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Welfare cost of childhood- and adolescent-onset epilepsy: A controlled national study

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ABSTRACT

Objectives: Epilepsy is associated with a significant burden to patients and society. We calculated the factual excess in direct and indirect costs associated with childhood- and adolescent-onset epilepsy.
Methods: Using records from the Danish National Patient Registry (1998–2002), we identified 3123 and 5018 patients with epilepsy aged 0–5 years and 6–20 years at the time of diagnosis, respectively. The two age groups of patients with epilepsy were matched to 6246 and 10,036 control persons without epilepsy, respectively, by gender, age, and geography. The controls were randomly chosen from the Danish Civil Registration System. Welfare costs included outpatient services, inpatient admissions, and emergency room visits based on the Danish National Patient Registry and information from the primary health-care sector based on data from the Danish Ministry of Health. This allowed the total health-care cost of epilepsy to be estimated. The use and costs of drugs were based on data from the Danish Medicines Agency. The frequencies of visits to outpatient clinics and hospitalizations and costs from primary sectors were based on data obtained from the National Patient Registry.
Results: Children with epilepsy had higher welfare costs than controls. The highest cost was found one year after diagnosis, with higher costs up to 10 years after diagnosis compared with controls. Children aged 0–5 years incurred greater health-care costs than those aged 6–20 years.
Conclusion: Epilepsy has major socioeconomic consequences for the individual person with epilepsy and for society.

1. Introduction

Epilepsy is one of the most important and common chronic neurological disorders and affects persons of all ages. It is strongly associated with significant comorbidities, mortality, stigma, reduced quality of life, and educational and professional problems and, consequently, has a substantial socioeconomic impact [1–4]. Estimation of the total societal burden of epilepsy is necessary to provide information for health planning. Studies on the economic impact of epilepsy have mainly focused on model information, questionnaires, and other direct or indirect information in selected groups of patients, and estimates of the economic burden extracted from this information have been primarily reported for adults [5–21]. However, the association between epilepsy in children and direct and indirect costs has not often been described [2,22–26]. There are limited data about long-term costs in children with epilepsy based on prospective studies. Recently, we described factual direct and indirect costs in children and adults diagnosed with epilepsy in Denmark [27]. These data suggested that epilepsy causes a substantial burden, not only at the time of diagnosis and after but also before diagnosis. However, this study assessed the total costs from the whole national population; there has been little focus on the welfare cost in children.

For the Danish population, using a unique identification number, it is possible to identify persons with and without epilepsy and to link this status to health and socioeconomic information. We aimed to evaluate the long-term welfare consequences of early onset epilepsy.

2. Methods

2.1. The cohort of persons with epilepsy and control subjects

Patients hospitalized with epilepsy in Denmark between 1998 and 2002 were identified from historical medical archives and matched by

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age, gender, and geographic region to a randomly chosen control group from the background population. Detailed information about education, employment, welfare benefits, family relations, hospital contacts, visits to general practitioners, and use of medication for the total Danish population was drawn from several nationwide registers. These data enabled us to identify the long-term social effect of epilepsy with a follow-up time of 10 years after diagnosis. Since April 1968, all Danish citizens have been assigned a unique identification number (Central Personal Registration number), which is recorded in the Danish Civil Registration System along with information about place of birth, place of residence, vital status, and marital status. In Denmark, all patient contacts are recorded in the Danish National Patient Registry (NPR) by time of contact and primary diagnosis. The NPR also includes administrative information and diagnostic and treatment procedures using several international classification systems including the International Classification of Disorders (ICD-10). The NPR is a time-based national database with details of all patient contacts, so the data may be considered representative of all patients in Denmark who have received a diagnosis of epilepsy in public and private hospitals.

To analyze the health consequences (costs and comorbidity) in the first 10 years after a diagnosis of epilepsy (index date), a cohort of patients with epilepsy alive 10 years after the index date was identified. The patients in the cohort were diagnosed with epilepsy for the first time between years 1998 and 2002 and followed up to the end of 2012.

All patients were individually matched to two control persons by age, gender, and living location. The use and costs of drugs were based on data from the National Danish Medicine Agency, including the retail price of the drug (with dispensing costs) multiplied by the number of transactions.

The control group was not matched to patients' education, because it is not possible to obtain a perfect match for the entire population based on child age. Instead, we controlled systematically for parental education i.e., skilled or college (short, medium, and long-term education) by including a dichotomous explanatory variable distinguishing trained and not trained in the statistical analysis.

The analysis was based on a prediction of annual health-care costs for patients with epilepsy and their controls over a 10-year period after diagnosis (postindex period).

Postindex health expenses were divided into those for outpatient services, hospital admissions, accident and emergency, primary health sector, and medication prescriptions redeemed.

Redemption of prescriptions, hospitalizations, outpatient visits, and accident and emergency visits were included after the index date. Index diagnosis costs of hospitalization, ambulatory visits, and accident and emergency visits were therefore not included.

Annual health-care costs were predicted from a generalized estimating equation (GEE) model in which parents' education (skilled and college) was also included as an explanatory variable (0 = neither parent trained, 1 = least one parent trained).

3. Results

Three thousand one hundred twenty-three patients aged 0–5 years and 5018 patients age 6–20 years at the time of diagnosis of epilepsy were identified and compared with 6246 and 10,036 controls, respectively. Patient characteristics are shown in Table 1. More boys than girls had epilepsy, although the distribution between the sexes was approximately equal for older children and adolescents. The parental educational level was lower among parents of children with epilepsy.

3.1. Health-care cost estimation for the 10-year postindex period

Outpatient services, inpatient admissions, accident and emergency, primary health-care sector, uses of medication, and consequently, total health-care costs were all significantly higher in 0- to 5- and 6- to 20-year-old patients (Tables 2A and 2B and Fig. 1 and 2). The costs in children with epilepsy diagnosed at age 0–5 years were higher than in patients aged 6–20 years at diagnosis (Fig. 2). The welfare costs were highest during the first year after diagnosis. For patients aged 0–5 years at the time of diagnosis, the cost of inpatient admissions constitutes the major part of the costs associated with epilepsy (Table 2A). The costs were lower for children diagnosed at 6–20 years of age, especially those of hospital admissions (Table 2B).

4. Discussion

This is one of the largest studies evaluating the welfare cost of childhood- and adolescent-onset epilepsy in a national cohort with gender-, age-, and geographically-matched controls. Compared with those in controls, the welfare costs were higher in both age groups of patients for all domains including general practice, hospital visits, emergency room visits, and medication use. The costs were highest during the first year after diagnosis and were higher for up to 10 years after the index date. Welfare costs were highest with early-onset epilepsy.

Onset of epilepsy in childhood, adolescence, and younger adulthood had a significant welfare impact. Total health costs were more than four

Table 1
Basic characteristics of persons with epilepsy aged 0–5 and 6–20 years at time of epilepsy diagnosis compared with controls.

	Diagnosis of epilepsy at age 0–5 years					Diagnosis of epilepsy at age 6–20 years				
	Persons with epilepsy		Controls		P	Persons with epilepsy		Control		P
	N = 3123		N = 6246			N = 5018		N = 10,036		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Age at diagnosis of epilepsy (index date)	2.2	1.7				12.1	4.2			
	N	%	N	%	P	N	%	N	%	P
Gender										
Male	1693	54.2				2603	51.9			
Female	1430	45.8				2415	48.1			
Education										
Parents' highest level of education at index date										
Primary	507	16.2	688	11.0	<0.001	908	18.1	1.466	14.6	<0.001
Secondary	136	4.4	281	4.5	<0.001	149	3.0	273	2.7	<0.001
Vocational	1366	43.7	2670	42.7	<0.001	2268	45.2	4343	43.3	<0.001
College	1099	35.2	2578	41.3	<0.001	1648	32.8	3820	38.1	<0.001
Unknown	15	0.5	29	0.5	<0.001	45	0.9	134	1.3	<0.001

Table 2A
Predicted health-care costs in 10 years after the initial diagnosis for the 0- to 5-year-old group with epilepsy and their controls. Adjusted for parenteral education.

Year	N		Outpatient services			Inpatient admissions			Accident and emergency			Primary health sector			Prescription medicine			Total health-care costs		
	Epilepsy 0–5 years	Control	Epilepsy 0–5 years	Control	P	Epilepsy 0–5 years	Control	P	Epilepsy 0–5 years	Control	P	Epilepsy 0–5 years	Control	P	Epilepsy 0–5 years	Control	P	Epilepsy 0–5 years	Control	P
	N	N	€	€		€	€		€	€		€	€		€	€		€	€	
1	3123	6246	402	51	<0.001	5066	510	<0.001	42	22	<0.001	403	247	<0.001	297	40	<0.001	6211	871	<0.001
2	3074	6192	202	47	<0.001	1805	248	<0.001	36	21	<0.001	352	207	<0.001	321	37	<0.001	2715	558	<0.001
3	3045	6176	178	44	<0.001	1413	187	<0.001	32	22	<0.001	290	172	<0.001	321	33	<0.001	2202	459	<0.001
4	3029	6143	161	50	<0.001	1162	140	<0.001	31	22	<0.001	277	157	<0.001	324	31	<0.001	1953	400	<0.001
5	3015	6128	152	49	<0.001	1172	169	<0.001	34	21	<0.001	289	138	<0.001	340	33	<0.001	1943	412	<0.001
6	2997	6114	160	54	<0.001	943	147	<0.001	33	23	<0.001	308	120	<0.001	356	37	<0.001	1798	381	<0.001
7	2991	6100	167	64	<0.001	929	182	<0.001	31	24	<0.001	348	110	<0.001	386	45	<0.001	1860	424	<0.001
8	2979	6094	158	59	<0.001	938	167	<0.001	32	27	0.003	394	108	<0.001	401	55	<0.001	1921	417	<0.001
9	2971	6080	205	70	<0.001	1151	175	<0.001	34	28	0.001	403	110	<0.001	431	62	<0.001	2216	446	<0.001
10	2966	6070	192	94	<0.001	933	199	<0.001	33	29	0.050	405	111	<0.001	432	66	<0.001	1998	500	<0.001

Table 2B
Predicted health-care costs in 10 years after the initial diagnosis for the 6- to 20-year-old group with epilepsy and their controls. Adjusted for parenteral education.

Year	N		Outpatient services			Inpatient admissions			Accident and emergency			Primary health sector			Prescription medicine			Health-care costs total		
	Epilepsy 6–20 years	Control	Epilepsy 6–20 years	Control	P	Epilepsy 6–20 years	Control	P	Epilepsy 6–20 years	Control	P	Epilepsy 6–20 years	Control	P	Epilepsy 6–20 years	Control	P	Epilepsy 6–20 years	Control	P
	N	N	€	€		€	€		€	€		€	€		€	€		€	€	
0	5018	10,036	285	52	<0.001	1810	151	<0.001	54	25	<0.001	196	103	<0.001	431	53	<0.001	2803	385	<0.001
1	4975	9958	158	61	<0.001	620	160	<0.001	47	28	<0.001	180	105	<0.001	517	58	<0.001	1527	412	<0.001
2	4951	9926	166	66	<0.001	604	178	<0.001	47	30	<0.001	186	106	<0.001	552	61	<0.001	1555	441	<0.001
3	4923	9893	144	72	<0.001	539	198	<0.001	50	32	<0.001	192	113	<0.001	545	68	<0.001	1475	485	<0.001
4	4918	9873	187	92	<0.001	582	187	<0.001	53	33	<0.001	210	119	<0.001	526	74	<0.001	1555	506	<0.001
5	4901	9848	203	104	<0.001	623	210	<0.001	50	34	<0.001	225	127	<0.001	519	81	<0.001	1622	556	<0.001
6	4886	9828	236	126	<0.001	700	220	<0.001	50	34	<0.001	242	135	<0.001	514	89	<0.001	1742	605	<0.001
7	4879	9834	264	151	<0.001	747	260	<0.001	48	34	<0.001	254	150	<0.001	501	92	<0.001	1813	689	<0.001
8	4873	9804	264	171	<0.001	632	294	<0.001	42	31	<0.001	255	165	<0.001	483	99	<0.001	1679	762	<0.001
9	4850	9782	273	186	<0.001	692	290	<0.001	41	29	<0.001	268	170	<0.001	483	105	<0.001	1764	780	<0.001

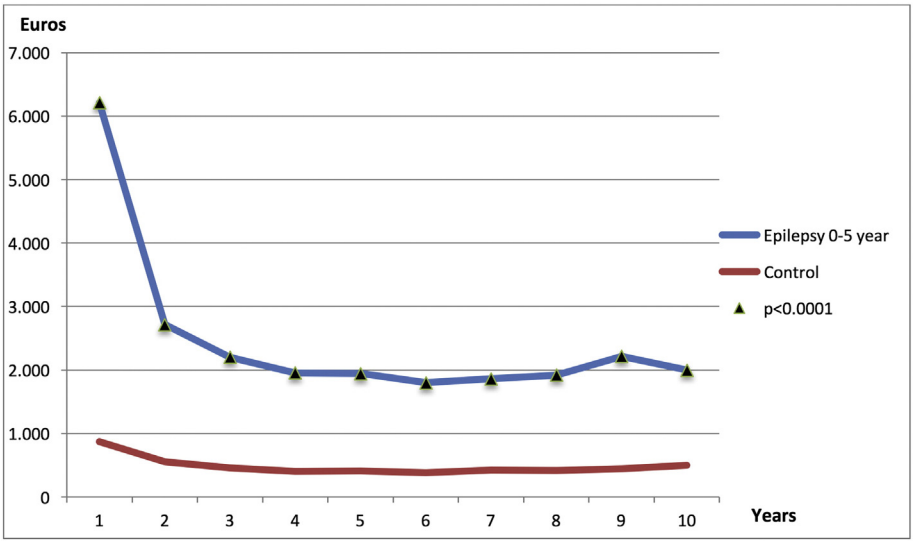

Fig. 1. Predicted health-care costs in 10 years after the initial diagnosis for the 0- to 5-year-old group with epilepsy and their controls, adjusted for parental education.

times higher in childhood- and adolescent-onset epilepsy than in controls, with hospital contacts contributing in particular to the total health costs. Those with early onset-epilepsy (0–5 years) suffered from significantly higher health-care costs compared with children and adolescents, probably because of early-onset epilepsy severity with consequent disease consequences affecting the developing brain, greater prevalence of comorbidities, and duration and chronicity of disease. Epilepsy often has an early onset and therefore has a significant influence on indirect costs including welfare, education, employment, and other socioeconomic factors [27].

Cost-of-illness methods aim to estimate the specific economic burden caused by disease and illness within a defined population. The costs of illness are usually broken down into a) direct costs, which are those borne by the health-care system, community, and patients' families to address the illness and b) indirect costs, which are mainly productivity losses to society caused by the health problem or disease. In this study, the cost of illness is isolated by comparing the patient group with a control group with similar characteristics but without the specific disease. The estimate of the cost of illness therefore includes all the welfare costs attributable to epilepsy and its comorbidities. The result of the study reflects the yearly excess welfare cost of a living person with epilepsy compared with that of a similar person without epilepsy. We were able to follow all study participants and exclude those who died, which is a major strength of this study because deceased persons do not consume any health-care resources. However, the difference in absolute mortality rate is small, so the impact on the total cost of illness estimate is negligible.

As in most other cost-of-illness analyses, it was difficult to isolate the cost of epilepsy from the cost of comorbid conditions. The estimates of cost found in this study should be interpreted as the yearly excess direct health cost and the cost of lost productivity for a living person diagnosed with epilepsy compared with those in a person without epilepsy regardless of comorbid disorders.

Epilepsy is a chronic neurological disorder that not only has a considerable negative economic impact but also may have major effects on patients' social competence and family relationships [25,28–35]. This may be even more pronounced in children and young adults for whom the disorder influences self-perception [36,37], stigma [8,30,38], education [2], employment [27,39], social prognosis, and income [27,33,40]. In this study, a gender-, age-, and geographically-matched control group

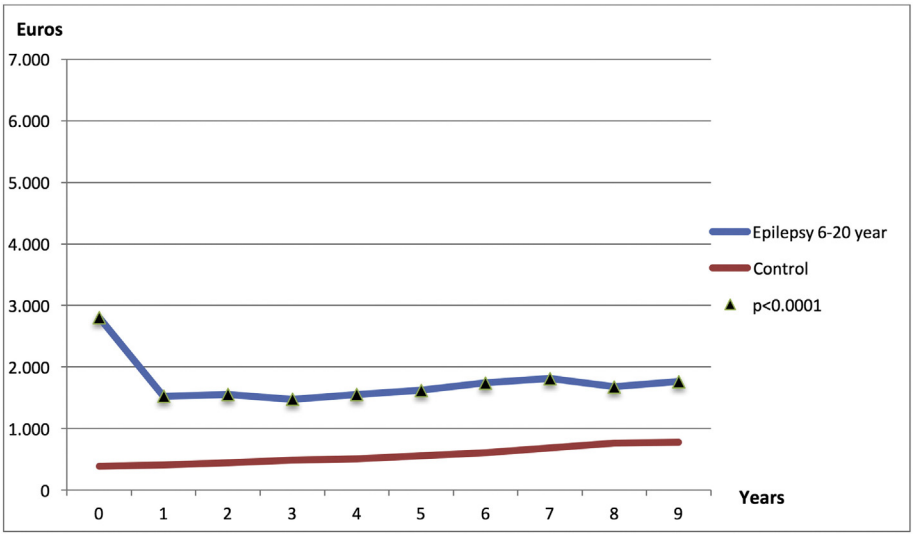

Fig. 2. Predicted health-care costs in 10 years after the initial diagnosis for the 6- to 20-year-old group with epilepsy and their controls, adjusted for parental education.

was randomly selected; these individuals might suffer from other diseases but not epilepsy. If we had compared patients suffering from epilepsy with healthy controls from the general population, the estimated differences and socioeconomic impact would have been more pronounced.

Previous studies on the burden of epilepsy have focused on the direct costs of hospital services, on using treatment procedures such as medication, and on psychological issues [2,22,25,26,30], among others. Epilepsy significantly reduces the quality of life for patients, family members, and caregivers [25]. Several studies have documented the increased direct cost (including diagnosis, management, and treatment) of epilepsy using quality-of-life or model estimates, evaluation of the effect of pharmacological treatment, or aspects of management related to the care of patients with epilepsy, including the effect on caregivers and families, as well as the influence on economic and other costs [6,8–10,13,16,18,19,23,25,30,41–54]. However, our study suggests that these estimates are less than the factual costs and that the indirect costs are even higher, possibly because we aimed to include all welfare costs.

Subanalyses of costs associated with epilepsy could potentially evaluate costs for each epilepsy subtype and epilepsy-related treatment and procedure, but this would require adjustments for comorbid diseases. Epilepsy is a disorder often associated with other brain disorders, including psychiatric disorders, which may also contribute to the disease course and its consequences [55]. We have not yet evaluated these factors in detail; this would require a careful consideration of the subjects' comorbid conditions before and after the diagnosis of epilepsy, since, for example, epilepsy may cause depression, but patients with depression are also at greater risk of developing epilepsy [56]. The rate of psychiatric comorbidities is however controversial, e.g., in a multicenter, multinational study, no increased rate of depression was found; however, the study also identified significant differences between diagnostic activities in the rate of depression [57].

Our studies show that daily functioning is affected by the age of the patient when epilepsy is diagnosed [27]. Prevention, effective treatment, and early intervention would therefore be necessary to prevent the full consequences of epilepsy being realized. Most treatment modalities focus on reducing the frequency and severity of seizures and, to a lesser degree, the effect on social and educational parameters [58]. Any new intervention could potentially lower morbidity, mortality, and health-care costs and thereby improve the welfare of a person with epilepsy. Furthermore, measurements of factors that reduce the social consequences are likely to have a significant impact on the burden and economic consequences of epilepsy.

We based our current study on reports from a complete national patient sample from all Danish outpatient clinics and hospitals registered in the NPR. This was possible because all Danes are registered using social security codes, enabling the collection of linked health, medication, and social and employment data. These calculated costs include those of all contacts with the primary and secondary health sectors, including diagnostic and treatment procedures at the time of diagnosis.

A limitation of the study is that we have not included costs of home care and physiotherapy, although these are likely to be low for children. We aimed to identify the health cost of an epilepsy diagnosis and included all the cases in the national sample with a primary diagnosis of epilepsy. Epilepsy diagnoses in the NPR have formerly been validated; the diagnoses are, in general, valid for the major but not subclassification of epilepsy [59]. We aimed to identify all national cases to be able to estimate the national burden of the disease and not subclasses of epilepsy. The control group was not defined as a group of healthy subjects; they were selected on the basis of age, gender, and geography (the latter to allow adjustment for social factors). Control subjects may therefore have suffered from other disorders, whose costs have been included in the values. Consequently, the study presents the factually determined health costs of epilepsy.

In conclusion, the current study found that epilepsy is associated with significantly higher health-related costs. It also identified a significant health-related impact of the disease, which highlights the need to address further the importance of measuring the effects of managing the disease. Health-care professionals should be aware of the possibilities for detecting, diagnosing, and managing epilepsy and ensure that patients receive adequate information about the disorders. Appropriate treatment and management must be provided not only to increase quality of life but also to help patients continue to take part in their personal and professional lives. Additional research is needed to facilitate early disease identification and management, to ameliorate the negative effects of epilepsy on quality of life, socioeconomic factors, work capability, and health care and social needs, so that the costs to patients and society can be reduced.

Author contributions

Poul Jennum (PJ) and Jakob Kjellberg (JK): creation, initiation, and management of the project. PJ is the main author. JK and RI performed the statistical analyses and commented on the manuscript. JC commented on the methods and critically revised the manuscript. All authors approved the final version of the manuscript.

Conflict of interest

None of the authors reports any conflict of interests.

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