Epilepsy in immigrants and Swedish-born

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Epilepsy in immigrants and Swedish-born: a cohort study of all adults 18 years of age and older in Sweden

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Abstract

Purpose We aimed to study the association between country of birth and incident epilepsy in several immigrant groups using Swedish-born individuals as referents.

Method The study population included all adults aged 18 years and older in Sweden, living and deceased, 6,690,598 in the first-generation and 6,683,125 in the second-generation sub-study. Epilepsy was defined as having at least one registered diagnosis of epilepsy in the National Patient Register. The incidence of epilepsy in different immigrant groups, using Swedish-born as referents, was assessed by Cox regression, expressed as hazard ratios (HRs) and 95% confidence intervals (CI). The models were stratified by sex and adjusted for age, geographical residence in Sweden, educational level, marital status, and neighbourhood socioeconomic status.

Results In the first-generation sub-study, totally 76,541 individuals had at least one registered diagnosis of epilepsy (1.14% in total; men 1.22% and women 1.07 %), and in the second-generation study 72,545 (1.09%; men 1.18% and women 0.99%). After adjusting for confounders, in first-generation immigrants compared to their Swedish-born counterparts the incidence was somewhat lower among both men (HR 0.92, 0.90-0.96) and women (HR 0.93, 0.90-0.96), and in the second-generation immigrants among women (HR 0.95, 0.92-0.99) but not men (HR 0.99; 0.96-1.02). Among immigrant groups, a higher incidence of epilepsy was observed among first-generation women from Africa and Iraq, and second-generation men and women from Bosnia, and women from Finland.

Conclusions: Risk of epilepsy was lower in immigrants in general compared to the Swedish-born population; but with higher incidence in some specific groups.

Keywords: epilepsy; gender; immigrants; neighborhood; socioeconomic status

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]. Epilepsy could affect people in all ages, and with a higher incidence in small children, and in elderly aged 65 years and older [2]. Based on studies from the 1990'ies, unprovoked epileptic seizures among subjects aged 17 years and older has been shown to have an incidence of 56 in 100,000 person-years [3, 4], with a cumulative incidence of unprovoked seizures of 4.6% among those in the ages of 17 and 84 years. A more recent Swedish study, found the crude incidence in all ages for first unprovoked seizures and epilepsy to be 33.9/100,000 person years in the years 2001-2004 [5], and no cause could be identified in most of these incident cases, i.e. 62.4%. A recent Canadian case-control study, aimed to characterize epilepsy in an elderly population, observed that the most common etiology of epilepsy (48%) in this population was unknown [6]. A review of epilepsy in the Nordic countries based on studies between 1966 and 2014 found prevalence of active epilepsy in adults with results ranging from 5.5 to 9.0 per 1 000 inhabitants [7], and an incidence from 24 to 56 per 100 000 person-years. Epilepsy seem to have similar age-adjusted incidence worldwide, with most studies from Europe and the US [2], however with a higher incidence reported from South America according to data from 1992 [8].

As migration worldwide is increasing, Sweden is an ideal setting for studies of epilepsy in immigrants; it is estimated that foreign-born individuals account for approximately 17% of the registered Swedish population in 2015 (data from Statistics Sweden) [9]. In general, the health of immigrants often tends to be better than that of the native population upon arrival to the new country; and the migrating populations seem to be in better health than people remaining in the country of origin; this is known as the "healthy migrant effect" [10]. However, the health of immigrants tends to decline as time goes by in their new home country [11, 12], especially in comparison with the native population.

The literature on epilepsy among immigrant groups is scarce. An Israeli study on males in the years 16-17 years of age in connection to patronage for military service during a period of 50 years concluded, that there was no significant change over the studied period in the prevalence of epilepsy by country of birth [13]. In a study of second-generation immigrant children in Sweden the risk of epilepsy was lower among girls with foreign-born parents compared to children with Swedish-born parents, while the risk among boys was lower only when adjusting for co-morbidity [14]. Thus, further studies on this topic are warranted, both for increased knowledge of this topic overall and for health care planning. As there are different causes and patterns of epilepsy in adults compared to children, with causes such as brain tumor, degenerative disease, stroke, and head injury [6], we restricted this study only to adults, i.e. individuals 18 years of age and older. Therefore, the aim of this study was to examine the risk of being diagnosed with epilepsy among first- and second-generation immigrants in the ages 18 years and older in Sweden as compared to Swedish-born individuals or individuals with two Swedish-born parents, as well as to compare the specific risk of being diagnosed with epilepsy among different immigrant groups.

2. Methods

2.1 Design

The registers used in the present study were the Total Population Register and the National Patient Register. Subjects aged 18 years of age and above 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, 6,690,598 individuals were included in the first-generation study, out of whom 76,541 individuals had a registered epilepsy event. In the second-generation study 6,683,125 individuals were included, with 72,545 with a registered epilepsy event.

2.3 Outcome variable

Time was calculated from January 1, 1998 until hospitalization/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), dementia (F00-F03, F10.7A, G30), head injury (S06, S07, S09.7, S09.8), and alcoholism and related disorders (F10, K70). These conditions were adjusted for in the analyses.

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

Neighborhood socioeconomic status (SES) The neighborhood 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 neighborhood SES.

2.6 Statistical analysis

Continuous variables are presented as mean and standard deviations, and categorical variables are presented as counts and percentages. 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 the Swedish-born population 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 adjusted for age, region of residence in Sweden, educational level, marital status and neighborhood SES, to examine to what extent SES 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. In addition, a sensitivity analysis was performed in which first-generation immigrants moving to Sweden within the last five years of follow-up were excluded, to examine if time in Sweden influenced the results.

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 [15], 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.

We also performed a sensitivity analysis, including patients without epilepsy before 2005, with follow-up between 2005 and 2015.

2.7 Data availability statement

Data could not be shared according to legal and ethical reasons.

3. Results

Characteristics of the study population of the first- and second-generation immigrants are shown in Table 1, with in the first-generation study a total of 1.14 % being registered with a diagnosis of epilepsy (1.22 % among men and 1.07 % among women; Supplementary Table 1), and in the second-generation study 1.09% (1.18% among men and 0.99% among women; Supplementary Table 2). The proportion of immigrants was lower among individuals with epilepsy than in the studied populations. Among co-morbidities, rates were higher among individuals with epilepsy compared to the studied populations for all the included co-morbidities, i.e. stroke, alcoholism and related disorders, head injury, brain tumours and dementia.

Among the co-morbid conditions (Supplementary Tables 3a, 3b, 4a and 4b), stroke was the most common condition, in first-generation study 25-37 %, with higher rates among men and among Swedish-born, and second-generation study 10-24 %, also with higher rates among men and among Swedish-born. Alcoholism and related disorders were also common, with rates between 6 % and 21 %, and being more common in men and in immigrants, both first- and second-generation. The three other co-morbidities, i.e. brain tumor, head injury and

dementia, showed in first-generation study rates of 5-10%, with a slightly increased risk of dementia among Swedish-born. In the second-generation study head injury showed a higher rate, 8-15%, with higher risk among men, and lower rate of dementia, 1.5-4 %, with higher risk among individuals with Swedish-born parents.

Tables 2a and 2b show the HRs of incident epilepsy for male and female immigrants compared to Swedish-born individuals. Compared to Swedish-born individuals, and after adjustment for socio-demographics, neighborhood deprivation and co-morbidities, incidence of epilepsy was lower in immigrant men from Nordic countries, Western Europe, Southern Europe and Central Europe, and in women from Southern Europe, Eastern Europe and Turkey. Higher incidence of epilepsy than that in Swedish-born population was observed in women from Africa, Iraq and Poland; and in men from Finland (however, only in model 2, i.e. with adjustment for socio-demographic factors but not co-morbidity).

Tables 3a and 3b show the HRs for second-generation immigrants with men and women, with slightly lower HRs in the females with foreign-born parents compared to those with Swedish-born parents, but with no significantly different HR among men. Only few groups showed higher HRs, i.e. men from Finland but only in model 1, and from Bosnia in models 2 and 3; and women from Finland and Bosnia in all three models. Many groups showed lower HRs, i.e. men from Southern Europe, and from Western Europe but not in model 3; and women from Iceland and Norway in Nordic countries, UK and Ireland, former Yugoslavia (except Bosnia), from Northern America and Asia.

We also assessed PAFs (Supplementary Tables 5a and 5b), with summarized PAFs for the five comorbidities for the four groups for the first-generation immigrants that ranged between 42.9% (foreign-born women) and 59.2 % (Swedish-born men), and in the second-generation immigrants between 27.9 % (women with foreign-born parents) and 48.6 % (men with Swedish-born parents). In the first-generation immigrants the PAFs of dementia were lowest,

and ranged between 3.4 % (foreign-born men) and 5.0 % (Swedish-born women); for head injuries from 4.6 % (foreign-born women) to 6.7 % (Swedish-born men); for brain tumors 6.5 % (foreign-born women) to 8.4 % (Swedish-born women); for alcoholism and related disorders 4.5 % (Swedish-born women) to 12.8 % (foreign-born men); and for stroke 21.8 % (foreign-born women) to 30.2 % (Swedish-born men). In the second-generation samples the corresponding PAFs of dementia were 1.0 % (women with foreign-born parents) to 2.4 % (women with Swedish-born parents); for head injuries 5.7 % (women with Swedish- and foreign-born parents) to 9.3 % (men with foreign-born parents); for brain tumors 6.1 % (men with foreign-born parents) to 8.3 % (women with Swedish-born parents); for alcoholism and related disorders 5.9 % (women with Swedish-born parents) to 14.0 % (men with foreign-born parents); and for stroke 8.1 % (women with foreign-born parents) to 19.2 % (men with Swedish-born parents).

The sensitivity analysis included patients without epilepsy before 2005, and with incident cases during follow-up 2005-2015 (Supplementary Tables 6a, 6b, 7a and 7b). Results were similar as in the primary analysis, although some estimates were non-significant, and with lower HRs among second-generation men and women with parents from Bosnia (Supplementary Tables 7a and 7b).

4. Discussion

In this nationwide cohort study of more than 6 million individuals aged 18 years and older in the respective sub-studies of first- and second-generation immigrants, we analyzed the risk of epilepsy among immigrants in Sweden. After adjustment for socio-demographics, neighbourhood deprivation and comorbidities, we observed a lower risk of epilepsy in general among first-generation male and female immigrants compared to Swedish-born. However,

some groups were at increased risk, such as first-generation women from Africa, Iran and Iraq, and second-generation women from Finland and Bosnia, and second-generation men from Bosnia.

There are no similar studies analyzing epilepsy risk in immigrants. The earlier cited Israeli study found no significant difference in the prevalence of epilepsy between foreign-born individuals compared to individuals born in Israel [13].

Regarding differences between Swedish-born and foreign-born individuals, or in the second-generation study between individuals with Swedish-born parents and individuals with foreign-born parents, for co-morbidities, or possible causal conditions, we observed the lower rates and PAFs of stroke in especially second-generation immigrants and to some extent also in first-generation immigrants. On the other hand, the PAFs of alcoholism and related disorders were higher among the immigrant groups compared to Swedish-born or individuals with Swedish-born parents. The Finnish group in Sweden has been the largest until recent years, and in general been associated with worse health [16], and higher rate alcohol related morbidity [17], with side effects that include epilepsy. However, the excess risk in second-generation women from Finland was marginal.

Regarding findings in the second-generation study, with higher risks in the Finnish and Bosnian groups this is a special finding. The Bosnian group has also been shown to exhibit higher rates of other diseases, such as atrial fibrillation [18], a known risk factor for stroke and thus also for epilepsy. Besides, owing to the earlier war in Bosnia, the rate of refugees within the group is rather high, as among immigrants from Iran and Iraq [19].

The risk was found to be lower in many groups, and the PAFs for stroke were indeed lower in general among immigrants, especially in the second-generation study. In contrast to the Finnish group, immigrants from non-European countries, especially from the Middle East region, have lower rates of hypertension [20, 21]. Besides, dietary factors could be of

importance for the development of cardiovascular diseases, and of dementia. For instance, the Mediterranean diet in the South European countries is associated with a lower risk of CHD [22], AF [23], and dementia [24]. Besides, the "healthy migrant" effect, i.e. that the migrating populations in general exhibit a better health than those of the same populations remaining in the country of origin, could be of importance when interpreting the low risk in many groups [25]. However, a Danish study concluded that the healthy migrant hypothesis should be used with caution when interpreting results [26]. Despite this objection, when looking at the low risks among many immigrant groups, it is tempting to ascribe the healthy migrant effect an important role for many migrants, e.g. Nordic countries, Western Europe, Southern Europe and Central Europe.

In the clinical situation it is of importance to pay attentions to immigrant groups with a higher risk of epilepsy, i.e. first-generation women from Africa, Iran and Iraq, and second-generation men and women from Bosnia.

Regarding SES, we found a lower rate of higher educational level among individuals with incident epilepsy. In general, low SES is associated with higher risk of epilepsy [27, 28]. However, this association might go in both directions, as presence of epilepsy in early adult life may also have a negative effect on higher education and employment. Many immigrant groups do have lower SES, which then might affect the epilepsy risk. However, adjusting for socio-economic factors only affected the estimates marginally, except for immigrants from Bosnia, with markedly increased estimates among first-generation men and second-generation men and women after adjustment for the socio-economic factors.

Regarding co-morbidities, stroke was very common with PAFs of 25-30% in the first-generation study, confirming the high risk of this association [29, 30]. In contrast, dementia showed low PAFs of 3-5%, this in line with figures from the Swedish Dementia Register [31].

There are limitations with this study. We chose to set the statistical significance limit at $p<0.05$, with the risk of over-interpreting results owing to mass significance. This should be in mind when looking at the different sub-groups of immigrants, and we recommend that results from the specific subgroups are interpreted as secondary, and rather with an exploratory approach. From a clinical point of view, on the other hand, considering the differences between the sub-groups of immigrants, it could be questioned to merge all immigrants into a large group, why analyses of the specific groups of country or region of origin is interesting. Identified co-morbid conditions may have been underestimated owing to the possibility to capture all ICD-10 codes. Our intention was to study both first-generation and second-generation immigrants, but 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 men and women from different types of sociodemographic backgrounds.

In conclusion, we found a lower incidence of epilepsy among first-generation men and women compared to Swedish-born, and a slightly lower incidence among second-generation women with foreign-born parents compared to women with Swedish-born parents. However, some groups showed a higher incidence, i.e. first-generation women from Africa, Iran and Iraq, and second-generation men and women from Finland and Bosnia. In the clinical situation these groups may of interest for special attention or more thorough investigation.

Ethics

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.

Disclosures

The authors have no conflict of interest to disclose.

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Table 1. Baseline characteristics and incident cases of epilepsy in the study population

	First generation individuals				Second generation individuals			
	Population		Epilepsy		Population		Epilepsy	
	No.	%	No	%	No.	%	No	%
Total population	6690598		76541		6683125		72545	
Gender								
Males	3171225	47.4	38803	50.7	3410329	51.0	40159	55.4
Females	3519373	52.6	37738	49.3	3272796	49.0	32386	44.6
Immigrant status*								
Swedish	5513793	82.4	67350	88.0	5560476	83.2	63160	87.1
Foreign born	1176805	17.6	9191	12.0	1122649	16.8	9385	12.9
Educational level								
≤ 9	2095474	31.3	28775	37.6	1579989	23.6	24184	33.3
10-12	1641090	24.5	21461	28.0	1477290	22.1	20315	28.0
> 12	2954034	44.2	26305	34.4	3625846	54.3	28046	38.7
Region of residence								
Large cities	2116866	31.6	28864	37.7	2047052	30.6	26514	36.5
Southern Sweden	2762397	41.3	33695	44.0	2653725	39.7	31961	44.1
Northern Sweden	1811335	27.1	13982	18.3	1982348	29.7	14070	19.4
Marital status								
Married	4928688	73.7	56519	73.8	4527759	67.7	44877	61.9
Not married	1761910	26.3	20022	26.2	2155366	32.3	27668	38.1
Neighborhood deprivation								
Low	916278	13.7	10584	13.8	939435	14.1	10145	14.0
Middle	3114607	46.6	37950	49.6	2978271	44.6	35769	49.3
High	738273	11.0	9639	12.6	684247	10.2	9475	13.1
Unknown	1921440	28.7	18368	24.0	2081172	31.1	17156	23.6
Hospital diagnosis of alcoholism	164450	2.5	8189	10.7	221323	3.3	9820	13.5
Hospital diagnosis of stroke	435236	6.5	25747	33.6	173633	2.6	14616	20.1
Hospital diagnosis of brain tumor	38630	0.6	6134	8.0	31096	0.5	5785	8.0
Hospital diagnosis of head injury	176592	2.6	7887	10.3	207366	3.1	8092	11.2
Hospital diagnosis of dementia	174094	2.6	6976	9.1	37262	0.6	2686	3.7

*Immigrant status in the second-generation individuals based on the country of birth in parents.

Table 2a. The results of Cox-regression analyses with Hazard Ratios (HRs) estimating the risk of incident epilepsy in first-generation male immigrants compared to Swedish-born population

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All foreign-born	**0.86**	**0.83**	**0.88**	**0.91**	**0.88**	**0.94**	**0.92**	**0.90**	**0.96**
Nordic countries	**0.94**	**0.89**	**0.98**	0.96	0.91	1.00	**0.91**	**0.87**	**0.96**
Denmark	**0.76**	**0.67**	**0.86**	**0.77**	**0.68**	**0.87**	**0.82**	**0.73**	**0.93**
Finland	1.04	0.99	1.11	**1.07**	**1.01**	**1.13**	0.96	0.91	1.02
Iceland	**0.58**	**0.37**	**0.89**	**0.63**	**0.41**	**0.98**	0.74	0.47	1.14
Norway	**0.70**	**0.60**	**0.81**	**0.72**	**0.63**	**0.84**	**0.77**	**0.67**	**0.89**
Southern Europe	**0.45**	**0.38**	**0.52**	**0.47**	**0.40**	**0.55**	**0.62**	**0.52**	**0.73**
France	**0.49**	**0.31**	**0.79**	**0.55**	**0.34**	**0.89**	**0.61**	**0.38**	**0.99**
Greece	**0.30**	**0.22**	**0.41**	**0.32**	**0.23**	**0.44**	**0.45**	**0.33**	**0.62**
Italy	**0.60**	**0.45**	**0.78**	**0.63**	**0.48**	**0.83**	0.81	0.62	1.06
Spain	**0.52**	**0.35**	**0.77**	**0.55**	**0.37**	**0.82**	0.69	0.46	1.03
Other Southern Europe	**0.48**	**0.29**	**0.80**	**0.49**	**0.29**	**0.81**	0.61	0.37	1.01
Western Europe	**0.75**	**0.68**	**0.83**	**0.81**	**0.73**	**0.90**	**0.87**	**0.78**	**0.96**
The Netherlands	0.83	0.59	1.17	0.92	0.65	1.30	1.11	0.79	1.58
UK and Ireland	**0.80**	**0.65**	**0.98**	0.89	0.73	1.09	0.90	0.73	1.10
Germany	**0.74**	**0.64**	**0.85**	**0.79**	**0.69**	**0.92**	**0.85**	**0.74**	**0.98**
Austria	**0.72**	**0.53**	**0.97**	0.77	0.57	1.04	0.77	0.56	1.04
Other Western Europe	**0.55**	**0.32**	**0.93**	0.62	0.36	1.04	0.77	0.46	1.30
Eastern Europe	**0.86**	**0.79**	**0.93**	0.93	0.85	1.01	0.94	0.86	1.02
Bosnia	1.06	0.90	1.26	**1.35**	**1.14**	**1.60**	1.18	0.99	1.40
Yugoslavia	**0.82**	**0.73**	**0.92**	**0.85**	**0.76**	**0.95**	**0.88**	**0.79**	**0.99**
Croatia	0.74	0.48	1.14	0.74	0.48	1.15	0.84	0.54	1.30
Romania	**0.62**	**0.44**	**0.89**	**0.67**	**0.47**	**0.95**	**0.69**	**0.48**	**0.98**
Bulgaria	0.58	0.30	1.11	0.63	0.33	1.21	0.72	0.37	1.38
Other Eastern Europe	1.06	0.75	1.51	1.19	0.83	1.69	1.21	0.85	1.72
Baltic countries	0.87	0.70	1.09	0.93	0.75	1.17	0.84	0.67	1.05
Estonia	0.88	0.68	1.12	0.93	0.72	1.19	0.82	0.64	1.05
Latvia	0.84	0.51	1.40	0.95	0.57	1.58	0.94	0.57	1.56
Central Europe	**0.76**	**0.67**	**0.86**	**0.79**	**0.70**	**0.90**	**0.82**	**0.72**	**0.93**
Poland	0.85	0.72	1.01	0.90	0.76	1.07	0.90	0.76	1.07

Other Central Europe	**0.58**	**0.40**	**0.83**	**0.61**	**0.43**	**0.88**	**0.68**	**0.47**	**0.97**
Hungary	**0.71**	**0.56**	**0.89**	**0.73**	**0.58**	**0.91**	**0.76**	**0.60**	**0.96**
Africa	1.04	0.92	1.18	**1.15**	**1.01**	**1.31**	**1.13**	**1.00**	**1.29**
Northern America	0.63	0.49	0.80	0.70	0.55	0.90	0.79	0.62	1.01
Latin America	**0.76**	**0.65**	**0.89**	**0.79**	**0.68**	**0.92**	0.90	0.77	1.05
Chile	0.85	0.71	1.02	0.87	0.72	1.05	0.99	0.82	1.19
South America	**0.62**	**0.47**	**0.81**	**0.67**	**0.51**	**0.88**	**0.76**	**0.58**	**0.99**
Asia	0.93	0.87	0.99	1.01	0.95	1.08	1.09	1.02	1.16
Turkey	**0.80**	**0.68**	**0.94**	**0.84**	**0.71**	**0.99**	0.90	0.77	1.06
Lebanon	1.19	0.98	1.44	**1.21**	**1.00**	**1.46**	**1.41**	**1.16**	**1.70**
Iran	0.96	0.84	1.10	1.03	0.90	1.18	**1.20**	**1.05**	**1.37**
Iraq	1.06	0.93	1.21	**1.27**	**1.11**	**1.45**	**1.19**	**1.05**	**1.37**
Other Asia countries	**0.83**	**0.74**	**0.94**	0.91	0.80	1.03	0.97	0.86	1.10
Russia	0.85	0.62	1.17	0.94	0.69	1.30	0.89	0.65	1.23

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

Table 2b. The results of Cox-regression analyses with Hazard Ratios (HRs) estimating the risk of incident epilepsy in first-generation female immigrants compared to Swedish-born population

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All foreign-born	**0.91**	**0.88**	**0.94**	**0.91**	**0.88**	**0.94**	**0.93**	**0.90**	**0.96**
Nordic countries	0.95	0.91	1.00	**0.94**	**0.90**	**0.98**	**0.94**	**0.90**	**0.98**
Denmark	0.91	0.80	1.03	0.89	0.78	1.01	0.95	0.84	1.08
Finland	0.96	0.91	1.01	0.95	0.90	1.00	**0.93**	**0.88**	**0.98**
Iceland	0.69	0.46	1.04	0.68	0.45	1.03	0.85	0.56	1.28
Norway	1.00	0.90	1.12	0.98	0.88	1.10	0.99	0.89	1.11
Southern Europe	**0.54**	**0.45**	**0.66**	**0.53**	**0.44**	**0.65**	**0.68**	**0.56**	**0.83**
France	0.95	0.63	1.43	1.03	0.68	1.55	1.21	0.80	1.82
Greece	**0.35**	**0.24**	**0.50**	**0.33**	**0.22**	**0.48**	**0.46**	**0.31**	**0.67**
Italy	**0.46**	**0.28**	**0.74**	**0.47**	**0.29**	**0.75**	**0.60**	**0.37**	**0.96**
Spain	**0.59**	**0.36**	**0.98**	**0.60**	**0.36**	**0.99**	0.69	0.41	1.14
Other Southern Europe	0.93	0.59	1.48	0.88	0.56	1.40	0.95	0.60	1.52
Western Europe	**0.74**	**0.66**	**0.83**	**0.77**	**0.69**	**0.86**	**0.81**	**0.72**	**0.91**
The Netherlands	0.97	0.65	1.45	1.04	0.70	1.56	1.08	0.72	1.61
UK and Ireland	**0.45**	**0.32**	**0.65**	**0.47**	**0.33**	**0.68**	**0.58**	**0.40**	**0.84**
Germany	**0.81**	**0.70**	**0.93**	**0.85**	**0.74**	**0.97**	**0.85**	**0.74**	**0.98**
Austria	**0.44**	**0.27**	**0.73**	**0.46**	**0.28**	**0.76**	**0.45**	**0.27**	**0.75**
Other Western Europe	0.95	0.59	1.52	1.03	0.64	1.65	1.26	0.78	2.03
Eastern Europe	**0.78**	**0.71**	**0.86**	**0.78**	**0.70**	**0.86**	**0.82**	**0.74**	**0.91**
Bosnia	0.91	0.76	1.10	1.02	0.84	1.22	1.03	0.86	1.24
Yugoslavia	**0.75**	**0.66**	**0.86**	**0.71**	**0.62**	**0.82**	**0.76**	**0.67**	**0.87**
Croatia	0.79	0.49	1.27	0.76	0.47	1.22	0.88	0.54	1.41
Romania	**0.53**	**0.36**	**0.78**	**0.56**	**0.38**	**0.82**	**0.58**	**0.39**	**0.85**
Bulgaria	0.70	0.38	1.30	0.76	0.41	1.40	0.83	0.45	1.54
Other Eastern Europe	0.97	0.66	1.43	0.92	0.63	1.35	0.95	0.65	1.40
Baltic countries	0.86	0.68	1.07	0.93	0.74	1.16	0.82	0.65	1.02
Estonia	0.81	0.63	1.06	0.87	0.67	1.13	0.76	0.59	0.99
Latvia	0.99	0.65	1.53	1.12	0.73	1.72	1.03	0.67	1.58
Central Europe	0.98	0.88	1.09	1.02	0.91	1.13	1.04	0.93	1.16
Poland	1.11	0.98	1.26	**1.14**	**1.01**	**1.30**	**1.17**	**1.03**	**1.33**
Other Central Europe	0.47	0.30	0.73	0.50	0.32	0.78	0.54	0.35	0.83
Hungary	0.90	0.70	1.15	0.93	0.73	1.19	0.95	0.74	1.21

Africa	**1.27**	**1.10**	**1.46**	**1.25**	**1.08**	**1.43**	**1.31**	**1.14**	**1.51**
Northern America	**0.72**	**0.56**	**0.93**	**0.77**	**0.59**	**0.99**	0.86	0.67	1.10
Latin America	1.06	0.92	1.21	1.05	0.92	1.21	1.13	0.99	1.30
Chile	1.04	0.86	1.25	1.00	0.84	1.21	1.10	0.91	1.32
South America	1.08	0.88	1.33	1.13	0.92	1.39	1.19	0.97	1.46
Asia	**0.92**	**0.86**	**0.99**	**0.91**	**0.85**	**0.98**	0.96	0.89	1.03
Turkey	**0.67**	**0.55**	**0.82**	**0.60**	**0.49**	**0.74**	**0.64**	**0.53**	**0.79**
Lebanon	1.06	0.84	1.34	0.97	0.77	1.23	1.03	0.82	1.31
Iran	1.10	0.94	1.28	1.15	0.98	1.33	**1.24**	**1.06**	**1.44**
Iraq	**1.15**	**1.00**	**1.32**	**1.19**	**1.03**	**1.38**	**1.19**	**1.03**	**1.37**
Other Asia countries	**0.83**	**0.74**	**0.93**	**0.82**	**0.74**	**0.92**	**0.87**	**0.78**	**0.97**
Russia	0.87	0.68	1.11	0.96	0.75	1.23	0.93	0.72	1.19

Model 1: adjusted for age and region of residence in Sweden; model 2: adjusted for age, region of residence in Sweden, educational level, and marital status; model 3: model 2 + neighborhood deprivation.

Table 3a. The results of Cox-regression analyses with Hazard Ratios (HRs) estimating the risk of incident epilepsy in second-generation male immigrants compared to men with Swedish-born parents

	Men								
	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All born by foreign-born parents	0.99	0.96	1.02	0.98	0.95	1.01	0.99	0.96	1.02
Nordic countries	1.07	1.03	1.11	1.01	0.97	1.05	1.01	0.97	1.05
Denmark	1.00	0.91	1.10	0.94	0.86	1.04	1.00	0.91	1.09
Finland	**1.10**	**1.05**	**1.16**	1.04	0.99	1.09	1.01	0.97	1.06
Iceland	0.53	0.31	0.92	0.50	0.29	0.87	0.58	0.33	0.99
Norway	1.03	0.94	1.12	0.99	0.91	1.08	1.02	0.93	1.11
Southern Europe	**0.72**	**0.62**	**0.84**	**0.69**	**0.60**	**0.81**	**0.76**	**0.65**	**0.89**
France	**0.58**	**0.36**	**0.92**	**0.60**	**0.38**	**0.95**	**0.62**	**0.39**	**0.98**
Greece	**0.70**	**0.54**	**0.90**	**0.65**	**0.50**	**0.84**	**0.76**	**0.59**	**0.99**
Italy	0.82	0.63	1.08	0.80	0.61	1.05	0.89	0.68	1.16
Spain	0.76	0.52	1.11	0.73	0.50	1.06	0.71	0.49	1.03
Other Southern Europe	0.68	0.39	1.16	0.65	0.38	1.12	0.69	0.40	1.19
Western Europe	**0.85**	**0.78**	**0.93**	**0.87**	**0.80**	**0.95**	0.96	0.88	1.06
The Netherlands	0.94	0.67	1.32	0.96	0.69	1.36	1.06	0.75	1.49
UK and Ireland	**0.74**	**0.58**	**0.96**	**0.76**	**0.59**	**0.98**	0.83	0.64	1.07
Germany	**0.89**	**0.80**	**0.99**	0.90	0.81	1.01	1.01	0.91	1.13
Austria	0.76	0.57	1.02	0.78	0.58	1.04	0.84	0.63	1.12
Other Western Europe	0.81	0.51	1.28	0.84	0.53	1.34	0.90	0.57	1.43
Eastern Europe	0.99	0.89	1.10	1.06	0.95	1.18	1.09	0.98	1.22
Bosnia	1.16	0.92	1.46	**1.74**	**1.37**	**2.20**	**1.67**	**1.32**	**2.11**
Yugoslavia	0.93	0.81	1.06	0.94	0.82	1.07	0.97	0.85	1.11
Croatia	0.63	0.30	1.32	0.64	0.30	1.34	0.67	0.32	1.40
Romania	1.14	0.78	1.65	1.19	0.82	1.72	1.25	0.86	1.81
Bulgaria	1.23	0.66	2.29	1.31	0.71	2.44	1.37	0.74	2.55
Other Eastern Europe	1.17	0.61	2.25	1.28	0.66	2.45	1.33	0.69	2.56
Baltic countries	0.87	0.73	1.02	0.92	0.77	1.08	0.94	0.79	1.11
Estonia	0.89	0.75	1.07	0.94	0.79	1.12	0.95	0.79	1.14
Latvia	0.72	0.44	1.15	0.77	0.48	1.24	0.85	0.53	1.37
Central Europe	0.91	0.80	1.04	0.92	0.81	1.05	0.93	0.82	1.06
Poland	1.00	0.84	1.19	1.03	0.87	1.23	1.02	0.86	1.21

Other Central Europe	0.84	0.60	1.16	0.86	0.62	1.19	0.89	0.64	1.24
Hungary	0.80	0.62	1.02	0.78	0.61	1.00	0.80	0.63	1.03
Africa	1.13	0.94	1.36	1.19	0.99	1.44	1.11	0.92	1.34
Northern America	0.90	0.76	1.06	0.94	0.79	1.11	0.96	0.81	1.14
Latin America	0.95	0.79	1.14	0.92	0.76	1.10	0.91	0.75	1.09
Chile	0.85	0.66	1.09	0.80	0.62	1.03	0.79	0.61	1.01
South America	1.10	0.83	1.45	1.12	0.85	1.48	1.13	0.85	1.49
Asia	0.99	0.91	1.09	1.03	0.94	1.12	1.03	0.95	1.13
Turkey	0.90	0.75	1.07	**0.83**	**0.69**	**0.99**	0.86	0.72	1.03
Lebanon	1.07	0.81	1.40	1.07	0.81	1.40	1.06	0.81	1.39
Iran	1.13	0.93	1.39	**1.22**	**1.00**	**1.50**	1.21	0.99	1.48
Iraq	**1.29**	**1.06**	**1.57**	**1.58**	**1.30**	**1.92**	**1.49**	**1.22**	**1.81**
Other Asia countries	**0.83**	**0.70**	**0.99**	0.87	0.73	1.04	0.89	0.75	1.06
Russia	0.97	0.74	1.28	1.01	0.77	1.33	0.98	0.75	1.29

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

Table 3b. The results of Cox-regression analyses with Hazard Ratios (HRs) estimating the risk of incident epilepsy in second-generation female immigrants compared to women with Swedish-born parents

	Model 1			Model 2			Model 3		
	HR	95% CI		HR	95% CI		HR	95% CI	
Sweden	1			1			1		
All born by foreign-born parents	**0.96**	**0.93**	**0.99**	**0.93**	**0.89**	**0.96**	**0.95**	**0.92**	**0.99**
Nordica countries	1.03	0.99	1.07	0.99	0.95	1.03	1.00	0.96	1.05
Denmark	1.04	0.94	1.15	0.94	0.84	1.04	0.97	0.88	1.08
Finland	**1.07**	**1.02**	**1.13**	**1.05**	**1.00**	**1.11**	**1.06**	**1.00**	**1.11**
Iceland	**0.49**	**0.27**	**0.89**	**0.40**	**0.22**	**0.73**	**0.47**	**0.26**	**0.85**
Norway	**0.90**	**0.81**	**1.00**	**0.86**	**0.77**	**0.95**	**0.88**	**0.79**	**0.98**
Southern Europe	**0.75**	**0.64**	**0.88**	**0.70**	**0.60**	**0.83**	**0.79**	**0.67**	**0.93**
France	0.78	0.51	1.20	0.79	0.51	1.21	0.86	0.56	1.32
Greece	**0.70**	**0.53**	**0.92**	**0.63**	**0.47**	**0.83**	**0.74**	**0.56**	**0.98**
Italy	**0.67**	**0.48**	**0.93**	**0.65**	**0.46**	**0.91**	**0.70**	**0.50**	**0.99**
Spain	0.83	0.56	1.22	0.80	0.54	1.18	0.86	0.58	1.27
Other Southern Europe	1.03	0.66	1.61	0.88	0.56	1.38	0.95	0.61	1.49
Western Europe	**0.88**	**0.80**	**0.97**	**0.90**	**0.82**	**0.99**	0.97	0.88	1.07
The Netherlands	0.69	0.44	1.06	0.68	0.44	1.05	0.75	0.49	1.17
UK and Ireland	**0.61**	**0.46**	**0.82**	**0.60**	**0.45**	**0.81**	**0.64**	**0.48**	**0.86**
Germany	1.00	0.89	1.12	1.02	0.91	1.15	1.11	0.99	1.24
Austria	0.76	0.55	1.05	0.80	0.58	1.10	0.83	0.60	1.15
Other Western Europe	0.79	0.48	1.31	0.82	0.49	1.35	0.92	0.55	1.53
Eastern Europe	0.94	0.84	1.05	0.91	0.81	1.02	0.96	0.85	1.07
Bosnia	**1.26**	**1.00**	**1.59**	**1.50**	**1.19**	**1.89**	**1.55**	**1.23**	**1.95**
Yugoslavia	**0.84**	**0.73**	**0.97**	**0.78**	**0.67**	**0.90**	**0.82**	**0.70**	**0.95**
Croatia	0.65	0.31	1.37	0.61	0.29	1.29	0.66	0.31	1.38
Romania	1.24	0.85	1.80	1.21	0.83	1.77	1.30	0.89	1.89
Bulgaria	0.69	0.29	1.65	0.67	0.28	1.61	0.74	0.31	1.78
Other Eastern Europe	1.01	0.48	2.11	0.87	0.41	1.82	0.96	0.46	2.01
Baltic countries	1.02	0.86	1.21	1.11	0.93	1.33	1.15	0.97	1.37
Estonia	1.03	0.85	1.25	1.12	0.93	1.35	1.16	0.96	1.39
Latvia	0.94	0.59	1.50	1.06	0.67	1.68	1.15	0.72	1.82
Central Europe	1.00	0.87	1.14	0.97	0.85	1.11	0.98	0.86	1.12
Poland	1.12	0.94	1.33	1.07	0.90	1.28	1.08	0.90	1.28
Other Central Europe	0.78	0.54	1.13	0.77	0.53	1.12	0.84	0.58	1.22

Hungary	0.90	0.70	1.17	0.88	0.68	1.14	0.88	0.68	1.14
Africa	0.99	0.81	1.21	0.93	0.76	1.14	0.91	0.75	1.12
Northern America	**0.70**	**0.56**	**0.86**	**0.70**	**0.56**	**0.86**	**0.72**	**0.58**	**0.89**
Latin America	0.98	0.81	1.18	0.89	0.74	1.08	0.89	0.74	1.08
Chile	0.93	0.73	1.19	0.84	0.66	1.07	0.83	0.65	1.07
South America	1.05	0.78	1.41	0.99	0.73	1.33	1.00	0.74	1.35
Asia	**0.80**	**0.72**	**0.89**	**0.75**	**0.68**	**0.83**	**0.78**	**0.71**	**0.87**
Turkey	**0.76**	**0.62**	**0.94**	**0.70**	**0.57**	**0.86**	**0.76**	**0.62**	**0.93**
Lebanon	**0.70**	**0.50**	**0.99**	**0.61**	**0.44**	**0.86**	**0.64**	**0.46**	**0.90**
Iran	1.10	0.89	1.37	1.06	0.86	1.32	1.06	0.86	1.32
Iraq	0.77	0.60	1.00	**0.76**	**0.59**	**0.99**	0.79	0.61	1.02
Other Asia countries	**0.72**	**0.59**	**0.87**	**0.68**	**0.56**	**0.82**	**0.71**	**0.58**	**0.86**
Russia	0.93	0.68	1.27	0.96	0.70	1.31	0.93	0.68	1.26

Model 1: adjusted for age and region of residence in Sweden; model 2: adjusted for age, region of residence in Sweden, educational level, and marital status; model 3: model 2 + neighborhood deprivation.