THE LANCET

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplemental table 1. Risks of natural causes of death after diagnosis with epilepsy, stratified by diagnostic threshold, sex, severity, patient type, epilepsy subtype, age group, birth order, and time after first diagnosis of epilepsy.

	Natural causes of death		Deaths from neoplasms		Deaths caused by diseases of the nervous system	
No epilepsy (n=660,869)	2,791 (57.1%)	1.0 (ref)	1,146 (23.4%)	1.0 (ref)	124 (2.5%)	1.0 (ref)
Epilepsy						
Sex						
Male (n=36,999)	711 (81.2%)	14.9 (13.9-16.0)	757 (20.0%)	12.3 (10.9-13.9)	750 (19.8%)	60.6 (46.4-79.1)
Female (n=32,996)	2,108 (89.0%)	16.4 (15.0-17.8)	659 (27.8%)	10.2 (9.0-11.5)	559 (23.6%)	93.3 (64.0-136.2)
Threshold						
≥1 diagnoses (n=69,995)	5,183 (84.2%)	15.5 (14.6-16.4)	1,416 (23.0%)	11.2 (10.3-12.2)	1,309 (21.3%)	71.1 (57.3-88.4)
≥2 diagnoses (n=48,105)	3,619 (87.1%)	16.7 (15.6-17.8)	918 (22.1%)	11.1 (10.0-12.4)	1,034 (24.9%)	91.5 (70.0-119.7)
Severity						
Less severe (n=62,143)	3,804 (82.6%)	13.7 (12.9-14.6)	1,100 (23.9%)	10.4 (9.5-11.5)	948 (20.6%)	60.0 (47.7-75.5)
More severe (n=7,852)	1,379 (89.0%)	26.9 (23.4-30.9)	316 (20.4%)	14.6 (11.9-18.0)	361 (23.3%)	193.8 (95.0-395.3)
Source						
Inpatient (n=50,071)	4,932 (84.8%)	16.5 (15.6-17.5)	1,316 (22.6%)	11.6 (10.6-12.8)	1,258 (21.6%)	77.2 (61.2-97.4)
Outpatient only (n=19,924)	251 (74.7%)	8.2 (6.8-9.8)	100 (29.8%)	7.6 (5.8-10.0)	51 (15.2%)	35.1 (18.6-66.4)

Type of seizures *						
Complex partial (n=8,382)	375 (87.0%)	13.4 (11.2-16.1)	431 (43.9%)	15.7 (12.2-20.3)	73 (16.9%)	54.6 (27.6-108.1)
Other partial (n=5,857)	310 (84.9%)	14.0 (11.4-17.3)	163 (44.7%)	19.6 (14.7-26.1)	68 (18.6%)	30.3 (14.7-62.5)
Generalized (n=15,315)	1,281 (87.7%)	13.0 (11.5-14.7)	214 (14.7%)	5.5 (4.5-6.8)	439 (30.1%)	92.2 (56.0-151.6)
Other and unspecified (n=40,441)	3,217 (82.5%)	17.0 (15.9-18.3)	850 (21.8%)	11.6 (10.4-13.0)	729 (18.7%)	74.8 (56.6-98.9)
Type of epilepsy **						
Focal (n=12,841)	559 (91.0%)	14.6 (12.6-16.8)	305 (49.7%)	18.4 (15.1-22.5)	108 (17.6%)	51.2 (29.8-88.1)
Generalized (n=7,593)	146 (85.9%)	8.4 (6.6-10.8)	27 (15.9%)	3.0 (1.9-4.7)	51 (30.0%)	92.6 (33.2-258.6)
Encephalopathy & mixed (n=1,894)	195 (95.1%)	56.1 (38.5-81.8)	41 (20.0%)	18.6 (10.6-32.7)	51 (24.9%)	236.7 (55.3-1,012.7)
Special syndromes (n=894)	109 (73.6%)	23.2 (15.4-35.0)	19 (12.8%)	6.7 (3.6-12.4)	15 (10.1%)	85.1 (10.8-667.9)
Other epilepsy (n=710)	46 (85.2%)	21.4 (12.4-36.7)	16 (29.6%)	24.0 (9.4-61.7)	11 (20.4%)	55.6 (11.6-266.6)
Unspecified epilepsy (n=29,997)	1,839 (83.9%)	17.4 (15.9-18.9)	557 (25.4%)	12.7 (11.1-14.6)	398 (18.2%)	81.6 (57.9-115.1)
Age at death						
0-15 (n=69,995)	1,070 (96.0%)	74.6 (56.0-99.3)	97 (8.7%)	14.2 (8.0-25.2)	791 (29.1%)	196.5 (77.0-501.3)
16-25 (n=68,877)	778 (85.2%)	34.6 (27.2-44.1)	135 (14.8%)	14.3 (9.2-22.1)	310 (34.0%)	525.5 (126.9-2,176.4)
26-35 (n=67,963)	992 (78.2%)	18.6 (16.1-21.5)	331 (26.1%)	20.2 (16.0-25.4)	295 (23.3%)	65.3 (39.3-108.5)
36-45 (n=66,691)	1,298 (79.3%)	13.3 (12.1-14.7)	465 (28.4%)	12.1 (10.5-13.9)	256 (15.6%)	59.5 (40.1-88.4)

46-56 (n=65,055)	1,045 (85.4%)	10.0 (9.1-11.0)	388 (31.7%)	8.6 (7.4-9.9)	124 (10.1%)	31.7 (21.3-47.2)
Birth order						
Firstborn (n=21,131)	1,572 (85.7%)	15.5 (14.1-17.2)	462 (25.2%)	12.1 (10.4-14.1)	373 (20.3%)	74.3 (48.9-112.9)
Not firstborn (n=27,306)	1,741 (84.7%)	17.6 (16.0-19.5)	435 (21.2%)	11.7 (10.0-13.8)	485 (23.6%)	89.1 (60.6-131.0)
No siblings (n=21,558)	1,870 (82.6%)	13.8 (12.6-15.2)	519 (22.9%)	9.6 (8.4-11.0)	451 (19.9%)	55.9 (39.7-78.8)
Time period						
0-182 days (n=69,995)	799 (89.2%)	91.5 (69.0-121.4)	340 (37.9%)	151.5 (91.9-249.6)	140 (15.6%)	316.8 (50.6-1985.4)
183-365 days (n=69,096)	446 (88.5%)	43.6 (33.4-57.0)	197 (39.1%)	62.5 (40.5-96.5)	74 (14.7%)	139.1 (29.2-662.4)
≥ 366 days (n=68,592)	3,938 (82.8%)	12.4 (11.7-13.2)	879 (18.5%)	7.3 (6.6-8.0)	1,095 (23.0%)	66.2 (52.8-82.9)

Note: Adjusted odds ratios (aOR) report odds of mortality in individuals with epilepsy compared to general population controls (matched for age and sex, and adjusted for income, and marital and immigration statuses).

* Complex partial (ICD-8: 345.31; ICD-9: 345M, 345N; ICD-10: G40.2); Other partial (ICD-8: 345.30, 345.38, 345.39; ICD-10: G40.0, G40.1); Generalized (ICD-8: 345.00, 345.09, 345.10, 345.11; ICD-9: 345J, 345K; ICD-10: G40.3); Other & unspecified (ICD-8: 345.18, 345.19, 345.20, 345.29, 345.32, 345.33 345.9; ICD-9: 345L, 345P, 345Q, 345W, 345X; ICD-10: G40.4, G40.5, G40.6, G40.7, G40.8, G40.9, G41).

** Focal (ICD-10: G40.0, G40.1, G40.2); Generalized (ICD-10: G40.3); Encephalopathy & mixed (ICD-10: G40.4); Special syndromes (ICD-10: G40.5); Other epilepsy (ICD-10: G40.8); Unspecified epilepsy (ICD-10: G40.6, G40.7, G40.9).

Supplemental table 2. Associations of natural causes of death in epilepsy with psychiatric comorbidity

Diagnostic group	Natural causes of death		Deaths from neoplasms		Deaths caused by diseases of the nervous system	
	n (%)	aOR (95% CI)	*n* (%)	aOR (95% CI)	*n* (%)	aOR (95% CI)
No epilepsy, no psychiatric disorder	1,984 (0.3%)	1.0 (ref)	972 (0.2%)	1.0 (ref)	89 (0.1%)	1.0 (ref)
No epilepsy, any psychiatric disorder	807 (1.2%)	2.8 (2.6-3.1)	174 (0.3%)	1.3 (1.1-1.5)	35 (0.1%)	3.6 (2.2-5.9)
Epilepsy, no psychiatric disorder	2,397 (5.8%)	17.7 (16.2-19.3)	1,087 (2.6%)	17.8 (15.8-20.0)	540 (1.3%)	70.2 (49.0-100.4)
Epilepsy, any psychiatric disorder	2,786 (9.8%)	21.9 (20.0-24.0)	329 (1.2%)	5.4 (4.6-6.3)	769 (2.7%)	120.8 (82.6-176.8)

Note: Number of deaths in epilepsy and associated controls, stratified by psychiatric diagnoses, and odds ratios adjusted for income, and marital and immigration statuses. aOR=adjusted odds ratio. Results are stratified into individuals with or without epilepsy and with or without any psychiatric disorder.

Appendix 1. STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1
Objectives	3	State specific objectives, including any prespecified hypotheses	1
Methods			
Study design	4	Present key elements of study design early in the paper	1-2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	2-3
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	2-4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	2-3
Bias	9	Describe any efforts to address potential sources of bias	3-4
Study size	10	Explain how the study size was arrived at	2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	2-4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	3-4
		(*b*) Describe any methods used to examine subgroups and interactions	3-4
		(*c*) Explain how missing data were addressed	3
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	3
		(*e*) Describe any sensitivity analyses	3-4

Results

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	--
		(c) Consider use of a flow diagram	--
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	2,4
		(b) Indicate number of participants with missing data for each variable of interest	2
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	4
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	4-6

Discussion

Key results	18	Summarise key results with reference to study objectives	6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6-8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-8

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	8

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org