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Urban-Rural Differences in the Associations of Risk Factors With Epilepsy Based on the California Health Interview Survey: A Multiple Logistic Regression Analysis

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Abstract

Background: Previous studies provided inconsistent associations of smoking, stroke, and serious psychological distress (SPD) with epilepsy while urban-rural differences in the associations of risk factors with epilepsy are not well documented.
Objectives: This study aimed to evaluate the associations of lifestyle, health conditions, and SPD with epilepsy and to examine whether the associations differ between urban and rural areas.
Patients and Methods: A total of 604 adults with epilepsy and 42416 controls were selected from the 2005 California Health Interview Survey. Weighted univariate and multiple logistic regression analyses were used to estimate the associations of potential factors (behavioral factors, SPD, social factors and health conditions) with epilepsy. The odds ratios (ORs) with 95% confidence intervals (CIs) were estimated.
Results: The overall prevalence of epilepsy was 1.3% and the prevalence was higher in urban area than rural area (1.4 vs. 1.1%). The prevalence of SPD was 11% in cases and 4% in controls, respectively. The percentage of stroke was higher in cases than in controls (9% vs. 2%). After adjusting for other factors using multiple logistic regression, current smoking, stroke, cancer, SPD and living in urban were positively significantly associated with epilepsy (OR = 1.74, 95% CI = 1.28 - 2.38; OR = 4.81, 95% CI = 3.13 - 7.41; OR = 1.52, 95% CI = 1.12 - 2.06; OR = 2.02, 95% CI = 1.39 - 2.92, and OR = 1.4, 95% CI = 1.08 - 1.81, respectively); while binge drinking was negatively associated with epilepsy (OR = 0.65, 95% CI = 0.43 - 0.99). Stratified by residence, in the urban area, current smoking and race were only associated with epilepsy. Stroke and SPD showed stronger association with epilepsy in the rural area (OR = 7.63, 95% CI = 3.68 - 15.8, and OR = 3.14, 95% CI = 1.52 - 6.47, respectively) comparing with urban region (OR = 4.51, 95% CI = 2.79 - 7.28 and OR = 1.9, 95% CI = 1.27 - 2.86, respectively).
Conclusions: Smoking, stroke, and SPD were associated with epilepsy; while the associations differed between urban and rural areas.

Keywords: Epilepsy, Prevalence, Smoking, Stroke, Cancer, Binge Drinking

1. Background

Epilepsy is a category of neurological disorders in which cortical neuronal is disturbed, causing sporadic episodic lapses in brain function which may result in a wide variety of symptoms and sensations potentially including abnormal behavior and/or impaired consciousness. Epilepsy affects about 2 million Americans (1); while globally, it costs most countries up to 1% of their total national health care expenditure (2). Epilepsy may considerably negatively affect people's day-to-day functioning (3). The causes of epilepsy may be linked to various factors, genetic, developmental or acquired factors. A number of potential factors have been reported to be associated with epilepsy, including reduced cognitive function, memory loss (4), adverse drug reactions to antiepileptic drugs (AEDs) (5), smoking among pregnant women with the disorder (6), cancer (7), psychosocial burden including anxiety and serious psychological distress (SPD) (8), employment status (9), stroke (10, 11), and depression (12). It has been systemically reviewed about the association between demographic, psychosocial, and condition-related factors and health-related quality of life, resource utilization or costs in adults with epilepsy (13).

Due to the high burden of epilepsy on society and in-

dividual patient, identification of these risk factors is central to improve health care and quality of life for epilepsy patients. Furthermore, there are inconsistent findings related to smoking, stroke and SPD with epilepsy in some studies, especially due to small sample size and different designs (14). In addition, little is known about urban-rural differences in the associations of mental health and behavioral factors with epilepsy.

2. Objectives

We conducted a secondary data analysis with large sample size (n = 43020) using logistic regression models to estimate the associations of behavioral factors, SPD, social factors and health conditions with epilepsy and to examine whether such associations differ between urban and rural residential status.

3. Patients and Methods

3.1. Study Population

The California Health Interview Survey (CHIS) is conducted by a collaborative study of the University of California, Los Angeles (UCLA) center for health policy research, the California department of health services, and the public health institute. The 2005 CHIS data is from the third CHIS data collection cycle since 2001. From each household, one adult respondent aged 18 years or older was randomly selected. Details about the sampling design can be found at http://healthpolicy.ucla.edu/chis/design/Pages/overview.aspx. In the current study, 43020 adults were included. For the CHIS 2005 data, the overall response rate was 26.9%, which is calculated based on a 49.8% success rate in initial screening and 59.3% of respondents completing the entire survey. The data collection and analysis procedures were approved by the institutional review boards (IRBs) at the participant universities and agencies. The present study was approved by the IRB of authors' university.

3.2. Measurements

3.2.1. Assessment of Epilepsy

Subjects were considered to have had epilepsy if they responded "yes" to the question "Have you ever been told by a doctor that you have a seizure disorder or epilepsy?" In total, 604 adults with epilepsy and 42416 controls were available for the 2005 CHIS.

3.2.2. Behavioral Factors

Smoking status was categorized as never smoking, current smoking, or past smoking. Other behavioral factors were coded as yes/no, including binge drinking and obesity. Adult was considered to have obesity when the body mass index (BMI) was 30.0 or greater. Binge drinking was defined for women when the individuals had 4 or more drinks at one time during the last 30 days and for men when the individuals had 5 or more drinks at one time during the last 30 days (15).

3.2.3. SPD

SPD has been used as a nonspecific psychometrically validated measure of psychological distress to discriminate among diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV) cases from non-cases (16, 17). SPD is defined by the Kessler 6 (K6) scale, which consists of 6 questions asking how often during the past 30 days a person felt: "so sad that nothing could cheer them up," "nervous," "restless," "hopeless," "worthless," or that "everything was an effort." Responses are scored from 0 (none of time) to 4 (all the time) and then the scores are summed to produce a total score (0 to 24); a total score of 13 or greater defines SPD (16). The K6 scale has been widely used to screen for DSM-IV mood and anxiety disorders in the previous studies (18, 19).

3.2.4. Social Factors

Gender was coded as either male or female based on self-report. Age was categorized as young (18 - 44 years), middle aged (45 - 64 years), and elderly (65 years or older). Employment status was classified as yes or no. Race was made of two subgroups: white and non-white. Residence was coded as urban and rural based on zip code.

3.2.5. Health Condition

Individuals were considered to have experienced a stroke if they responded "yes" to the question "doctor ever told had a stroke". Adults were considered to have had a cancer if they responded "yes" to the question "doctor ever told had cancer".

3.3. Statistical Analysis

In this cross-sectional study, we referred subjects with epilepsy as cases and subjects without epilepsy as controls. Sas Proc Surveymeans was used to estimate the overall prevalence and Sas Proc Surveyfreq was used to estimate population proportions in cases and controls for behavioral factors, health conditions, SPD, and social factors. The chi-square test was applied to compare the prevalence of epilepsy across gender, age and race. Then the Sas Proc

Surveylogistic procedure was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the relation between potential risk factors and epilepsy. First, simple logistic regression (univariate logistic regression analysis) was used to examine the unadjusted association of each potential factor with epilepsy. After that, multiple logistic regression analysis was used to simultaneously adjust for all potential factors of epilepsy using enter method. First order effect modification/interaction with residential status was explored in relation with all important variables. In view of significant effect modification of residential status, a stratified analysis by residential status was performed to determine the association of risk factors with epilepsy using multiple logistic regressions. All the analyses were performed using SAS statistical software, version 9.2 (SAS Institute, Cary, NC, USA). A jackknife method was used to properly estimate confidence intervals considering the survey's multistage sampling design.

4. Results

4.1. Subjects Characteristics and Prevalence

The characteristics of the epilepsy cases and controls are listed in Table 1. The prevalence of current smoking was higher in cases than that in controls (24% vs. 15%). There were 25% of cases and 21% of controls who were obese. The percentage of SPD in cases and in controls was 11% and 4%, respectively. For the elders (65 years of age or older), the percentage was lower in cases than in controls (9% vs. 15%). Most subjects were unemployed (52%) in the patient group, but fewer controls were unemployed (39%). For health factors, prevalence of stroke was higher in cases (9%) compared to the control group (2%) and prevalence of cancer was higher in cases than controls (11% vs. 8%). The prevalence of epilepsy by gender, age and race is presented in Table 2. The overall prevalence of epilepsy was 1.3% (1.2% for males and 1.5% for females, respectively); while the prevalence was higher in urban area than that in rural area (1.4 vs. 1.1%). The prevalence in stroke (5.4%) was higher than those without stroke, while the prevalence in SPD (3.7%) was higher than those without SPD (1.2%).

4.2. Logistic Regression Analysis for the Whole Sample

Table 3 presents the results from both univariate and multiple logistic regression analyses. By univariate analyses, current smoking, stroke, cancer, SPD, older ages, and employment were associated with epilepsy. After adjusting for other factors using multiple logistic regression, current smoking, stroke, cancer, SPD and living in urban were still positively significantly associated with epilepsy (OR = 1.74, 95% CI = 1.28 - 2.38; OR = 4.81, 95% CI = 3.13 - 7.41; OR = 1.52, 95% CI = 1.12 - 2.06; OR = 2.02, 95% CI = 1.39 - 2.92, and OR = 1.4, 95% CI = 1.08 - 1.81, respectively); while binge drinking was negatively associated with epilepsy (OR = 0.65, 95% CI = 0.43 - 0.99). In addition, middle-aged and elderly, employed were negatively associated with epilepsy (OR = 0.79, 95% CI = 0.63 - 0.99; OR = 0.21, 95% CI = 0.13 - 0.33; and OR = 0.56, 95% CI = 0.43 - 0.72, respectively).

4.3. Interactions with Residential Status

After adjusting for all potential risk factors in the multiple logistic regression models, age group, smoking, stroke, cancer status, obesity, SPD, race, and employment showed significant interactions ($P < 0.05$) with residential status. Stroke, SPD, cancer, obesity and white race showed positive interactions with residential status ($P < 0.0001$ with OR = 4.51; $P = 0.0012$ with OR = 1.93; $P = 0.0284$ with OR = 1.49; $P = 0.0439$ with OR = 1.28; and $P = 0.0065$ with OR = 1.37; respectively); while comparing with never smoking, current smoking revealed significant interaction with residential status ($P = 0.0004$ with OR = 1.81). Thus, a stratified analysis by residential status was performed and reported in Table 4.

4.4. Logistic Regression Analysis of Urban-Rural Differences

The urban-rural differences in the associations of behavioral factors, health conditions, SPD, and social factors with epilepsy are shown in Table 4. Current smoking and race were only associated with epilepsy in urban area (OR = 1.77, 95% CI = 1.26 - 2.49; OR = 1.34, 95% CI = 1.03 - 1.73). Age, stroke, cancer, SPD and employment were associated with epilepsy in both urban and rural areas; whereas stroke and SPD showed stronger association with epilepsy in the rural area (OR = 7.63, 95% CI = 3.68 - 15.8, and OR = 3.14, 95% CI = 1.52 - 6.47, respectively) comparing with urban region (OR = 4.51, 95% CI = 2.79 - 7.28 and OR = 1.9, 95% CI = 1.27 - 2.86, respectively).

5. Discussion

In this study, we found the prevalence of epilepsy was significantly higher in adults being current smoking, with stroke or SPD than in those without these conditions. After adjusting for covariates, we identified several factors (current smoking, stroke, cancer, and SPD) significantly associated with an increased odds for having epilepsy based on a total of 43020 adults. Especially, we found urban-rural differences in the association of several factors with epilepsy.

The overall prevalence of epilepsy in the California population was 1.3% (1.5% for female and 1.2% for male), which is quite similar to those in previous studies (20, 21). Our findings further showed that the prevalence of

Table 1. Characteristics of Cases and Controls[a]

Variables	Cases (n = 604)	Controls (n = 42416)
Gender		
Male	211 (46)	17261 (49)
Female	393 (54)	25155 (51)
Age group, y		
18 - 44	228 (56)	16222 (54)
45 - 64	287 (35)	16450 (31)
> 65	89 (9)	9744 (15)
Smoking status		
Never	292 (51)	23813 (60)
Current	133 (24)	6033 (15)
Past	179 (25)	12570 (25)
Binge drinking		
No	542 (87)	36335 (82)
Yes	62 (13)	6081 (18)
Stroke		
No	525 (91)	41167 (98)
Yes	79 (9)	1249 (2)
Cancer		
No	502 (89)	37520 (92)
Yes	102 (11)	4896 (8)
Obesity		
No	453 (75)	33618 (79)
Yes	151 (25)	8798 (21)
SPD		
No	513 (89)	40708 (96)
Yes	83 (11)	1575 (4)
Employment		
No	363 (52)	19416 (39)
Yes	241 (48)	23000 (61)
Residence		
Rural	117 (10)	7933 (12)
Urban	487 (90)	34443 (88)
Race		
White	424 (57)	28555 (52)
Non-white	180 (43)	13861 (48)

Abbreviation: SPD, serious psychological distress.
[a]Values are presented as No. (%).

epilepsy in stroke (5.4%) was higher than those without stroke (1.2%) and also suggest that people with stroke are more likely (adjusted OR of 4.81) to have epilepsy compared with people without a history of stroke. A previous study has shown that stroke can cause epilepsy, especially in the elderly stroke is the most common cause of new-

Table 2. The Prevalence of Epilepsy (%) According to Considered Factors

Variables	Total	No. of Cases	Prevalence, %	95% CI	P Value
Gender					
Male	17472	211	1.2	0.9 - 1.5	0.259
Female	25548	393	1.5	1.2 - 1.6	
Age group, y					
18 - 44	16450	228	1.4	1.1 - 1.6	0.0026
45 - 64	16737	287	1.5	1.3 - 1.7	
> 65	9833	89	0.8	0.5 - 1.0	
Smoking status					
Never	24105	292	1.1	0.9 - 1.3	0.0002
Current	6166	133	2.1	1.5 - 2.6	
Past	12749	179	1.4	1.1 - 1.7	
Binge drinking					
No	36877	542	1.4	1.2 - 1.6	0.00857
Yes	6143	62	1.0	0.6 - 1.4	
Stroke					
No	41692	525	1.2	1.1 - 1.4	< 0.0001
Yes	1249	79	5.4	3.7 - 7.1	
Cancer					
No	38022	502	1.3	1.1 - 1.5	0.0125
Yes	4998	102	1.9	1.4 - 2.3	
Obesity					
No	34071	453	1.3	1.1 - 1.5	0.0967
Yes	8949	151	1.5	1.2 - 1.8	
SPD					
No	41221	513	1.2	1.0 - 1.4	< 0.0001
Yes	1658	83	3.7	2.6 - 4.8	
Employment					
No	19779	363	1.7	1.5 - 2.0	< 0.001
Yes	23241	241	1.1	0.8 - 1.3	
Residence					
Rural	8090	117	1.1	0.8 - 1.3	0.0869
Urban	34930	487	1.4	1.2 - 1.6	
Race					
White	28979	424	1.5	1.3 - 1.7	0.0766
Non-white	14041	180	1.2	0.9 - 1.4	
Overall	43020	604	1.3	0.8 - 1.5	

Abbreviation: SPD, serious psychological distress; CI, Confidence Interval.

onset epilepsy (22). Recently, the frequency of seizures in stroke victims was estimated to vary from 5 to 20% and stroke was positively associated with seizures and epilepsy (23). The incidence of post-stroke epilepsy in a European

Table 3. Univariate and Multiple Logistic Regression Analyses for the Relationship Between All Potential Risk Factors and Epilepsy

Variables	Crude OR	95% CI	P Value	Adjusted OR	95% CI	P Value
Gender						
Male	1			1		
Female	1.15	0.89 - 1.48	0.277	1.04	0.80 - 1.35	0.772
Age group, y						
18 - 44	1			1		
45 - 64	1.09	0.87 - 1.37	0.459	0.79	0.63 - 0.99	0.0427
> 65	0.49	0.33 - 0.72	0.0003	0.21	0.13 - 0.33	< 0.0001
Smoking status						
Never	1			1		
Current	1.89	1.39 - 2.57	< 0.0001	1.74	1.28 - 2.38	0.0005
Past	1.19	0.90 - 1.58	0.213	1.30	0.97 - 1.75	0.0792
Binge drinking						
No	1			1		
Yes	0.73	0.49 - 1.07	0.105	0.65	0.43 - 0.99	0.0422
Stroke						
No	1			1		
Yes	4.51	3.15 - 6.46	< 0.0001	4.81	3.13 - 7.41	< 0.0001
Cancer						
No	1			1		
Yes	1.49	1.10 - 2.02	0.0096	1.52	1.12 - 2.06	0.0069
Obesity						
No	1			1		
Yes	1.24	0.98 - 1.57	0.0692	1.19	0.94 - 1.50	0.149
SPD						
No	1			1		
Yes	3.14	2.21 - 4.49	< 0.0001	2.02	1.39 - 2.92	0.0002
Employment						
No	1			1		
Yes	0.60	0.47 - 0.77	< 0.0001	0.56	0.43 - 0.72	< 0.0001
Residence						
Rural	1			1		
Urban	1.26	0.97 - 1.63	0.0876	1.40	1.08 - 1.81	0.0117
Race						
Non-white	1			1		
White	1.27	0.98 - 1.63	0.0613	1.37	1.08 - 1.73	0.0096

Abbreviation: CI, confidence interval; OR, odds ratio; SPD, serious psychological distress.

population was 8.2%, which is higher than that in previous studies (2 - 4%) (10). Stroke and epilepsy coexist, so the mechanisms underlying this association need further investigation (24).

Epilepsy patients reported to have greater SPD than controls (11% vs. 4%) which is in the line with previous

Table 4. Multiple Logistic Regression Analyses for the Relationship Between All Potential Risk Factors and Epilepsy by Urban and Rural Areas

Variables	Adjusted OR (Rural Residence)	95% CI	P Value	Adjusted OR (Urban Residence)	95% CI	P Value
Gender						
Male	1			1		
Female	1.30	0.70 - 2.41	0.4	1.02	0.78 - 1.33	0.908
Age group, y						
18 - 44	1			1		
45 - 64	0.55	0.29 - 1.04	0.0674	0.82	0.64 - 1.06	0.126
> 65	0.12	0.04 - 0.32	< 0.0001	0.22	0.13 - 0.37	< 0.0001
Smoking status						
Never	1			1		
Current	1.45	0.74 - 2.83	0.277	1.77	1.26 - 2.49	0.0011
Past	1.51	0.67 - 3.41	0.316	1.27	0.92 - 1.76	0.146
Binge drinking						
No	1			1		
Yes	0.36	0.13 - 1.01	0.0525	0.69	0.45 - 1.05	0.0858
Stroke						
No	1			1		
Yes	7.63	3.68 - 15.8	< 0.0001	4.51	2.79 - 7.28	< 0.0001
Cancer						
No	1			1		
Yes	1.96	1.13 - 3.41	0.0169	1.45	1.01 - 2.09	0.0448
Obesity						
No	1			1		
Yes	0.90	0.48 - 1.70	0.753	1.23	0.96 - 1.55	0.089
SPDa						
No	1			1		
Yes	3.14	1.52 - 6.47	0.002	1.90	1.27 - 2.86	0.0019
Employment						
No	1			1		
Yes	0.36	0.19 - 0.67	0.0013	0.58	0.44 - 0.76	0.0001
Race						
Non-white	1			1		
White	1.81	0.79 - 4.15	0.16	1.34	1.03 - 1.73	0.0266

Abbreviation: CI, confidence interval; OR, odds ratio; SPD, serious psychological distress.

observations that depression and anxiety were associated with epilepsy or seizure disorders (20, 25). Psychiatric disorders such as anxiety and depression have been more common comorbidities with epilepsy than in the general population (24). Few studies have investigated the effects of SPD on epilepsy. Previous study (8) reported that the adjusted OR for SPD with epilepsy was 2.24, which is similar to our results (adjusted OR = 2.02). Our results further indicated that the prevalence of epilepsy in SPD (3.7%) is significantly higher than subjects without SPD (1.2%). Increasing evidence suggests that epilepsy patients without seizure control may have higher levels of psychological distress, a deleterious cycle of loss of self-efficacy, and social disadvantage (26). In light of this significant association

between SPD and epilepsy, SPD was found as the strongest predictors of health-related quality of life among epilepsy patients (27), a rehabilitation approach and partnership with general practitioners and nurses are warranted to assess psychological distress and reduce distress for people with epilepsy (8, 26).

The current findings also provide additional evidence of a strong association between cancer and epilepsy. Previous study revealed that the lifetime risk of having epileptic seizures may increase significantly for patients with cancer; while patients with primary brain tumors may increase a lifetime risk of epilepsy about 20 - 80% (28). The treatment for seizures in patients with cancer is multifaceted and may involve surgery, radiation, chemotherapy, and antiepileptic drugs.

Cigarette smoking is associated with increased risk of epilepsy, which is consistent with previous studies (21, 29, 30). The present study further adds to this finding and suggests that current smoking is associated with epilepsy, particularly in urban residence in California, indicating the complex effect of smoking on epilepsy. It has been proposed that the studies on the association between tobacco smoking and seizures or epilepsy are insufficient and future works on testing unique constituents of tobacco smoke and smoking cessation agents and better understanding of their mechanisms of action will be required to deeply understand the underlying pathophysiology of seizures and epilepsy, which may lead to the development of more effective treatments (30). Previous studies suggested that mild to moderate alcohol consumption may decrease risk of seizures (31, 32) or moderate alcohol use did not have association with seizure or epilepsy (29). Furthermore, binge drinking during pregnancy (11 - 16 weeks gestation) may be associated with the development of seizures in infants (33). Another study reported a dose-response relationship between the daily amount of alcohol use and the probability of the onset of epilepsy (34). Few studies have focused on the binge drinking with epilepsy. In the present study, multiple logistic regression analyses showed that binge drinking was negatively associated with epilepsy in the entire cohort and separate group analysis based on residency status.

The finding of increasing of unemployment rates among patients with epilepsy also added to previous observations. It has been reported that the full-time employment rates for patients with epilepsy were lower in various populations reported in Australia (35), and Malaysia (36). However, only 42% of adults with epilepsy reported employment compared with 70% of people without epilepsy in a U.S. population (37). The findings from our current study demonstrated that employment is a reduced risk for having epilepsy (Table 2). Therefore, it is important to understand employment patterns of people with epilepsy, which inform optimization of legislative, pharmacological, and nonpharmacological health strategies. To our knowledge, no study attempted to investigate the urban-rural differences in the associations of behavioral factors, health conditions, SPD, and social factors with epilepsy in the U.S. population. The present study provided new findings on current smoking and race were associated with epilepsy only in urban residence; while age, stroke, cancer, SPD and employment were associated with epilepsy in both urban and rural areas; whereas stroke and SPD showed stronger association with epilepsy in the rural area compared to urban region.

The study has several strengths such as the diversity of the population. For example, five languages (English, Spanish, Mandarin Chinese and Cantonese Chinese, Vietnamese, and Korean) facilitated inclusion in subjects who could neither speak English nor speak English well enough to otherwise participate. Furthermore, this large subject sample was randomly selected and included comprehensive information with a wide age range on epilepsy and social, behavioral, and health characteristics. The large sample made us possible to adjust for numerous factors. Moreover, we provided the prevalence estimates for epilepsy in lifestyle, health condition, SPD and urban and rural areas. In addition, we examined the urban-rural differences in the associations of behavioral factors, health conditions, SPD, and social factors with epilepsy in the California population.

Several limitations need to be acknowledged. First, a cross-sectional design cannot make decision about the causal relationships between these potential factors and epilepsy. Second, for a telephone survey, the institutionalized adults, who did not have a landline telephone or cell phone, and who could not answer the phone due to other reasons were impossible to be included, which may cause a potential selection bias between participants and nonparticipants. For instance, younger adults may have higher chance to possess a phone and answer the call. In addition, self-reported data may be subject to misclassification.

Importantly, the epidemiology of epilepsy has been widely used to identify the frequency, causes, and progress of epilepsy. Only 20 - 30% of epilepsy cases have a clearly etiological acquired cause (such as head trauma, stroke). The evidence suggests that there is a twofold to fourfold increase in epilepsy risk in first degree relatives and 70% heritability derived from twin studies of epilepsies without known cause (38). A number of candidate genes such as SLC2A1, STXBP1, and SCN1A have been identified to be associated with epilepsy (39). In the near future, research discoveries on epidemiology, genetics, and epigenetic mechanisms will continue to drive our inextricable move towards

prevention, high-throughput genetic diagnosis, targeted therapies, and personalized medicine for patients who suffer from epilepsy.

In conclusion, we identified a number of potential factors associated with epilepsy, including current smoking, stroke, cancer, unemployment and SPD; while the associations differed between urban and rural areas. Intervention strategies that target risk reduction of epilepsy may be tailored accordingly.

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Footnote

Authors' Contribution: Ke-Sheng Wang, Chun Xiang Mao, and Chun Xu managed the literature searches and analyses, edited the references, and wrote the draft of the manuscript. Xuefeng Liu offered critical guidance on the statistical analysis and contributed for statistical expertise and improvement of the manuscript. Alok Dwivedi, Javier Ordonez, and Lewis R Rubin provided a substantive review of the manuscript. All authors read and approved the manuscript.

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