Appendix S1. Questionnaire for medical history and treatment

In the health examination, each participant completed a self-administered questionnaire covering medical history of epilepsy and other diseases, and a list of prescription drugs (including antiepileptic agents and any other drugs prescribed from hospitals or clinics).

The following is an English translation of the questionnaire (originally in Japanese).

What illnesses have you had in the past?

Please note any disease(s) you have had in the past using the list below.

If applicable, please provide the name of the hospital/clinic you visited for treatment, and the date (month/year) of disease onset or hospital visit.

1. Stroke
2. Myocardial infarction
3. Angina pectoris or coronary intervention
4. Other heart diseases (e.g., arrhythmia, valvular heart diseases)
5. Arterial disease in the leg
6. Cancer
7. Pulmonary tuberculosis
8. Other pulmonary diseases (e.g., pneumonia, bronchial asthma)
9. Liver diseases
10. Gastric or duodenal ulcer
11. Polyps in the gastrointestinal tract
12. Gynecology diseases
13. Trauma or injury
14. Surgical operation
15. Depression or anxiety
16. Epilepsy, convulsions, or seizures
17. Blood transfusion
18. Others

What medicines are you currently prescribed by hospitals or clinics?

Please attached a copy of prescription (or a list of drugs) that you receive from hospitals or clinics.

Appendix S2. Supplemental Methods

Classification of the causes of epilepsy

The etiology of epilepsy was classified into the following categories on the basis of the clinical records—including medical history, brain imaging, and electroencephalogram reports, if available—which were collected from clinics or hospitals. If the clinical records were unavailable, classification was determined by a face-to-face or telephone interview with the participant or his/her attending physician. If the participant or physician did not have any information, the cause of epilepsy was classified as "unknown causes". The classifications used in the Rochester Study[1,2] and the Veterans Affairs Cooperative Study[3] were modified for the present study. In this study, no subjects were classified as having "other neurological diseases".

1. **Cerebrovascular diseases:**

   Active epilepsy after an identified insult caused by vascular occlusion, embolism, or intracerebral or subarachnoid hemorrhage was included.

2. **Congenital diseases:**

   Active epilepsy presumed to be due to congenital or perinatal neurological diseases was included, irrespective of age at first episode of seizure.

3. **Head trauma:**

   Active epilepsy subsequent to a significant head injury such as skull fracture, open head injury, or intracranial hematoma was included.

4. **Other neurological diseases:**

   Active epilepsy subsequent to other identified neurological diseases (e.g., brain tumor, encephalopathy) was included.

5. **Epilepsy with no focal lesions**:

   Active epilepsy with no primary neurological diseases was included. In this category, the focus of epilepsy was not detected in brain imaging (computed tomography or magnetic resonance imaging).

6. **Unknown causes:**

   Active epilepsy which was not classified into any of the categories above because clinical information and brain imaging were lacking, unavailable, or insufficient.

Definitions of variables other than epilepsy

Each participant completed a self-administered questionnaire covering medical history of epilepsy and cerebrovascular diseases, treatment for hypertension and diabetes, smoking habits, and alcohol intake. Blood pressure was measured three times using an automated sphygmomanometer in the sitting position after resting for ≥ 5 min. The mean of the three measurements was used for the analysis. Hypertension was defined as blood pressure levels $\geq 140/90$ mmHg or current treatment with antihypertension agents. Plasma glucose levels were measured with the hexokinase method. Diabetes mellitus was defined as a fasting plasma glucose level of ≥ 7.0 mmol/L, 2-h post-loaded or casual glucose level of ≥ 11.1 mmol/L, or current use of oral hypoglycemic agents or insulin. Serum total cholesterol was measured enzymatically. Body height and weight were measured with the subject in light clothing

without shoes, and the body mass index was calculated. Smoking habits and alcohol intake were categorized as current use or not. Activities of daily living of subjects were evaluated by modified Rankin Scale, and disability was defined as modified Rankin Scale ≥2.

Statistical analysis

SAS 9.4 (SAS Institute, Cary, NC, USA) was used for the statistical analyses. The 95% confidence intervals (CIs) of the prevalence of epilepsy were estimated using a binominal distribution. The prevalence of categorical variables and the mean values of continuous variables were compared by chi-square test and t-test, respectively. Values of $P<0.05$ were considered statistically significant.

References

1. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. *Epilepsia* 1993;34:453-468.

2. Hauser WA, Annegers JF, Kurland LT. Prevalence of epilepsy in Rochester, Minnesota: 1940-1980. *Epilepsia* 1991;32:429-445.

3. Ramsay RE, Rowan AJ, Pryor FM. Special considerations in treating the elderly patient with epilepsy. *Neurology* 2004;62:S24-29.

Table S1. Baseline characteristics of subjects with and without epilepsy.

	Epilepsy (-) (n=3,310)	Epilepsy (+) (n=23)	*P* value
Age at examination, mean±SD	65±13	74±14	<0.001
Age at first episode of seizure, n (%)			
0-19 years	-	4 (17)	
20-39 years	-	1 (4)	
40-64 years	-	4 (17)	
≥65 years	-	13 (57)	
Unknown	-	1 (4)	
Women, n (%)	1,887 (57.0)	16 (69.6)	0.23
Hypertension, n (%)	1,782 (53.8)	8 (34.8)	0.07
Diabetes mellitus, n (%)	590 (17.8)	4 (17.4)	0.96
Serum total cholesterol, mmol/L, mean±SD	5.21±0.95	5.14±1.11	0.72
Body mass index, kg/m^2, mean±SD	23.0±3.5	20.4±4.1	<0.001
Current smoking, n (%)	528 (16.0)	2 (8.7)	0.34
Current drinking, n (%)	1,575 (47.6)	7 (30.4)	0.10
History of cerebrovascular diseases, n (%)	148 (4.5)	14 (60.9)	<0.001
Disability (modified Rankin Scale ≥2), n (%)	394 (11.9)	16 (69.6)	<0.001
Hospitalized or institutionalized at a nursing home, n (%)	93 (2.8)	12 (52.2)	<0.001