FULL-LENGTH ORIGINAL RESEARCH

Long-term socioeconomic consequences and health care costs of childhood and adolescent-onset epilepsy

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Summary

Objective: **To estimate long-term socioeconomic consequences and health care costs of epilepsy with onset in childhood and adolescence.**

Methods: **A historical prospective cohort study of Danish individuals with epilepsy, age up to 20 years at time of diagnosis between January 1981 and December 2012. Information about marital status, parenthood, educational level, employment status, income, use of the health care system, and cost of medicine was obtained from nationwide administrative and health registers.**

Results: **We identified 12,756 and 28,319 people with diagnosed with epilepsy, ages 0–5 and 6–20 years at onset, respectively. Using follow-up data for a maximum of 30 years, 1,394 of those ages 0–5 years at onset were compared with 2,897 controls persons without epilepsy, and 10,195 of those ages 6–20 years at onset were compared with 20,678 controls without epilepsy. Compared with people without the epilepsy, those with epilepsy tended to have a lower level of education, to be less likely to be married, to be more likely to live alone, and to have higher divorce and unemployment rates, lower employment rates, and people with epilepsy were more likely to receive disability pension and social security. Income was lower from employment, which in part was compensated by social security, sick pay, disability pension and unemployment benefit, sick pay (public-funded), disability pension, and other public transfers. Predicted health care costs 30 years after epilepsy onset were significantly higher among persons with epilepsy onset at 0–5 and 6–20 years, including costs for outpatient and inpatient services (hospital services), emergency room use, primary health care sector (general practice), and use of medication.**

Significance: **The long-term negative effects on all aspects of health care and social domains, including marital status, parental socioeconomic status, educational level, employment status, and use of welfare benefits compared with controls without epilepsy calls for increased awareness on childhood- and adolescent-onset epilepsy.**

KEY WORDS: **Epilepsy, Children, Social, Education, Employment.**

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Key Points

- Epilepsy with onset in childhood and adolescence has major long-term effects on welfare, use of medication, educational level, and social course
- The effects were observed among 30-year-olds, who were unlikely to return subsequently to the social level of those without epilepsy
- The observed effects were all significant also after adjustment for social factors, for example, parenteral status
- These results underscore the need for continued efforts toward better disease education, management, and research to reduce the long-term consequences of epilepsy

Epilepsy is one of the most serious chronic neurologic disorders, affecting a significant proportion of the population of all ages from childhood to old age.[1] Significant progress has been made toward understanding the underlying pathophysiology, improving diagnostic accuracy and management of epilepsy with improved care and diagnostic and treatment opportunities.[2] Despite these advances, epilepsy is still an important disorder, with significant implications for personal health and social functioning, and for society as a whole.[3] Early intervention focuses on reducing the severity of epilepsy and its associated morbidity and mortality. Epilepsy, not only in adults,[4] but also in children and adolescents, is strongly associated with social stigma, educational and professional problems, and reduced quality of life for patients, and therefore also has a substantial socioeconomic impact.[5–8]

Studies of the economic effects of epilepsy have focused primarily on model information, questionnaires, and other direct or indirect information in selected groups of patients (primarily adults), and estimates of the economic burden extracted from this information.[9–16] There is a small amount of information from long-term prospective studies in children, which indicates a significant socioeconomic impact of the disorder.[5,25–28] These studies have primarily addressed direct (health care) costs, since labor market participation and social transfers often are difficult to estimate. For this reason, no attempt has been made previously to estimate the concrete national total cost of the disease for a patient group compared with an appropriate control group. We recently described direct health costs and impact on labor market participation and social transfer payment in children and adult patients with epilepsy diagnoses in Denmark.[4] These cost estimates in children and adults suggested that epilepsy is associated with a substantial disease burden, not only at the time of diagnosis and after, but also in the years before diagnosis. There is limited information regarding the long-term welfare consequences of childhood-onset epilepsy; therefore, we aim to describe the long-term consequence of childhood- and adolescent-onset epilepsy.

In Denmark, it is possible to identify subjects with epilepsy from health registers and link them individually with data on health, educational level, employment status, and income level. Direct health costs and impact on the labor market participation and social transfer payments may be calculated from this information. We conducted the current national population-based study to evaluate the long-term social consequences of early onset epilepsy.

Methods

All analysis was performed in SAS 9.4 and the significance level is set to 0.05.

People with epilepsy and controls

Since April 1968, all Danish citizens have been assigned a unique identification number (Central Personal Registration [CPR] number), which is recorded in the Danish Civil Registration System along with information on place of birth, place of residence, vital status, and marital status.[29]

In Denmark, all patient contacts are recorded in the Danish National Patient Registry (NPR) with respect to date of contact and diagnoses. The NPR is a time-based national database of administrative information, diagnoses, and diagnostic and treatment procedures using several international classification systems, including the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). It contains details of all patient contacts, so the data may be considered representative of all patients in Denmark who have received a diagnosis of epilepsy (G40x) in the secondary sector in public and private hospitals. The year of diagnosis was defined as the first time a person was recorded in the NPR between 1980 and 2012. Patients were followed until death, emigration, or 31 December 2012, whichever event was earliest. A first-time diagnosis is defined if the diagnosis has not been recorded for a minimum of 3 years (<2 years for the 0–2-year-olds).

We subdivided people with a first diagnosis of epilepsy into two groups—those who received their diagnosis when aged 0–5 years and those with received their diagnosis when aged 6–20 years—to distinguish early and later-onset childhood and adolescent epilepsies. We defined a randomly selected control group by age, gender, and county at time of first diagnosis. The controls had no diagnosis of epilepsy, but may have other diseases. We did not control for parental social factors, since epilepsy is associated with lower parenteral socioeconomic status. We selected two controls per person with epilepsy. Accordingly, we were able to describe the total morbidity, mortality, health care costs, and sociodemographic variables (education, occupation, and income) for the cohort. Information about health was obtained from the NPR; information about all social

variables, including education, was obtained from the Danish Civil Registration System (CRS). The use and costs of all drugs were based on data from the Danish National Prescription Registry, which includes the retail price of each drug (including dispensing costs) and the number of reimbursements.

Analysis of long-term health and socioeconomic consequences of epilepsy

We compared the socioeconomic status of people with epilepsy at 30 years of age with that of the control group. Socioeconomic status was analyzed with respect to educational level, employment status, and income based on predicted income, taking into account the level of education of at least one parent.

Separate analyses were done for those with epilepsy diagnosed at 0–5 years and those with epilepsy diagnosed at 6–20 years of age.

Educational status of people with epilepsy

Educational status was defined as the highest level attained by the members of the cohorts at 30 years of age. Four levels were considered: primary (elementary school), secondary (high school), vocational (skilled), and college (short-, medium- and long-term education, including to PhD level). We evaluated the parenteral educational (but not the

Table 1. Characteristics of people with epilepsy and age- and sex-matched controls by age at epilepsy onset

	Age at epilepsy onset 0–5 years						Age at epilepsy onset 6–20 years					
	Epilepsy N = 1,394			Controls N = 2,897			Epilepsy N = 10,195			Control N = 20,678		
Age	Mean	SD	Median	Mean	SD	p-Value	Mean	SD	Median	Mean	SD	p-Value
Average age at the epilepsy index date	3.2	1.6	3				13.9	4.2	14			
Gender	N	%					N	%				
Male	757	54.3					5.084	49.9				
Female	637	45.7					5.111	50.1				
Marital status age 30 years	N	%					N	%				
Co-living	400	28.7		1.101	38.0	0.000	2,986	29.3		7,387	35.7	0.000
Married	289	20.7		772	26.6		2,685	26.3		6,093	29.5	
Single	701	50.3		1.011	34.9		4,483	44.0		7,047	34.1	
Unknown	4	0.3		13	0.4		41	0.4		151	0.7	
Divorced>1	46	3.3		80	2.8	0.328	489	4.8		725	3.5	0.328
Never divorced	1,348	96.7		2,817	97.2		9,706	95.2		19,953	96.5	
Education at age 30 years	N	%		N	%		N	%		N	%	
Education completed												
Primary	546	39.2		468	16.2	0.000	3.641	35.7		3.456	16.7	0.000
Secondary	72	5.2		208	7.2		667	6.5		1.733	8.4	
Vocational	396	28.4		998	34.4		3.305	32.4		7.686	37.2	
College	342	24.5		1,206	41.6		2,431	23.8		7,733	37.4	
Unknown	38	2.7		17	0.6		151	1.5		70	0.3	
Parents' highest level of education (index date)												
Primary	411	29.5		572	19.7	0.000	2,883	28.3		4,605	22.3	0.000
Secondary	30	2.2		80	2.8		123	1.2		284	1.4	
Vocational	619	44.4		1.335	46.1		4.463	43.8		9.145	44.2	
College	329	23.6		888	30.7		2.611	25.6		6.319	30.6	
Unknown	5	0.4		22	0.8		115	1.1		325	1.6	
Employment	N	%		N	%		N	%		N	%	
Employment status 30 years of age												
Employed[a]	835	59.9		2,389	82.5	0.000	6,989	68.6		17,619	85.2	0.000
Student[b]	28	2.0		65	2.2		215	2.1		537	2.6	
Unemployed	135	9.7		237	8.2		1,000	9.8		1,410	6.8	
Disability pension	282	20.2		48	1.7		1.230	12.1		193	0.9	
Social security	48	3.4		33	1.1		318	3.1		283	1.4	
Other—outside the labor force	66	4.7		125	4.3		443	4.3		636	3.1	

[a]The group of employed includes students working >9 h per week.
[b]The employment code for students is missing for 2013. Therefore, the number of students is underestimated and the group "Other" is overestimated for 2013.

income) level. The highest completed educational level of each individual's parents at the time of diagnosis was also included in the statistical analysis to adjust for confounding. The odds ratios of having a particular educational level (case–control) were estimated by logistic regression, including parental education as a dummy explanatory variable, with values of 0 signifying that neither parent had received higher education (i.e., only educated to primary or secondary school level) and values of 1 indicating that at least one parent had received higher education (vocational or college level).

The estimated odds ratio for earned grade point average (conditional logit) was adjusted for parental education.

Employment status

The employment status of people with epilepsy at 30 years of age was compared with that of the control group. Employment status was categorized into five classes: in a job, active student, unemployed, early retirement, and receiving social assistance. A logistic regression (conditional logit) model was used to estimate the odds ratio for employment, which in turn takes into account at least one of the parents having more than basic education (vocational or college level).

Income prediction

In the analysis of income, we compared the annual income of the 30-year-old people with epilepsy with their control groups. Income was classified on the basis of whether it was derived from income/independent, transfer payments, social compensation, sick payment, early retirement, and other (including training aid). Income for the cohorts of 30-year-old people with epilepsy and the control groups was estimated from a prediction of income when parents' education (vocational or college level) was included as a dichotomous explanatory variable (0 = neither parent highly educated; 1 = least one parent highly educated).

Health economic analysis

The health economic analysis is a prediction of annual costs for 30-year-olds with epilepsy and their control in the year they became 30 years old. The prediction was made with a generalized estimating equation model in which parental education (vocational or college level) was included as an explanatory variable. We used an exchangeable working correlation structure, since there can be sources of unmeasured variation within the clusters. Because the population is large, the choice of correlation structure is less sensitive for this model. Health expenses were divided into outpatient visits (outpatient services), admissions (inpatient services), emergency (emergency room), primary sector (primary health sector), and medication prescription dispensed. The period of investigation was 1980–2012, but health economic data were available only from 1998, so only patients who were 30 years old in 1998 and thereafter were included in this analysis.

Results

The study included 12,756 people aged 0–5 years, and 28,319 people aged 6–20 years between 1980 and 2012. Of these, 6,807 people with epilepsy onset at 0–5 years of age

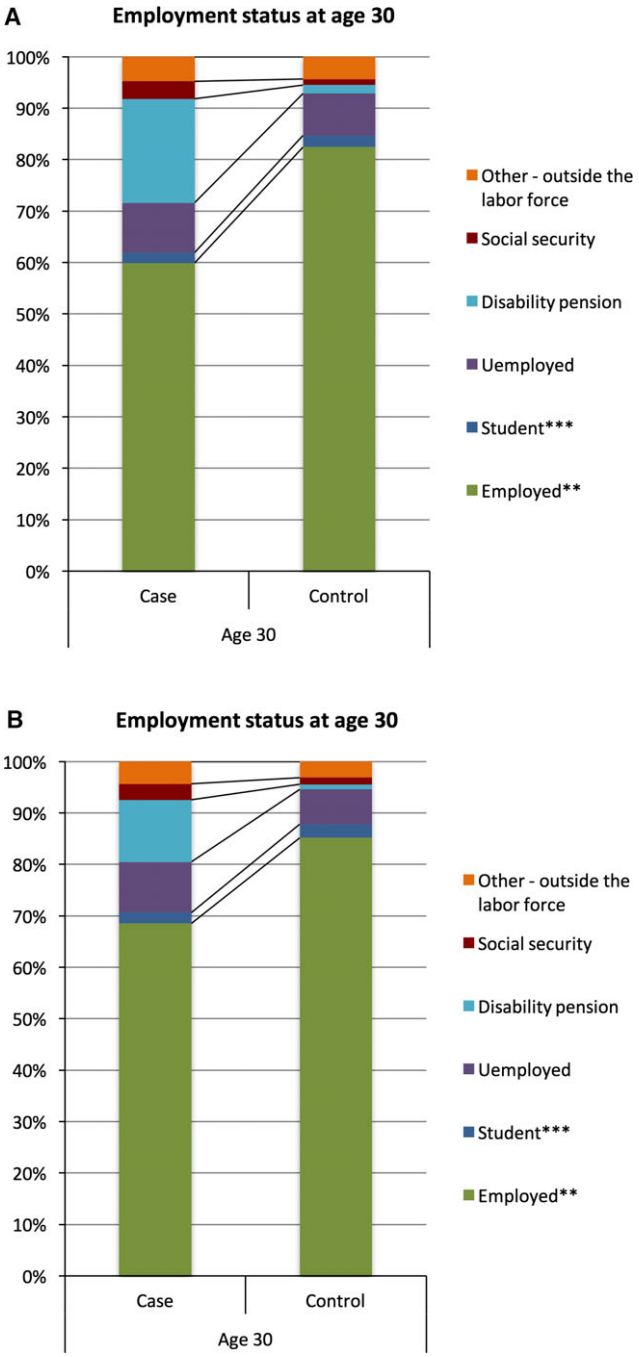

Figure 1.
Employment status at 30 years of age for people with a first diagnosis of epilepsy at 0–5 years (**A**) and 6–20 years (**B**) of age.
Epilepsia © ILAE

Table 2. Odds ratio of education level for people with epilepsy compared with controls, adjusting for parental education level

Education completed at 30 years of age	Odds ratio of education level at 30 years of age		
	Odds ratio	95% confidence limits Lower	Upper
Age 0–5 years at time of first epilepsy diagnosis			
Primary	–	–	–
Secondary	**0.30**	0.22	0.41
Vocational	**0.35**	0.29	0.42
College	**0.25**	0.20	0.30
Unknown	**1.92**	1.01	3.64
Age 6–20 years at time of first epilepsy diagnosis			
Primary	–	–	–
Secondary	**0.36**	0.32	0.40
Vocational	**0.40**	0.37	0.42
College	**0.28**	0.26	0.30
Unknown	**2.00**	1.49	2.70

Logistic regression was used to calculate odds ratios for people with epilepsy whose parents' highest education level was included as an explanatory variable. Significant results are indicated in bold.

Table 3. Estimated income in Euros at age 30 years for people with epilepsy and their controls

	Estimated income at 30 years of age		
	People with epilepsy €	Controls €	p-Value[a]
Age 0–5 years at first epilepsy diagnosis			
N	1,394	2,897	
Income from employment and other income	26,218	40,899	0.000
Public transfer income			
Social security and unemployment benefit	2,547	2,011	0.001
Sick pay (public funded)	966	1,038	0.535
Disability pension	5,396	377	0.000
Other public transfers	1,960	1,584	0.000
Total income	38,559	45,406	0.000
Age 6–20 years at first epilepsy diagnosis			
N	10,195	20,678	
Income from employment and other income	28,918	39,416	0.000
Public transfer income			
Social security and unemployment benefit	3,139	2,120	0.000
Sick pay (public funded)	955	965	0.814
Disability pension	2,927	228	0.000
Other public transfers	1,822	1,556	0.000
Total income	38,738	43,843	0.000

[a]Income was analyzed using a generalized estimating equation including only people for whom we could identify their parental education level (vocational or college education at index date).

were compared with 14,197 controls for a follow-up at 20 years old. For a 30-year-old at follow-up the corresponding figures were 1,394 patients and 2,897 controls. For children with disease onset at 6–20 years there were 10,195 cases and 20,678 for a 30-year follow-up period. We took advantage of the opportunity to analyze the 30-year maximum follow-up, since all the data considered were also present and significant in the 20-year cohort. The demographic details of this group are presented in Table 1.

Marital status, education, and employment

More boys than girls were diagnosed with epilepsy in the youngest age group (0–5 years at diagnosis), whereas there was no gender difference for those diagnosed with epilepsy at age 6–20 years (Table 1).

For both age groups at 30 years of age, people with epilepsy were less likely to be married, more likely to live alone, and had higher divorce rates (Table 1). Those with epilepsy had a lower level of education, as did their parents (Table 1). Employment rates among those with epilepsy were lower than in controls (Fig. 1A,B show the rates for epilepsy onset at 0–5 and 6–20 years, respectively). The rates for unemployment, disability pension, and social security were higher among those with epilepsy onset at 0–5 and 6–20 years of age.

Table 4. Estimated health care costs in Euros at age 30 years for people with epilepsy and their controls

	Predicted health care cost at age 30 years		
	Epilepsy Cost = €	Control Cost = €	p-Value[a]
Age 0–5 years at time of first epilepsy diagnosis			
N[b]	945	1.963	
Health care cost[b]			
Outpatient services	334	298	0.282
Inpatient admissions	572	481	0.165
Emergency room (ER)	24	15	0.000
Primary health sector	396	198	0.000
Medicine (prescription medicine)	398	99	0.000
Health care cost total	1,731	1.089	0.000
Age 6–20 years at time of first epilepsy diagnosis			
N[b]	8,747	17,745	
Health care cost[b]			
Outpatient services	344	243	0.000
Inpatient admissions	841	484	0.000
Emergency room (ER)	37	19	0.000
Primary health sector	299	199	0.000
Medicine (prescription medicine)	666	124	0.000
Health care cost total	2,181	1,073	0.000

[a]Estimates are based on a generalized linear model (GLM) where parents with an education at index date (vocational and college) was included as an explanatory variable.

[b]Health costs are calculated on the basis of economic health data from 1998 to 2012. Only patients who were 30 years in 1998 or later were included.

We estimated the likelihood (odds ratio) of the educational level of people with epilepsy, adjusting for parental education: epilepsy was still associated with low educational level for early and late-onset epilepsy (Table 2).

Income level and social security

The income of people with epilepsy was significantly lower than that of controls at 30 years of age, regardless of their age at epilepsy onset (Table 3). Income was lower as a total value, and when subdivided into income from employment and income from social security, disability pension, unemployment benefit, sick pay (public funded), and other public transfers (Tables 1 and 3).

Health care costs

Predicted health care costs at 30 years of age at follow-up was significantly higher in people with epilepsy than in controls, including costs from outpatient and inpatient services (hospital services), emergency room use, primary health care (general practice), and use of prescription medication (Table 4). We estimated the effect of parental education on health care costs using a generalized estimating equation model. The effects of parental education on outpatient services, inpatient admissions, emergency room use, primary health care, and use of prescription medication were all primarily explained by the presence of epilepsy (Table 5).

Discussion

We identified significant long-term socioeconomic consequences and higher personal health care costs associated with childhood- and adolescent-onset epilepsy in a large cohort of epilepsy patients with a follow-up to 30 years of age. To our knowledge, this is the largest study and the one with the longest follow-up to focus on childhood- and adolescent-onset epilepsy. Even after adjusting for parental educational level, the associations were all highly statistically significant. The results show that people with epilepsy, even many years after diagnosis, are neither able to compensate nor catch up in relation to overall health, education, and social status.

We observed that income from regular employment was significantly lower among those with epilepsy onset in childhood and adolescence. To our knowledge, no previous studies have looked at the impact of epilepsy on income level in adulthood.

Epilepsy has complex etiologies, ranging from severe brain diseases in which seizures are only part of the general neurologic deficits, to a presentation of "idiopathic" epilepsies with few or very few seizures and minimal or no comorbidity. The prognosis also varies from episodic seizures and spontaneous remission to severe epilepsy with drug-resistant seizures, as is reflected in this long-term follow-up

Table 5. Estimated health care costs at 30 years of age for people with epilepsy and their controls

	Age at epilepsy onset (0–5 years)				Age at epilepsy onset (6–10 years)			
Income GLM	Estimate	SE	5–95% CI	p-Value	Estimate	SE	5–95% CI	p-Value
Outpatient services								
Intercept	5.79	0.13	5.54 to 6.05	0.000	5.60	0.07	5.47 to 5.74	0.000
Epilepsy	0.12	0.11	−0.09 to 0.32	0.282	0.35	0.07	0.22 to 0.48	0.000
Parental education (vocational or college)	−0.10	0.13	−0.36 to 0.17	0.469	−0.11	0.08	−0.28 to 0.05	0.188
Inpatient admissions								
Intercept	6.41	0.12	6.17 to 6.64	0.000	6.28	0.05	6.17 to 6.38	0.000
Epilepsy	0.17	0.12	−0.07 to 0.42	0.165	0.55	0.07	0.41 to 0.69	0.000
Parental education (vocational or college)	−0.23	0.13	−0.48 to 0.02	0.072	−0.09	0.06	−0.22 to 0.03	0.141
Emergency room visit								
Intercept	2.99	0.12	2.77 to 3.22	0.000	3.24	0.04	3.17 to 3.31	0.000
Epilepsy	0.46	0.12	0.23 to 0.70	0.000	0.66	0.04	0.59 to 0.73	0.000
Parental education (vocational or college)	−0.28	0.12	−0.52 to −0.05	0.019	−0.28	0.04	−0.36 to −0.20	0.000
Primary health care								
Intercept	5.26	0.06	5.13 to 5.38	0.000	5.30	0.02	5.26 to 5.34	0.000
Epilepsy	0.69	0.07	0.56 to 0.83	0.000	0.40	0.02	0.36 to 0.45	0.000
Parental education (vocational or college)	0.03	0.07	−0.11 to 0.17	0.658	0.00	0.02	−0.05 to 0.04	0.893
Medicine costs (prescription medicine)								
Intercept	4.97	0.14	4.69 to 5.25	0.000	4.77	0.04	4.69 to 4.85	0.000
Epilepsy	1.39	0.11	1.17 to 1.62	0.000	1.68	0.05	1.59 to 1.77	0.000
Parental education (vocational or college)	−0.38	0.14	−0.66 to −0.10	0.008	0.05	0.05	−0.04 to 0.14	0.270
Health care cost total								
Intercept	7.17	0.08	7.02 to 7.32	0.000	7.03	0.03	6.97 to 7.10	0.000
Epilepsy	0.46	0.07	0.32 to 0.60	0.000	0.71	0.04	0.64 to 0.78	0.000
Parental education (vocational or college)	−0.18	0.08	−0.34 to −0.02	0.026	−0.06	0.04	−0.13 to 0.02	0.141

Estimates were based on generalized linear model, restricted to people with information on parental educational level.

study. Epilepsy is associated with significant morbidities and increased health care use, including medication use.[13,30] The few available studies of the cost of childhood epilepsy show a significant impact on the direct health care costs and costs related to reduced labor market participation associated with epilepsy,[5,25,31,32] although they all have shorter follow-up.

Although not directly comparable, it is worth mentioning that other severe or chronic diseases with onset in childhood or adolescence, such as diabetes, multiple sclerosis (MS), narcolepsy, and cancer, seem to have a similar impact on employment rate and income. A recent Danish study showed that not only was the employment rate considerably lower among MS patients, but also that the income level of employed MS patients was significantly lower than that of control subjects.[33] Among children treated for central nervous system (CNS) cancer, 20% received disability pension at the age of 16–67 years, and yearly income and working ability were considerably lower than among controls.[34] Diabetes without complications does not seem to affect a person's working ability or income, although the presence of diabetic complications strongly influences the ability to work and has a negative influence on income.[35] Patients with narcolepsy—a disease with onset that frequently occurs in childhood—have significant impairment of their education and experience serious social consequences[36] that are almost as severe as those associated with epilepsy. However, narcolepsy is a primary brain disease with almost no comorbid conditions at disease onset, so it is likely that epilepsy per se is a major contributor to the negative effect on social and health factors. The societal burden of a disease is not the same as the excess health and social burden that might be reduced by management. There are almost no data supporting this in children. As such, there is an unmet need to document the prospective effects of health, social and educational interventions in people with epilepsy to counteract the negative impact of epilepsy.

The current study has many strengths, all of which stem from the fact that all Danes are included in national registers: the large number of people included, the completeness of the registration of people with epilepsy and of all comorbidities, the long-term follow-up with minimal loss to follow-up, the identification of family members and of comparable controls, the linkage of data to other health care contacts, and the educational and socioeconomic information.

The major limitation of the study is the validity and classification of epilepsy and its subtypes, and the completeness of the registration, since people with epilepsy who are followed only by their general practitioner are not registered in the National Hospital Register. The validity of the epilepsy diagnoses in the Danish National Hospital Register has a moderate to high positive predictive value for epilepsy, but a relatively low predictive value for epilepsy syndromes.[37] Despite this inhomogeneity, we aimed to evaluate the total, national consequences of patients with a diagnosis of epilepsy. Therefore, we used diagnoses of all epilepsies, independent of subtype or cause. We did not have information on seizure frequency or freedom, and we therefore could not include severity of epilepsy as an explanatory variable in our analyses.

To estimate whether the employment profile and health care costs of people with epilepsy differed from expectations, we compared epilepsy patients with an age- and gender-matched group of Danes who lived in the same period. Among this control group, some people may have had undiagnosed epilepsy if their disorder had not required hospitalization or evaluation in an outpatient clinic. Few children and adolescents with epilepsy are likely *not* to have had contact with the hospital system at some stage of their disorder and therefore to have been included in the NPR, so this misclassification is unlikely to have had a major impact on the overall results of this study.

Conclusion

In conclusion, the present investigation suggests that a diagnosis of epilepsy in childhood and adolescence has a major long-term effect on health care utilization, use of medication, educational level, and social course. The effects were observed among 30-year-olds, who were unlikely to return subsequently to the levels of those without epilepsy. These results underscore the need for continued efforts toward better disease education, management, and research to reduce the long-term consequences of epilepsy. We believe that these data should focus on the management of childhood onset epilepsy, not only in terms of diagnosis and treatment, but also earlier educational and social intervention to improve social and health outcome.

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Disclosures

None of the authors report any conflicts of interests. 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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