inc., Santa Clara, CA, USA). A double-entry procedure was employed to assure a high level of data accuracy. Statistical analyses

**Table 1**
Sociodemographic and clinical characteristics of the cohorts.

| | 2003 cohort [7] n = 101 | 2008 cohort [22] n = 151 | 2013 cohort n = 198 | p-Value |
|---|---|---|---|---|
| Age in years[a] | 40.7 ± 15.7 range: 18–78 | 41.0 ± 14.9 range: 18–82 | 39.6 ± 15.0 range:18–84 | 0.387[b] |
| Disease duration in years[a] | 18.1 ± 15.4 range: 0.1–52 | 19.4 ± 15.2 range: 0.1–68 | 14.6 ± 14.1 range: 0.1–63 | 0.028[b] |
| Antiepileptic drugs (AEDs) | | | | |
| Mean number of AEDs[a] | 1.7 ± 0.9 | 1.8 ± 0.8 | 1.8 ± 0.8 | 1.000[b] |
| No AEDs, % (n) | 4.0 (4) | 5.3 (8) | 1.0 (2) | |
| Monotherapy, % (n) | 39.6 (40) | 30.5 (46) | 39.9 (79) | |
| 2 AEDs, % (n) | 33.6 (34) | 48.3 (73) | 37.9 (75) | |
| ≥3 AEDs, % (n) | 22.8 (23) | 15.9 (24) | 21.2 (42) | |
| Sex | % (n) | % (n) | % (n) | |
| Male | 46.5 (47) | 46.4 (70) | 49.5 (98) | 0.561[c] |
| Female | 53.5 (54) | 53.6 (81) | 50.5 (100) | |
| Epilepsy syndrome | % (n) | % (n) | % (n) | |
| Focal epilepsy | 76.2 (77) | 76.8 (116) | 75.8 (150) | 0.817[c] |
| With simple partial seizures only | 5.9 (6) | 0.7 (1) | 5.6 (11) | |
| With complex partial seizures | 27.7 (28) | 15.5 (28) | 47.5 (94) | |
| With secondarily generalized tonic–clonic seizures | 43.6 (43) | 57.6 (87) | 35.9 (71) | |
| Idiopathic generalized epilepsy | 19.8 (20) | 13.9 (21) | 18.2 (36) | |
| Unclassified | 4.0 (4) | 9.3 (14) | 6.1 (12) | |

[a] Mean ± standard deviation.
[b] p-Values calculated using two samples *t*-test comparing 2008 and 2013 cohort.
[c] p-Values calculated using chi-square test comparing 2008 and 2013 cohort.