Seizure: European Journal of Epilepsy 117 (2024) 20–27

Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

The changing incidence of childhood epilepsy in Finland

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ARTICLE INFO

Keywords:
Childhood onset epilepsy
Shifting incidence
Population trends
Validity of national health registers
Perinatal factors

ABSTRACT

Introduction: to investigate the childhood epilepsy incidence, population trends, associated factors, and validate the national population registers.

Methods: a comprehensive comparative analysis of childhood epilepsy in the population during two distinct time intervals using medical records, appropriate national medical and population registers, and two random samples for control.

Results: In 1961–1964, the average incidence of epilepsy was 38/100,000 and during 1991–2000 65.9 (95 % CI 59.6 to 72.2) and 65.6/100,000 person-years after adjustment for the European Standard Population. This increase was significant ($p<0.0001$) as was a decline ($p<0.003$) from 1991 to 1995 to 1996–2000. The decline in incidence for girls occurred at a younger age compared to boys. Epilepsy cases associated with prenatal and perinatal factors were 50 % lower in 1991–2000 than in 1961–1964, especially related to asphyxia, infections, pre-eclampsia, and imminent abortion. The national Register for Healthcare independently identified 94.5 % of relevant cases (University Hospital alone 81.2 %, and Drug Register alone 74.3 %).

Discussion: Over the past five decades, the incidence rate of childhood epilepsy has exhibited a dynamic pattern, with a notable increase until the 1990's, followed by a stabilization at an incidence rate of approximately 60–70 per 100,000 person-years. Our findings, in line with other recent Finnish research, support a significant decrease in incidence since the mid-1990's. The underlying reasons for the increase and decrease remain unclear. Finnish national registers for epilepsy have established themselves as highly dependable resources for conducting epidemiological research.

Conclusion: Childhood epilepsy incidence in Finland is similar to other industrialized countries, but there are signs of a declining trend emerging.

1. Introduction

It is increasingly accepted that the incidence of epilepsy in childhood is in slow decline. However, there are recent population-based studies that show wide variation within and between countries. For example, investigators from Italy reported a rate of 31 per 100,000 children in 2014 [1] and 79 per 100,000 ([2] in 2019 while in Finland the rate varied from 38 [3] to 87 per 100,000 ([4]). Few studies have reported changes in the incidence of childhood epilepsy in the same population. A Danish study [5] and a Finnish study ([4]) found an increase in incidence until the 1990s, but also suggested a deceasing incidence since the 1990s. Similar changes in the middle-2000s were reported by Hernández-Ronquillo et al. [6]. However, there are few other reports of the trends in incidence since 1990.

We now report changes in the incidence and associated factors of childhood-onset epilepsy between 1961 and 1964 and 1991–2000 in the same source population. We established the validity of the national epilepsy registers in Finland and used these registers to establish temporal changes in the incidence of childhood-onset epilepsy. Our hypothesis was that there are non-linear changes in the incidence of epilepsy in the last half of the 20th century.

2. Method

2.1. Main features of the Finnish child healthcare system

The Finnish system for child neurological services in both the public and private sectors is comprehensively detailed in a previous publication

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https://doi.org/10.1016/j.seizure.2024.01.008
Received 23 October 2023; Received in revised form 10 January 2024; Accepted 11 January 2024
Available online 13 January 2024

[7]. In brief, the country is divided into 21 central hospital districts, five of which hold university hospital status with extended teaching and research functions. Each district is responsible for a designated geographic catchment area. Across the country, children requiring neurological services experience minimal waiting times, typically within a few days. This is attributed to a remarkable density of trained specialists, reasonably evenly distributed in the country, reaching 11.9 per 100,000 children under 16 years or 12.7 per 100,000 under 15 years (as of 2018), likely the highest or one of the highest worldwide.

The training program for child neurologists encompasses supervised clinical work as a resident, theoretical coursework, healthcare management courses, and successful completion of a national written examination. In addition to the public healthcare system, specialists are authorized to practice concurrently in the private sector. A close partnership exists with third-sector lay organizations.

Referrals to hospital outpatient clinics for specialist evaluations primarily come from pediatricians, child neurologists, or general practitioners. Notably, a significant percentage of cases involve emergencies, with approximately one-third of children experiencing a first seizure falling into this category. A longstanding rule in Finland mandates the referral of every child experiencing a first seizure event for a hospital child specialist evaluation, a practice that is effectively implemented.

2.2. Setting

The 1991–2000 cohort. The source population comprised 82,500 children (mean in 1991–2000) less than 16 years of age and resident in the catchment area of Turku University Hospital (TUH), Southwest Finland (mean total population 450,000). Data were collected from several sources: TUH hard copies; TUH electronic medical records (AURIA); records of all other hospitals in the area or outside, primary care units, and private offices potentially caring for children; national Register for Healthcare (HILMO); and national Refundable Drugs Register (RDR). AURIA, maintained by the TUH District, included children treated in the Department of Pediatrics and Adolescent Medicine, presently called the TUH Lighthouse hospital. National data register (HILMO), maintained by the National Institute for Health and Welfare, listed the national healthcare data for all of Finland. The medical events of patients treated as outpatients or inpatients in any public primary, secondary or tertiary care hospitals or private offices are documented in HILMO including municipality code of permanent residence and treatment abroad. RDR, maintained by the Social Insurance Institution (SII), includes all children who have been granted a 100 % refund for drug expenses, including antiseizure medication. A statement of a diagnosis of epilepsy is required by a specialist in child neurology, adult neurology, or pediatrics for the 100 % reimbursement for any listed antiseizure medication. The SII refunds begin at the first documentation of the diagnosis of epilepsy. Thus, the date of a first entitled antiseizure drug reimbursement for epilepsy was used as the date of the diagnosis of new-onset epilepsy unless it was more accurately documented elsewhere. Seizure onset was from January 1, 1991 and December 31, 2000.

The overwhelming majority of the children with paroxysmal and other neurological problems, are treated in the TUH that has a mandate to treat the designed population in the area. TUH is one of the 21 tertiary care centers in Finland, called Central hospitals, with their network covering the whole country. The catchment areas of the Central hospitals are not geographically overlapping. However, five of the Central Hospitals have an extended teaching and research status as University Hospitals, and some of those five, including TUH, are designated as specialty centers for patients from any part of the country for problems such as rare diseases or pediatric epilepsy surgery.

In the Finnish National Health Services system, it is mandatory for every municipality to belong to one of the Central Hospital Districts. All public and private healthcare contacts of Finnish citizens have to be entered into the public healthcare registers. Patients are expected to use the services of their "own" Central Hospital District, and nearly all do, but they are entitled, at will, to use medical services of any public healthcare units, even in other countries, but the health data are still registered in HILMO.

Data were available for all children who resided in the study area regardless of where they were treated: (1) Department of Pediatrics and Adolescent Medicine, TUH Lighthouse Hospital (formerly U-Hospital), the main unit of child neurological services in the area; (2) its sub-units of TUH Turunmaa Hospital, TUH Salo Hospital and TUH Loimaa Hospital; (3) Municipal Child Neurological Outpatient Unit of the City of Turku with the recruitment area overlapping more than one third of the TUH Hospital District population; (4) private child neurology offices and (5) all relevant national registers that cover all the hospitals caring for children, primary care units, and private medical offices in Finland. In addition, data for children cared for abroad were, in principle, available for the study.

All child neurologists are certified specialists, because, in Finland, all child neurologists require board-certification. All EEG investigations were carried out at the TUH neurophysiology laboratory or at one collaborating, certified private EEG laboratory.

2.3. Participants

The inclusion criteria were two or more unprovoked seizures separated by more than 24 h ([8–10]. Although recently it has been suggested that epilepsy may be diagnosed in some patients with only one unprovoked seizure, we used the older definition for comparison with the 1961–1964 cohort. All patients were age <16 years at seizure onset.

Children were enrolled at the beginning of the year of their first (index) unprovoked seizure at which time they had to be residing in the county of Southwest Finland, the geographically defined TUH catchment area of the city of Turku or in the surrounding 28 urban, sub-urban and rural municipalities. Excluded were patients with only neonatal seizures (onset before the age of 28 days), acute provoked seizures or non-epileptic seizures only. Those with only two unprovoked seizures separated by more than five years were also excluded.

The study database was constructed in three stages. 1) A detailed chart review identified all potentially eligible patients from AURIA, 2) A chart review was undertaken of potentially eligible patients treated beyond the TUH Lighthouse Hospital using the national HILMO register, 3) The national RDR was searched for patients who had been granted a 100 % refund for drugs for the therapy of epilepsy, 4) Based on the chart reviews, patients were removed if they were misclassified as children with epilepsy, that is, if they had non-epileptic or acute provoked seizures or one unprovoked seizure only. All study data were encoded by a trained nurse under direct supervision of one of the authors, or by that senior author himself (MS).

Initially chosen were the original medical records of all children who had any of the following diagnoses in either the AURIA or HILMO or RGR databases, coded according to the International Classification of Diseases ICD-9: 330, 332A, 345, 7790A, 7802A, 7802B, 7802X, 7803A, and ICD-10: G40, G41, G90, F48.8, F80.3, F90, R55, R56.0, R56.8, I45, T67.1 and T67.2. The explanations of the codes are in Supplementary Table 1.

All the referral and discharge diagnoses of ascertained or suspected epilepsy or any potential paroxysmal brain or heart-related event ("faints, fits or funny turns" [11]were checked carefully for epilepsy and the epilepsies also reclassified in accordance with the current classification of epilepsies ([12]). In addition to seizure semiology and other clinical data, all included epilepsy patients had a conventional, night-and-day EEG or video-EEG examinations. Overall 80 % of cases had a brain MRI or CT scan.

To minimize intra-observer variability, the data were checked by two independent observers three times, each one with at least three months interval. All the data were encoded using a web-based application Research Electronic Data Capture (REDCap).

The 1961–1964 cohort. The 1961–1964 cohort has been described

previously [13,14]. That cohort excluded a few cases with a brain tumor or neurometabolic cause for seizures. To maintain the comparability with the 1991–2000 cohort, they are included in the current study.

Validation cohorts. For validation purposes, the charts of two TUH non-epilepsy patient groups were reviewed. A random sample of children with ascertained diabetes mellitus (ICD-9 250*, ICD-10 250*, ICD-10 E10*) was drawn from the TUH database. The diabetes group served as a method of estimating the accuracy of the AURIA to document children whose treatment was invariably started in hospital. To ensure randomization, every child diagnosed with new-onset diabetes on any of the first 15 calendar days of a month between 1991 and 2000 was recruited.

Another validation group was a random sample of 240 children (120 girls and 120 boys) whose previous history was uneventful for seizures or similar events or diabetes. Since no reliable estimates of expected number of misdiagnosed epilepsies were available, no formal power analysis was performed. Instead, the sample was stratified by time and sex by including one girl and one boy from each of the 120 months of the study period. This random sample served as a control for potential failure to identify relevant patients with epilepsy.

2.4. Statistical analysis

Confidence intervals for incidence estimates were calculated with Poisson regression models, whereas age class, gender, and their interaction were included, as well as calendar year as classified (1991–1995, 1996–2000) and calendar year (as classified) by age class interaction. Differences between categories and the 95 % confidence intervals were calculated. In addition, 95 % confidence intervals were calculated for relative risks and Fisher's exact test was made to compare two time periods. Statistical analyses were done with SAS System for Windows, release 9.4 (SAS Institute, Cary, NC, USA).

2.5. Ethics

The study was based on register data, patients were not contacted, and informed consent of the participants was not required, according to the Finnish legislation on studies limited to register data. The permissions to use the relevant databases were obtained from the TUH (#J8/2019/4.3.2019), the Finnish Institute for Health and Welfare (#THL/2167/5.05.00/2019/17.3.2020), the Social Insurance Institution of Finland (#164/522/2019/6.3.2020) and Statistics Finland (#TK-53–57–20).

3. Results

Data collection and validation of TUH electronic records (AURIA). Altogether 543 new-onset cases of epilepsy were identified as having epilepsy with two or more unprovoked seizures.

Table 1 shows data collection from AURIA in 1991–2000. There were 1464 potential patients but after applying the inclusion/exclusion criteria listed above and chart review, 439 of all 543 children with a diagnosis of epilepsy (two or more unprovoked seizures) remained for closer analyses.

Patients who proved to have epilepsy were admitted to the TUH through a referral by public sector in 59 % (health center 26 %, other hospital 14 %, Turku city child neurological outpatient clinic 9 %, internal transfer from TUH ward other than child neurological one 8 %, child welfare center 1 %, school health doctor 1 %) and by private sector in 6 %. One third (34 %) of children with epilepsy arrived without referral as emergency cases. No referral data were available on 1 %.

The sample of patients with diabetes ($n = 133$) proved to comprise all the intention-to-find cases (100 %). Analysis of the random population sample ($n = 240$) did not detect any case of incident diabetes or incident epilepsy. There was, however, one prevalent case of epilepsy, that is, seizures had appeared before the beginning of the observation period.

Table 1
Data collection for the incidence study of children with epilepsy in 1991–2000.

Participants	N	%
Potential participants	1568	100.0
Excluded:	1025	65.4
-no index event	196	19.1
-resident outside the study area at onset of study period	117	11.4
-febrile seizures only	378	36.9
-acute provoked seizures only	15	1.5
-psychogenic non-epileptic seizures only	173	16.9
-one unprovoked seizure only	81	7.9
-other	32	3.1
-no data available	33	3.2
Included:		
-two or more unprovoked epileptic seizures (for incidence calculations)	543	34.6
-two or more unprovoked epileptic seizures (for closer analysis)	439	28.0
Total	1568	100.0

3.1. Data from registers other than AURIA

All the participants who were identified from the medical records were detected in the TUH electronic database AURIA ($n = 439$). They comprised 81.2 % of the final cohort. A further 102 (18.8 %) participants were registered in HILMO, but not in AURIA or TUH medical records. This was because they had been treated outside TUH. Inclusion of those participants raised the coverage to 99.6 %. Notably, the contribution of Refundable Drugs Register was little, because only two children with epilepsy, who met the inclusion criteria, were identified from the Refundable Drugs Register, but not from any other data source. On the other hand, HILMO had erroneously included three patients who only had one unprovoked epileptic seizure and were, by definition, excluded from the present study: one with two seizures (one febrile seizure plus one unprovoked seizure), another with three seizures within a couple of hours and one with unprovoked status epilepticus. Overall, AURIA alone detected 81.2 % of all cases (100.0 % of cases treated in TUH), HILMO alone 94.5 % and RDR alone 74.3 % of all cases.

3.2. Incidence of epilepsy

The mean incidence of epilepsy in 1991–2000 was 65.9 (95 %CI 59.6–72.2) per 100,000 person years, age-adjusted for the Finnish general population (Statistics Finland 2021 https://www.stat.fi) (Table 2).

There was a significant ($p = 0.0030$) overall lowering trend in the incidence among both girls and boys from 1991 to 1995 to 1996–2000.

Fig. 2 shows that the incidence of epilepsy was affected by age differently in boys and girls. For girls, there was a significant ($p<0.0001$) difference in incidence for those <2 years of age, but no significant difference for those aged 12 years or more compared with those less than 12 years. On the other hand, in boys, there was no significant difference between those aged less than two years compared with those aged 2–11 years, but there was a highly significant difference ($p<0.0001$) when comparing boys aged 12–15 years to those less than 2 years. Additionally, the incidence is highly significantly ($p<0.0002$) lower in boys aged 12–15 years compared to those aged 2–11 years (Fig. 2).

3.3. Changes in etiologies of epilepsy

Table 3 shows that, compared with the 1961–1964 data, genetic structural causes were almost fourfold and presumed genetic syndromes also significantly (30 %) higher in 1991–2000. Associated prenatal and perinatal factors were almost 50 % less frequent in 1991–2000, especially asphyxia, infections, pre-eclampsia and imminent abortion. Substantially more participants had a known cause for epilepsy and lesional brain disorders were significantly fewer in 1991- 2000 than in

Table 2
Incidence of childhood epilepsy per 100,000 person-years by gender and age in the 1990's in Finland. (CI=confidence interval).

		N	Mean (SD)	Lower 95 % CI for mean	Upper 95 % CI for mean
All		543	65.94 (57.28)	59.64	72.24
Gender					
	Girls	261	64.85 (61.43)	55.26	74.44
	Boys	282	67.04 (52.97)	58.77	74.44
Age					
	<2	108	105.99 (78.12)	81.01	130.98
	2–11	340	66.18 (52.57)	58.85	73.51
	12–15	95	45.34 (45.07)	35.31	55.36
Calendar years					
	1991–1995	310	75.18 (60.22)	65.77	84.58
	1996–2000	233	56.71 (52.77)	48.47	64.95

The incidence, age-adjusted to the European Standard Population (https://seer.cancer.gov/seerstat/tutorials/aarates/step3.html, 2013) was virtually the same, 65.6 per 100,000. Fig. 1 shows the changes in the incidence of childhood epilepsy by year of onset and age group.

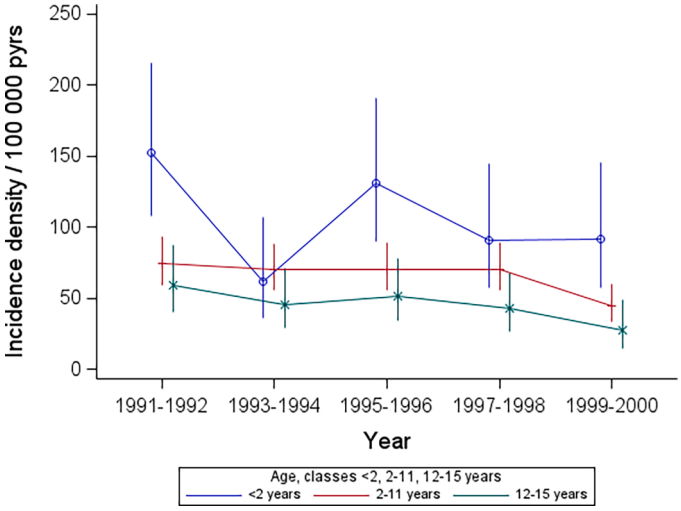

Fig. 1. Incidence of epilepsy in Finnish children by year of onset and age group.

1961–1964. The incidences of single genetic or presumed genetic syndromes did not significantly change in any age group (Table 4). In addition, the distribution of epilepsy syndromes was the same in both cohorts, although small numbers of subjects in most specific syndrome categories was usually too small for a confident comparison.

4. Discussion and conclusions

In this study we found a mean annual incidence of childhood epilepsy of 66 per 100,000 in the years 1991–2000 that is similar to other reports of the overall population-based incidences of childhood epilepsy from the 1990s that vary from 40 to 68 per 100,000. Our findings are also in line with other data from Finland. The median annual incidence in western Finland between 1986 and 2008 was 70 per 100,000) [4] and in eastern Finland 87 per 100,000 [15]. Hirvonen et al. [16] reported the incidence of 62.3 per 100,000 children born in Finland in 1991–2001. Sokka et al. [3] found an incidence of 38 per 100,000 in children less than 15 years in eastern Finland in 1989–2007, a result that is, in all probability, an underestimate, but the reasons are unknown.

The methodology of present study was comprehensive - hard copies of the medical records of TUH, and three population registers. We found that 81.2 % of the patients residing in the catchment area of one university hospital are treated in their "own" hospital. One fifth were treated elsewere. The hard copy medical records (virtually equal to AURIA) and HILMO data cover 99.6 % of all relevant subjects. In Finland, every child with identified or suspected epileptic seizures has to be referred to a specialist care hospital [14]([17]). The coverage of the registers for epilepsy was excellent. The validity of the enrolment method was further emphasized with a random sample of new onset diabetes.

The published literature shows a recognizable upward trend in the incidences of childhood epilepsy from the latter half of the 1900's to the early 2000's (Supplementary Table 2). Our previous results from 1961 to 1964 [14] showed an incidence of 35 per 100,000. Corrected to match the inclusion criteria of the other studies – including patients with an associated expansive or degenerative brain disorder - the attained incidence was 38 per 100,000 person-years and well in line with another Finnish study (36/100,000) from 1968 to 1972 [18], 41 per 100,000 in a Canadian study [19] from 1977 to 1985 and 50 per 100,000 by Brorson [20] from 1961 to 1964 in Sweden.

The incidences of childhood epilepsy from the 1960's to the 1980's are lower than what is expected today. There is no doubt that the rates reported in the literature from that period reflected data which were available and accessible to the contemporary researchers. In all probability, a number of children with unprovoked epileptic seizures did not present to the medical care system for reasons such as stigmatization or diagnostic failures and therefore remained outside the data collection methods.

In Finland, the rise of the annual incidence of childhood-onset epilepsy (recurrent unprovoked seizures) was highly significant ($p<0.0001$), from 38 per 100,000 in 1961–1964 [13,14] to the present 66 per 100,000 in 1991–2000 from the population of the same geographic area.

The reasons for the increase in incidence from the 1960's to the 1980's and then the decreasing incidence in the late 1990's are not clearcut. However, several potential influences may be suggested.

In the early 1960's in Finland, convulsive seizures were considered a family emergency, prompting immediate medical attention. On the other hand, non-convulsive seizures and fits were often overlooked as epileptic, either due to ignorance or were recognized but ignored and concealed due to shame. According to one of the senior authors (MS), whose personal experience on epilepsy spans from 1961 to the present, a shift in attitude towards epilepsy began to occur in the latter half of the 1960's.

During this period, significant changes in Finnish society's approach to epilepsy were observed. In 1967, the first regional layman epilepsy association was established, followed by the foundation of the national Epilepsy Association and a network of regional associations across the country. The initiation of the Finnish Epilepsy Journal for laymen further contributed to this evolving perspective. The repeal of a law regarding epilepsy as a marriage impediment in 1968 marked a positive signal to public in attitudes toward epilepsy. This likely empowered individuals with epilepsy to be more open about their condition and seek medical support. [21]. Attitude polls conducted in various countries have shown a gradual reduction in prejudices toward epilepsy and decreased stigmatization among the population [22,23]. This societal shift could have played a role in increasing awareness and knowledge of epilepsy among the general public, thereby reducing stigmatization and fostering a greater willingness to seek medical care for even subtle seizures. Importantly, these changing circumstances undoubtedly contributed to the improved recognition of non-convulsive seizures and encouraged individuals to seek medical attention.

In 1967–1969, the first four physicians were listed as trained child

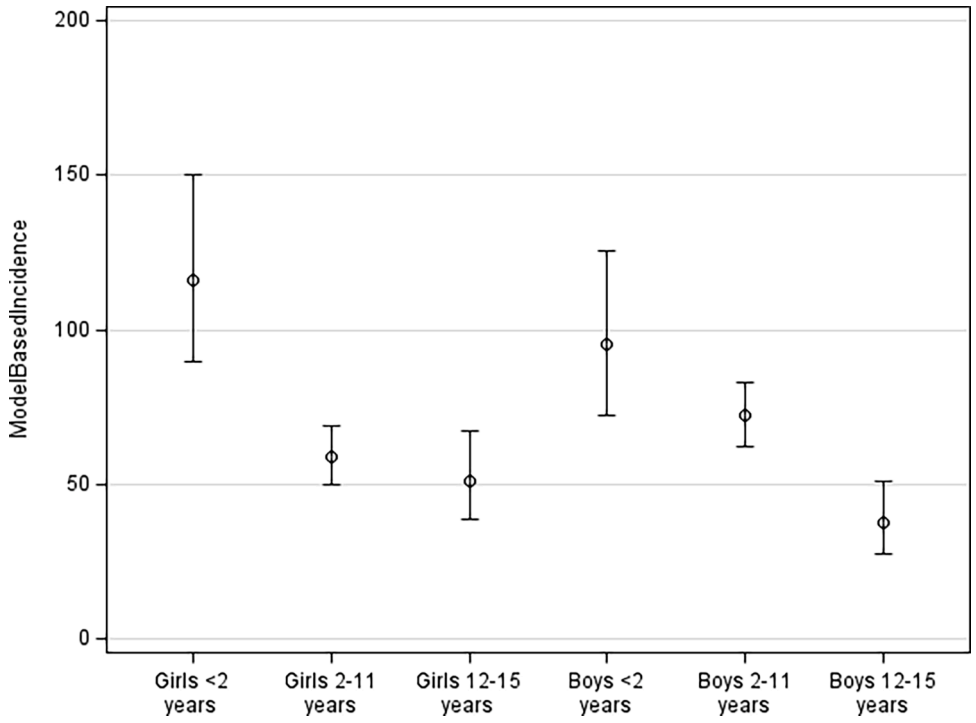

Fig. 2. Model-based incidence estimates of epilepsy (and 95 % confidence intervals) in Finnish children by gender and age group.

neurology specialists, followed by a linear quantitative increase and numbering 73 specialists in 2000. As described above, virtually all central hospital districts had their child neurology department or ward offering services with a few days waiting time. In addition to a high frequency attendance in international epilepsy congresses of Finnish child neurologists, the national continued professional education was organized by establishing the Finnish Epilepsy Society (in 1986) and the Finnish Epilepsy Research Foundation (1992), a continuation of the Finnish Chapter of ILAE (in 1976). [21]. A reasonably even distribution and accessibility to child neurological specialist services without doubt increasingly prompted identification of new-onset epilepsy.

In the years 1967–1969, the initial four physicians were board-certified as trained child neurology specialists, marking the commencement of a continuous quantitative expansion up to 74 specialists by the year 2000 and 150 by 2018. As delineated earlier, all central hospital districts boasted a dedicated child neurology department or ward, providing services with minimal waiting times. Concurrently, Finnish child neurologists very actively participated in international epilepsy congresses, while the national landscape of continued professional education was enriched through the establishment of the Finnish Epilepsy Society in 1986 and the Finnish Epilepsy Research Foundation in 1992, following the legacy of the Finnish Chapter of ILAE since 1976. [21]. This deliberate effort contributed to a more even distribution and enhanced accessibility to child neurological specialist services, undoubtedly facilitating the identification of new-onset epilepsy.

Examining national Finnish statistics on infant mortality (Finland Infant Mortality Rate 1950–2023, retrieved on 2023–12–14) reveals a significant reduction in the infant mortality rate, declining from 21.547 in 1961 to 18.249 in 1964, and further decreasing from 5.347 in 1991 to 3.587 in 2000, ultimately reaching 1.422 per 1000 live-born. Currently, Finland holds the fourth position globally in terms of the lowest mortality rate, following Iceland, Hong Kong, and Singapore. Further, annual neonatal mortality decreased from 11.13 in 1969 to 2.46 per 1000 in 2004 in Finland [24]

Contrary to a widespread hypothesis positing that the reduction in perinatal mortality and the subsequent increase in survival rates might lead to a higher postnatal neurological morbidity rate, existing evidence does not support this claim, at least for cerebral palsy (CP). This holds true for both preterm and term births, even with a substantial rise in cesarean delivery rates [25]. CP, a typical brain injury-related disorder, has not become more incident despite modern advancements in monitoring and imaging technology. This conclusion is supported by extensive reviews spanning from 1966 to 1996 [25], the landmark study by Hagberg covering 1954–1994 [26], and investigations by Himmelmann and Uvebrant [27] from 1959 to 2006. While we are not aware of such long-term incidence studies on epilepsy, it is plausible to infer a similar trend based on the evidence. Certain signs point to a potential rise in inherited and other congenital malformations, often linked to epilepsy [28]. In conclusion, the reverse of enhanced perinatal care may not result in a higher occurrence of significant neuromorbidity. Furthermore, the coding practice, which remained unchanged throughout the study, did not contribute to incidence rate.

The recognition of Child Neurology as a recognized full-time specialty in 1978, led to an increase in specialist education and establishment of new specialist posts which likely improved the case-finding and ascertainment of epilepsy. The density of child neurologists in Finland (11.9 per 100,000 children) is probably highest in the world, and the services are reasonably evenly distributed all over the country [7]. Research into epilepsy was supported by newly-established professional organizations, the Finnish Epilepsy Society and the Finnish Epilepsy Research Foundation. The development of diagnostic methods, such as video-EEG recording, CT scans, MRI, PET, and magnetoencephalography, likely improved the accuracy of epilepsy diagnosis.

During the 1990's and the present observation period, there seems to have been a saturation in the identification of undiagnosed or latent cases of epilepsy, leading to a largely plateaued incidence curve [19]. Some other studies have suggested a decline in the incidence. For instance, a British study observed "a near halving of the cumulative incidence of recorded epilepsy at age 5 years for children born between 1994 and 1996 and 2003–2005″, with a 33 % lower cumulative incidence among children born in 2003–2005 compared to those born in 1994–1996. According to their findings, the annual incidence declined significantly by 4–9 % per annum between 2001 and 2008. Similarly,

Table 3
Etiological features of epilepsies in 1961–1964 and in 1991–2000.

Number of subjects	*N* = 164	*N* = 439	p	RR	95 %CL
Number of symptoms/signs	n (%)	n (%)			
Genetic structural	**8 (4.9 %)**	**83 (19 %)**	<0.0001	3.88	1.92–7.83
Corpus callosum, agenesis/hypoplasia	0	13		NA	
Cortical dysplasia	0	6		NA	
Septo-optic dysplasia	0	3		NA	
Hemimegalencephaly, asymmetry	0	2		NA	
Cerebellar hypoplasia	0	1		NA	
Cerebral tumor	4*	9	0.7572	0.84	0.26–2.69
astrocytoma		4		NA	
ganglioglioma		2		NA	
dysembryotic epithelioma		1		NA	
malignant meningeoma		1		NA	
hamartoma		1		NA	
primitive neuroectodermal tumor		1		NA	
Lissencephaly	0	2		NA	
Cortical/subcortical band heterotopia	0	2		NA	
Pachygyria, polymicrogyria	0	3		NA	
Heterotopia	0	1		NA	
Dysmyelination	0	11		NA	
Vascular malformation	0	8		NA	
Fragile-X syndrome	1	0		NA	
Monosomy 1p36 syndrome	0	1		NA	
Wisconsin syndrome (3p deletion)	0	1		NA	
Wolf-Hirschhorn syndrome (del chr. 4)	0	1		NA	
Angelman syndrome (part. monosomy 15q12)	0	1			
Patau syndrome (trisomy 13)	0	1		NA	
Chromosome 15q12–14 anomaly	0	3		NA	
Down syndrome (trisomy 21)	0	2		NA	
Sotos syndrome (5q35.2–q35.3)	0	1		NA	
Supernumerary marker chromosome 46	0	1		NA	
Dehydro-pyridin-dehydrogenase defect	0	1		NA	
Factor V Leiden mutation	0	1		NA	
Leigh syndrome	0	1		NA	
Mucopolysaccharidosis II (Hunter syndrome)	0	1		NA	
Muscle-eye-brain disease (1p.32–34)	0	1		NA	
Infantile neuronal ceroid lipofuscinosis (1p32)	0	1		NA	
Late onset neuronal ceroid lipofuscinosis (13q21–22)	0	1		NA	
Rett syndrome (Xq27-q28)	0	2		NA	
Genetic neurometabolic	**3**	**9**	1.0000	1.12	0.31–4.09
Presumed genetic	**54 (34 %)**	**194 (44 %)**	0.0155	1.34	1.05–1.71
Pre/perinatal	**56 (34 %)**	**79 (18 %)**	<0.0001	0.53	0.39–0.71
Asphyxia	21 (13 %)	10 (6.1 %)	<0.0001	0.12	0.09–0.37
Pre-eclampsia	9 (5.5 %)	5 (1.2 %)	0.0037	0.21	0.07–0.61
Infection	11 (6.7 %)	5 (1.2 %)	0.0005	0.16	0.06–0.48
External mechanical trauma	2	1	0.1812	0.19	0.02–2.05
Imminent abortion	5	1	0.0066	0.07	0.01–0.63
Stroke	1	3	1.0000	1.12	0.12–10.70
Hemorrhage	10 (6.1 %)	15 (3.4 %)	0.1676	0.56	0.26–1.22
Unknown	30 (18 %)	47 (11 %)	0.0191	0.59	0.38–0.89
Postnatal infection	**5 (3.0 %)**	**7 (1.6 %)**	0.3233	0.52	0.17–1.62
Postnatal traumatic brain injury	**8 (4.9 %)**	**5 (1.2 %)**	0.0091	0.23	0.08–0.70
Postnatal cerebral hemorrhage	**1**	**0**		NA	
Immunological	**0**	**0**		NA	
Unknown	**66 (40 %)**	**112 (26 %)**	0.0006	0.64	0.50–0.81

* Data on histopathology no more available.

Christensen et al. [5] found that the incidence of epilepsy modestly decreased in all pediatric age groups from 1995 to 2003, except for a substantial decline in children less than one year old.

Recent longitudinal population studies from Finland are the first to reveal a significantly declining incidence of childhood epilepsy. Incidence rates between 76.8–92.1 per 100,000 in different parts of the country in 1995 decreased to 62.1–70.6 per 100,000 in 2000 [15]. Further evidence from Finland indicated a decline in the incidence of childhood epilepsy between 1995 and 2000. In boys, the incidence decreased from 85.2 to 67.8 per 100,000, and in girls, it decreased from 74.2 to 59.6 per 100,000 during this period [29]. Similarly, in West Finland, the incidence of childhood epilepsy decreased from 76.8 to 62.1 per 100,000 between 1995 and 2000 [15]. Countrywide data from Finland during the same observation period [4] further confirmed a significant declining trend for boys and girls in all pediatric age groups from 1988 to 1992 to 1998–2002. The present study confirms a significant decrease beginning in the 1990's.

Preterm birth and low socioeconomic status are widely recognized as significant risk factors for unfavorable outcomes [30]. The observed decline in the incidence of preterm birth can be attributed, at least in part, to advancements in prenatal and perinatal care, leading to a reduction in the occurrence of brain injuries [31]. One indicator of successful prevention of epilepsy is the reduction in the number of preterm births, as children born prematurely are notably more susceptible to epilepsy compared to those born at term or post-term [16]. In Finland, the incidence of very preterm births exhibited a gradual decrease from 253 to 51 per 100,000 births during the period of 1991–1995 [32]. Notably, socioeconomic disparities were also narrowing during this time [32]. To our knowledge, there are no research data on a direct correlation between improved socioeconomic status and a decreased incidence of epilepsy. Postnatal traumatic brain injuries were decreasing in the 1990's in Finland [33,34].

Our study has several strengths. The initial TUH dataset spanning from 1991 to 2000 was meticulously recorded, with particular emphasis on validating the epilepsy diagnoses of each patient. Throughout the documentation phase in 1991–2000, a child neurological specialist, who

Table 4
Distribution of childhood epilepsy types and syndromes in 1961–1964 ($N = 164$) and 1991–2000 ($N = 439$). Reclassified according to the ILAE 2017 classification (GTCS=generalized tonic-clonic seizures; GTS=generalized tonic seizures; GCS=generalized clonic seizures; GATS=generalized atonic seizures).

Number of subjects Number of characteristics	$N =$ 164 n (%)	$N =$ 439 n (%)	p	RR	95 %CI
Syndrome					
Genetic or presumed genetic syndromes	76 (46 %)	236 (54 %)	0.1195	1.16	0.96–1.40
1 Neonatal period/infancy (0–11 months)	12 (7.3 %)	40 (9.1 %)	0.62	1.25	0.67–2.31
11 Self-limited epilepsy syndromes	0	4		NA	
111 Familial neonatal/ infantile epilepsy	0	0		NA	
112 Genetic epilepsy with febrile seizures plus	0	0		NA	
113 Myoclonic epilepsy in infancy (MEI)	0	4		NA	
12 Developmental and epileptic encephalopathies	12 (7.3 %)	36 (8.2 %)	0.8659	1.12	0.60–2.10
121 Early myoclonic encephalopathy	0	1		NA	
122 Early-infantile epileptic encephalopathy	1	3	1.0	1.12	0.11–10.70
123 Epilepsy of infancy with migrating focal seizures	0	0		NA	
124 Infantile spasms syndrome	5 (3.0 %)	17 (3.9 %)	0.81	1.27	0.48–3.39
125 Dravet syndrome	0	2		NA	
126 Sturge-Weber syndrome	0	2		NA	
127 Hypothalamic hamartoma with gelastic seizures	0	0		NA	
128 Angelman syndrome	0	1		NA	
129 Neurodevelopmental brain tumors	5 (3.0 %)	10 (2.3 %)	0.57	0.75	0.26–2.15
2 Childhood (1–12 years)	51 (31 %)	153 (35 %)	0.4392	1.12	0.86–1.46
21 Self-limited focal epilepsies	17 (10 %)	51 (12 %)	0.7727	1.12	0.67–1.88
211 Epilepsy with centrotemporal spikes	16	43	1.0	1.00	0.58–1.73
212 Epilepsy with autonomic seizures	1	7	0.6897	2.62	0.32–21.09
213 Childhood occipital visual epilepsy	0	1		NA	
214 Photosensitive occipital lobe epilepsy	0	0		NA	
22 Generalized epilepsies	34 (21 %)	102 (23 %)	0.5843	1.12	0.79–1.58
221 Idiopathic generalized epilepsies	6 (3.7 %)	14 (3.2 %)	0.7996	0.87	0.34–2.23
2211 Childhood absence epilepsy	6 (3.7 %)	14 (3.2 %)	0.7996	0.87	0.34–2.23
222 Genetic generalized epilepsy	28 (17 %)	69 (16 %)	0.7092	0.92	0.62–1.37
221 Epilepsy with GTCS/ GTS/GCS/GATS	25 (15 %)	67 (15 %)	1.0	1.00	0.66–1.53
2222 Epilepsy with eyelid myoclonia	0	2		NA	
2223 Epilepsy with myoclonic absence	1 (0.6 %)	1 (0.2 %)	0.4703	0.37	0.02–5.93
2224 Self-induced photosensitive epilepsy	2	0		NA	
223 Developmental and epileptic encephalopathies	7 (4.3 %)	18 (4.1 %)	1.0	0.96	041–2.26
2231 Myoclonic-atonic epilepsy	1 (0.06 %)	1 0.02 %)	0.4703	0.37	0.02–5.93
2232 Lennox-Gastaut syndrome	6 (3.7 %)	10 (2.3 %)	0.3936	0.62	0.23–1.69
2233 D/EE-SWAS and Kleffner syndrome	0	7		NA	
2234 Febrile infection-related epilepsy syndrome	0	0		NA	
2235 HHE syndrome	0	0		NA	
3 Adolescence-adulthood (13+ years), all ages	13 (7.9 %)	43 (9.8 %)	0.5319	1.24	0.68–2.24
31 Idiopathic generalized epilepsies	13 (7.9 %)	43 (9.8 %)	0.5319	1.24	0.68–2.24
311 Juvenile absence epilepsy	3 (1.8 %)	18 (4.1 %)	0.2181	2.24	0.69–7.51
312 Juvenile myoclonic epilepsy	3 (1.8 %)	14 (3.2 %)	0.5903	1.70	0.51–5.91
313 Epilepsy with tonic-clonic seizures alone	7 (4.3 %)	11 (2.5 %)	0.2839	0.59	0.23–1.49
314 Progressive myoclonus epilepsy	0	0		NA	
Non-genetic syndromes	66 (40 %)	133 (30 %)	0.0251	0.75	0.60–0.95

is one of the authors, conducted a double-check of the epilepsy diagnoses for accuracy and reliability. The national health and population registers were cross-referenced for the TUH data and proved very valid for epilepsy and associated data.

To conclude, the Finnish national registers for epilepsy are valid and offer a reliable basis for epidemiological studies of epilepsy. The incidence of childhood-onset epilepsy in Finland does not differ from the data reported from other developed countries. While the incidence of childhood epilepsy was increasing during the last half of the 2000th century, a turning point was likely reached in the 1990s followed by a significant declining trend. The recent decline in incidence is welcome although not completely understood.

Declaration of competing interest

The authors disclose no conflicts of interest

Acknowledgments

We owe thanks to Maiju Saarinen, MSc, for her help and assistance in the data collection and initial analysis, and Auria Clinical Informatics unit for delivering us the medical records data. This study was financially supported by the Governmental Research Grant and Pro Humanitate Foundation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.seizure.2024.01.008.

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