Supplementary Online Content

Gorton HC, Webb RT, Carr MJ, DelPozo-Banos M, John A, Ashcroft DM. Risk of unnatural mortality among people with epilepsy. *JAMA Neurol*. Published online April 9, 2018. doi:10.1001/jamaneurol.2018.0333

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Explanation of the Matching Process Applied to Delineate the Matched-Cohort Study

Separately in the CPRD and the SAIL Databank, people with epilepsy were matched to up to 20 individuals who had never received a diagnostic code for epilepsy and were alive on the date that follow-up began. They were matched on gender, year of birth (+/-2 years) and registered general practice; and followed up from the same day as the corresponding individual in the epilepsy cohort. We employed an algorithm that used nearest-neighbor matching. Individuals were ineligible for inclusion in the comparison cohort if they ever had a diagnostic code for epilepsy. In both the epilepsy and comparison cohorts, at least one day of follow-up after the entry date was required. The matching ratio of up to 20:1 was used to improve statistical power to detect rare outcomes, in line with evidence reported by Hennessy et al. that there are benefits to increasing the matching ratio for case-control studies above 5:1 when the exposure prevalence is low among control subjects. (1) Therefore, an increased matching ratio will be beneficial for the matched cohort design when incidence is very low in the comparison cohort. It enables more precise estimation of relative risks for exceptionally rare specific causes of death such as homicide. Whilst this matching ratio was desired, in practice it was not possible to match all individuals with epilepsy to 20 people. This was because there were not enough individuals who were the same gender, had the same year of birth (+/- 2 years), were registered in the same general practice and who had never had a diagnosis of epilepsy. Each individual was matched to as many individuals as possible who satisfied the matching criteria. In the CPRD there was a median of 19 (IQR 18-19) individuals in the comparison cohort for each individual in the epilepsy cohort. The median was 20 (IQR 20-20) in the SAIL Databank.

Reference:

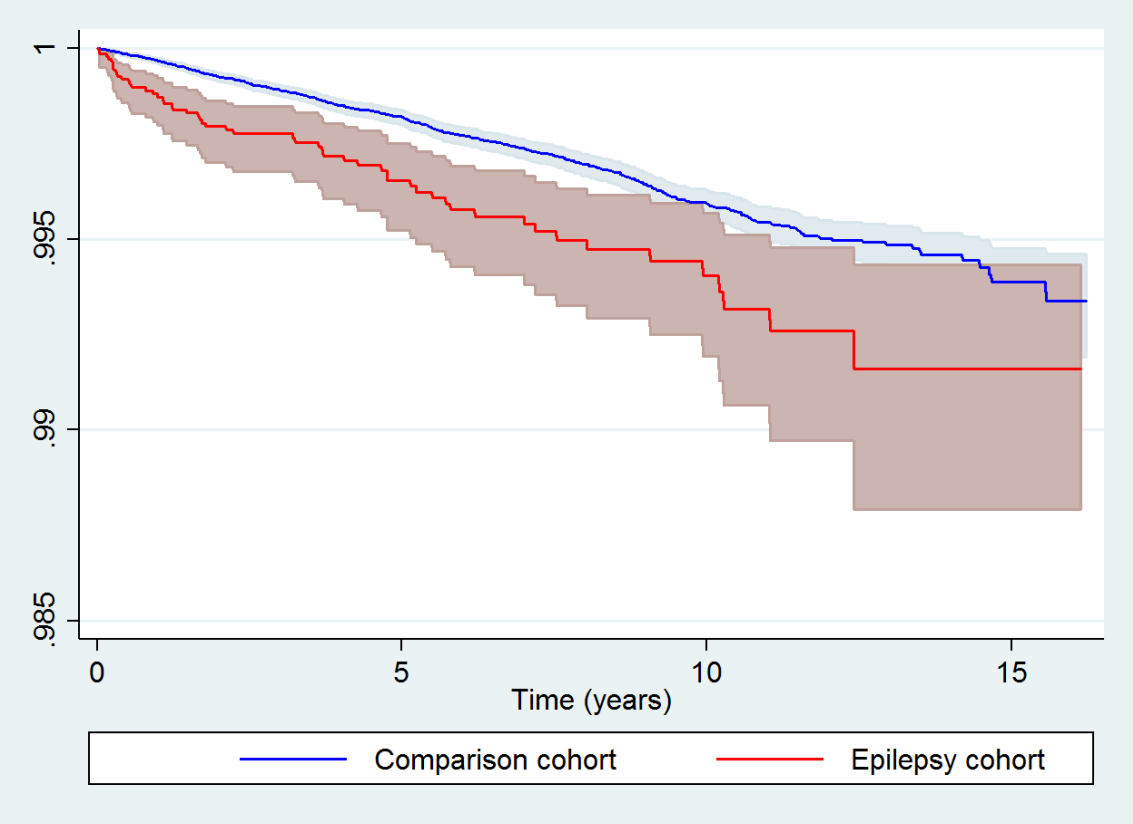
1. Hennessy S, Bilker WB, Berlin JA, Strom BL. Factors influencing the optimal control-to-case ratio in matched case–control studies. Am J Epidemiol. 1999;149(5):489.

eTable. *ICD-10* Codes Used to Classify Medication Taken in Fatal Poisonings

Medication Group	Codes
Psychotropic medication	T40.5, T40.7, T40.8, T40.9, T42.4, T43.0-9, T50.5
Opioid	T40.0-4, T40.6
Non-opioid	T39
Antiepileptic Drugs	T42.0-3, T42.5-7
Other	T36-38,T41,T42.8,T44-49,T50.0-4, T50.6-9

ICD-10 codes listed in supplementary cause of death fields in the ONS mortality record

e**Figure 1.** Kaplan-Meier Plot Depicting Probability of Cause-Specific Survival in Relation to Unnatural Mortality in the CPRD



eFigure 2. Kaplan-Meier Plot Depicting Probability of Cause-Specific Survival in Relation to Unnatural Mortality in the SAIL Databank