

## Economic and social cost of epilepsy in Poland: 5-year analysis

Joanna Jędrzejczak, Department of Neurology and Epileptology Centre of Postgraduate Medical Education, Warsaw, Poland

Beata Majkowska-Zwolińska, Epilepsy Diagnostic and Therapeutic Center, Foundation of Epileptology, Warsaw, Poland

Anna Chudzicka-Bator, HTA Consulting, Krakow, Poland

Iwona Żerda, HTA Consulting, Krakow, Poland

Magdalena Władysiuk, HTA Consulting, Krakow, Poland

Brian Godman, SIPBS, Strathclyde University, Glasgow, UK; School of Pharmacy, SMU, Pretoria, South Africa

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### Abstract

**Introduction:** Epilepsy affects nearly 50 million people around the world. As a common and chronic disease generates a high cost burden for healthcare system and patients. **Aim:** We aimed to determine the most current direct and indirect costs of epilepsy in Poland from the social perspective for the years 2014–2018, to analyze the changes of expenditures over time, indicate trends and to determine key cost-drivers. **Material and Methods:** Direct and indirect costs using a top-down approach were estimated based on the public institutions' data for the ICD-10 codes G40 and G41. Direct costs included pharmacotherapy, hospitalizations, outpatient specialist care and rehabilitation. A human capital approach was used to estimate loss of productivity due to sick leaves and long-term inability to work. **Results:** Annual total direct and indirect costs related to epilepsy accounted for EUR 410 million in 2014 and decreased in subsequent years to EUR 361 million in 2018. The indirect costs were dominant (76–83% of total costs) and in the majority related to the long-term absenteeism (87–92% of total indirect costs). In 2014–2018 patients with epilepsy generated EUR 341 million to EUR 282 million of indirect costs. Annual direct costs for patients with epilepsy were EUR 69 million in 2014 and increased to EUR 80 million in 2018. The biggest expenses were the costs of AEDs (>50%) and hospitalizations (~ 40%). **Conclusions:** Epilepsy is an expensive disorder in terms of consumption of resources and social costs. Decision-makers should take it under special consideration.

**Key words:** epilepsy, direct costs, indirect costs, productivity loss, absenteeism

# 1. Introduction

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiological, cognitive, psychological, and social consequences of this condition [1]. Currently, it is estimated that up to 50 million people worldwide have epilepsy, making epilepsy one of the most common neurological conditions [2–4]. Overall, it is estimated that approximately five million people are diagnosed with epilepsy each year [3]. According to Polish Ministry of Health [5] in 2016 in Poland lived over six hundred and forty-three thousand people with epilepsy (registered in the public health system after 2009). Prevalence rates are likely to grow due to rising life expectancy worldwide with an increase in the number of people over 80 years of age with potentially epileptogenic brain insults including brain injury, tumors, infections of the brain, and stroke [3, 4].

As a common and chronic disease, epilepsy is associated with a considerable economic burden for both healthcare systems and patients [6, 7], since in most cases epilepsy requires lifelong treatment. Expenses are associated with drug prescriptions, medical consultations, and hospital care as well as surgery where pertinent. Significant costs are related to the treatment of seizures, especially drug resistant epilepsy and status epilepticus. Apart from medical issues epilepsy adversely affects the economic, psychological and social aspects of patients' life measured by reduced quality of life and indirectly also their family, friends, and relatives [8].

Epilepsy has significant economic implications in terms of health care needs and lost productivity at work, reflected by high rates of disability life years (DALYs) [2–4, 9]. According to the World Health Organization (WHO), International League Against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE), epilepsy accounts for over 13 million disability-adjusted life years (DALYs) globally and is responsible for more than 0.5% of the global burden of disease (GBD) [10]. It is ranked as the second most burdensome neurologic disorder worldwide in terms of DALYs [11]; however, this is decreasing [2]. Epilepsy also has a considerable burden on patients and their families [12–14]. An increase in seizure frequency and severity combined with co-morbid conditions appreciably reduces health related quality of life of patients with epilepsy. However, the burden of epilepsy is very often neglected in public health at a global and national level leading to calls by the WHO for countries to take increased action against epilepsy and its consequences [3].

Current data on economic burden of epilepsy in European countries, in particular in Poland, is limited. A systematic review by Allers et al. [6] shows that previously conducted analyses on burden of epilepsy had focused mainly on direct costs of illness, while indirect costs had been neglected since they are not easy to estimate due to lack of reliable and sufficient data. Since then, more recent studies have estimate both the direct and indirect costs of epilepsy [15–23]. However, estimated costs in epilepsy do vary among countries due to differences between healthcare and social benefit systems.

In publications discussing the economic burden for Poland different methods have been used (bottom-up design [24] and top-down approach [20]), which makes it challenging to compare the results and to draw clear conclusions.

Consequently, we wanted to address this concern in Poland given the increasing recognition of the clinical and economic burden of epilepsy and the need to instigate pertinent policies to enhance the care of such patients and their families.

## **1.1. Aim**

In view of this, the aims of this study were multiple. Firstly, to determine current direct and indirect costs of epilepsy in Poland from a social perspective based on the data from public institutions for 2014–2018. Secondly, to analyze the changes in different aspects of expenditure over time and indicate pertinent trends. Lastly, to determine key cost-drivers that could influence future treatment policies.

# 2. Material and Methods

## **2.1. General costs and sources**

We estimated costs using a top-down approach since detailed patient level data is currently not available in Poland.

Bottom-up costing methods are more feasible where procedures are frequently performed and/or detailed resource use data are available as seen with patient-level data. In such cases bottom-up calculations provide more detailed analysis particularly for selected risk factors as well as to compare subgroup results. In comparison, top-down methods require access to expenditure data from centralized systems, which often is difficult or even may not be possible. Nevertheless, once that engagement is established and access is provided, top-down method may provide more general insight in the costs related with epilepsy in a given country [25].

For this study, data from the Narodowy Fundusz Zdrowia (NFZ, National Health Fund), Zakład Ubezpieczeń Społecznych (ZUS, Social Insurance Institution) and Kasa Rolniczego Ubezpieczenia Społecznego (KRUS, Agricultural Social Insurance Fund) databases for the ICD-10 codes G40 and G41 were collected. The analysis covers data for both patients with epilepsy and patients with status epilepticus.

In Poland the public health insurance system is obligatory for the vast majority of the population, and it is not possible to opt out. The official coverage in 2018 was approx. 88%. The percentage is however an underestimate due to the inclusion of Polish citizens living abroad but still registered as residents in Poland. The private care system in Poland exists but its extent is limited. Consequently, this data was not included in analysis. In addition, we wanted to focus on the public healthcare system.

The NFZ remains the principal payer in the public health care system [26]. There is no cost-sharing for patients attending primary care, outpatient specialist care, emergency medical care or inpatient care; however, co-payment for medicines is relatively high. Typically, there is a flat-rate co-payment (PLN 3.20, i.e. EUR 0.74) coupled with a 0%, 30% and 50% co-payment of medicines on the reimbursement limit. Hospitalizations are financed based on their Diagnosis Related Groups (DRGs) and separate benefit catalogues. Health care products in the catalogues are defined through specific diagnoses (according to ICD-10 classification) or procedures (according to ICD-9 classification), and hospitals receive a flat payment per admission based on the point value of a given condition. That payment is calculated to cover all hospital costs incurred during a patient's hospital stay and includes medical consultations, diagnostic tests, medicines, and procedures. The main groups dedicated to epilepsy in the DRG system are A66, A67, and P23 (only for children) and the tariffs imposed by NFZ are EUR 219.8, EUR 997.4, and EUR 808.4 respectively. Funding of outpatient specialist care is based on the catalogue of visits classified by the type and number of services that can be provided within the visit with a flat point value calculated to cover their costs. The cost of the basic neurological visit imposed by NFZ is approximately EUR 7.9 for adults and EUR 8.1 for children. Funding of rehabilitation is similar at EUR 59.5 per day.

The disability pensions and sickness insurances in Poland as a part of the social insurance system are managed mainly by two main institutions: ZUS and KRUS. They both cover each year 15.8 and 1.4 million of people respectively, which represents 54% of Polish citizens aged 15 years or more [27, 28].

## **2.2. Direct and indirect costs**

The economic and social costs included in this study include both direct and indirect costs. All costs were measured in the Polish currency and were converted into euros using the middle exchange rate for EUR/PLN in the years 2014–2018 provided by National Bank of Poland [29]. Estimations in PLN are provided in the Supplementary Material.

### **2.2.1. Direct costs**

Data collected include the costs of pharmacotherapy excluding patients' co-payment, hospitalizations (including pharmacological, surgical treatment, and stimulation methods), outpatient specialist care and rehabilitation. In the analysis, NFZ resource use and expenditure data for each year in 2014–2018 for children and adults who have been registered in the NFZ system with the ICD-10 codes G40 and/or G41 were included in the analysis. We excluded patient co-payments as the focus for direct costs was the public payer, i.e. NFZ.

### **2.2.2. Indirect costs**

Estimates were based on the data provided and published by ZUS and KRUS [27, 28] on the number of disability living allowances (DLA). These were grouped by the duration of DLA and the age of the transition to DLA, and the number of days of sick leave due to epilepsy (G40 and/or G41 according to the ICD-10 classification) issued in each year between 2014 and 2018, as well as data of the on the Polish general population age structure [30].

The indirect costs were calculated according to the methodology outlined in consensus paper by Władysiuk et al. 2014 for INFARMA (the association of innovative pharmaceutical companies in Poland) [31]. Only the loss of productivity due to employee sickness absence, i.e. short-term and long-term absenteeism, due to epilepsy was considered. Because of the lack of quality data, the cost of productivity loss caused by a decrease in employee's productivity in the workplace (presenteeism) and premature death were omitted.

The Human capital approach (HCA) was used to assess indirect costs as this is the predominant method applied to evaluate productivity costs in the vast majority of published health economics studies. The unit cost of productivity loss was estimated using Gross Domestic Product (GDP) per worker. As the use of GDP per employee can lead to an overestimation of indirect costs, it was necessary to adjust the results with a coefficient that describes the relationship of marginal productivity of labor to the average productivity of labor. The analysis was performed with reference to working days reduced by paid annual leave, i.e. 26 days. The results were discounted with an annual discount rate [32]. Parameters used to estimate indirect costs are summarized in Online Resource 1.

The cost of short-term absenteeism was calculated using the number of days of absence due to illness. The cost associated with procurement of disability pension, i.e. fixed-term and permanent disability living allowance (DLA) and social pensions, i.e. benefits granted to adults whose health condition does not allow them to take up any work and the deterioration of the health condition had to take place before the age of 18 or during education before the age of 25, was determined based on the number of decisions issued, the average duration of DLA and social pension, as well as the average age of the transition to DLA and to social pension. It was assumed that the permanent pension is paid until the end of the employee's working age in Poland, i.e. for women up to 60 and for men up to 65 years of age, or death. A fixed-term pension is paid for a specified period determined individually. The results were adjusted by mortality of pensioners based on life tables for the Polish general population in 2014–2018 [30]. In addition, it was assumed that people with both partial and complete inability to work do not work at all. Consequently, no additional correction was applied when calculating the cost of DLA due to partial inability to work.

### **2.2.3. Expenses of ZUS**

ZUS expenses do not belong to either direct nor indirect costs, but are considered as social transfers. Available data on ZUS expenses incurred for benefits related to an inability to work due to epilepsy include disability pensions, social pensions, sickness absence benefits and rehabilitation benefits. ZUS expenses are paid for sickness

absence of an employee for longer than 33 days (expenses related to sickness absence lasting up to 33 days are covered by the employer) and childcare or other family members care regardless of the length of absence.

## **3. Results**

### **3.1. Direct costs**

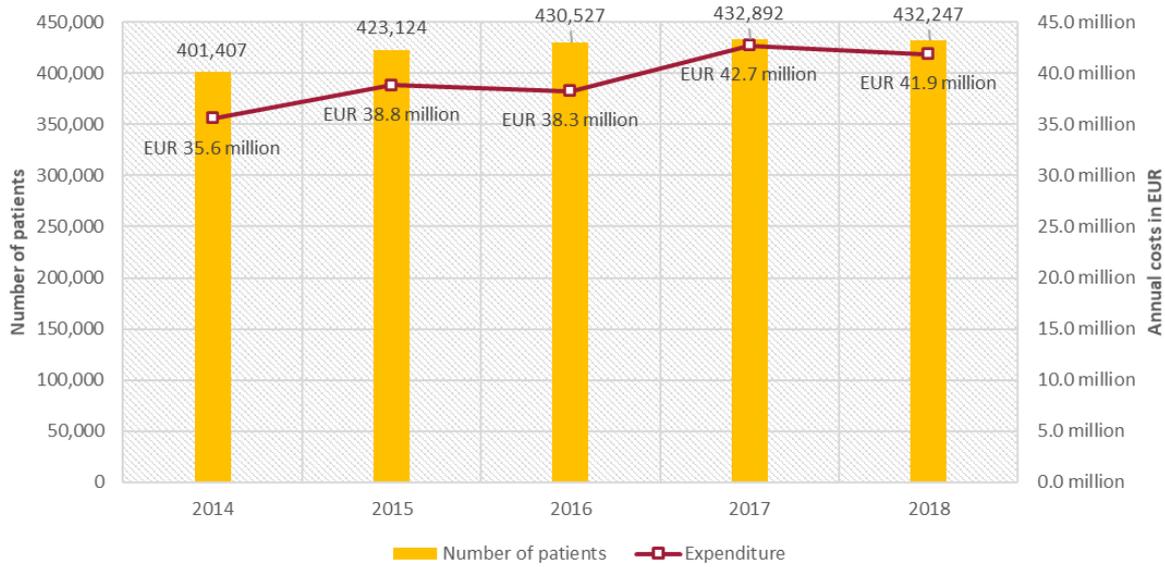
#### **3.1.1. Antiepileptic drugs**

In Poland between 2014-2018, 20 medicines were available for patients with epilepsy reimbursed by NFZ. These include carbamazepine, clonazepam, ethosuximide, gabapentine, lamotrigine, levetiracetam, lacosamide, magnesium valproate, oxcarbazepine, phenobarbital, phenytoin, pregabalin, primidone, retigabine, sodium valproate, tiagabine, topiramate, valproic acid, valproic acid + sodium valproate and vigabatrin. Except for retigabine (withdrawn in 2015), lacosamide (registered in 2008, refunded by NFZ since 2014) and stiripentol (registered in 2007, refunded by NFZ since 2016 in Dravet syndrome and epilepsy of infancy with migrating focal seizures; not available for other patients with epilepsy) all medicines were registered in 2000 at the latest. None of the medicines registered by EMA for the management of epilepsy after 2010, i.e. brivaracetam and perampanel, were financed by the NFZ between 2014-2018. The number of patients with epilepsy in Poland treated with AEDs reimbursed by NFZ has been growing slightly since 2014 from 401,000 up to 431,000 in 2016 and stabilized in the next years (Figure 1). In reported years, patients were most often prescribed drugs containing valproic acid (37%) and carbamazepine (21%, data for 2018). Overall, patients who were prescribed older AEDs accounted for between 65–72% of all patients prescribed AEDs between 2014–2018 but the trend is slowly downwards. The share of patients with epilepsy, especially those with drug resistant epilepsy, treated with newer medicines including lacosamide and stiripentol was less than 1%.

#### **3.1.2. Antiepileptic drugs costs**

The costs of antiepileptic drugs (prescribed to adults and children) in epilepsy between 2014–2018 were increasing from year to year, from EUR 36 million to EUR 42 million (Figure 1), i.e. from EUR 89 to EUR 99 per patient treated with AEDs reimbursed by NFZ. The actual increase in the pharmacotherapy cost is lower than the increase in AEDs consumption in reported years due to an observed decrease in the unit price of AEDs during this period. This may have been influenced by the increasing availability of lower cost multiple sourced products.

**Figure 1.**  
**Number of patients with epilepsy using AEDs reimbursed by NFZ and associated NFZ costs, years 2014–2018**



Authors' analysis based on NFZ data.

### 3.1.3. Hospital care

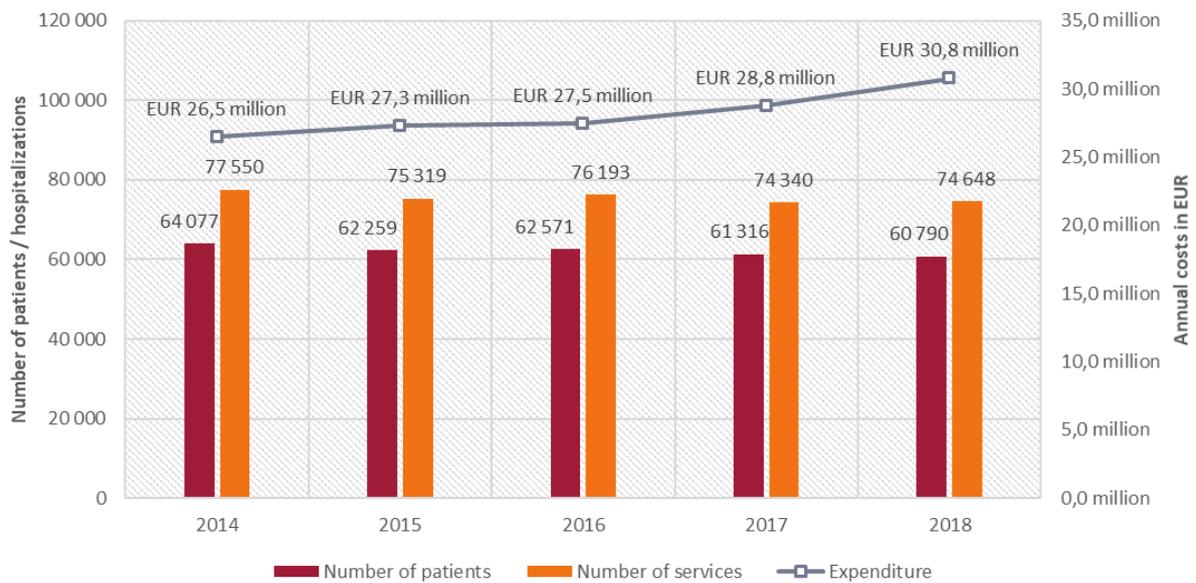
Between 2014 and 2018, the number of hospitalizations for patients with epilepsy decreased from 64,000 patients and 78,000 hospitalizations in 2014 to 61,000 patients and 75,000 hospitalizations in 2018 (Figure 2). This works out at approximately 1.2 hospitalizations per patient each year with, on average, patients with epilepsy being hospitalized for 2.9 days each year.

At least 19-23% of all hospitalizations were for pediatric patients with the increasing tendency.

### 3.1.4. Hospital care costs

The costs of epilepsy-related hospitalizations amounted to EUR 26 million in 2014, increasing to EUR 31 million in 2018 (Figure 2), i.e. EUR 414 to EUR 506 per patient hospitalized. Despite a declining number of hospitalizations, hospital costs increased as a result of a change in the valuation of the services' tariffs. Taking into account only hospitalizations that are dedicated to diagnosis or treatment of epilepsy, costs of hospitalizations in pediatric patients constituted 41–44% of total costs with the remaining 56–59% accounted for by adult patients.

**Figure 2.**  
**Number of hospitalized patients with epilepsy and associated costs, years 2014–2018 – hospital care**



Authors' analysis based on NFZ data.

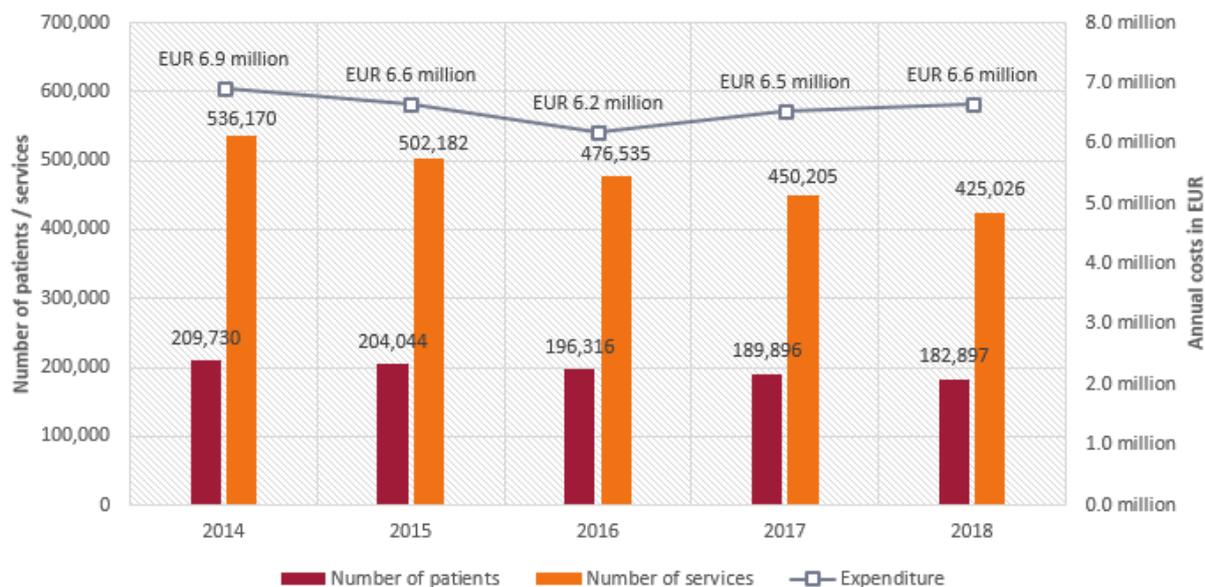
### 3.1.5. Outpatient specialist care use

The number of outpatient visits for patients with epilepsy decreased: from 536,000 visits and 210,000 patients in 2014 to 425,000 visits and 183,000 patients in 2018 (Figure 3). The number of specialized visits in outpatient care per year per patient with epilepsy decreased from 2.6 to 2.3. The outpatient specialist care was provided mainly at neurologist clinics (96% of visits).

### 3.1.6. Outpatient specialist care costs

The costs of epilepsy-related ambulatory services amounted to EUR 6.9 million in 2014. In the following years, these costs fluctuated around EUR 6.5 million (Figure 3). In spite of a clear decline in the number of specialized visits, the reduction of costs was observed only until 2016. In 2017 and 2018 there was an escalation of costs for these services. The costs per patient using outpatient services also behaved in the same manner ranging from EUR 31 to EUR 36 in these years. On average, pediatric patients accounted for 25% of public costs of neurological visits for patients with epilepsy compared with 75% for adult patients.

**Figure 3.**  
**Number of patients with epilepsy using specialized services and associated costs, years 2014–2018 – outpatient care**



Authors' analysis based on NFZ data.

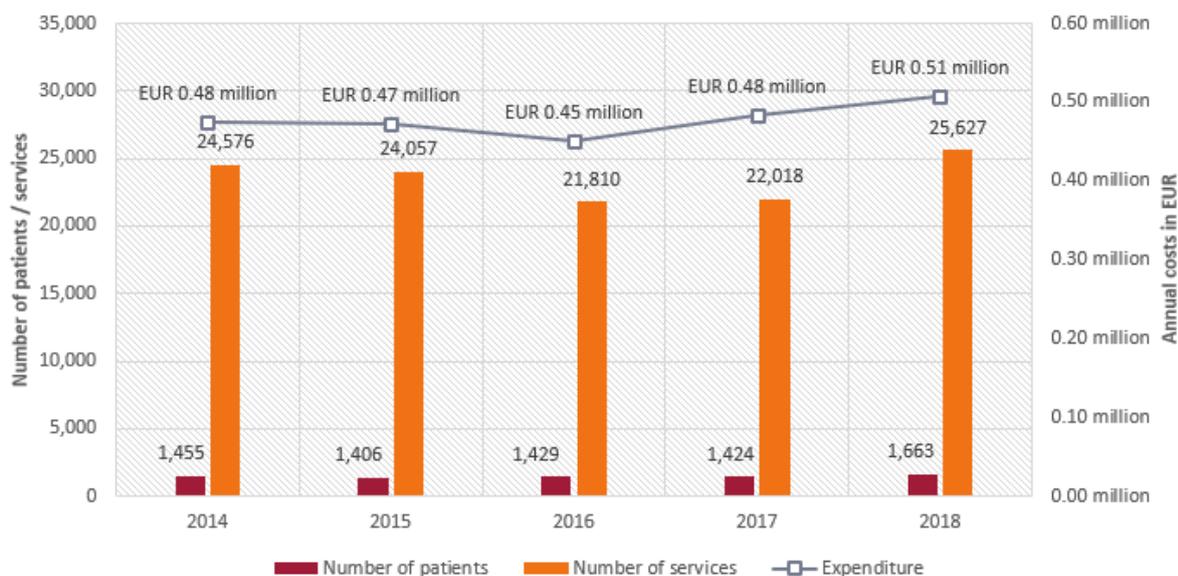
### 3.1.7. Rehabilitation use

The number of patients who were provided with rehabilitation amounted for 1,455 in 2014, increasing to 1,663 in 2018 (Figure 4). The number of rehabilitations increased as well from 24,600 in 2014 to 25,600 in 2018. There were 16.9 rehabilitations per patient in 2014 which decreased to 15.4 in 2018. Despite the fact that there were less rehabilitated children than adults (41% vs 59% on average), young patients more often benefited from these services. On average, each year there were 25 rehabilitations per child and 10 rehabilitations per adult with epilepsy.

### 3.1.8. Rehabilitation costs

Between 2014 to 2018, the costs of rehabilitation in epilepsy remained stable at EUR 0.5 million with the majority (76–87% with a decreasing trend) incurred in children (Figure 4). In contrast, costs per patient were fluctuating due to an irregular number of patients using rehabilitation. These ranged in 2014-2018 from EUR 305 to EUR 339.

**Figure 4.**  
**Number of patients with epilepsy using specialized services and associated costs, years 2014–2018 – rehabilitation**

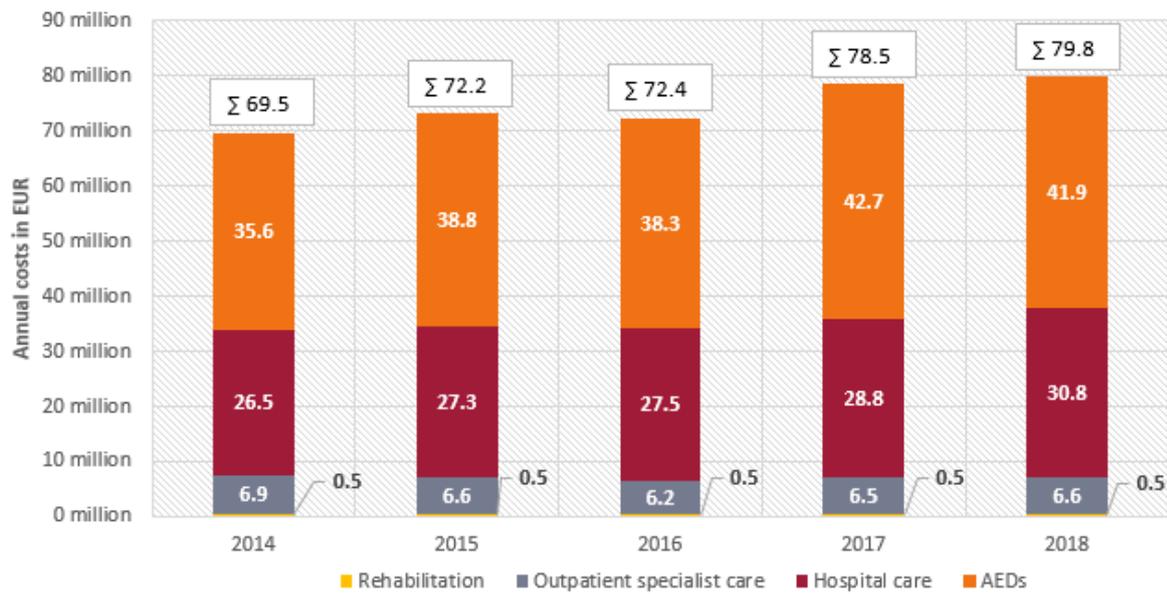


Authors' analysis based on NFZ data.

### 3.1.9. Summary of direct costs

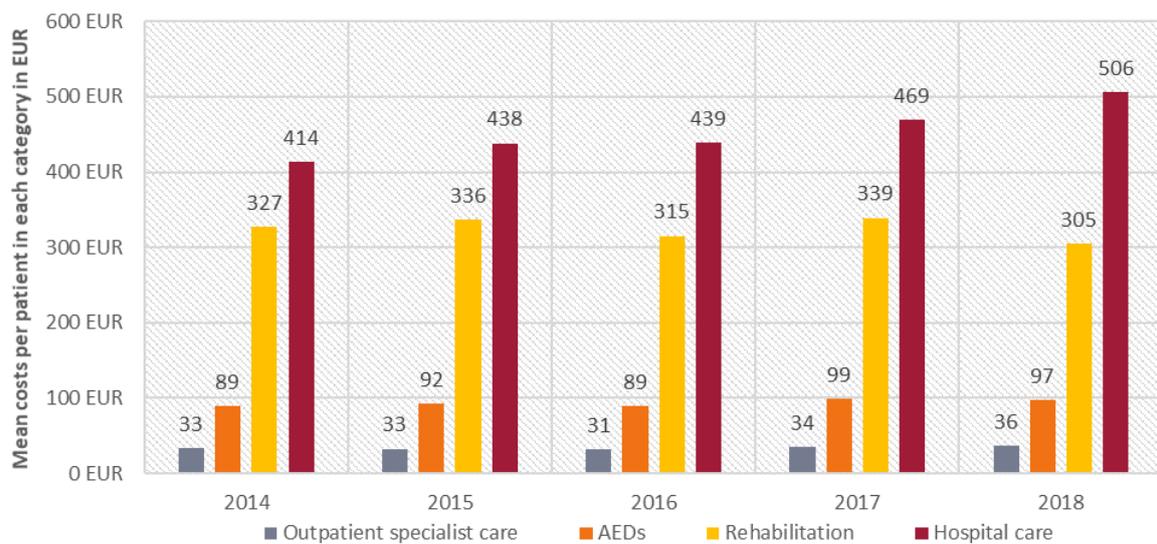
The annual direct costs for patients with epilepsy in Poland were EUR 69 million in 2014, increasing to EUR 80 million in 2018. Details are presented in Figure 5 and Online Resource 3. The costs associated with the use of antiepileptic drugs and hospital care were the principal cost drivers. The cost of antiepileptic drugs accounted for 51–54% of all analyzed cost categories. An increase in the costs of AEDs resulted in an overall increase of NFZ expenditures in epilepsy by approximately 15%. Hospital care accounted for approximately 38% of total costs. In general, direct costs of treating patients with epilepsy in Poland continuously grew from 2014 to 2018 (except for 2016 when a decrease by 1% was observed). The growth was mainly caused by increasing use of AEDs (7-8%) and annual costs of hospitalization and AEDs per patient (22% and 9%, respectively) as the number of specialized services and hospitalizations decreased in subsequent years. Mean direct costs related with epilepsy per patient in each of analyzed category are presented in Figure 6 and Online Resource 4.

**Figure 5.**  
Direct costs related with epilepsy in Poland [EUR], years 2014-2018



Authors' analysis based on NFZ data

**Figure 6.**  
Mean direct costs related with epilepsy per patient in each category in Poland [EUR], years 2014-2018



## 3.2. Indirect costs

### 3.2.1. Disability pensions

Between 2014 and 2018, the number of disability pensions (fixed-term and permanent) issued for patients with epilepsy decreased from 4721 in 2014 to 3720 in 2018 (Table 1). In last two years, a limited growth was observed; however, this was preceded by significant decrease in 2015 and 2016 for fixed-term pensions and in 2016 for permanent pensions. The majority (approximately 90%) of pensions were issued for partial incapacity to work.

Between 2014 and 2018, the number of social pensions issued for patients with epilepsy only slightly decreased from 687 to 627. There was a significant decrease in 2016; however, increases in the remaining years. 92% of all social pensions were fixed-term.

### 3.2.2. Sick leave

The total number of days of sick leave due to epilepsy was stable in 2014–2018 at approximately 360,000 days a year (Table 1). The average length of sick leave was 13 days. Each year, approximately 75% of certificates were issued for more than 7 days (Online Resource 2).

**Table 1.**  
**Number of DLAs, social pensions and days lost due to sick leave in patients with epilepsy in Poland, years 2014–2018**

Parameter	Year 2014	Year 2015	Year 2016	Year 2017	Year 2018
<b>Number of fixed-term DLAs</b>	4,379	3,640	2,764	2,844	3,128
<b>Number of permanent DLAs</b>	342	364	312	496	592
<b>Number of social pensions</b>	687	739	584	606	627
<b>Number of days lost due to sick leave</b>	357,380	354,347	357,046	366,970	357,443
<b>Number of medical certificates</b>	5,379	5,176	4,718	4,250	4,301

Authors' analysis based on ZUS and KRUS data.

### 3.2.3. Summary of indirect costs

In 2014, the indirect costs of patients with epilepsy in Poland was EUR 341 million. In the following years, indirect costs due to lost productivity fluctuated; however, this did not exceed 2014 levels. As showed in Figure 7, fixed term DLAs were the principal cost-driver (87–92% of total indirect costs). It should be noted that costs presented for 2018 do not include KRUS data. As can be seen, there is a large variation in results between years. This is due to significant fluctuations in number of both types of DLAs, particularly fixed-term DLAs which number dropped by 1/3 between 2014-2016, so as social pensions. The reason of that fluctuations could be introduction of some restrictions on entitlement to DLA for patients with epilepsy in 2016 but the official rationale is unknown.

**Figure 7.**  
Indirect costs related to epilepsy in Poland, years 2014–2018



Authors' analysis based on ZUS, KRUS and CSO data

### 3.3. Total (direct and indirect) costs

Annual total direct and indirect costs in patients with epilepsy accounted for EUR 410 million in 2014, decreasing to EUR 296 million in 2016 (Table 2). Indirect costs were dominant representing 76–83% of the total costs. The proportion of indirect costs declined in the first three years with growth thereafter.

**Table 2.**  
Total costs related with epilepsy in Poland, years 2014–2018

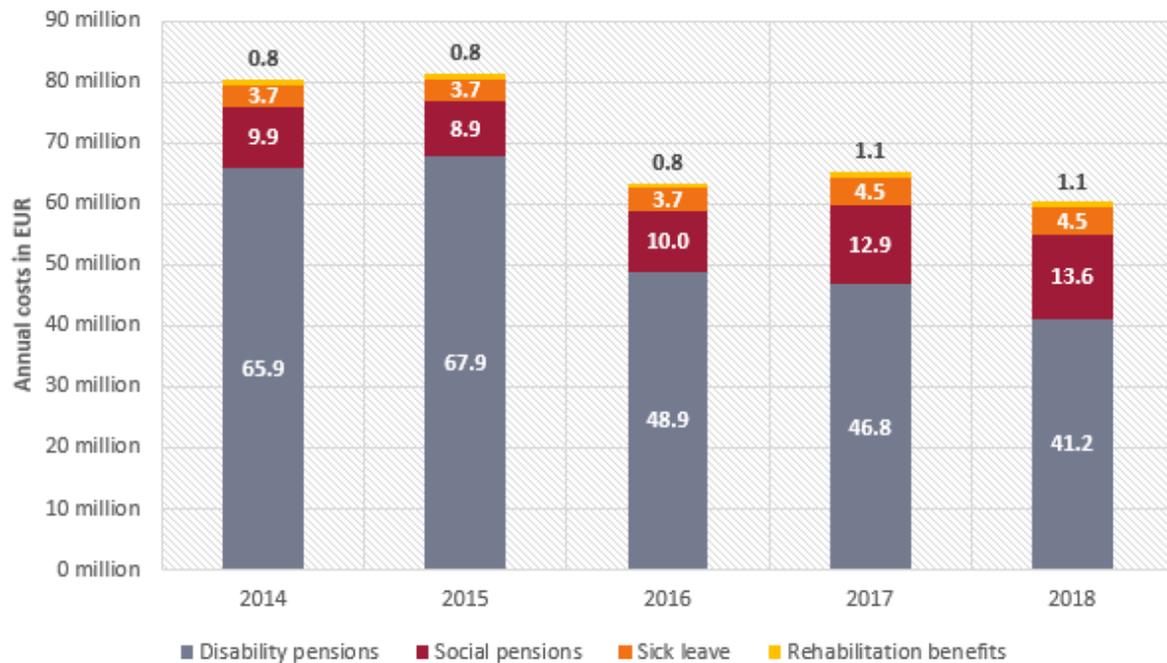
Cost category	Year 2014	Year 2015	Year 2016	Year 2017	Year 2018
<b>Direct costs</b>	69.5 (16.9%)	73.2 (20.0%)	72.4 (24.4%)	78.5 (23.3%)	79.8 (22.1%)
<b>Indirect costs</b>	340.8 (83.1%)	293.7 (80.0%)	223.9 (75.6%)	258.1 (76.7%)	281.5 (77.9%)
<b>Total</b>	<b>410.2</b>	<b>366.9</b>	<b>296.3</b>	<b>336.6</b>	<b>361.3</b>

Authors' analysis based on NFZ, ZUS, KRUS and CSO data. Shares of total direct and indirect costs respectively are reported in brackets.

### 3.4. ZUS expenses

The ZUS expenses incurred for benefits related to epilepsy decreased from approximately EUR 80 million per year in 2014–2015 to approximately EUR 63 million in 2016–2018. The largest share in ZUS expenses due to epilepsy belonged to disability pensions (on average 77%) and social pensions (on average 15%). A significant decrease in ZUS expenses was observed in 2016 probably as a consequence of the decrease in the number of fixed-term pensions issued that year. Nevertheless, the downward trend in these costs was seen in subsequent years despite an increase in the number of issued pension (Figure 8). This suggests decreasing amounts in ZUS benefits in 2017 and 2018.

**Figure 8.**  
**Structure of ZUS expenses on benefits related to inability to work due to epilepsy in 2014–2018**



## 4. Discussion

In this paper direct and indirect costs for the epilepsy population in Poland were estimated from the social perspective. We believe this is the most comprehensive set of public institution data concerning health and social aspects of epilepsy for Poland addressing some of the concerns with earlier studies. Mela et al. [20] determined direct and indirect costs of epilepsy in Poland in the years 2014–2016 using data from national databases (NFZ and ZUS). Our study covers the longer period of observation, contains more detailed data from available currently public sources (NFZ, ZUS and KRUS) and patients with status epilepticus (not included in earlier studies). This allowed for a more comprehensive insight into the public expenditures in epilepsy in Poland and investigating their changes in the past years.

Our results show that epilepsy causes an appreciable socioeconomic burden for Poland principally indirect costs. Total direct and indirect costs due to epilepsy were EUR 354 million in 2014, decreasing to EUR 270 million in 2018. Our results are in line with Mela et al. [20]. Having longer observation time, we showed that the trend of total expenditure decreased persists. The direct expenses on epilepsy in Poland were growing by approximately 10% between 2014 and 2018, but indirect costs were decreasing.

Indirect costs constituted the majority of costs incurred in patients with epilepsy at between 70 to 80% of total costs. However, contrasting with other recent studies where indirect costs constitute between 18–72% of total costs of epilepsy [18–20, 22, 23]. The wide range of the estimates probably results from differences in the social benefit systems and costing methodologies used. The estimations of indirect costs for Poland were primarily related with

a long-term incapacity to work. This is a major concern in patients with epilepsy, European data suggests that between 28–59% of patients with epilepsy are not economically active [15–19, 33–35], with a study published in 2012 showing that in Poland only 49% of patients with epilepsy are employed, of whom 67% work full-time [34].

Gupta et al. [15, 16] found that employees with epilepsy absent from work on average for 25–29 days per year. In Poland, insured patients with a sick leave due to epilepsy were absent from work on average for 28 days, but only 25% of sick leaves were issued for 7 days or less [36]. These observations suggest that the data used for productivity loss in our study could be biased by high unemployment rate among patients with epilepsy in Poland. The fact that at least some employees with epilepsy did not claim sick leave due to that condition means that real absenteeism per year may well be higher.

Whilst a significant decrease was observed in the number of disability pensions issued in 2016–2018, mainly associated with a fixed-term DLAs, a drop in the average annual number of decisions by 1/3 in relation to 2014 to 2015, the productivity costs stayed relatively high. In reported years, the costs of sick leaves were at stable but much lower level, constituting between 10–17% of total indirect costs. A similar conclusion was seen a study by Jennum et al. [18] in the Netherlands where sick leaves issued in 2011 represented approximately 8.7% of total indirect costs.

The comparison of costs of epilepsy reported for several European countries has shown that direct costs differ between healthcare systems. It is difficult to determine whether the differences are due to different unit costs or to different use of health-care resources. However, in general, papers present that AEDs usage and hospital care are major costs contributors in direct cost category with a smaller impact of outpatient care [20–22]. Bolin et al. [21, 22] using data of national healthcare registries show that in Sweden most money (47%) is spent on medicines. Nevertheless, the proportion between costs of AEDs and hospital care may differ. For instance, Strzelczyk et al. [23] compared epilepsy-related costs in newly diagnosed patients during the first and second year after diagnosis with costs in patients with established epilepsy in Germany. Newly diagnosed patients during the first year after diagnosis had significantly higher share of hospital care costs (59%). The more time passed since diagnosis, the more costs were driven by use of medicines (from 30% up to 63%). These findings are in line with the study by Jennum et al. [18] showing that in Denmark at the time of diagnosis the costs are elevated due to hospitalization and diagnostic procedures (58%). Outpatient care was related with smaller costs in range of 6–21% of total health care costs of epilepsy reported in these papers.

Significant costs are related to the treatment of seizures, especially status epilepticus, and may differ depending on severity of illness. So far, there are a few cost-of-illness studies regarding this medical condition. Kortland et al. [37] and Strzelczyk et al. [38] showed that treatment of status epilepticus in Germany, including refractory and super refractory status epilepticus was associated with prolonged length of hospital stay (19 and 21 days on average, respectively). In comparison, mean length of stay for patients with epilepsy was barely 8 days. In consequence, status epilepticus was associated with higher costs of treatment than epilepsy. Kortland et al. estimated these costs nearly to EUR 15,000 per admission, while Strzelczyk et al. to approx. EUR 11,500 per admission. For the most severe cases costs of treatment was about EUR 50,000 per admission.

There are concerns with the limited use of newer AEDs such as lacosamide and stiripentol especially in refractory patients with their expenditure amounting to less than 1% of total expenditure on medicines, with a similar situation for brivaracetam observed in 2019. Increased availability of low cost generics may help to release resources to spend on newer AEDs especially for refractory patients as well as where there are concerns with existing treatments [39–42]. This is particularly important given WHO concerns about the lack of focus on epilepsy among countries and the need to treat patients well in view of the morbidity, mortality and costs associated with epilepsy [4, 6, 12, 13]. For instance, in November 2018, reimbursement of the first generics for lacosamide was started in Poland, which resulted in savings of approximately EUR 4 million per year [43]. However, care is needed when prescribing generic AEDs due to concerns with substitution with for instance the authorities in Sweden not mandating compulsory generic substitution for AEDs unlike other medicine classes and the authorities in the UK advocating care with substitution apart from selected AEDs [44, 45].

Among services, hospital care was the main cost-driver with approximately 38% of the public health costs of epilepsy in Poland despite the fact that most patients were managed in outpatient settings. This suggests expenditures on this type of care remain low. The reason of this could be significantly lower costs for neurological visits in Poland in comparison to Western European countries, e.g., GBP 160 per neurological visit for adults and GBP 332 per neurological visit for pediatric patients in the UK based on published NHS [46] data versus below GBP 8 for a basic neurological visit in Poland according to NFZ [47]. On the other hand, it should be noticed that in Poland medical outpatient visits are provided by both public and private service providers. In case of healthcare services provided outside the NFZ system, all costs are covered by the patients themselves and not reported in the public healthcare system. Consequently, the costs of outpatient care for epilepsy in Poland are probably much higher than estimated in this paper. This situation is caused mainly by limited access to public services in Poland and potentially a lower chance of therapeutic success, disease control and normal life. This may also explain the decreasing number of patients with epilepsy treated in outpatient settings via NFZ in the reported years. This needs also to be addressed within a public healthcare system as it is against the European ideals of equitable healthcare for all.

It is important to know that the children's share among each reported cost category was highly diverse and represented only 11% for AEDs (i.e., costs of AEDs reported for 2017–2018), 25% for outpatient care (neurological visits), as much as 41–44% for hospital care and 76–87% for rehabilitation. At the same time, 19–23% of hospitalizations related with epilepsy involved children. Both observations show that the use and costing of services in pediatric patients is higher than in adults with epilepsy in Poland.

We believe the strength of our approach is that both direct and indirect costs for patients with epilepsy in Poland were estimated from the social perspective. In addition, the most recent and comprehensive set of public institutions data concerning health and social aspects of epilepsy were collected. Consequently, we believe our results show possibly the most reliable estimates of actual costs of epilepsy in the past years in Poland providing information about key cost drivers and extent of costs changes over subsequent years. It is hoped that these results will inform further research into the cost burden of epilepsy in Poland and help to improve quality of treatment and the management of patients with these conditions.

We are aware though that our study had several limitations. Firstly, the healthcare data used covered only publicly funded benefits. While hospitalizations in Poland are financed mainly by NFZ, pharmacotherapy, outpatient specialist care and rehabilitation could be co-funded by patients or even provided outside the NFZ system and fully financed by patients if they attend private service. Nowadays, a significant part of outpatient care in Poland is provided outside the public system with some estimating that the average cost of a private visit is 13 times higher than visits financed by NFZ [5, 24]. However, this analysis was performed from the public payer perspective.

The NFZ data on primary care in epilepsy were not provided. However, the annual cost per person within the system is flat regardless of the health care use and relatively small at EUR 35/year. Consequently, we believe this does not affect the results, especially in Poland where patients with epilepsy are under the care of neurologists not of general practitioners.

In addition, the KRUS data on the number of lost days due to sick leave in 2018 and on the number of medical certificates received for G40 were not available. Consequently, the linear prediction was made based on data from previous years. What is more, the KRUS data on DLAs for epilepsy were provided. The values were estimated from the aggregated number of DLAs due to any neurological disorder (ICD-10 code G00–G99) issued by KRUS using the epilepsy share within DLAs due to neurological disorder issued by ZUS.

Data on social pensions in epilepsy were also limited. Social pensions are paid by ZUS only; consequently, there is a lack of KRUS data. ZUS data did not include (except 2018) the age of pensioners and duration of the pensions. The average age of pensioners was estimated from the data for social pensions issued in Poland in 2018 regardless of the underlying condition (lack of data explicitly for epilepsy). Permanent pension share and duration of the fixed-term pension for 2014–2017 years was assumed the same as reported in 2018.

To avoid possible double-counting of long-term absenteeism related with premature death and permanent pensions in patients with epilepsy (in 2014–2018 there were 440–512 deaths due to epilepsy and 342–592 permanent DLAs issued) the data on epilepsy-related mortality in Poland were omitted. Including these data in the calculations would result in an increase in estimated indirect costs by on average 40%.

Alongside this, due to a lack of relevant data, the indirect cost of lost productivity concerned with decreased productivity in the workplace (presenteeism) has been omitted. Such data are collected usually individually among patients and therefore not compatible with the costing method applied in this analysis (top-down). At the same time, there is no doubt the phenomena of presenteeism in patients with epilepsy occurs and generates costs. Gupta et al. [15, 16] showed that presenteeism was a major contributor to productivity loss in patients with idiopathic generalized epilepsy and focal epilepsy. In comparison to absenteeism, it was 2.5 times greater in patients with idiopathic and 3.4 times greater in patients with focal epilepsy. Consequently, we are confident of our findings since, if anything, the estimates of indirect costs between 2014 and 2018 are a considerable under-estimate.

In conclusion, there can be considerable costs associated with managing patients with epilepsy in terms of both direct as well as indirect costs including social expenses. Detailed insight into the burden of epilepsy including its associated cost can help inform decision-makers when allocating resources to improve the care of patients within public healthcare systems. In the last years in Poland, there has been a decline in total costs of epilepsy but due to

high disproportion between indirect and direct costs this information does not mean much. Direct costs of epilepsy in Poland are growing, driven mostly by spending on AEDs and hospital care. However, most of the AEDs prescribed are currently the older AEDs with high share of low-cost generics (about 90%). Consequently, there is an undeniable need to change prescription patterns to use newer AEDs especially for refractory patients in line with WHO guidance to improve the care of patients with epilepsy across countries. Concurrently with this, the costs of epilepsy-related ambulatory services that involve most of the patients with epilepsy in Poland are stable and low (approximately 8-10% of direct costs), a future public health system changes should be aimed at shifting the care of patients with epilepsy from hospital to outpatient settings. Indirect costs of epilepsy in Poland are substantially decreasing mainly due to a significant fall in the number of disability pensions issued for epilepsy. It shows that more and more often people with epilepsy can function in a normal way returning to the labor market. All of discussed system changes would allow to further develop this process and could be additionally strengthened by reinvestment of saved funds to improve the care of people with epilepsy in Poland.

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