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Transfer of Finnish adolescents with epilepsy to adult care: a population-based study

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ABSTRACT

Background: Transferring adolescents with epilepsy (AWE) to adult care is a complex process, yet there is limited data on its overall epidemiology and clinical implications.
Objective: This population-based study analyzes the long-term clinical trajectories and predictors of transfer among AWE within a robust Finnish healthcare system.
Methods: A cohort of 439 AWE was followed for a mean of 10.28 years. Transfer outcomes, care settings, and long-term seizure control were evaluated for patients reaching transfer age, focusing on predictors of public adult specialty care.
Results: Of 222 AWE reaching transfer age, 189 (85.1 %) were transferred to adult services, with 64 % entering university hospital care. Remission was achieved in 23 % during extended follow-up, while 27 % remained drug-resistant. Multivariable analysis identified developmental and epileptic encephalopathy, specific developmental disorders, and comorbidities such as asthma, allergies, and obesity as significant predictors for public adult specialty care. Notably, changing the transfer age from 16 to 18 years had no significant effect on transfer rates.
Conclusion: Transfer to adult specialty care affects the vast majority of AWE, imposing considerable demands on public health systems. These findings underscore the need for early identification of high-risk patients to inform resource planning and individualized care strategies.

1. Introduction

Transferring from adolescent to adulthood medical care involves profound developmental changes, even for individuals without health concerns [1,2]. Adolescents with chronic neurological conditions such as epilepsy face additional medical, social, and environmental challenges.

Over the past three decades, a number of reports have emphasized the importance of transitioning adolescents with epilepsy (AWE) to adult healthcare service [3–9], some few with reservations [9]. These transition studies focus on preparing adolescents to move from pediatric- to adult-centered care. AWE frequently encounter distinct psychosocial and medical challenges during this transition [4,10,11]. Crucial domains include education, employment, driving, reproductive health, hobbies, independence, and the broader socioeconomic implications [6,12,13]. We focused, however, exclusively on the event of transfer, without considering preceding structured transition programs. Despite the significant impact of epilepsy on the transition process, empirical data quantifying the rate of transfer and identifying factors associated with successful outcomes remain scarce, if any. As a matter of fact, to the best of our knowledge, neither the Goselink group (email communication) nor other study teams have such data.

We sought to determine: (1) what proportion of AWE are transferred to adult care; (2) which factors predict transfer; (3) the post-transfer distribution of care providers; and (4) the overall treatment burden placed on university hospital-related public adult specialty healthcare. In our study, the transfer involved patients from all pediatric units in the region of the Department of Neurology at the University Hospital (TUH). We assessed the prevalence and potential predictors of transfer to provide a comprehensive overview of the issue and to identify key risks within a highly developed national public healthcare system.

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2. Participants and methods

The initial source population comprised 82,500 children under 16 years old residing in the TUH catchment area (regional mean population ~ 450,000) during the period 1991–2000. Data were obtained from national hospitals, primary care units, and national registers, covering 99.6 % of relevant cases and validated through rigorous analysis [7]. System details and validation methods are described in Sillanpää et al [14].

From 1991 to 2000, data were gathered via detailed chart reviews of children receiving care at the TUH Department of Child Neurology or the Department of Pediatrics and Adolescent Medicine —the primary pediatric and child neurological center serving the city of location and 28 surrounding municipalities. The inclusion criteria consisted of children experiencing recurrent unprovoked seizures separated by more than 24 h [15–17], who resided within the study area and had their first seizure during the review period. Exclusion criteria included neonatal seizures only, acute provoked seizures, non-epileptic seizures, and cases involving only two unprovoked seizures more than five years apart [14].

Eligible patients were identified via AURIA, TUH's electronic patient register. Their transfer to adult care was subsequently examined. Data were entered into the Research Electronic Data Capture (REDCap) system by a trained healthcare professional under the supervision of one of the authors (MS).

The cohort included 439 children with epilepsy, resulting in an incidence rate of approximately 65.8 per 100,000 children, adjusted according to the European Standard Population [14].

When transferring to adult neurological care, children had several options for caregivers: TUH outpatient and inpatient units offering both secondary and tertiary services for the entire catchment area; public district hospitals with neurology services; regional institutions for individuals with intellectual disabilities; university hospital municipal health center for primary care, however, with pediatric and neurology services and private neurology/pediatric neurology group clinics. All of these patients were cared for in settings that included neurological expertise. In this study, the TUH-transferred patients were more thoroughly assessed both in terms of their need for specialized neurological care and from the perspective of TUH's economic burden, since it is our impression that outpatient and inpatient services are significantly more expensive at the university hospital than in lower-level healthcare units. Patients without further need of neurologic services could choose to withdraw from continued care.

The primary outcome variable was transfer to adult neurological specialty care. For analytical consistency, an age cutoff of 16 years was applied. During the 1990s, this transfer point was nationally mandated for administrative and financial reasons (e.g., budgeting, personnel, bed availability). Consequently, medical records spanned ages 0–15. Due to the use of "continuing records" (lifelong documentation within a single patient file), we accessed the pediatric data of individuals whose care continued into adult units. In the 2000s, the age of transfer shifted to 18.

Predictors were found on the basis of ICD-10 codes. Single predictors were combined in case of low frequency. Potential predictors included in the analysis were as follows: age at onset of epilepsy; comorbidity (allergic diseases, bronchial asthma, cerebral palsy, migraine and headache, neurotic, stress-related or somatoform, obesity, specific neurodevelopmental disorders); caregiver in continued care (See Table 1); continued care (yes, no); continued care in University Hospital, reason (seizures, other, which one?); developmental/epileptic encephalopathy (developmental, epileptic, both); drug therapy at age 16 years (no, mono, poly); drug therapy at the end of follow-up; duration of follow-up; epilepsy type (See Table 2); etiology of seizures (structural, genetic, unknown); febrile seizures (yes, no); gender (girl, boy); obesity (BMI $\geq$ 30, <30); photosensitivity (clinical, EEG, both); remission at age 16 years; remission at the end of follow-up; remission, $\geq$5 years (yes, no); response to drug therapy (self-limited, pharmaco-responsive, drug-resistant); status epilepticus or prolonged seizure (yes, no); time from epilepsy onset to 16 years of age; year of death. The predictors that we finally entered into the multivariable analysis are shown in Table 3.

Table 1
Caregiver of 222 transferred adolescents with epilepsy.

Caregiver	Total
	N (%)
University Hospital (TUH)	143 (64.4)
Other– University municipality healthcare center	14 (6.3)
– district hospital	8 (3.6)
– regional institution for patients with intellectual disability	5 (2.2)
– private group practice	11 (5.0)
– unknown caregiver	3 (1.4)
– no need for adult care*	33 (14.9)
– unknown	5 (2.2)
Total	222 (100.0)

* No need for adult care means pre-transfer 5-year remission without medication at the age of eligibility for transfer.

Obesity was defined per WHO standards as a BMI $\geq$ 30. Developmental and epileptic encephalopathy was defined using the criteria set by Scheffer and Liao [18] and Ago et al [19]. Neurodevelopmental disorders included conditions affecting speech and language, academic skills, motor functions, autism spectrum disorder, and attention-deficit/hyperactivity disorder. Patients who had no further need for transfer to adult services were defined as having a 5-year terminal remission of seizures without further anti-seizure medication.

2.1. Statistical analysis

To assess differences between transferred and non-transferred patients, Fisher's exact test was used. Both univariable and multivariable analyses were conducted using modified Poisson regression with robust standard errors to calculate relative risk [20]. Results are reported as relative risks (RR) with 95 % confidence intervals (CI), and p-values in univariable analyses were Bonferroni-corrected for multiple comparisons. Statistical analyses were performed using R (version 4.5.1).

2.2. Ethics

This registry-based study did not involve direct contact with participants and, according to the national legislation, did not require informed consent. Approvals were obtained from: the University Hospital (J8/2019/04.03.2019); National Institute for Health and Welfare (THL/2167/5.05/2919/06.03.2020); and the national statistical central bureau (TK-53–57-20).

3. Results

Mean follow-up for the overall cohort (n = 439) was 10.28 years (SD 5.90, median 11.01, range 0–28.23), for the transferred patients (n = 189); 10.28 years (SD 4.25, media 13.97, range 0–28.23); and for the patients transferred to TUH (n = 129) 13.90 years (SD 4.37, median 14.13, range 0–28.23).

At the end of follow up, 226 of the 439 AWE (51 %) were considered pharmaco-responsive; 113 (26 %) were drug-resistant; 75 (17 %) experienced self-limited epilepsy; and 25 (6 %) had unknown response. Seventy-nine (18 %) were diagnosed with developmental encephalopathy; 5 (1 %) with epileptic encephalopathy; and 45 (10 %) with both. Table 2 indicates that the distribution of epilepsy types at transfer age was similar to that of the children who had not yet reached transfer age.

Between 1991 and 2000, 222 adolescents with epilepsy (AWE)—representing 50.5 % of the total cohort of 439—reached the legal transfer age of 16 years. At transfer, 189 (85 %) of 222 individuals required ongoing neurological care. All 189 transferred AWE received adult neurological services. Patients treated at TUH continued their care within TUH, while others were referred to alternative arrangements,

Table 2
Transfer of adolescents with epilepsy to public specialty care at age 16 years by epilepsy type (ICD-10 codes). No need for adult care means pre-transfer 5-year remission without medication.

Epilepsy type	All	Non-transferred			Transferred
		No need fortransfer at age 16	Age less than 16	All non-*trans*-ferred	
	n(%)	n(%)	n(%)	n%)	n(%)
Total	439/100.0 %)	33(7.5)	184(41.9)	217(49.4)	189 (43.1)
G40.0–40.2 Focal with seizures of localized onset	239(100.0)	27(11.3)	104(43.5)	131(54.8)	108(45.2)
G40.0–40.2 with awared consciousness	57(100.0)	23(40.3)	27(47.4)	50(87.3)	7(12.3)
G40.00 focal idiopathic (rolandic)	38(100.0)	15(39.5)	20(52.6)	35(92.1)	3(7.9)
G40.09 other idiopathic	12(100.0)	8(66.7)	4(3.3)	12(100.0)	0
G40.10 non-idiopathic with simpleseizures	7(100.0)	0	3(42.9)	3(42.9)	4(57.1)
G40.11–40.22 focal with impairedconsciousness	182(100.0)	4(2.2)	77(42.3)	81(44.5)	97(55.5)
G40.11 focal with complex seizures	62(100.0)	2(3.2)	30(48.4)	32(51.6)	30(48.4)
G40.12 focal with sec. generalization	4(100.0)	0	0	0	4(100.0)
G40.20 focal with complex non-convulsive seizures	14(100.0)	0	6(42.9)	6(42.9)	8(57.1)
G40.21 focal complex with automat-isms and disturbed awareness	25(100.0)	1(4.0)	1(4.0)	2(4.0)	23(92.0)
G40.22 focal complex with sec.Generalization	75(100.0)	1(1.3)	29(38.7)	30(40.0)	45(60.0)
G40.30–40.39 Generalized onset idiopathic	125(100.0)	6(4.8)	39(31.2)	45(36.0)	80(64.0)
G40.30 generalized with motorseizures	73(100.0)	4(5.5)	19(26.0)	23(31.5)	50(68.5)
G40.33–40.39 generalized with non-motor seizures	52(100.0)	2(3.8)	20(38.5)	22(42.3)	30(57.7)
G40.4 Other generalized	39(100.0)	0	26(66.7)	26(33.3)	13(33.3)
G40.51–40.89 Other specified	29(100.0)	0	11(37.9)	18(62.1)	18(100.0)
G40.9 Unspecified	7(100.0)	0	4(57.1)	4(57.1)	3(42.9)

Table 3
Predictors of transfer of adolescents with childhood-onset epilepsy to public specialty care (University Hospital, TUH). BMI = body mass index.

Determinant	Transferred to TUH N = 143	Transferred elsewhere N = 79	Univariate analysis		Multivariate analysis	
	n (%)	n (%)	RR (95 % Cl)	p	RR (95 % Cl)	p
Bronchial asthma and allergic disorders (yes vs. no)	28 (19.6 %)	6 (7.59 %)	1.34 (1.11–1.63)	0.033	1.44 (1.18–1.76)	0.0003
Developmental or epileptic encephalopathy or combination (yes vs. no)	25 (17.9 %)	4 (5.41 %)	1.39 (1.15–1.67)	0.0065	1.42 (1.16–1.74)	0.0006
Specific neurodevelopmental disorders (yes vs. no)	25 (17.5 %)	6 (7.59 %)	1.31 (1.06–1.60)	0.14	1.36 (1.11–1.69)	0.0034
Time from epilepsy onset to age 16: <2 years vs. 2 + years	8(5.6%	1 (1.27 %)	1.40 (1.09–1.81)	0.12	1.48 (1.13–1.93)	0.0043
Obesity BMI ≥ 30 vs. < 30	10(7.0%)	1 (1.27 %)	1.44 (1.16–1.79)	0.010	1.32 (1.04–1.66)	0.022
Remission at age 16: <2 years vs. ≥ 2 years	85 (58.0 %)	26 (32.9 %)	1.33 (1.09–1.62)	0.078	1.20 (0.97–1.49)	0.094
Drug therapy at age 16: Yes vs. no	124 (86.7 %)	60 (76.0 %)	1.35 (0.97–1.88)	>0.99	1.21 (0.87–1.69)	0.25
Etiology of seizures: structural vs. other	42 (29.4 %)	18 (22.8 %)	1.12 (0.92–1.38)	>0.99		
Gender: boys vs. girls	76 (53.2 %)	36 (45.6 %)	1.11 (0.90–1.29)	>0.99		
Focal non-idiopathic (ICD-10 G40.1) vs. other types	139 (97.2 %)	59 (74.7 %)	1.07 (0.88–1.30)	>0.99		
Clinical or EEG photosensitivity: absent vs. present	22 (15.4 %)	10 (12.7 %)	1.08 (0.84–1.40)	>0.99		
Age at onset of epilepsy: <2 years vs. 2 + years.	14 (9.79 %)	8 (10.1 %)	0.99 (0.71–1.38)	>0.99		
Status epilepticus yes vs. no	27 (18.9 %)	15 (19.0 %)	0.99 (0.78–1.28)	>0.99		

including the university hospital municipal primary care services, a unit staffed by a neurological team. The remaining persons opted to attend private neurological group practices situated in the university hospital municipality or surroundings.

Of the 222 eligible for transfer, 64 % moved to TUH adult specialty care, 12 % to district institutions, and 5 % to private care; 4 % had unknown caregivers. The remaining subset of 33 patients (15 %) had achieved five-year terminal remission without medication by age 16 and were considered “cured”. These subjects were not transferred, as they were no longer deemed to require ongoing neurological care. Of these 33, 29 (88 %) had been treated solely for seizures. All the remaining five (12 %) had at least one comorbidity: all five had tension headache, two had mental health issues, and one had comorbid asthma.

Of the 189 requiring ongoing therapy, 170 (90 %) received public care and 19 (10 %) private or undocumented care. (Table 1).

Table 2 demonstrates that children presenting with seizures of localized onset – including focal self-limited epilepsies such as Rolandic and related epilepsies – were less likely to be transferred to adult care compared to those with generalized onset idiopathic epilepsy ($p = 0.02$). When stratifying by seizure type with impaired awareness, this difference was not significant ($p = 0.31$).

Of 189 post-transfer individuals, 38 (20.1 %) achieved five-year remission; 86 (45.5 %) reached five-year terminal remission off medication; 46 (24.3 %) failed to achieve a 2-year remission and were classified as drug-resistant; and 19 (10.1 %) had undetermined outcomes due to insufficient follow-up data.

Multivariable analysis identified four significant predictors for transfer to public adult specialty care: developmental and/or epileptic encephalopathy; specific developmental disorders (speech, motor, academic); non-neurological comorbidities: asthma, allergies, and obesity; and epilepsy onset near age 16, which typically necessitated transfer due to limited pediatric treatment duration (Table 3).

Following the study period, the statutory age for transfer was raised to 18 years. Of the 189 patients treated at TUH, longitudinal data were available up to age 16 (but not 18) for 39 individuals (21 %), while 150 patients (79 %) were followed through to age 18. Comparative analysis between these two cohorts revealed no significant differences in the predictive variables for transfer.

4. Discussion and conclusions

This population-based study, supported by high-quality national healthcare data [14] demonstrates that three out of four adolescents with epilepsy (76 %) transferred into public, adult, high-level specialty

care. An additional 18 % of AWE were transferred to less specialized adult care – no longer needing care; receiving treatment via local healthcare units; or private adult practice. No prior studies have quantified transfer rates in this patient group. The percentage of transferred adolescents was higher than expected. Our hypothesis was that drug-resistance would be the main, reason for transfer. Our results showed, however, that there are additional reasons, including certain comorbidity, neurodevelopmental issues and recent onset of epilepsy that must be considered. We were not able to reliably divide our patients in terms of whether they were mainly transferred for seizures, comorbidity or their combination. Though not dealt with in the present study, we can speculate that continuation of treatment in the setting of high-level specialty care might be partly influenced by the fact that the pediatric and adult units are geographically close with a high level of collaboration.

While seizures and continued antiseizure therapy are typical reasons for transfer, neurological and non-neurological comorbidity may be as important. Many of our patients with epilepsy had distinct comorbidities, that appeared to have an important influence on transfer.

We did identify a number of variables on multivariable analysis that were associated with transfer to the University Hospital versus settings with less comprehensive neurological care. Some of these variables are well known to be associated with difficult to treat epilepsy, including developmental and epileptic encephalopathies and short periods of seizure remission. Two associated variables were surprising – asthma and obesity.

Both bronchial asthma and obesity are common disorders in childhood and adolescence, as shown in several national population-based studies [e. g. [21]]. According to a population study from Taiwan, epilepsy and asthma are bidirectionally associated with each other [22,23]. Asthma is known to be weakly associated with epilepsy also in children with febrile seizures [24,25]. Our results lend support to those findings. No causative factors are established, but chronic inflammation is central to both conditions [26]. Epilepsy may involve neuroinflammation and then influence systemic immune responses and predispose to asthma. One may also speculate that antiseizure drugs influence immune responses [27]. Epileptic seizures may present with autonomic signs, but it is unknown whether they could influence the brain-lung axis.

Obesity is more common in children with epilepsy than their healthy peers [28]. The worldwide prevalence of childhood and adolescence obesity is estimated 20–25 % and found to be 23.8 % (BMI $\geq$ 95th percentile) by Rifas-Shiman [29]. Causal relationships are unclear, although immune dysfunction has been suggested [26]. Another cause could be antiseizure drugs, such as valproate, carbamazepine, oxcarbazepine, phenytoin, gabapentin, and pregabalin [27]. However, a high frequency of obesity is seen also in children with newly diagnosed, untreated epilepsy [28]. The role of epilepsy as a direct cause of obesity has not been demonstrated, but the ketogenic diet is known to reduce the number of seizures in difficult-to-treat epilepsies and promote weight loss [30]. The mechanism of action may be an impact on neuronal metabolism and neurotransmitter function. Interestingly, metformin, a drug commonly used for diabetes, may also control comorbid epileptic seizures [31]. It is also possible that the influence of obesity and asthma on transfer to the more specialized care offered at University Hospital related to a need for more comprehensive care rather than more complicated epilepsy.

Transfer imposes a considerable medical and economic burden on public adult neurological services. Still, all AWE are initially managed by child neurologists in this country, with post-transfer care provided by adult neurology specialists across outpatient, inpatient, primary, or private sectors. The university municipality health center illustrates an effective model of continuous specialty care. In that municipality, as well as across the country, nearly all child neurologists are based in hospitals. However, it is common and permitted for hospital-affiliated child neurologists to also maintain independent private practices. These offices are typically located within larger private healthcare centers that offer a broad range of specialist services.

The diversity of post-transfer care options in our patients was probably influenced by financial considerations and aligned with the principle of subsidiarity that favors services located geographically close to the patient. Nonetheless, the vast majority were transferred to TUH for complex care.

While literature highlights the importance of the transition process [32], it is still infrequently applied [33] and still fewer studies assess the epidemiology of the transfer itself, especially in chronic neurological conditions like epilepsy [34]. The current study contributes prevalence data and predictive insights for future planning. A recent registry study from Sweden suggested that 22 % of youth with epilepsy were lost to neurologic follow up following transfer to adult medical services. This suggests that transfer is not a guarantee of long-term care [7].

Transfers in our cohort were administratively driven without formal transition programs. Although international transfer ages range from 14 to 25 [35–37], Finland now legally mandates transfer at age 18. Notably, changing the transfer age from 16 to 18 had no significant impact on transfer rates, affirming the robustness of our findings.

Nabbout and Camfield [38] proposed three typologies of transferred AWE: early-onset with multidisciplinary needs, recent-onset with low remission likelihood, and complete remission with comorbidities. These categories resonate with our findings, though limited data prevented full classification.

Our study has limitations. The cohort was identified retrospectively; however, the case finding method was comprehensive and the outcome variable of transfer was reliably identifiable [14]. The study cohort was based on an unselected population from a geographically defined area and defined time period. In addition to medical factors, regional circumstances, such as easy access to specialist services may have affected the transfer rate. Another limitation is that we had no data on medical or social outcome of the patients whose continued care took place beyond the university hospital. Our study focused on the event of transfer only, without information about preceding transition programs that prepared patients for transfer.

In conclusion, adult specialty care systems must be ready to assume responsibility for the majority of children transferring from pediatric services. To optimize care and alleviate burden, targeted attention should naturally be given to patients with drug resistant epilepsy, epileptic encephalopathy and developmental disorders. In addition, further attention could be directed to those with asthma and obesity. These findings offer insights for policy development and resource planning across the continuum of epilepsy care.

CRediT authorship contribution statement

Matti L Sillanpää: Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Vivian Reinhold:** Writing – review & editing, Writing – original draft, Conceptualization. **Leevi Toivonen:** Writing – review & editing, Writing – original draft, Software, Methodology. **Peter R Camfield:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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