Epilepsy in young people: 23 year follow up of the British national child development study

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Abstract

Objective: To estimate the incidence and prevalence of epilepsy during childhood and early adult life in England, Scotland, and Wales.

Design: Prospective study of 17 414 children born in England, Scotland, and Wales between 3 and 9 March 1958, followed up at 7, 11, 16, and 23 years of age, with a review of those with epilepsy at age 28.

Subjects: People with epilepsy developing at or before age 23.

Main outcome measures: The age specific incidence, cumulative incidence, and prevalence of epilepsy.

Results: 124 young people had a confirmed diagnosis of epilepsy during their first 23 years (cumulative incidence 8.4 per 1000; 95% confidence interval 6.8 to 10.0). 6 had died by age 23. 46 (37%) had neurological impairment or another major health problem in addition to epilepsy. The prevalence of active epilepsy at age 23 was 6.3 per 1000 (4.9 to 7.7).

Conclusions: A wide variety of seizure disorders is included under the term epilepsy. A third of cases had generalised seizures. In only a quarter was the onset of seizures attributed to a specific cause. Children with additional health problems were more likely to continue to have seizures in early adult life than those with epilepsy alone. 1 in 8 were prescribed drug treatment for 6 years or more after their last seizure. All deaths occurred in young adults over the age of 16.

Introduction

Epilepsy is a common neurological disorder in childhood[1] and can have a major impact on a child's development.[2 3] In many children the seizures remit,[4] but in others the disorder continues and may affect adult life.[5] Despite a large amount of published literature from many countries on the incidence of epilepsy in childhood,[6] comparatively little is known about the long term prospects for those who have epilepsy in childhood.[7] Review articles emphasise the difficulty of comparing studies; variations in incidence rates may not only reflect differences in occurrence but also differences in case definition, diagnostic accuracy, and study populations. Variations in prevalence may also depend on the definition of active epilepsy.[8] The heterogeneous nature of seizure disorders causes additional complications: the term "epilepsy" is beginning to be replaced by increasingly well defined epileptic syndromes.[9] Some people have associated disabilities or additional health problems which influence the aetiology, prognosis, prevention of seizures, and management of the disease.[10]

An earlier paper based on the 1958 national child development study cohort explored the impact of epilepsy up to age 11.[11] We have used the follow up data collected from the cohort at ages 16 and 23 together with additional information we collected from the cohort members and their medical practitioners to extend the study of epilepsy into early adult life.

Subjects and methods

The 17 733 children born in England, Scotland, and Wales between 3 and 9 March 1958 were identified through the British perinatal mortality survey; data were collected on 17 414 (98%) at birth.[12] At follow up, information on health, social background, and education was collected by the national child development study; the response rate was 91% at ages 7 and 11, 87% at 16, and 76% at age 23.[11 13 14]

Incidences were calculated by using standard survival methods.[15] For the estimation of prevalence, cohort members were considered to have active epilepsy at a particular age if they were continuing to take antiepilepsy drugs or had had at least one seizure during the previous 2 years. Those who had not had a seizure for more than 2 years and were not currently receiving drug treatment for epilepsy were considered to be in remission.

As previously reported,[11] a screening question asked at ages 7 and 11 identified 1043 children who had had at least one fit, faint, or turn (table 1). For our study, these children were classified as possibly having epilepsy. For 346 of these children there were reports of recurrent episodes of loss of consciousness, prescription of anticonvulsant drugs, electroencephalographic investigations, or specific references to epilepsy; these children were classified as likely to have epilepsy. General practitioners and hospital consultants provided further details for the children. Analysis of all available data showed that 64 children had established epilepsy, which was defined as recurrent paroxysmal disturbances of consciousness, sensation, or movement that were primarily cerebral in origin and not associated with acute febrile episodes. Although a further 39 had been diagnosed by at least one doctor as having epilepsy, they did not meet the study definition and were regarded as unestablished cases.[11]

We did a similar case finding exercise using the cohort data collected at ages 16 and 23. Additional information on those likely to have epilepsy, as well as on the 64 cohort members already identified as having epilepsy, was obtained from general practitioners, medical specialists, and the cohort members to validate the diagnosis. During 1987 and 1988 those who had had active epilepsy at age 16 or older were interviewed using a structured questionnaire. A review of death certificates for cohort members who died by the age of 23 revealed two additional cases of epilepsy.

An independent neurologist reviewed clinical details and classified seizure types and epilepsy syndromes according to an established system.[16] Those with recognised syndromes or other severe conditions, and those who had required special educational

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Table 1 Numbers of cases of epilepsy identified in the national child development study cohort. Data on 17 414 children collected at birth

	Age at follow up (years)		
	7 and 11*	16	23
No traced	15 496	14 761	12 537
Possible epilepsy†	1 043	1 636	551
Likely epilepsy‡	346	60	100
Validated cases§	64	23	37¶

*Traced at age 7 or 11 or both.
†Includes children who had at least one fit, faint, or turn.
‡Includes children with recurrent episodes of loss of consciousness, prescription of anticonvulsant drugs, electroencephalographic investigations, or specific references to epilepsy.
§Validated cases were those in which children had recurrent paroxysmal disturbances of consciousness, sensation, or movement that were primarily cerebral in origin and not associated with acute febrile episodes.
¶Includes 2 cases identified from death certificate only.

provision because of physical, behavioural, or mental impairment were categorised as having additional health problems.

Results

At age 11, 64 children had been identified as having epilepsy (table 1).[11] Twenty three new cases were identified at age 16, and 35 at age 23. Eleven cohort members classified as likely to have epilepsy at age 16 or 23 either could not be traced or declined to participate further; they could neither be excluded nor confirmed as having epilepsy. Two cohort members had died at age 22 and had epilepsy mentioned on their death certificates, but neither had reported seizures at any follow up point; we assumed that their first seizures occurred after age 16. Over 80% (99/122) of the other cohort members with epilepsy were identified from information available at the first follow up after the reported onset of seizures. Nine cohort members identified at age 16 and nine identified at age 23 had their first seizure before age 12, but had not been identified during the earlier study; this includes nine children whose first seizure occurred before age 8. Five young people who began having seizures between ages 12 and 16 were not identified until they were 23. Altogether, 124 cohort members were accepted as having a validated history of epilepsy by age 23: 66 males and 58 females.

Age specific incidence, cumulative incidence, and prevalence

For the 19 children for whom the age at first seizure was not recorded, the onset of seizures was assigned to the midpoint of the age range in which it occurred. Annual incidence of the onset of seizures during the study averaged 0.35/1000 (range 0 to 14 new cases a year). Sixty two of the cohort members with epilepsy identified in this study had their first seizure before age 8 (early onset) and 82 before age 12. Table 2 shows the age specific and cumulative incidence of onset of seizures.

The prevalence of active epilepsy and age at follow up is shown in table 3. At age 7 prevalence is almost the same as the cumulative incidence (figure). By age 23 the cumulative incidence had more than doubled and prevalence increased by 60%. Because epilepsy is not necessarily persistent the prevalence of active epilepsy depends on the cumulative incidence and the definition of remission. The age specific incidence declined steadily (table 2) ($P < 0.001$, test for trend) but was slightly higher than the rate of remission, so the prevalence of active epilepsy rose gradually from 3.9/1000 at age 7 to 6.3/1000 at age 23 (figure).

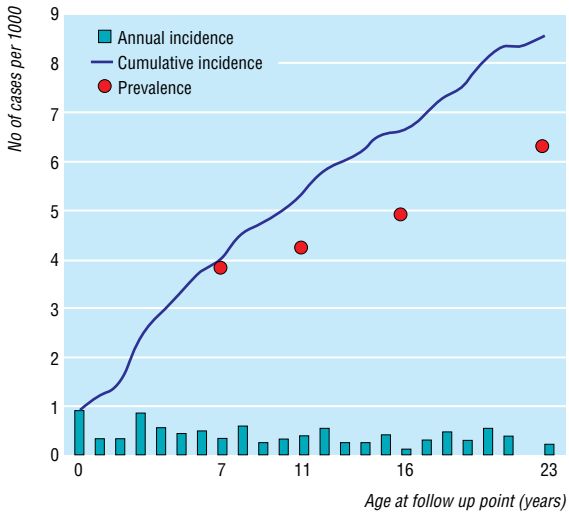
Seizure type, additional health problems, and cause of epilepsy

Type of seizure could not be classified on the basis of the information available in 23 of the 124 cohort members (table 4); two of the 23 had additional neurological impairment and three had other medical conditions. Of the remaining 101 cohort members, 71

Table 2 Age specific and cumulative incidence of epilepsy in the national child development study cohort

Age (years)	No of new cases	No in cohort*	Incidence (per 1000)	
			Age specific	Cumulative (95% CI)
0	14	15 496	0.90	0.90 (0.43 to 1.38)
1	5	15 482	0.32	1.23 (0.68 to 1.78)
2	5	15 477	0.32	1.55 (0.93 to 2.17)
3	13	15 472	0.84	2.39 (1.62 to 3.16)
4	8	15 459	0.52	2.90 (2.06 to 3.75)
5	6	15 451	0.39	3.29 (2.39 to 4.19)
6	7	15 445	0.45	3.74 (2.78 to 4.70)
7	4	15 438	0.26	4.00 (3.01 to 4.99)
8	8	15 434	0.52	4.52 (3.46 to 5.57)
9	3	15 426	0.19	4.71 (3.63 to 5.79)
10	4	15 423	0.26	4.97 (3.86 to 6.08)
11	5	15 419	0.32	5.29 (4.15 to 6.43)
12	7	14 679	0.48	5.77 (4.54 to 6.99)
13	3	14 672	0.20	5.97 (4.73 to 7.21)
14	3	14 669	0.20	6.17 (4.91 to 7.44)
15	5	14 666	0.34	6.51 (5.21 to 7.81)
16	1	14 661	0.07	6.58 (5.27 to 7.88)
17	3	12 436	0.24	6.82 (5.38 to 8.26)
18	5	12 433	0.40	7.22 (5.74 to 8.70)
19	3	12 428	0.24	7.46 (5.95 to 8.96)
20	6	12 425	0.48	7.94 (6.38 to 9.49)
21	4	12 419	0.32	8.26 (6.67 to 9.84)
22	0	12 415	0.00	8.26 (6.67 to 9.84)
23	2	12 415	0.16	8.42 (6.82 to 10.02)

*Population estimated from numbers traced at each follow up.



Age specific and cumulative incidence of epilepsy and prevalence of active epilepsy among children and adults up to age 23 in the national child development study cohort

Table 3 Prevalence of active epilepsy in the national child development study cohort

Age (years)	Proportion with active epilepsy	Prevalence (per 1000) (95% CI)
7	60/15 438	3.89 (2.90 to 4.87)
11	66/15 419	4.28 (3.25 to 5.31)
16	72/14 661	4.91 (3.78 to 6.04)
23	78/12 415	6.28 (4.89 to 7.68)

Table 4 Classification of epilepsy and other health problems in children with epilepsy in the national child development study cohort

Type of epilepsy	Epilepsy alone	Neurological impairment	Other conditions	Total
Unclassified	18	2	3	23
Localised	32	0	4	36
Localised with handicap	0	30	3	33
Lennox-Gastaut syndrome	0	2	0	2
Generalised	28	0	2	30
Total	78	34	12	124

had localisation related epilepsy; 32 of these (including two with Lennox-Gastaut syndrome) had neurological impairment and seven had other conditions. The remaining 30 cohort members had generalised epilepsy; this included two with other conditions (see below). Overall 78 cohort members had epilepsy alone and 34 also had some type of neurological impairment; 12 had additional health problems other than a neurological impairment (Addison's disease, hearing loss, deaf mutism after meningitis, congenital heart disease, cancer of the bladder, or psychiatric disorder). Altogether 11 cohort members had multiple problems.

Half of those with epilepsy (62) had an early onset of seizures. Of these, 28 had additional health problems, compared with only 18 of the 62 cohort members whose seizures started later ($P = 0.064$).

In about a quarter of the cases (32) epilepsy was attributed to a specific factor or event: congenital defect or syndrome including tumour (11 (9%)); birth trauma or other unspecified problems in early infancy (3 (2%)); meningitis or encephalitis (7 (6%)); head injury (11 (9%)).

Remission of seizures

Four young people were lost to follow up between the ages of 8 and 18. Among the 62 children with early onset of epilepsy at least 14 (23%) no longer had active epilepsy by age 12. Twenty five of the 82 (30%) children whose seizures started before they were 12 no longer had active epilepsy at age 16, and 35 of the 101 whose epilepsy began before age 17 no longer had active epilepsy at age 23.

A total of 114 cohort members with epilepsy survived to age 23; six died and four were lost to follow up. Of the 72 with epilepsy alone, 27 (38%) were in remission compared with nine (21%) of the 42 who had additional health problems ($P = 0.076$).

Drug treatment

Three of the 124 cohort members had never been prescribed drug treatment. Four members who had stopped drug treatment reported a later seizure. Thirty seven cohort members continued drug treatment for more than 2 years after their last seizure; this includes eight who had not had a seizure for between 6 and 10 years and seven who had not had a seizure for more than 10 years. Of these 37, three cohort members with neurological impairment were no longer receiving drug treatment when they were last contacted. The other 34 members had epilepsy alone; most had not started having seizures until they were teenagers, and all but two were continuing to take drug treatment when contacted in their late 20s.

Mortality

No deaths from epilepsy were recorded before age 17; six young people died between ages 17 and 23. Three more are known to have died by age 28. Those with additional health problems had a higher death rate (5/46, 11%) than those with epilepsy alone (4/78, 5%) but this difference was not significant ($P = 0.201$, Fisher's exact test). At least five of the nine deaths were directly associated with seizures; the other four were associated with airway obstruction from inhaling a bone, metastatic carcinoma, bronchopneumonia, and athetoid cerebral palsy.

Discussion

This study defines the minimum incidence and prevalence of epilepsy in a large, nationally representative, cohort of births in England, Scotland, and Wales.

Case ascertainment

Use of a prospectively identified cohort with repeated follow up examinations ensured that cases of epilepsy were included which might not have fulfilled the case definition at one screening. For example, one of the 39 children who was regarded as an unestablished case at age 11 was identified as a confirmed case from information obtained at age 23. Some of those who were not identified at the first follow up after the onset of seizures had probably had only one seizure at that time and did not yet satisfy the criteria for case definition. Recognition of other cases of epilepsy may have been delayed because the focus was initially on other health problems or because the respondent (either the parent or the cohort member) did not want to report seizures.

Despite the advantages offered by the prospective nature of the national child development study and repeated follow up, case ascertainment may have been incomplete. We did not identify any cases of epilepsy among the 423 children who died before the age of 7,[11] but no special search was made other than a review of death certificates. In the later cohort study of children born in 1970, in whom the incidence of epilepsy in the first 10 years of life was 4.3/1000, review of the hospital records of those who died identified six children with epilepsy, all of whom died before age 7.[17] Some older cohort members may have developed a seizure disorder and died between two follow up points without epilepsy being mentioned on the death certificate. Additionally, the few cohort members who refused to take part in the national child development study could have included an excess number of members with seizures, and those who took part might not have disclosed a history of seizures. We could not confirm or exclude a diagnosis of epilepsy in 11 young people classified as likely to have epilepsy at ages 16

Key Messages

- A cause of epilepsy was identified in only about a quarter of cases in the national child development study cohort
- 35% of those diagnosed with epilepsy by age 16 no longer require drug treatment and are free from seizures by age 23
- 30% of young people in this cohort continued taking drugs for epilepsy for more than 2 years after their last seizure; 15 of these young people had not had a seizure for 6 or more years
- Continuing epilepsy is more likely in those with neurological impairment or other additional medical conditions
- After age 16 there is a high death rate in young people with epilepsy. This emphasises the importance of maintaining supportive relationships between health care professionals and people with epilepsy as they become independent adults

and 23; they either could not be traced or declined to supply further information.

Defining prevalence and classifying seizure types

Other studies have used different definitions of active epilepsy—for example, taking antiepilepsy drugs regardless of the time since the last seizure,[4] or having had a seizure in the previous 3 years.[18] Changing the definition used in this study would make only a small difference to the prevalence estimates. With our definition of receiving drug treatment at age 23 or having had at least one seizure in the previous 2 years, 6.3/1000 cohort members had active epilepsy at age 23. However, using other definitions, 5.8/1000 were taking antiepilepsy drugs at age 23, whereas 6.5/1000 were either receiving drug treatment or had had a seizure in the previous 3 years.

For 19% of cohort members the type of epilepsy was unclassifiable (table 4). Among those with classified epilepsy, over two thirds had an anatomically localised condition. The proportion who had epilepsy associated with neurological impairment or another condition declined as the age of onset rose. Whatever their age at onset, cohort members with epilepsy and additional health problems were more likely than those with epilepsy alone to have active epilepsy at age 23.

Comparisons with other studies

This study did not identify any children with epilepsy who died before age 17. Five of the nine deaths identified at between 17 and 29 years were associated with seizures; four young people who died had epilepsy alone, four had neurological impairment, and one had cancer. This contrasts with results found in earlier studies such as that by Harrison and Taylor,[19] in which an overall death rate of 10.1% was found, with most deaths occurring in the first year of life and 65% before the age of five; however, they included children with febrile convulsions and fits associated with illness, such as cerebral infection. A high death rate was also reported from the 1946 cohort of the national survey of health and development, in which 30% of those with two or more seizures before the age of 26 died by age 36, compared with 6.7% of the whole cohort.[7]

Hauser and colleagues reviewed the literature on mortality (having included patients with epilepsy of much later onset than were included in our study)[20] and found that patients with idiopathic epilepsy had about twice the expected mortality for the first 10 years after diagnosis. They also found a substantially higher rate in those with associated neurological dysfunction. Our study supports this observation, although our sample is too small for the results to reach significance. Review of death certificates and medical notes yielded little additional information about those who died, but in at least four cases death from epilepsy was unexpected. The deaths occurred as these young people moved into adult life, a time when particular and sensitive attention should be paid to preventive management.[21]

This study was made possible by the active cooperation of the people who form the cohort of the study (and in earlier times, their parents). The data from the national child development study are held at the Social Statistics Research Unit, City University, London, and we are grateful to Peter Shepherd for his help in accessing and using the data. We are also grateful to the late Dr Anthony Hopkins for reviewing clinical cases and assessing diagnostic categories; to Melissa Preece, Flo Green, and Doris Fadden, who did many of the home interviews; to Professor Catherine Peckham, in whose department the project was based; and to the many family doctors, paediatricians, and other specialists who willingly provided supplementary information to verify diagnoses and the clinical course of epilepsy.

Contributors: ZK was the principal investigator; discussed core ideas; participated in the collection and analysis of data; and participated in writing the paper. ER carried out the earlier study which identified young people with epilepsy in this cohort; initiated the current study; discussed core ideas; participated in the analysis of the data and writing the paper; and is guarantor for the study. PT discussed core ideas; traced the subjects and their doctors; coordinated and participated in the collection and analysis of data; and participated in writing the paper.

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