Epilepsy in second-generation immigrants


#greatminds
IN OUR WORLD, A STEADY FLOW KEEPS PATIENTS ALIVE.
LET'S TAKE CARE OF IT. TOGETHER.
Driving Excellence in Neurology.
Be part of one of humankind's most ambitious projects to help uncover the workings of the nervous system. EAN connects 45,000 specialists in neurology in 47 countries across Europe. Promoting excellence, cutting-edge science and innovative therapies for a better life for more than 430 million patients in Europe alone. Read more on ean.org
Great Minds.
ean
european academy of neurology

PROFESSOR PER WÄNDELL (Orcid ID : 0000-0001-5169-2965)

Article type : Original Article

Epilepsy in second-generation immigrants: a cohort study of all children up to 18 years of age in Sweden

Corresponding author email id : per.wandell@ki.se

Revised version 24 June 2019

Per Wändell[1]*, Sten Fredrikson[2], Axel C Carlsson[1], Xinjun Li[3], Danijela Gasevic[4,5], Jan Sundquist[3,6,7] and Kristina Sundquist[3,6,7]

[1] Division of Family Medicine and Primary Care, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Huddinge, Sweden

[2] Department of Clinical Neuroscience, Division of Neurology, Karolinska Institutet Huddinge, Stockholm, Sweden

[3] Center for Primary Health Care Research, Lund University, Malmö, Sweden

[4] Usher Institute of Population Health Sciences and Informatics, College of Medicine and Veterinary Medicine, University of Edinburgh, Edinburgh, UK

[5]School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia

[6]Department of Family Medicine and Community Health, Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, USA

[7] Center for Community-based Healthcare Research and Education (CoHRE), Department of Functional Pathology, School of Medicine, Shimane University, Japan

Running title: Epilepsy among immigrants

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ene.14049

*Corresponding author: Tel: (+ 46) 08-52488708
Per Wändell, Division of Family Medicine and Primary Care, NVS Department, Karolinska Institutet, Alfred Nobels Allé 23, SE-141 83 Huddinge, Sweden.

Funding

This work was supported by ALF funding awarded to Jan Sundquist and Kristina Sundquist and by grants from the Swedish Research Council (awarded to Kristina Sundquist), the Swedish Council for Working Life and Social Research (Jan Sundquist).

Abstract

Objective To study association between country of birth and incident epilepsy in second-generation immigrants in Sweden.

Methods Study population included all children (n=4,023,149) aged up to 18 years of age in Sweden. Epilepsy was defined as at least one registered diagnosis of epilepsy in the National Patient Register. The incidence of epilepsy, using individuals with Swedish-born parents as referents, was assessed by Cox regression, expressed in hazard ratios (HRs) and 95% confidence intervals (95% CI). All models were stratified by sex and adjusted for age, geographical residence in Sweden, educational level, marital status, neighbourhood socioeconomic status and comorbid conditions, also using data from the Total Population Register.

Results A total of 26,310 individuals had a registered epilepsy event, i.e. 6.5/1000 (6.6/1000 among boys and 6.3/1000 among girls). After adjustment, the risk of epilepsy was lower than in children of Swedish-born parents. Among girls, the significant HR was 0.85 (95% CI, 0.81-0.88) but in boys only when adjusting also for co-morbidity (HR = 0.96, 0.92-0.99). Among specific immigrant groups, a higher incidence of epilepsy was observed among boys with parents from Turkey and Africa, but not when adjusting for co-morbidity, and a lower risk in many other groups (boys with parents from Latvia, girls with parents from Finland, Iceland, Southern Europe, countries from the former Yugoslavia, and Asia).

Significance: Risk of epilepsy was lower in second-generation immigrant children compared to children with Swedish-born parents, however, with substantial differences between different immigrant groups.

Keywords: epilepsy; gender; second-generation immigrants; incidence; socioeconomic status

Key points:

Among second-generation immigrant children, risk of epilepsy was lower than in children of Swedish-born parents

A higher incidence of epilepsy was observed among boys from Turkey and Africa, but not when adjusting for co-morbidity

Introduction

Epilepsy is one of the most common neurological diseases globally that affects about 50 million people of all ages of which almost 80% live in low- and middle-income countries (WHO) [1]. It is the most frequent chronic neurologic condition in children and, according to a literature summary, the incidence of epilepsy ranges from 41 to 187 per 100,000 person-years [2], being higher in developing countries and especially in rural areas. The prevalence of epilepsy ranges between 3.2-5.5/1000 persons in developed and 3.6-44/1000 persons in developing countries [2]. A review of epilepsy in the Nordic countries reported an incidence of 25 to 82 per 100 000 person-years and the prevalence of active epilepsy in all children ranged from 3.2 to 5.1 per 1 000 inhabitants [3].

There is a lack of studies on the risk of epilepsy in immigrant children although Immigration to Sweden has increased during the last decades; today, around 17% of the Swedish population is foreign-born [4]. An Israeli study that researched the differences over

time in the prevalence of epilepsy in 17-18 year old males observed no significant change in the prevalence of epilepsy between the different countries of birth [5]. In an American study of prematurely born children it was found that first- and second-generation children of immigrants had "comparable or better developmental outcomes than preterm children of US born parents despite socioeconomic disadvantage" [6]. Comparisons between Afro-Americans and Caucasians in the US have showed a higher risk of epilepsy in the ages 5-19 years of age [7]. Besides, the epilepsy patterns seem to be different in different ethnic groups, with a lower rate of generalized epilepsy among African-Americans compared to Caucasians [8], which suggest that "there may be geographical differences in the distribution of epilepsy susceptibility genes and an effect of genetic background on epilepsy phenotype".

There are also different causes and patterns among children compared to adults [9], why preferably epilepsy should be studied separately in children and adults. In children, causes such as cerebral palsy [10], intellectual disability [11, 12], or autism [13], are more common.

Therefore, the aim of this study was to describe the risk of being diagnosed with epilepsy among second-generation immigrants up to 18 years of age in Sweden as compared to Swedish-born individuals with two Swedish-born parents, as well as to compare the specific risk of being diagnosed with epilepsy among specific second-generation immigrant groups.

2. Methods

2.1 Design

The registers used in the present study were the Total Population Register and the National Patient Register. The Total Population Register includes data of all citizens in Sweden, with socio-economic data and country of birth. The National Patient Register includes medical data from hospitals, both in-hospital care and out-care clinics. Subjects aged up to18 years of age were included in the study. The follow-up period ran from January 1, 1998 until

hospitalisation/out-patient treatment of epilepsy at age of diagnosis of 18 years or more, death, emigration or the end of the study period on December 31, 2015, whichever came first. Out-patient diagnoses were included nationwide from 2001 and onwards from specialist care, not primary health care.

2.2 Study population

In total, 4,023,149 individuals were included, out of whom 26,310 individuals had a registered epilepsy event. Our initial intention was to include both first- and second-generation immigrant children. However, the number of first-generation immigrants was too low, so we restricted the study population to second-generation immigrants, i.e. children born in Sweden but with foreign-born parents.

2.3 Outcome variable

Time was calculated from January 1, 1998 until hospitalisation/out-patient treatment of epilepsy (ICD-code G40), death, emigration or the end of the study period on December 31, 2015, whichever came first.

Co-morbidities

We also identified co-morbidities according to ICD-10 for the following diagnoses: Cerebrovascular diseases (I60-69), brain tumor (D32, D33, C70, C71), developmental delay/intellectual disability (F70, F71, F72, F73, F78, F79, F84.2), autism spectrum disorders (F84), cerebral palsy (CP; G80), and head injury (S06, S07, S09.7, S09.8).

2.4 Demographic and socioeconomic variables

The study population was stratified by *sex*.

Age was used as a continuous variable in the analysis.

Educational attainment was categorised as ≤9 years (partial or complete compulsory schooling), 10–12 years (partial or complete secondary schooling) and >12 years (attendance at college and/or university).

Geographic region of residence was included in order to adjust for possible regional differences in hospital admissions and was categorised as (1) large cities, (2) southern Sweden and (3) northern Sweden. Large cities were defined as municipalities with a population of >200,000 and comprised the three largest cities in Sweden: Stockholm, Gothenburg and Malmö.

2.5 Neighbourhood deprivation

Neighbourhood socioeconomic status (SES) The neighbourhood deprivation index was categorized into four groups: more than one standard deviation (SD) below the mean (low deprivation level or high SES), more than one SD above the mean (high deprivation level or low SES), and within one SD of the mean (moderate SES or moderate deprivation level) used as reference group, and also unknown neighbourhood SES.

2.6 Statistical analysis

Cox regression analysis was used for estimating the risk (hazard ratios (HR) with 95% confidence intervals (CI)) of incident epilepsy in different immigrant groups compared to individuals with Swedish-born parents during the follow-up time. All analyses were stratified by sex. Three models were used in our analyses:

Model 1 was adjusted for age and region of residence in Sweden.

Model 2 was as Model 1, but also adjusted for educational level and marital status of the parents, and also neighbourhood SES, to examine to what extent marital status and SES of parents explained the association between country of birth and epilepsy incidence.
Model 3 was constructed as Model 2 with the inclusion of relevant co-morbidities to examine if other diagnoses explained the association between country of birth and epilepsy incidence. The factors being used were included regardless if being statistically significant or not. For Cox regression analyses, we ensured that the proportional hazards assumption was met using individual and global $\chi 2$ tests and examination of Schoenfeld residual plots.

The adjusted population attributable fraction (PAF), or population attributable risk (PAR), was estimated in percent for risk factors as prevalence (%) among cases multiplied by HR-1/HR [14], using adjusted HRs for the different factors. PAF is useful in order to compare the impact of different risk factors on the incidence of the outcome, in this case epilepsy.

3. Results

Characteristics of the study population of the second-generation immigrant children are shown in Table 1. A total of 0.65 % of children were registered with a diagnosis of epilepsy (0.66 % among boys and 0.63 % among girls).

Tables 2 and 3 present the HRs for second-generation immigrant boys and girls compared to boys and girls with Swedish-born parents. For both boys and girls, after adjusting for all confounders (Model 3), the risk of epilepsy was lower in second-generation immigrant children compared to children with Swedish-born parents. However, there were differences in the risk of epilepsy among second-generation immigrant children. Compared to boys of Swedish-born parents (Table 2), the risk of epilepsy was higher in boys from Turkey and Africa (in Models 1 and 2, but not in the fully adjusted Model), but lower in boys with parents born in Latvia. Among boys with parents from Turkey and Africa the rate of

developmental delay was higher in the whole groups, 1.6% and 1.4%, respectively, vs. 0.8% among boys with Swedish-born parents. The risk of epilepsy was also lower in Model 2 for boys with parents from the Nordic countries, or Western Europe, while boys with parents from Iraq only showed a lower risk in the fully adjusted Model. Compared to girls of Swedish-born parents (Table 3), the risk of epilepsy was lower in girls with parents from Finland, Iceland, Southern Europe, former Yugoslavia or Asia.

When looking at registered co-morbid conditions, patterns were similar between boys and girls, and among individuals with foreign-born parents compared to those with Swedish-born parents (Table 1). However, there were higher rates among children with foreign-born parents for developmental delay and cerebral palsy, but lower rates for head injuries. Rates were higher among boys in general for autism spectrum disorders. The most frequent condition was developmental delay (18-25%), followed by CP (9-13%) and autism spectrum disorders (9-14%). Other co-morbid conditions were more infrequent, such as head injuries (5-8%), and brain tumor and stroke (both 1-2%).

We assessed PAFs (Supplementary Table 1), with summarized PAFs for the six comorbidities for the four groups that ranged between 36.7% (girls with Swedish-born parents) and 46.9 % (boys with foreign-born parents). In general, the PAFs were similar to the rates in Table 1. PAFs for boys and girls with foreign-born parents were higher compared to boys and girls with Swedish-born parents as regards developmental delay, 23.0% (95% CI 22.7-23.2) and 21.5% (95% CI 21.3-21.6) vs 18.1% (95% CI 18.0-18.2) and 16.9% (95% CI 16.8-17.0), respectively, and as regards CP, 12.4% (95% CI 12.2-12.5) and 11.4% (95% CI 11.3-11.6) vs 10.1% (95% CI 10.0-10.1) and 8.2% (95% CI 8.1-8.3).

4. Discussion

In this nationwide cohort study of more than 4 million individuals, we found the risk of epilepsy in children (< 18 years of age) to be lower in second-immigration girls compared to girls with Swedish-born parents, while the risk in second-immigration boys was similar to that in boys with Swedish-born parents albeit lower when also adjusting for co-morbidities.

The patterns were different between boys and girls, with a lower risk among girls with foreign-born parents in all statistical models, while for boys with foreign-born parents a higher risk was present in the model adjusted only for age and region of residence, and the lower risk appeared in the model adjusted for co-morbidities. Thus, a marginally increased risk for epilepsy among boys with foreign-born parents seemed to be explained by a lower educational level of the parents and a higher risk of co-morbidities, especially developmental delay. However, the reason for the different gender patterns is unclear.

There are conflicting factors in the health among children to immigrant parents, i.e. the "Healthy Migrant Factor" [15], and the higher risk for adverse birth outcomes for immigrant parents described in Sweden and other developed countries [16]. The concept of the "Healthy Migrant Paradox" implies, that immigrants have comparable or better perinatal health outcomes than natives in many developed countries, despite low socio-economic circumstances in the host country [15, 17]. This "Healthy Migrant" thus might explain the better outcomes among girls to foreign-born parents.

However, the opposite factor, a higher risk of adverse birth outcomes for immigrant parents in Sweden [16], might then be at hand for boys to foreign-born parents. The risk of small-for-gestational age is found to be higher among immigrants in Sweden, especially from South-European, African and Asian countries [18]. The risk of pre-term birth is also higher in immigrants [19]. When looking at potentially causal factors to epilepsy in children, the most common factors were developmental delay, autism spectrum disorders and CP.

Developmental delay and CP were slightly more common with higher PAFs in immigrant boys and girls compared to individuals with Swedish-born parents. As CPs are related to childbirth this could be a sign of more complications to deliveries of foreign-born women, which actually is described especially for women from Africa and to some extent also from the Middle East in Sweden [20]. A Danish study found a similar risk of CP among children immigrant compared to those of Danish-born parents, while the risk of bilateral spastic CP was higher among children of non-Western immigrants, especially for Turkey and Pakistan and of unilateral spastic CP lower [21]. An Australian study found a higher risk of some perinatal outcomes for children of mothers from East Africa [22]. Perinatal outcomes are also more common in low socio-economic areas [23]. Besides, there are also studies showing a higher risk of hospitalization of children with parents originating from some areas, especially sub-Saharan Africa [24].

As regards the two groups among boys showing higher risk of epilepsy, i.e. boys with parents from Turkey and Africa, the finding was not present when adjusting also for co-morbidity. Thus, the excess risk in these groups seems to be mediated or confounded by the listed co-morbidities [8], especially a higher rate of developmental delay compared to boys with Swedish-born parents, also to some extent supported by the earlier studies listed above. In general, male fetus and infants seem to be more sensitive to factors during pregnancy and early childhood than female.

There might also be genetic differences in "the distribution of epilepsy susceptibility genes and an effect of genetic background on epilepsy phenotype" [8]. In our study we could neither confirm nor rebut this owing to lack of genetic data.

There are limitations with this study. We used register data, and had no access to detailed clinical data from medical records, and thus to the epilepsy phenotype. Thus, we lack a validation of the diagnoses, and also of data regarding family history. The quality of Swedish

national registers is generally high [25], even if the diagnosis of epilepsy has not been studied for validity. It is possible that misclassifications with over-diagnosis has been performed. We studied associated co-morbid conditions as probable mediators or confounders. Identified co-morbid conditions may have been underestimated owing to the difficulties to capture all ICD-10 codes, especially in regards to developmental delay. However, from a numerical point of view missed conditions were most probably few. We chose to set the statistical significance limit at $p<0.05$, which may be questioned when analyzing many groups. However, we based the main results on second-generation immigrants general compared to the referent groups, and consider the specific subgroups as secondary and an exploratory approach. From a clinical point of view, on the other hand, it could be questioned to merge all immigrants into a total group, why analyses of the specific groups of country or region of origin is interesting. Our intention was to study both first-generation and second-generation immigrants; however the number of cases in the first-generation study was too low. Despite these limitations, a major strength of this study is the linkage of diagnoses from individual patients to national demographic and socioeconomic data. Besides, as we could use national Swedish data it was possible to analyse individuals from different types of sociodemographic backgrounds. Furthermore, this is the first study to look into this topic.

In conclusion, we found a slightly lower incidence of epilepsy among girls with foreign-born parents compared to girls with Swedish-born parents, while the risk among boys with foreign-born parents was lower compared to boys with Swedish-born parents but only when adjusting for co-morbid conditions. However, among boys, two groups showed a higher incidence, i.e. Turkey and Africa, while many groups, especially among girls, showed a lower risk (boys from Latvia, girls from Finland, Iceland, Southern Europe, countries from the former Yugoslavia, and Asia).

Ethical statement

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. Ethical approvals were obtained from regional boards at Karolinska Institutet and the University of Lund. Informed consent from participants was not obtained, as anonymous data from registers were used.

Disclosure

The authors have no conflict of interest to declare.

Acknowledgements

This work was supported by ALF funding awarded to Jan Sundquist and Kristina Sundquist and by grants from the Swedish Research Council (awarded to Kristina Sundquist).

References:

[1]. WHO. https://www.who.int/news-room/fact-sheets/detail/epilepsy (accessed 8 February 2018.

[2]. Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. *Epileptic Disord*. 2015 **17:** 117-123.

[3]. Syvertsen M, Koht J, Nakken KO. Prevalence and incidence of epilepsy in the Nordic countries. *Tidsskr Nor Laegeforen*. 2015 **135:** 1641-1645.

[4]. Statistics Sweden. Foreign-born persons in Sweden by country of birth, age and sex. Year 2000 - 2015. Statistics Sweden, 2016.

[5]. Farfel A, Green MS, Shochat T, Noyman I, Levy Y, Afek A. Trends in specific morbidity prevalence in male adolescents in Israel over a 50 year period and the impact of recent immigration. *Isr Med Assoc J*. 2007 **9:** 149-152.

[6]. Bediako PT, BeLue R, Hillemeier MM. Immigrant Generational Status and Developmental Problems among Prematurely Born Children. *J Immigr Minor Health*. 2018 **20:** 422-430.

[7]. Haerer AF, Anderson DW, Schoenberg BS. Prevalence and clinical features of epilepsy in a biracial United States population. *Epilepsia*. 1986 **27:** 66-75.

[8]. Friedman D, Fahlstrom R. Racial and ethnic differences in epilepsy classification among probands in the Epilepsy Phenome/Genome Project (EPGP). *Epilepsy Res*. 2013 **107:** 306-310.

[9]. Cowan LD. The epidemiology of the epilepsies in children. *Ment Retard Dev Disabil Res Rev*. 2002 **8:** 171-181.

[10]. Hollung SJ, Vik T, Lydersen S, Bakken IJ, Andersen GL. Decreasing prevalence and severity of cerebral palsy in Norway among children born 1999 to 2010 concomitant with improvements in perinatal health. *Eur J Paediatr Neurol*. 2018.

[11]. Nordin V, Olsson IB, Tomson T. [Epilepsy and comorbid neurodevelopmental disorders]. *Lakartidningen*. 2018 **115**.

[12]. Selassie AW, Wilson DA, Martz GU, Smith GG, Wagner JL, Wannamaker BB. Epilepsy beyond seizure: a population-based study of comorbidities. *Epilepsy Res*. 2014 **108:** 305-315.

[13]. Sundelin HE, Larsson H, Lichtenstein P, *et al.* Autism and epilepsy: A population-based nationwide cohort study. *Neurology*. 2016 **87:** 192-197.

[14]. Miettinen OS. Proportion of disease caused or prevented by a given exposure, trait or intervention. *American journal of epidemiology*. 1974 **99:** 325-332.

[15]. Juarez SP, Ortiz-Barreda G, Agudelo-Suarez AA, Ronda-Perez E. Revisiting the Healthy Migrant Paradox in Perinatal Health Outcomes Through a Scoping Review in a Recent Host Country. *J Immigr Minor Health*. 2017 **19:** 205-214.

[16]. Urquia ML, Qiao Y, Ray JG, Liu C, Hjern A. Birth outcomes of foreign-born, native-born, and mixed couples in Sweden. *Paediatr Perinat Epidemiol*. 2015 **29:** 123-130.

[17]. Juarez SP, Revuelta-Eugercios BA. Exploring the 'Healthy Migrant Paradox' in Sweden. A Cross Sectional Study Focused on Perinatal Outcomes. *J Immigr Minor Health*. 2016 **18:** 42-50.

[18]. Li X, Sundquist K, Sundquist J. Risks of small-for-gestational-age births in immigrants: a nationwide epidemiological study in Sweden. *Scand J Public Health*. 2012 **40:** 634-640.

[19]. Li X, Sundquist J, Sundquist K. Immigrants and preterm births: a nationwide epidemiological study in Sweden. *Matern Child Health J*. 2013 **17:** 1052-1058.

[20]. The National Board of Health and Welfare. Socio-economic factors influence on women and child's health after childbirth (In Swedish). Stockholm: The National Board of Health and Welfare, 2016: 84.
[21]. Petersen TG, Forthun I, Lange T, *et al.* Cerebral palsy among children of immigrants in Denmark and the role of socioeconomic status. *Eur J Paediatr Neurol*. 2019.
[22]. Belihu FB, Davey MA, Small R. Perinatal health outcomes of East African immigrant populations in Victoria, Australia: a population based study. *BMC Pregnancy Childbirth*. 2016 **16:** 86.
[23]. Gudmundsson S, Bjorgvinsdottir L, Molin J, Gunnarsson G, Marsal K. Socioeconomic status and perinatal outcome according to residence area in the city of Malmo. *Acta Obstet Gynecol Scand*. 1997 **76:** 318-323.
[24]. Danielsson N, Ericsson A, Eriksson M, Kallen B, Zetterstrom R. Hospitalization in Sweden of children born to immigrants. *Acta Paediatr*. 2003 **92:** 228-232.
[25]. Ludvigsson JF, Andersson E, Ekbom A, *et al.* External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011 **11:** 450.

Table 1. Population in second-generation and number of cases of epilepsy diagnosis categorized by sex, and by Swedish- or foreign-born parents

	Boys								Girls							
	Swedish-born parents				Foreign-born parents				Swedish-born parents				Foreign-born parents			
	Pop		EP		Pop		EP		Pop		EP		Pop		EP	
	No.	%	No	%	No.	%	No	%	No.	%	No	%	No.	%	No	%
Total population	1477805		10094		591278		3870		1395840		9313		558226		3033	
Educational level																
≤ 9	214903	14.5	1396	13.8	178796	30.2	1072	27.7	203417	14.6	1365	14.7	168413	30.2	833	27.5
10-12	449532	30.4	3517	34.8	126973	21.5	930	24.0	425946	30.5	3279	35.2	120227	21.5	787	25.9
> 12	813370	55.0	5181	51.3	285509	48.3	1868	48.3	766477	54.9	4669	50.1	269586	48.3	1413	46.6
Neighborhood deprivation																
Low	84957	5.7	267	2.6	11164	1.9	32	0.8	80464	5.8	280	3.0	10602	1.9	33	1.1
Middle	254094	17.2	953	9.4	40257	6.8	159	4.1	239838	17.2	929	10.0	38375	6.9	142	4.7
High	51889	3.5	205	2.0	22192	3.8	91	2.4	49413	3.5	208	2.2	20827	3.7	71	2.3
Unknown	1086865	73.5	8669	85.9	517665	87.6	3588	92.7	1026125	73.5	7896	84.8	488422	87.5	2787	91.9
Hospital diagnoses:																
Stroke	1813	0.1	160	1.6	585	0.1	75	1.9	1610	0.1	130	1.4	437	0.1	39	1.3
Brain tumor	1535	0.1	174	1.7	421	0.1	58	1.5	1403	0.1	134	1.4	378	0.1	38	1.3
Developmental delay	12162	0.8	2000	19.8	6189	1.0	973	25.1	8512	0.6	1684	18.1	3698	0.7	692	22.8
Autism spectrum disorders	26699	1.8	1291	12.8	9293	1.6	532	13.7	12752	0.9	876	9.4	3672	0.7	275	9.1
Cerebral palsy	3796	0.3	1108	11.0	1579	0.3	518	13.4	2789	0.2	844	9.1	1135	0.2	379	12.5
Head injury	69992	4.7	798	7.9	17904	3.0	229	5.9	50475	3.6	680	7.3	11960	2.1	152	5.0

Table 2. HR of epilepsy in second-generation male immigrants

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All born with foreign-born parents	**1.05**	**1.01**	**1.09**	1.00	0.96	1.04	**0.96**	**0.92**	**0.99**
Nordica countries	0.98	0.91	1.06	0.95	0.87	1.02	0.98	0.91	1.07
Denmark	1.07	0.90	1.27	1.04	0.88	1.24	1.02	0.86	1.22
Finland	1.01	0.91	1.11	0.97	0.88	1.07	1.02	0.93	1.13
Iceland	0.83	0.52	1.31	0.78	0.49	1.24	0.76	0.48	1.21
Norway	0.86	0.71	1.04	**0.82**	**0.68**	**0.99**	0.87	0.72	1.05
Southern Europe	0.91	0.76	1.09	0.89	0.75	1.07	0.94	0.78	1.12
France	0.99	0.69	1.44	0.98	0.68	1.43	1.05	0.73	1.53
Greece	0.92	0.64	1.32	0.89	0.62	1.27	0.99	0.69	1.42
Italy	0.77	0.49	1.22	0.76	0.48	1.21	0.84	0.53	1.33
Spain	1.00	0.66	1.50	1.01	0.67	1.51	0.94	0.63	1.42
Other Southern Europe	0.85	0.54	1.33	0.82	0.52	1.28	0.82	0.52	1.29
Western Europe	0.87	0.75	1.00	**0.86**	**0.74**	**0.99**	0.89	0.77	1.02
The Netherland	0.85	0.55	1.30	0.83	0.54	1.27	0.90	0.58	1.38
England and Ireland	0.96	0.78	1.18	0.94	0.77	1.16	0.99	0.80	1.22
Germany	0.81	0.63	1.02	0.81	0.63	1.02	0.80	0.63	1.01
Austria	0.88	0.47	1.63	0.90	0.48	1.67	0.97	0.52	1.80
Other Western Europe	0.64	0.33	1.23	0.63	0.33	1.21	0.69	0.36	1.32
Eastern Europe	1.13	1.03	1.23	1.02	0.94	1.12	1.00	0.91	1.09
Bosnia	1.14	0.98	1.33	1.00	0.86	1.16	1.00	0.86	1.17
Yugoslavia	1.08	0.95	1.23	0.98	0.86	1.11	0.93	0.81	1.05
Croatia	0.98	0.53	1.82	0.93	0.50	1.74	0.93	0.50	1.73
Romania	1.20	0.89	1.61	1.18	0.88	1.59	1.25	0.93	1.68
Bulgaria	0.52	0.23	1.16	0.50	0.22	1.10	0.55	0.25	1.23
Other Eastern Europe	**1.48**	**1.14**	**1.92**	**1.39**	**1.07**	**1.81**	**1.32**	**1.02**	**1.71**
Baltic countries	**0.59**	**0.37**	**0.94**	**0.59**	**0.37**	**0.94**	**0.57**	**0.36**	**0.90**
Estonia	0.97	0.54	1.76	0.97	0.54	1.76	0.91	0.50	1.64
Latvia	**0.37**	**0.17**	**0.77**	**0.37**	**0.18**	**0.77**	**0.36**	**0.17**	**0.75**
Central Europe	0.98	0.84	1.14	0.97	0.84	1.13	1.01	0.87	1.18
Poland	0.99	0.83	1.17	0.98	0.82	1.16	1.01	0.85	1.20
Other Central Europe	1.04	0.59	1.83	1.04	0.59	1.84	1.19	0.68	2.10
Hungary	0.92	0.61	1.38	0.92	0.61	1.39	0.98	0.65	1.47
Africa	**1.36**	**1.24**	**1.49**	**1.29**	**1.17**	**1.41**	0.99	0.90	1.09
Northern America	0.84	0.65	1.09	0.83	0.64	1.07	0.83	0.64	1.07
Latin America	1.12	0.97	1.28	1.09	0.95	1.25	1.05	0.92	1.21
Chile	1.15	0.96	1.38	1.12	0.93	1.34	1.11	0.92	1.33
South America	1.08	0.88	1.32	1.05	0.86	1.30	0.99	0.81	1.22
Asia	1.05	0.99	1.12	0.99	0.93	1.05	**0.93**	**0.88**	**0.99**
Turkey	**1.25**	**1.09**	**1.43**	1.16	1.02	1.34	1.06	0.92	1.21
Lebanon	1.04	0.87	1.23	0.96	0.80	1.14	0.95	0.80	1.13
Iran	1.03	0.87	1.20	0.99	0.84	1.16	0.89	0.76	1.04
Iraq	1.07	0.97	1.19	0.98	0.88	1.09	**0.88**	**0.79**	**0.98**
Other Asia countries	0.98	0.89	1.08	0.94	0.85	1.03	0.94	0.85	1.03
Russia	0.97	0.72	1.30	0.95	0.71	1.27	0.90	0.67	1.21

Model 1: adjusted for age; model 2: adjusted for age, educational level, and marital status, and neighborhood deprivation; model 3: model 2 + comorbidities

Table 3. HR of epilepsy in second-generation female immigrants

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All born with foreign-born parents	**0.90**	**0.86**	**0.93**	**0.85**	**0.82**	**0.89**	**0.85**	**0.81**	**0.88**
Nordica countries	0.93	0.86	1.01	**0.89**	**0.81**	**0.96**	0.92	0.85	1.00
Denmark	1.03	0.86	1.24	1.02	0.85	1.23	1.02	0.85	1.22
Finland	0.90	0.81	1.00	**0.84**	**0.75**	**0.94**	**0.88**	**0.79**	**0.98**
Iceland	**0.43**	**0.23**	**0.83**	**0.42**	**0.22**	**0.81**	**0.48**	**0.25**	**0.91**
Norway	1.03	0.86	1.23	0.99	0.83	1.19	1.04	0.87	1.25
Southern Europe	**0.70**	**0.56**	**0.87**	**0.67**	**0.54**	**0.83**	**0.66**	**0.53**	**0.82**
France	0.76	0.49	1.18	0.75	0.49	1.17	0.77	0.49	1.19
Greece	0.75	0.50	1.13	0.69	0.46	1.04	0.73	0.49	1.10
Italy	**0.51**	**0.28**	**0.92**	**0.49**	**0.27**	**0.89**	**0.50**	**0.28**	**0.90**
Spain	0.66	0.39	1.12	0.64	0.38	1.09	**0.53**	**0.31**	**0.89**
Other Southern Europe	0.77	0.47	1.25	0.74	0.46	1.21	0.77	0.47	1.26
Western Europe	0.88	0.76	1.02	0.88	0.76	1.01	0.90	0.78	1.04
The Netherland	0.61	0.36	1.03	0.61	0.36	1.03	0.65	0.38	1.10
England and Ireland	0.83	0.65	1.05	0.81	0.64	1.03	0.90	0.71	1.14
Germany	0.88	0.70	1.12	0.89	0.70	1.12	0.84	0.66	1.06
Austria	1.39	0.84	2.31	1.41	0.85	2.33	1.56	0.94	2.60
Other Western Europe	1.25	0.77	2.05	1.25	0.77	2.05	1.19	0.73	1.94
Eastern Europe	**0.89**	**0.80**	**0.98**	**0.83**	**0.75**	**0.92**	**0.83**	**0.75**	**0.92**
Bosnia	0.95	0.80	1.13	0.87	0.73	1.04	0.92	0.77	1.09
Yugoslavia	**0.83**	**0.71**	**0.96**	**0.77**	**0.67**	**0.90**	**0.75**	**0.64**	**0.87**
Croatia	0.69	0.33	1.45	0.68	0.32	1.42	0.76	0.36	1.59
Romania	0.92	0.65	1.31	0.91	0.64	1.29	0.94	0.66	1.34
Bulgaria	0.56	0.25	1.25	0.55	0.25	1.22	0.52	0.24	1.17
Other Eastern Europe	1.17	0.86	1.61	1.11	0.81	1.52	1.01	0.73	1.38
Baltic countries	0.79	0.52	1.21	0.79	0.51	1.21	0.85	0.55	1.30
Estonia	0.70	0.33	1.46	0.69	0.33	1.46	0.71	0.34	1.50
Latvia	0.85	0.50	1.43	0.84	0.50	1.43	0.93	0.55	1.58
Central Europe	0.86	0.72	1.02	0.84	0.71	1.00	0.84	0.71	1.00
Poland	0.85	0.70	1.03	0.83	0.69	1.01	0.83	0.69	1.01
Other Central Europe	1.12	0.64	1.98	1.13	0.64	1.99	1.16	0.66	2.05
Hungary	0.76	0.47	1.23	0.76	0.47	1.23	0.74	0.46	1.19
Africa	1.03	0.92	1.15	0.97	0.87	1.09	0.95	0.85	1.05
Northern America	0.87	0.67	1.12	0.86	0.66	1.12	0.91	0.71	1.19
Latin America	0.85	0.72	1.00	**0.82**	**0.70**	**0.96**	0.85	0.72	1.00
Chile	0.87	0.70	1.08	0.82	0.66	1.02	0.84	0.68	1.04
South America	0.83	0.65	1.06	0.82	0.64	1.04	0.86	0.68	1.10
Asia	**0.87**	**0.82**	**0.93**	**0.82**	**0.77**	**0.88**	**0.79**	**0.74**	**0.84**
Turkey	0.90	0.76	1.07	**0.81**	**0.68**	**0.96**	**0.71**	**0.60**	**0.84**
Lebanon	0.96	0.79	1.15	0.88	0.73	1.06	0.84	0.70	1.02
Iran	0.87	0.72	1.04	0.85	0.71	1.02	0.84	0.70	1.01
Iraq	0.94	0.84	1.06	0.89	0.79	1.00	**0.82**	**0.73**	**0.92**
Other Asia countries	**0.79**	**0.71**	**0.89**	**0.76**	**0.68**	**0.84**	**0.76**	**0.68**	**0.85**
Russia	0.95	0.69	1.30	0.93	0.68	1.27	0.93	0.68	1.27

Model 1: adjusted for age; model 2: adjusted for age, educational level, and marital status, and neighborhood deprivation; model 3: model 2 + comorbidities