Supplementary Methods. Methodology of the National General Practice Study of Epilepsy and Epileptic Seizures

In the 1980s, the NGPSE was set up in an attempt to redress the prevalent selection bias introduced by studies of epilepsy largely being retrospective and hospital-based. The study received ethics approval from the joint committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology in London, and was reviewed and recommended by the UK Royal College of General Practitioners.

The first phase (1984 to 1987) was concerned with the setting up of the reporting network and the recruitment of General Practitioners (GPs) and then of people with newly suspected epileptic seizures. From the start the study was funded by the National Society for Epilepsy and the Brain Research Trust. The study was advertised to GPs in various medical magazines (Medicine Today, Pulse, Mimms Magazine, Hospital Update etc), and in a letter in the Journal of the Royal College of General Practitioners.[1] The cohort was then recruited from the practices of 275 GPs over a three-year period, with practitioners joining the study progressively over that period. GPs were asked to include all people in whom a new diagnosis of epilepsy, a single epileptic seizure or a febrile seizure (in children) was suspected. It was emphasised that all individuals should be included, regardless of aetiology or precipitants, age (apart from neonatal seizures), seizure type, the number of attacks and whether or not they were referred to hospital. Once an individual was identified, the initial questionnaire was completed by the GP. Collaborative workshops were held, and newsletters circulated, to inform GPs of the progress of the study and of new developments in epilepsy and to encourage them to keep going with the study.

The expected sample size of about 1200 was chosen because it was considered the maximum number the study was likely to enrol in the time available and because the anticipated number of 700 with epileptic seizures would be sufficient to estimate recurrence rates with 95% confidence.[2] In all, 1195 individuals were registered with the study. About fifteen percent (183 people) were excluded; on further inquiries 104 people were found to have a previous diagnosis of epilepsy (unknown to their current GP) and 79 people were found not to have epilepsy. Thus 564 people with a definite non-febrile epileptic seizure, 228 with a probable epileptic seizure and 220 children with febrile seizures were included in the cohort. The study was registered with the National Health Service Central Register, to enable follow-up of individuals who moved and notification of deaths.

The initial registration form contained details of medical history, family history, risk factors and circumstances of seizures, a seizure description (including a witnessed account where

possible) and a checklist of symptoms and signs. It also recorded details of any previous episodes (of previously undiagnosed seizures), and the date, time and duration of the seizure. Any treatment given and any hospital referral was also noted.[2] The GP was sent a green card with details of the individual's registration with the study to be inserted in the case notes. The seizure which led the individual to be registered with the study was designated the 'index' seizure.

After six months a follow-up form was sent to each GP and to the hospital consultant of those who were referred requesting details on recurrence of seizures, treatment, other developments and results of any investigations. At this time a study panel consisting of a neurologist with a special interest in epilepsy, a GP, a neurological research fellow and a paediatric neurologist, with access to all information received, classified each individual as having definite epileptic seizures, probable seizures, febrile convulsions or another (non-epilepsy) diagnosis (Sander *et al.,* 1990). The "probable" group included people in whom the diagnosis of epilepsy was still not clear (for example the index episode(s) were unwitnessed and therefore subject to ongoing diagnostic uncertainty). Diagnostic categories have remained unchanged throughout follow-up. Those with definite epileptic seizures, and subsequently those with probable seizures, were further classified as having idiopathic/cryptogenic seizures, remote symptomatic seizures, acute symptomatic seizures (occurring within three months of an acute insult) or associated with a congenital or perinatal abnormality.

Following the forms sent to GPs and hospital physicians at six months after the index seizure, a further follow-up form was sent to the GP at one year. After this, the same follow-up form was sent to the GPs of people classified as having definite or probable epileptic seizures each year until 1998, with a further questionnaire in 2001.

The most recent follow-up, in 2009-10 had many issues. At this point, following enactment of the Data Protection Act 1998[3] and the Health and Social Care Act 2001,[4] GPs were no longer able to release identifiable patient information without consent from the individuals concerned. Section 60 exemption of the Health and Social Care Act 2001 allows disclosure of such information without specific consent when it is impractical to obtain individual consent or when important public interest is at state. We believed that needing to obtain individual consent would inevitably result in a significant loss of information and probably also in bias concerning those who gave and those who withheld consent. Having obtained further ethics approval to continue with the study in 2007, we thus applied to the Department of Health Patient Information Advisory Group (PIAG) for this exemption.[5] Initial rejection of our application was followed by an appeal, at which exemption was allowed for people who had

had no seizures and who had taken no anti-epileptic drugs in the previous five years; for all others, consent was required. Partial completion of all forms (answering questions on occurrence of seizures and use of anti-epileptic drugs) was allowed in all cases without consent. We were also only permitted to ask for further information on seizure frequency in the previous five years and on antiepileptic drug usage and could no longer request information on comorbidities. We needed to obtain consent (via the GPs) for any individuals who had either had seizures or had taken antiepileptic drugs in the past five years to enable the GP to complete the questionnaire. Furthermore, for people enrolled in the study who lived in Scotland, there was no provision for this exemption as the Health and Social Care Act was enacted after Scottish devolution. Not only did we therefore need to obtain consent for each individual via the GP, but we were also not allowed direct contact with the GPs to emphasise the importance of the study and thus of obtaining consent.

Reference List

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3. UK Parliament Acts. European data Protection Act 1998. 1998. 18-10-2007.
4. British Parliament. Health and Social Care Act. 2001.
5. Neligan, A. The long term prognosis of epilepsy. 2011. University College London.