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Neurologist adherence to clinical practice guidelines and costs in patients with newly diagnosed and chronic epilepsy in Germany

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ABSTRACT

Purpose: The aim of this study was to evaluate physician adherence to the German Neurological Society guidelines of 2008 regarding initial monotherapy and to determine the cost-of-illness in epilepsy.
Methods: This was an observational cohort study using health data routinely collected at 55 outpatient neurology practices throughout Germany (NeuroTransData network). Data on socioeconomic status, course of epilepsy, anticonvulsive treatment, and direct and indirect costs were recorded using practice software-based questionnaires.
Results: One thousand five hundred eighty-four patients with epilepsy (785 male (49.6%); mean age: 51.3 ± 18.1 years) were enrolled, of whom 507 were newly diagnosed. Initial monotherapy was started according to authorization status in 85.9%, with nonenzyme-inducing drugs in 94.3% of all AEDs. Drugs of first choice by guideline recommendations were used in 66.5%. Total annual direct costs in the first year amounted to €2194 (SD: €4273; range: €55–43,896) per patient, with hospitalization (59% of total direct costs) and anticonvulsants (30%) as the main cost factors. Annual total direct costs decreased by 29% to €1572 in the second year, mainly because of a 59% decrease in hospitalization costs. The use of first choice AEDs did not influence costs. Chronic epilepsy was present in 1077 patients, and total annual direct costs amounted to €1847 per patient, with anticonvulsants (51.0%) and hospitalization (41.0%) as the main cost factors. Potential cost-driving factors in these patients were active epilepsy and focal epilepsy syndrome.
Conclusion: This study shows excellent physician adherence to guidelines regarding initial monotherapy in adults with epilepsy. Newly diagnosed patients show higher total direct and hospital costs in the first year upon diagnosis, but these are not influenced by adherence to treatment guidelines.

1. Introduction

Epilepsy is a common and chronic neurological disorder that imposes a substantial burden on individuals and society as a whole. The initial diagnosis of epilepsy is associated with the costs of diagnostic procedures and inpatient admissions [1,2]. After a first seizure or with a newly established diagnosis of epilepsy, patients are affected by social stigma, reduced employment opportunities, and impaired quality of life for themselves and their carers, resulting in increased indirect as well as intangible costs [3–8].

The long-term efficacy of antiepileptic drugs (AEDs) is crucial, as the seizures of up to 30% of patients remain refractory to medical treatment [9–12]. Patients with newly diagnosed and active epilepsy account for a high proportion of total costs [13–18]. As healthcare costs increase, reliable cost-of-illness (COI) estimates are essential as a scientific basis for health economic calculations, resource allocation, and health policy decision-making. In addition, the introduction of new AEDs and the use of generic medication can result in a considerable shift in the distribution of cost components [19,20].

To allow for the best possible therapy for patients with neurological diseases, the German Neurological Society (Deutsche Gesellschaft für Neurologie [DGN], Berlin) has been publishing clinical practice guidelines regularly since 2002. In general, guidelines are viewed by physicians as helpful in terms of increasing the quality of patient care and education and the presentation of information without bias

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[21–23]. However, there are limited data on the implementation of clinical practice guidelines in patients with epilepsy. In 2007, the pivotal SANAD studies [24,25] and a randomized controlled trial comparing controlled-release carbamazepine with levetiracetam [26] were published. As a consequence, the German clinical practice guidelines on epilepsy published in 2008 [27,28] named certain drugs as the first choice (i.e., lamotrigine and levetiracetam in focal epilepsy instead of carbamazepine), required physicians not to use strong enzyme-inducing drugs (i.e., carbamazepine, phenytoin, or phenobarbital), and gave warnings regarding the use of valproate in women of childbearing age. Table 1 shows anticonvulsive treatment options according to the authorization status of each individual drug for initial monotherapy as of January 1st, 2008 and recommendations from the guidelines.

The aim of this study was to evaluate the degree of physician adherence regarding the selection of AED to the clinical practice guidelines regarding "first epileptic seizure and epilepsy in adulthood" [27] published in 2008 to patients with newly diagnosed epilepsy between 2008 and 2013, to quantify healthcare utilization in these patients and to compare these patients with patients with epilepsy diagnosed before 2008. For this evaluation, we used a web-based digital NeuroTransData (NTD) data source that allows for avoiding labor-intensive paper-and-pencil questionnaires and simultaneous gathering of long-term disease and cost-of-illness (COI) data in patients with epilepsy [28,29]. Such a bottom-up approach is individual-related and gathers precise, epilepsy-specific cost estimates in daily routines, as shown in previous studies [28,29].

2. Patients and methods

2.1. Study design

This was an observational cohort study using health data routinely collected in 55 outpatient neurology practices that are members of the NeuroTransData (NTD) network. The NTD practices collect, systematically and chronologically, fully anonymous patient data since 2008. Each practice is certified according to ISO 9001:2008, and they provide outpatient care throughout Germany. This study includes outpatients with epilepsy 18 years of age or older, with newly diagnosed or chronic epilepsy, who gave informed consent to participate. The diagnosis was based on the definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy [30]. Patients were excluded when the diagnosis of epilepsy could not be determined without doubt.

2.2. Data acquisition

During clinical visits at least once every three-month period, the treating neurologist recorded in-time the following parameters: demographic data, type and frequency of seizures, daily dosage of antiepileptic medication, results of EEG and cerebral MRI, days of inpatient care in acute and rehabilitation hospitals, and days of work leave due to epilepsy. All participating medical staff are trained to document these data in-time in a standardized way in the web-based digital NTD data source. This data acquisition protocol was approved by the ethical committee of the Bavarian Medical Board (Bayerische Landesärztekammer, 14.06.2012). The data were pooled anonymously to form the database of the study.

2.3. Physician adherence to guidelines

The treatment decision processes for antiepileptic medication were supported by the electronic expert system EPI-Scout® (epilepsy scout), which suggests individual therapeutic options based on evidence-based guidelines for the diagnosis and treatment of patients with epilepsy considering the type of seizure as well as MRI and EEG results [28,29,31,32]. The evaluation of physician adherence to guidelines was confined to newly diagnosed patients with epilepsy. In patients with chronic epilepsy, too many confounding variables make a meaningful analysis impossible in a cohort study. The absolute and relative frequencies were calculated to reveal what proportion of the patients had been treated according to the clinical practice guidelines with regard to authorization status, the aim to reduce the prescription of enzyme-inducing drugs, and first choice AEDs. The details are presented in Table 1.

2.4. Cost assessment

The calculation of the direct and indirect costs of epilepsy was based on a semistructured interview of patients at each visit with patients being asked by the treating neurologist about the utilization of healthcare associated with their epilepsy. Direct costs including inpatient hospital and rehabilitation care, neurological outpatient service, and drug costs due to epilepsy were recorded and evaluated as defined in the German recommendations for performing health economic evaluations [29,33,34]. Indirect costs were confined to days off work due to epilepsy. The use of medical resources due to conditions other than epilepsy was excluded. For the evaluation of costs, a bottom-up approach was employed from the perspective of statutory health insurance (Gesetzliche Krankenversicherung [GKV]). Averaged drug costs were obtained from prescription reports [35]. Costs for inpatient care (hospitalization and rehabilitation) were calculated based on daily charges and the pricing defined by German Diagnosis Related Groups (G-DRG; www.g-drg.de). The costs for outpatient care were obtained from the official German doctor's fee scale (Einheitlicher Bewertungsmaßstab, EBM) [33]. Other direct costs, such as for cerebral imaging or laboratory investigations, were not evaluated in this study. Indirect costs for lost productivity due to days off were evaluated using the human capital approach for patients younger than 65 years.

Table 1
Authorization status of each individual drug for initial monotherapy, recommendation as first choice and specific restrictions from the clinical practice guideline published in 2008.

Epilepsy syndrome	Idiopathic (genetic) generalized epilepsy	Focal (structural/metabolic) epilepsy	Unknown epilepsy syndrome
ICD-10 coding	G40.3	G40.1/G40.2	G40.6–G40.9
AEDs authorized for initial monotherapy[a]	LTG, PB, PRM, TPM, VPA, ESM (absences only)	CBZ, GBP, LTG, LEV, OXC, PB, PRM, PHT, TPM, VPA	CBZ, GBP, LTG, LEV, OXC, PB, PRM, PHT, TPM, VPA[b]
Nonenzyme-inducing AEDs	LTG, TPM, VPA, ESM, LEV (Add-on only)	GBP, LTG, LEV, OXC, TPM, VPA	GBP, LTG, LEV, OXC, TPM, VPA[b]
Drug of first choice	LTG, VPA, TPM	LEV, LTG	LEV, LTG, TPM, VPA
Restrictions in first choice	VPA (childbearing age)	–	VPA (childbearing age)

CBZ = carbamazepine, ESM = ethosuximide, GBP = gabapentin, LEV = levetiracetam, LTG = lamotrigine, OXC = oxcarbazepine, PB = phenobarbital, PHT = phenytoin, PRM = primidone, TPM = topiramate, VPA = valproate.

[a] Authorization status as per January 1st, 2008.

[b] For patients with an unknown epilepsy syndrome at initial diagnosis, all approved AEDs for initial monotherapy were considered as appropriate as there might be a suspicion of focal epilepsy in this patient population.