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Original Article

Incidence of First-Episode Status Epilepticus and Risk Factors in Ontario, Canada

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ABSTRACT: ***Background:*** Status epilepticus (SE) is a neurological emergency characterized by prolonged seizures. However, the incidence of first-episode SE is unclear, as estimates vary greatly among studies. Additionally, SE risk factors have been insufficiently explored. Therefore, the objectives of this study were to estimate the incidence of first-episode SE in Ontario, Canada, and estimate the associations between potential sociodemographic and health-related risk factors and first-episode SE. ***Methods:*** We conducted a population-based retrospective cohort study using linked health administrative datasets. We included individuals who completed Canada's 2006 Census long-form questionnaire, lived in Ontario, were between 18 and 105, and had no history of SE. A Cox proportional hazards regression model was used to estimate the hazard ratios for SE within three years associated with each potential risk factor. ***Results:*** The final sample included 1,301,700 participants, 140 of whom were hospitalized or had an emergency department visit for first-episode SE during follow-up (3.5 per 100,000 person-years). Older age was the only significant sociodemographic SE risk factor (HR = 1.35, 95% CI = 1.33, 1.37), while health-related risk factors included alcohol or drug abuse (HR = 1.05, 95% CI = 1.02, 1.08), brain tumour or cancer (HR = 1.14, 95% CI = 1.12, 1.15), chronic kidney disease (HR = 1.32, 95% CI = 1.29, 1.36), dementia (HR = 1.42, 95% CI = 1.36, 1.48), diabetes (HR = 1.11, 95% CI = 1.09, 1.12), epilepsy or seizures (HR = 1.05, 95% CI = 1.01, 1.09) and stroke (HR = 1.08, 95% CI = 1.05, 1.11). ***Conclusion:*** The estimated incidence of SE in a sample of Ontario residents was 3.5 per 100,000 person-years. Older age and several comorbid conditions were associated with higher first-episode SE risk.

RÉSUMÉ : Incidence des premiers épisodes d'état de mal épileptique et facteurs de risque en Ontario (Canada) ***Contexte :*** L'état de mal épileptique (EME) est une urgence neurologique caractérisée par des crises convulsives prolongées. Cependant, l'incidence des premiers épisodes d'EME demeure méconnue dans la mesure où les estimations varient considérablement d'une étude à l'autre. En outre, les facteurs de risque de l'EME n'ont pas été suffisamment explorés. Par conséquent, les objectifs de cette étude étaient d'estimer l'incidence des premiers épisodes d'EME en Ontario (Canada) et d'estimer les associations entre ces mêmes premiers épisodes et des facteurs de risque sociodémographiques et liés à la santé. ***Méthodes :*** Nous avons ainsi mené une étude de cohorte rétrospective basée sur la population en utilisant des ensembles de données administratives liées à la santé. Nous avons inclus les individus ayant rempli le questionnaire détaillé du recensement canadien de 2006 qui vivaient en Ontario, qui avaient entre 18 et 105 ans et qui n'avaient pas d'antécédents d'EME. À cet égard, un modèle de régression des risques proportionnels de Cox a été utilisé pour estimer, sur une période de trois ans, les rapports de risque de l'EME associés à chaque facteur potentiel de risque. ***Résultats :*** Notre échantillon final comprenait 1 301 700 participants, dont 140 avaient été hospitalisés ou s'étaient rendus aux urgences en raison d'un premier épisode d'EME au cours d'un suivi (3,5 par 100 000 personnes-années). L'âge avancé d'un individu s'est révélé le seul facteur de risque sociodémographique significatif de l'EME (RRI = 1,35 ; IC 95 % = 1,33-1,37) tandis que les facteurs de risque liés à la santé ont inclus l'abus d'alcool ou de drogues (RRI = 1,05 ; IC 95 % = 1,02-1,08), la présence d'une tumeur cérébrale ou d'un cancer (RRI = 1,14 ; IC 95 % = 1,12-1,15), l'insuffisance rénale chronique (RRI = 1,32 ; IC 95 % = 1,29-1,36), la démence (RRI = 1,42 ; IC 95 % = 1,36-1,48), le diabète (RRI = 1,11 ; IC 95 % = 1,09-1,12), l'épilepsie ou des crises convulsives (RRI = 1,05 ; IC 95 % = 1,01-1,09) ainsi que les AVC (RRI = 1,08 ; IC 95 % = 1,05-1,11). ***Conclusion :*** L'incidence estimée de l'EME dans un échantillon de résidents de l'Ontario était de 3,5 par 100 000 années-personnes. De plus, l'âge avancé de ces résidents de même que plusieurs comorbidités ont été associés à un risque plus élevé d'être victime d'un premier épisode d'EME.

Keywords: Epidemiology; Epilepsy; Status epilepticus

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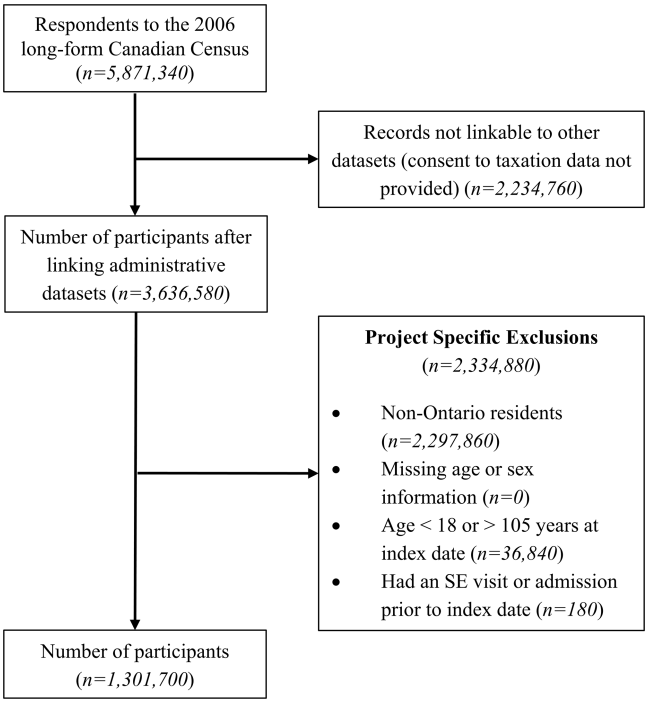

Figure 1: Flow diagram depicting the cohort build.

Introduction

Status epilepticus (SE), characterized by prolonged seizures,[1] is a neurological emergency with high rates of morbidity and mortality.[2] SE can occur in people with or without a diagnosis of epilepsy or prior seizures and can have an unknown or known etiology, such as intoxication or encephalitis.[3] The treatment of SE is often complex, requiring lengthy hospitalizations. One study conducted in Alberta found that over half of patients admitted to a hospital with SE required treatment in an intensive care unit (ICU), with a mean ICU length of stay of 6.5 days,[4] indicating that SE is a significant burden on the Canadian healthcare system.

Although there are many estimates of the frequency of SE, there are few estimates of the incidence of first-episode SE. Those that do exist vary considerably, ranging from 10.7 to 73.7 per 100,000 person-years.[5,6] Additionally, no estimates are available from Canadian study populations. Understanding the incidence of first-episode SE is essential to ensure that medical professionals are adequately educated about the likelihood of first-episode SE. In addition, a baseline incidence estimate should be available so that changes may be monitored over time. Therefore, incidence estimates from Canadian study populations are needed to clarify the incidence of first-episode SE in Canada.

Epilepsy is the most common risk factor for SE,[7] with an estimated 16%–61% of patients with SE having a previous epilepsy diagnosis.[8,9] Among those with epilepsy, patients who are non-adherent to their anti-seizure medications are at highest risk.[10] Other known SE risk factors include stroke, traumatic brain injury, alcohol abuse, brain tumors and infections.[7] However, less is known about non-health-related risk factors for SE, such as income, educational attainment, ethnicity and other socio-demographic characteristics. Social and economic factors are known to influence health, and identifying these factors is necessary to reduce health inequities.[11] Most studies that have examined sociodemographic characteristics as potential SE risk factors were among patients with epilepsy and included only age and sex, as clinical risk factors (e.g. the etiology and type of epilepsy) were of primary interest. Therefore, it is necessary to further explore sociodemographic characteristics as potential risk factors for SE, as any inequities identified would indicate the sub-populations that would benefit most from prevention strategies.

Therefore, the objectives of this study were to estimate the incidence of first-episode SE in Ontario, Canada, and the associations between potential sociodemographic and health-related risk factors and first-episode SE.

Methods

The objectives of this study were addressed using a retrospective cohort design and linked census and health administrative data from Ontario, Canada. The following datasets were linked on an individual patient level: Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD), CIHI National Ambulatory Care Reporting System (NACRS), Canada's 2006 Census long-form questionnaire (CENSUS), 2006 Canadian Census Health and Environment Cohort (CanCHEC), Canadian Vital Statistics – Death Database (CVSD), Canadian Mortality Database (CMDB), Canadian Cancer Registry (CCR), Postal Code Conversion File Plus (PCCF+), Historical Postal Code file and the Canadian Marginalization Index (CAN-Marg).

The DAD and NACRS contain the health administrative data that were used. The DAD database contains administrative and clinical data from acute inpatient facilities in Ontario.[12] The NACRS database contains emergency department, day surgery and clinic data from all Ontario facilities.[13] Full descriptions of the datasets used in this study can be found in the supplementary material (eTable 1).

Population

The study population included respondents to the 2006 Census long-form questionnaire who consented to the use of their taxation data to determine their place of residence. Approximately 20% of the Canadian population receives the long-form questionnaire; the remainder receives a shorter version. The long-form questionnaire requests additional demographic, social and economic information about the individuals in the household.[14] We included only long-form respondents because we required information that was only collected from these individuals. We excluded nonresidents of Ontario, those with missing age or sex information, were younger than 18 or older than 105, or had a prior hospital admission or emergency department visit for SE (Fig. 1).

Potential Risk Factors

Most potential sociodemographic risk factors were obtained from the Census using variables that directly correspond to these concepts. These include sex, age, educational attainment, marital status, employment status, race, immigration status, second-generation Canadian, speaks one or more of Canada's official languages, mother tongue, weekly number of hours spent on unpaid housework, childcare, senior care, household conditions (in need of repairs), individual-level household income and rurality.

Neighborhood household income and neighbourhood marginalization (dimensions: instability, deprivation, dependency and ethnic concentration) were assigned to participants using the PCCF + and CAN-Marg databases, respectively, using their postal

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Table 1: Risk factors of study sample by outcome

	Developed SE	Did not develop SE	Standardized difference
Total, *N* (%)	140	1,301,560	
Demographics			
Age (years), Mean (*SD*)	55.55 ± 18.84	47.26 ± 17.45	0.46
Age groups (years), *N* (%)			0.49
18–24	10 (7.14%)	141,580 (10.88%)	
25–34	15 (10.71%)	202,710 (15.57%)	
35–44	15 (10.71%)	262,850 (20.19%)	
45–54	25 (17.86%)	261,040 (20.05%)	
55–64	25 (17.86%)	197,310 (15.16%)	
65–74	25 (17.86%)	131,700 (10.12%)	
75–84	15 (10.71%)	83,530 (6.42%)	
85+	5 (3.57%)	20,840 (1.60%)	
Female, *N* (%)	75 (53.57%)	678,000 (52.09%)	0.01
Educational attainment, *N* (%)			0.60
Less than high school	60 (42.86%)	237,840 (18.27%)	
High school	25 (17.86%)	353,955 (27.19%)	
Post-secondary diploma	35 (25.00%)	369,635 (28.40%)	
University degree	20 (14.29%)	340,135 (26.13%)	
Marital status, *N* (%)			0.26
Divorced or separated	20 (14.29%)	134,060 (10.30%)	
Married	70 (50.00%)	760,070 (58.40%)	
Never married	35 (25.00%)	328,715 (25.26%)	
Widowed	20 (14.29%)	78,715 (6.05%)	
Employment status, *N* (%)			− 0.86
Employed	35 (25.00%)	836,250 (64.25%)	
Unemployed or not in labor force	105 (75.00%)	465,315 (35.75%)	
Race, *N* (%)			0.06
White	115 (82.14%)	1,023,010 (78.60%)	
Nonwhite	30 (21.43%)	278,555 (21.40%)	
Immigration status, *N* (%)			0.14
Nonimmigrant	95 (67.86%)	886,195 (68.09%)	
Immigrant	45 (32.14%)	405,895 (31.19%)	
Nonpermanent resident	0 (0.00%)	9,470 (0.73%)	
Second-generation Canadian, *N* (%)	20 (14.29%)	248,325 (19.08%)	−0.11
Speaks one or more of Canada's official languages, *N* (%)			0.14
English only or French only	115 (82.14%)	1,124,310 (86.38%)	
Both	15 (10.71%)	151,545 (11.64%)	
Neither	10 (7.14%)	25,710 (1.97%)	
Mother tongue, *N* (%)			0.16
English	90 (64.29%)	898,385 (69.02%)	
French	10 (7.14%)	64,690 (4.97%)	
Other	35 (25.00%)	338,490 (26.01%)	
Weekly number of hours spent on unpaid housework, *N* (%)			0.30
Less than 5 hours	60 (42.86%)	379,825 (29.18%)	
5–14 hours	35 (25.00%)	437,640 (33.62%)	

(*Continued*)

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Table 1: (*Continued*)

	Developed SE	Did not develop SE	Standardized difference
15–29 hours	25 (17.86%)	286,915 (22.04%)	
30 or more hours	20 (14.29%)	197,185 (15.15%)	
Weekly number of hours spent on unpaid childcare, *N* (%)			0.33
Less than 5 hours	115 (82.14%)	900,585 (69.19%)	
5–14 hours	10 (7.14%)	132,525 (10.18%)	
15 or more hours	15 (10.71%)	268,455 (20.63%)	
Weekly number of hours spent on unpaid senior care, *N* (%)			− 0.12
Less than 5 hours	135 (96.43%)	1,199,480 (92.16%)	
5 or more hours	10 (7.14%)	102,080 (7.84%)	
Household conditions: in need of repairs, *N* (%)			0.19
Not in need of repairs	90 (64.29%)	887,180 (68.16%)	
In need of minor repairs	35 (25.00%)	326,590 (25.09%)	
In need of major repairs	10 (7.14%)	77,595 (5.96%)	
Not applicable	5 (3.57%)	10,195 (0.78%)	
Individual-level household income, *N* (%)			0.59
Quintile 1	50 (35.71%)	190,845 (14.66%)	
Quintile 2	35 (25.00%)	232,585 (17.87%)	
Quintile 3	20 (14.29%)	252,205 (19.38%)	
Quintile 4 or 5	35 (25.00%)	625,930 (48.09%)	
Neighborhood-level household income, *N* (%)			0.41
Quintile 1	50 (35.71%)	254,330 (19.54%)	
Quintile 2	30 (21.43%)	260,780 (20.04%)	
Quintile 3	20 (14.29%)	253,520 (19,48%)	
Quintile 4	20 (14.29%)	251,260 (19.30%)	
Quintile 5	20 (14.29%)	280,250 (21.53%)	
Missing	0 (0.00%)	1,425 (0.11%)	
Rural Living, *N* (%)	15 (10.71%)	219,640 (16.88%)	−0.16
Neighborhood Marginalization, *N* (%)			
Instability			0.37
Quartile 1	40 (28.57%)	453,695 (34.86%)	
Quartile 2	25 (17.86%)	356,450 (27.39%)	
Quartile 3	30 (21.43%)	215,515 (16.55%)	
Quartile 4	45 (32.14%)	275,905 (21.20%)	
Deprivation			0.36
Quartile 1	35 (25.00%)	441,565 (33.93%)	
Quartile 2	30 (21.43%)	358,745 (27.56%)	
Quartile 3	35 (25.00%)	282,825 (21.73%)	
Quartile 4	45 (32.14%)	218,425 (16.78%)	
Dependency			0.23
Quartile 1	40 (28.57%)	370,165 (28.44%)	
Quartile 2	25 (17.86%)	340,120 (26.13%)	
Quartile 3	40 (28.57%)	297,390 (22.85%)	
Quartile 4	40 (28.57%)	293,885 (22.58%)	

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Table 1: (*Continued*)

	Developed SE	Did not develop SE	Standardized difference
Ethnic Concentration			0.14
Quartile 1	35 (25.00%)	263,515 (20.25%)	
Quartile 2	35 (25.00%)	281,135 (21.60%)	
Quartile 3	30 (21.43%)	299,150 (22.98%)	
Quartile 4	40 (28.57%)	293,885 (22.58%)	
Comorbidities, *N* (%)			
Alcohol or drug abuse	5 (3.57%)	5,175 (0.40%)	0.31
Brain surgery	5 (3.57%)	3,820 (0.29%)	0.32
Brain tumor or cancer	15 (10.71%)	26,385 (2.03%)	0.40
CKD	5 (3.57%)	4,780 (0.37%)	0.23
CNS infection or TBI	10 (7.14%)	5,525 (0.42%)	0.31
Dementia	5 (3.57%)	2,200 (0.17%)	0.28
Depression/anxiety	15 (10.71%)	20,950 (1.61%)	0.38
Diabetes	20 (14.29%)	14,870 (1.14%)	0.47
Epilepsy/seizures	30 (21.43%)	2,650 (0.20%)	0.76
Stroke	15 (10.71%)	5,595 (0.43%)	0.42

*Column of "Developed SE" does not always sum to 140 people, as cells were rounded to the nearest multiple of five. Standardized differences were calculated using unrounded values.

code of residence at baseline, the census administration date of May 16, 2006. Participants' baseline postal code of residence was available from the Historical Postal Code file.

We also investigated comorbid conditions that increase the risk of seizures, epilepsy, or SE as potential risk factors. Alcohol and drug abuse, chronic kidney disease (CKD) and diabetes increase the risk of provoked seizures.[15,16] These conditions were identified using International Classification of Diseases 10th Revision (ICD-10) codes in the DAD and NACRS databases within the two years before baseline. Brain tumors, central nervous system (CNS) infections, dementia, depression or anxiety, epilepsy or seizures, stroke and traumatic brain injuries (TBIs) are known to increase the risk of epilepsy or SE.[7,17,18] These comorbid conditions were identified using ICD-9 and ICD-10 codes in all available DAD and NACRS data before baseline (since 2000 for the DAD and 2002 for the NACRS). As cancer also increases the risk of epilepsy,[19] diagnoses within the five years before baseline were identified using the CCR. The specific ICD codes used to define these comorbid conditions are available in the supplementary material (eTable 2).

Outcome

Participants were followed from baseline, May 16, 2006, until they were admitted to a hospital or visited an emergency room for SE, their death, or the end of the follow-up period, May 15, 2009. First-episode SE was defined using ICD-10 code G41: status epilepticus identified in the primary diagnostic position in the DAD and NACRS databases. The CVSD and CMDB were used to identify deaths.

Statistical Analysis

We estimated the cumulative incidence and incidence rate of first-episode SE in our study population. We also age-standardized the estimated incidence rate using the full 2006 Canadian population.

In the bivariate analysis, we assessed whether there were differences in each potential risk factor between those who did and did not develop SE using standardized differences, with differences greater than 0.1 considered statistically significant. In the multivariable analysis, we included selected risk factors in the Cox proportional hazards regression model to estimate the hazard ratios (HRs) for their associations with first-episode SE. These risk factors were selected based on the standardized differences from the bivariate analysis and how common the risk factors were among patients who developed SE. For example, we excluded the variables for time spent on child and senior care, as few people who developed SE spent more than five hours per week on these tasks. A p-value of 0.05 was used to determine statistical significance.

Missing values for categorical variables were categorized into a separate "missing" category for all analyses. However, missing data from the Census was minimal since Statistics Canada follows up with respondents of incomplete questionnaires. Data analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC) software and standardized differences were estimated using a macro from Yang and Dalton.[20] Data were accessed through the Research Data Centre at Western University. Statistics Canada requires at least five individuals per table cell, except for quantiles, which require at least twenty. To meet this requirement, we combined categories as needed. We also randomly rounded the cells in Table 1 to multiples of five, which Statistics Canada also requires.

Results

We included 1,301,700 individuals in our study population. In the three years following the Census, 140 (0.011%) developed SE (3.6 per 100,000 person-years). The age-standardized incidence rate was 3.5 per 100,000 person-years. The total and mean follow-up time was 3,857,888 person-years and 3.0 (± 0.26) person-years, respectively. There were 31,140 (2.4%) deaths during follow-up.

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Table 2: Multivariable analysis of select risk factors and status epilepticus

	Hazard Ratio (HR)	95% CI	*P*-value
Demographics			
Age groups			
18–24	1.00 (reference)		
25–34	1.01	1.00–1.02	0.04
35–44	1.01	1.00–1.02	<0.01
45–54	1.01	1.01–1.02	<0.001
55–64	1.02	1.01–1.03	<0.001
65–74	1.04	1.03–1.05	<0.001
75–84	1.12	1.11– 1.13	<0.001
85+	1.35	1.33–1.37	<0.001
Sex			
Female	1.00 (reference)		
Male	1.01	1.00–1.01	<0.001
Educational attainment			
Less than high school	1.00 (reference)		
High school	1.00	0.99–1.00	0.08
Post-secondary diploma	1.00	0.99–1.00	0.10
University degree	0.99	0.99–1.00	0.02
Employment status			
Employed	1.00 (reference)		
Unemployed or not in labor force	1.01	1.01–1.01	<0.001
Race			
White	1.00 (reference)		
Nonwhite	1.00	0.99–1.00	0.24
Immigration status			
Nonimmigrant	1.00 (reference)		
Immigrant	1.00	0.99–1.00	0.02
Nonpermanent resident	0.99	0.97–1.02	0.57
Weekly number of hours spent on unpaid housework			
Less than 5 hours	1.00 (reference)		
5–14 hours	0.98	0.98–0.99	<0.001
15–29 hours	0.98	0.97–0.98	<0.001
30 or more hours	0.97	0.97–0.98	<0.001
Individual-level household income			
Quintile 1	1.00 (reference)		
Quintile 2	1.00	0.99–1.00	0.14
Quintile 3	0.99	0.99–1.00	0.04
Quintile 4	0.99	0.99–1.00	0.01
Quintile 5	0.99	0.99–1.00	<0.01
Rurality Living			
Urban	1.00 (reference)		
Rural	1.00	1.00–1.01	0.46
Comorbidities			
Alcohol or drug abuse	1.05	1.02–1.08	<0.001
Brain surgery	1.03	1.00–1.06	0.07

(*Continued*)

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Table 2: (*Continued*)

	Hazard Ratio (HR)	95% CI	*P*-value
Brain tumor or cancer	1.14	1.12–1.15	<0.001
Chronic kidney disease	1.32	1.29–1.36	<0.001
CNS infection or TBI	1.02	0.99–1.04	0.26
Dementia	1.42	1.36–1.48	<0.001
Depression/anxiety	1.02	1.00–1.03	0.01
Diabetes	1.11	1.09–1.12	<0.001
Epilepsy/seizures	1.05	1.01–1.09	0.02
Stroke	1.08	1.05–1.11	<0.001

Most differences in the distribution of potential risk factors between individuals who did and did not develop SE were statistically significant in the bivariate analysis (Table 1). In the multivariable analysis (Table 2), the sociodemographic factors that significantly increased the risk of first-episode SE included older age, male sex and being unemployed. Having a university degree, being an immigrant, spending more time on unpaid housework, and having a higher household income were protective. However, except for older age, all these hazard ratios were close to one and are likely of minimal clinical relevance. The comorbid conditions that statistically significantly increased the risk of first-episode SE include alcohol or drug abuse, brain tumor or cancer, chronic kidney disease, dementia, depression or anxiety, diabetes, epilepsy or seizures and stroke.

Discussion

The estimated cumulative incidence of first-episode SE over the three-year study period was 0.011%, and the age-adjusted incidence rate was 3.5 per 100,000 person-years. Risk factors included older age, alcohol or drug abuse, brain tumors or cancer, chronic kidney disease, dementia, diabetes, epilepsy or seizures and stroke.

Our incidence rate estimate is lower than those previously reported in other high-income countries.[5,21] Our lower estimate is likely due to the official International League Against Epilepsy (ILAE) definition of SE in use during the study period, the 1981 definition, which defined SE as a seizure with a minimum duration of 30 minutes.[22] Since the seizure duration defining SE was reduced to 5 minutes in 2015 by the ILAE, studies using data from after this date, are more likely to report a higher incidence rate.[1]

Inconsistencies between incidence rates estimated across studies could also be due to the ICD codes used to identify SE. Some studies, including ours, used ICD-10 code G41: status epilepticus, while others have used G40.301 and G40.311: generalized idiopathic epilepsy and epilepsy syndromes, intractable or not intractable, with status epilepticus. It is currently unclear which ICD codes should be used to identify SE in health administrative data, as no studies estimating their accuracy could be identified. We could not use G40.301 and G40.311 as they are not used in the DAD or NACRS databases. Therefore, using only G41 is appropriate and likely highly accurate for our data. However, as with all studies using health administrative data to estimate first-episode SE incidence, it is possible that SE could be coded as a seizure (G40) or that a seizure could be incorrectly classified as SE.

We identified several sociodemographic factors statistically significantly associated with first-episode SE, but most of their hazard ratios were close to one. However, age was positively associated with the first episode of SE, with a clinically relevant hazard ratio of 1.35, a finding that is consistent with previous studies.[10,21,23] We did not find meaningful associations with sex in the present study. Studies that have included sex as a risk factor have reported inconsistent findings, with most studies reporting a higher incidence in men,[9,21,24,25] another reporting a higher incidence in women,[26] and another reporting similar incidence rates in men and women.[27] Thus, it remains unclear whether sex is associated with SE.

In addition, we found no clinically relevant associations between first-episode SE and educational attainment, employment status, immigration status, individual-level household income, rurality, or race. We found a small but statistically significant reduced risk of first-episode SE among those who performed more than five hours of housework per week (5–14 hours: HR = 0.98, 95% CI = 0.98, 0.99; 15–29 hours: 0.98, 95% CI = 0.97, 0.98; 30+ hours: HR = 0.97, 95% CI = 0.97, 0.98). It is unclear why housework might be associated with a reduced risk of first-episode SE. However, the small risk difference may not be clinically meaningful.

Although few sociodemographic factors were associated with first-episode SE, we found multiple comorbid conditions associated with our outcome in the multivariable analysis. Comorbid conditions associated with SE include hypoxemia, systemic infection, dementia, TBI, cancer, drug poisoning, CNS infection, metabolic causes, alcohol-related causes and stroke.[28] In addition to estimating significant associations with some of these conditions, we also estimated significant associations with CKD and diabetes. These findings are expected, as it is well-known that both CKD and diabetes can cause provoked seizures.[15,16] Importantly, some comorbid conditions, such as alcohol abuse and diabetes, are more prevalent in the general population. Therefore, despite these conditions having smaller hazard ratios than others, such as CKD, they likely have a more significant effect on SE risk at the population level.

There are some limitations of this study. As we explored potential sociodemographic risk factors for first-episode SE, we required the linkage of census and health administrative data, which typically takes many years to become available. Therefore, although our estimate was measured using data from 2006, it was the most current data linked to the Census when we began the study. Additionally, gender is an essential sociodemographic variable we would have liked to include in this study. However, gender was not added to the Census until 2021[29] and was therefore unavailable.

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We also identified relatively few people who had first-episode SE over follow-up ($n = 140$), which limited the power of the multivariable analysis. The limited number of patients with SE also required us to combine risk factor categories to meet the minimum cell size requirements of Statistics Canada when reporting the bivariate analysis results. Additionally, we did not account for the competing risk of death, which may have resulted in an overestimation of the hazard ratios.

In addition, we likely did not identify all patients with the comorbidities included. As these variables were measured between 2000 and 2006, we would have identified patients with the condition only if they had either an emergency department visit or hospitalization for the condition within this period. Therefore, patients with preexisting but well-controlled conditions would be more likely to have been missed. Additionally, we would not have identified patients with the conditions diagnosed between the index date and the end of the follow-up period. Another study limitation is the potential that some adjusted potential risk factors mediate the associations between other potential risk factors and SE, which would result in an underestimation of the associations between the exposure and SE. For example, alcohol abuse may partially mediate the association between socioeconomic status and SE, and adjusting for both may bias the association between socioeconomic status and SE toward the null hypothesis. Therefore, mediation effects between the potential risk factors included in this study should be explored in future research.

As high-quality healthcare databases were used for this population-based study, we believe our results are generalizable to adult populations in many other regions, particularly other parts of Canada and other high-income nations. The generalizability of our study results to lower- and middle-income countries is unclear, as they may have higher incidence rates due to a higher prevalence of risk factors. In addition, some variables in our study may poorly represent the sociodemographic characteristics of people in other countries, such as mother tongue and race, making the estimates for some risk factors in this study less relevant for those populations.

The incidence of SE has a bimodal distribution across the lifespan, with peaks in early childhood and older adulthood. Therefore, since we did not include children, our results are not generalizable to pediatric populations. Additionally, since we used census data to identify the study population, generalizability to individuals who do not reside in private households, such as those in collective dwellings or who are unhoused, may be limited.[30]

Conclusion

The incidence of first-episode SE in our sample of Ontario adult residents between 2006 and 2009 was 3.5 per 100,000 person-years, somewhat lower than rates estimated in other high-income countries. Older age and several comorbid conditions, including alcohol or drug abuse, brain tumors or cancer, chronic kidney disease, dementia, diabetes, epilepsy or seizures and stroke, were associated with an increased risk of first-episode SE. This information can be used to educate medical professionals about the likelihood of first-episode SE and its risk factors and act as a baseline estimate to monitor changes over time. Future research should continue to explore sociodemographic and health-related risk factors for SE to confirm our findings.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2024.11.

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