Sudden unexpected death in epilepsy (SUDEP) in New Zealand; a retrospective review

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ABSTRACT

AIM: Sudden unexpected death in epilepsy (SUDEP) is well recognised and widely reported but remains poorly understood. SUDEP in young adults is 27 times more common than sudden death in control populations. The incidence of SUDEP in New Zealand is not known but up to 40 people with epilepsy may die from SUDEP every year. A review of coroner's reports of SUDEP was undertaken to learn more about SUDEP in New Zealand.

METHOD: Coroner's reports of all cases of possible SUDEP in New Zealand from 2007–2016 (n=190) were obtained and post-mortem and toxicology results were reviewed. Cases were categorised using published criteria.

RESULTS: We obtained reports of 190 cases from the coroner's office. Of these 190 cases, we determined that 123 were definite SUDEP, 40 were definite SUDEP plus, three were probable SUDEP, seven were possible SUDEP and 17 were probably not SUDEP. The number of cases per year varied from 11–26 (2013). Cases were aged 1.5–67 years, with 63% aged 15–45 (mean 37 years). Sixty-one percent were male. Eighty-seven percent of the deaths occurred at home, with 74% found dead in their bed or bedroom. The majority were not employed, with only 33% working or retired at the time of death; 15% were children or students. Information regarding work status was not available for 11%. Toxicology results were available for 155 cases; antiepileptic drug (AED) use was detected in 67% of these cases, with a single AED detected in 44%, two AEDs in 21%, and three AEDs in 3% of samples taken at autopsy. Approximately half who took an AED were taking either sodium valproate or carbamazepine.

CONCLUSION: This study suggests that people with epilepsy who die from SUDEP in New Zealand are young and are often compliant with their medication. We plan to establish a nationwide SUDEP registry using the EpiNet database to determine the incidence of SUDEP in New Zealand, and to track changes in SUDEP rates. We are also planning to take part in an international case-control study of SUDEP in the hope that we might learn more about risk factors that predispose people with epilepsy to SUDEP, and factors that might reduce the risk.

Epilepsy is a common neurological condition. The prevalence of epilepsy in developed countries is estimated at between 5–10/1,000 people, with most Western countries reporting a prevalence of about 0.7%.[1] Several studies have established that people with epilepsy have a lower life expectancy than that of the general population.[2–4] This lower life expectancy is explained, in part, by high rates of comorbidity, the risk of injury during seizures and status epilepticus. However, there is also a significant risk of sudden unexpected death in epilepsy (SUDEP).[2–4]

SUDEP is defined as sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death in patients with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus, in which post-mortem examination does not reveal a toxicological or anatomic cause of death.[5]

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Table 1: Nashef sudden unexpected death in epilepsy classification.[5]

Definite SUDEP	Sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death that occurs in benign circumstances in an individual with epilepsy, with or without evidence for a seizure, and excludes documented status epilpeticus, in which post-mortem examination does not reveal a cause of death.
Definite SUDEP plus	Death satisfying criteria for definite SUDEP, if a concomitant condition other than epilepsy is identified before or after death, if the death might have been due to the combined effect of both conditions, and if autopsy or direct observations or recording of the terminal event did not prove the concomitant condition to be the cause of death.
Probable SUDEP or probable SUDEP plus	Same definition as definite SUDEP or SUDEP plus, but without autopsy. The victim should have died unexpectedly while in a reasonable state of health, during normal activities, and in benign circumstances, without a known structural cause of death.
Possible SUDEP	A competing cause for death is present.
Not SUDEP	A clear alternative cause of death is known.
Unclassified	Incomplete information available; not possible to classify.

The incidence of sudden death in young adults with epilepsy is reported to be 27 times higher than the incidence of sudden death in control populations.[6] The annual incidence of SUDEP in patients with epilepsy is estimated to be 1.2 per 1,000 people.[7] When epilepsy begins in early childhood, the average cumulative risk of SUDEP is as high as 8% by 70 years.[7]

When the age at which SUDEP occurs is taken into account, SUDEP ranks second only to stroke, in terms of potential years of life lost.[7]

The strongest SUDEP risk factor appears to be poor control of tonic-clonic seizures.[8,9] Other potential risk factors are male sex, epilepsy onset before 16 years of age, longer duration of epilepsy and intellectual disability.[9]

Despite an increase in research into SUDEP, the underlying mechanisms remain unclear. Currently, there are no proven strategies to prevent SUDEP.

Here we present the results of a retrospective review of coroners' reports of people who have died of SUDEP in New Zealand between 2007 and 2016. Our aim was to obtain a better understanding of SUDEP in New Zealand and identify future areas of research.

Method

The coroner's office provided documentation for all cases between July 2007 and July 2016 where the cause of death was thought to have been SUDEP. Documentation included the coroner's verdict on the cause of death and whether an enquiry was opened into the cause of death. We reviewed these cases and extracted demographic data and information regarding the circumstances of death (date of death, place of death etc).

After approval from the Chief Coroner and the Health and Disability Ethics committee (Northern B; 18/NTB/28), the coroner's office also provided post-mortem and toxicology reports. We were then able to record additional information about the circumstances of death. We determined if anti-epileptic drugs were identified post-mortem, and whether other medications, alcohol and/or recreational drugs were detected.

The epilepsy fellow at Auckland Hospital (SS) used the Nashef criteria for SUDEP to categorise each case into definite SUDEP, definite SUDEP plus, probable SUDEP, probable SUDEP plus, possible SUDEP, not SUDEP or unclassified (Table 1).[5] Where there was uncertainty about the appropriate category, the case was reviewed by a second member of the research team (PB), and consensus was reached.

Table 2: Breakdown of SUDEP categories.

Definite SUDEP	Definite SUDEP plus	Probable SUDEP	Possible SUDEP	Not SUDEP	Unclassified
123	40	3	7	14	3

Results

The coroner's office identified 190 cases where the cause of death may have been SUDEP between July 2007 and July 2016.

Following our review, we concluded that 166 cases fulfilled the Nashef criteria for either definite SUDEP, definite SUDEP plus or probable SUDEP.

The breakdown of the different SUDEP categories can be seen in Table 2.

Five of the possible SUDEP cases also had significant cardiac disease which may have caused their deaths. One had a high level of methadone detected at post mortem, and one died following a fall and did not have a post mortem. Of the 14 patients that were considered not to have had SUDEP, we concluded that five patients had drowned, three probably died from a cardiac cause, two had died from probable status epilepticus, one died as a result of septicaemia, one was having palliative care and had stopped AEDs, and one died from suicide. The final patient had a probable symptomatic seizure, but he had not had previous seizures and did not have a diagnosis of epilepsy.

Demographics of 166 definite, definite + or probable SUDEP patients

The patients with definite SUDEP, definite SUDEP plus or probable SUDEP were aged between 1.5 years and 67 years (Figure 1). The mean age for this group was 37 years.

Sixty-one percent of all the SUDEP cases were male. Figure 2 shows the cases of SUDEP by year and gender.

The ethnicity was not recorded for 56 patients. Twenty-one patients were Māori and 77 were recorded as Caucasian.

The type of epilepsy was stated in less than one-third of cases. Information about seizure frequency was not available and duration of epilepsy was rarely stated.

Circumstances of death

One hundred and forty-six patients' (88%) deaths occurred at home; 74% were found in their bedroom and 7% of patients were found dead in the bathroom. One hundred and forty-four patients (87%) were alone when they died.

We also looked at what position the body was found in; in particular, whether the

Figure 1: Age at time of death.

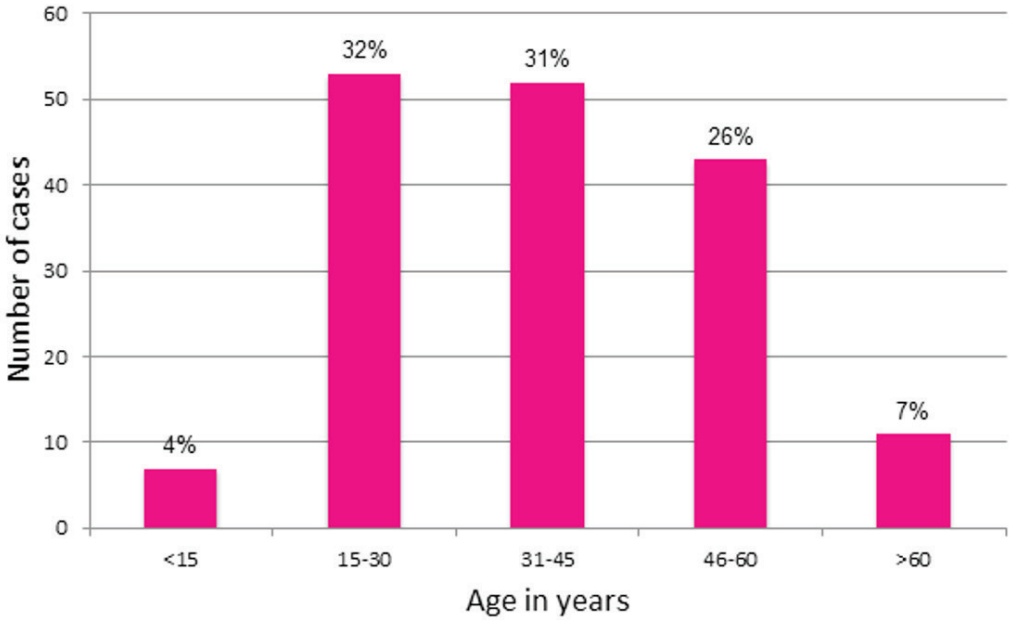

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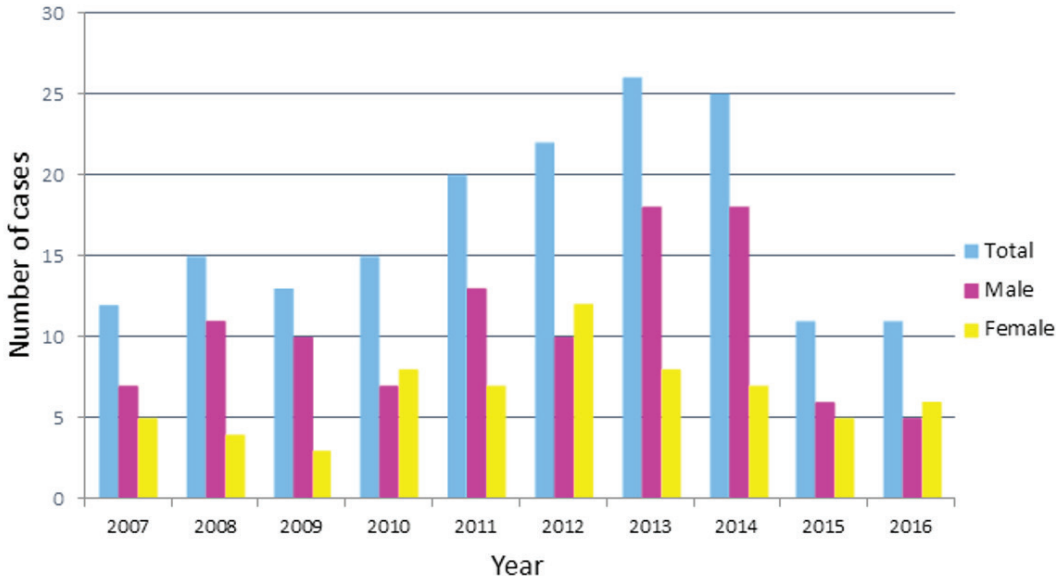
Figure 2: SUDEP cases by year and gender.



deceased was in bed, and if lying, whether supine or prone (Figure 3).

Toxicology

We obtained toxicology reports on 155 of the 166 definite and probable SUDEP cases. Anti-epileptic drugs (AED) were detected in 67% of the cases in which toxicology was performed; a single AED was detected in 68 people (44%), two AEDs were detected in 32 patients (21%), and three AEDs were detected in four people (3%) (Figure 4). Approximately half of those who took an AED were either taking sodium valproate or carbamazepine.

High alcohol levels were not identified in any patient. Recent cannabis use was detected in 20 people (12%) and other recreational drugs in six people (4%). Anti-depressants and antipsychotic medications were identified in small numbers of patients.

Figure 3: Position of body when found.

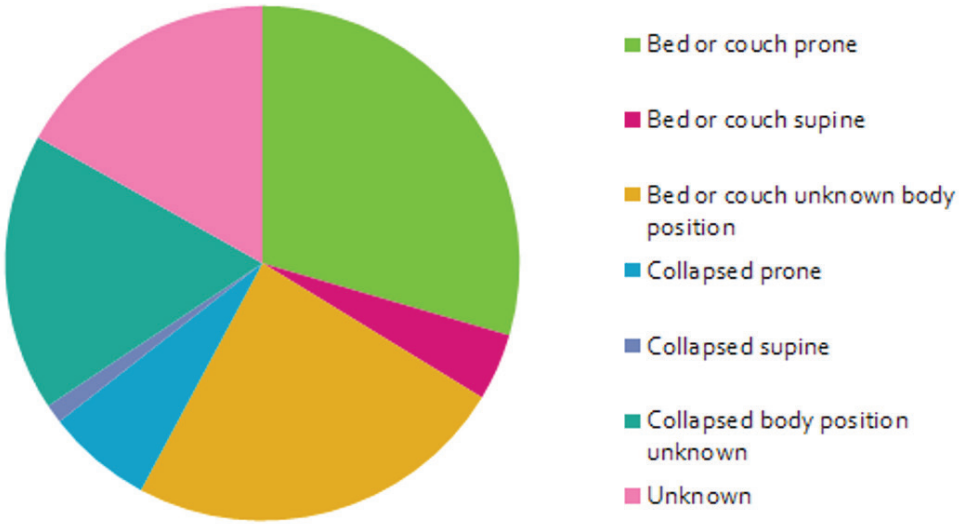
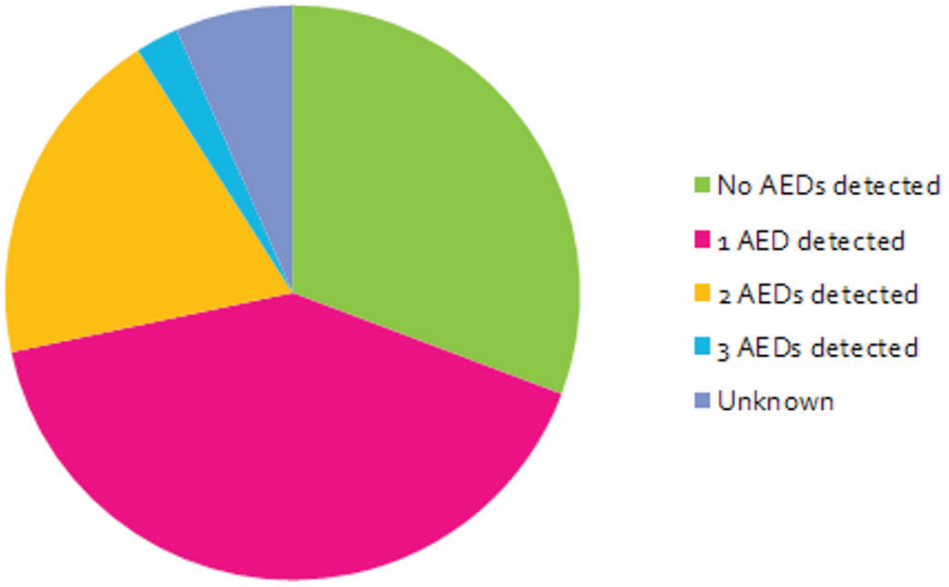


Figure 4: Number of AEDs at the time of death detected by toxicology.



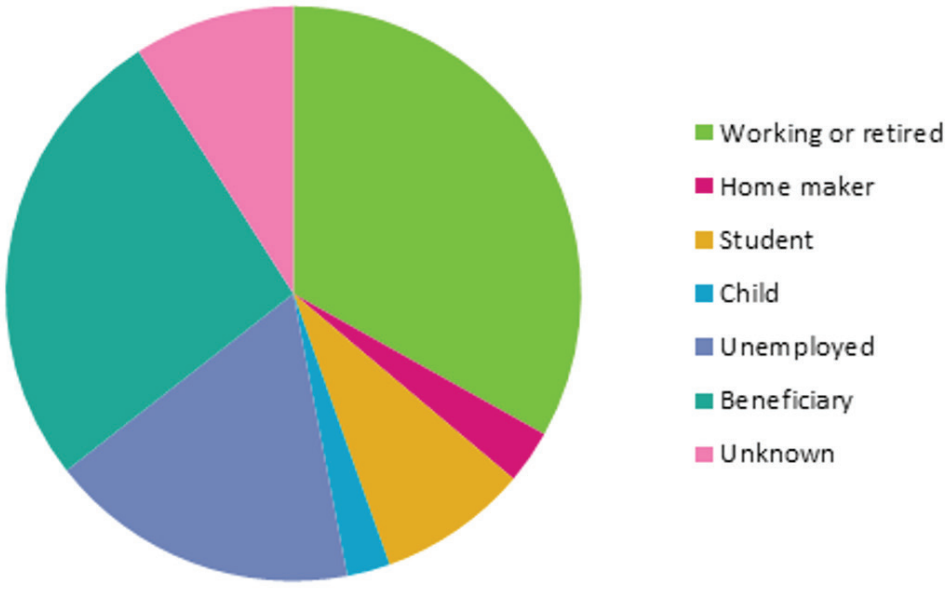
Employment status

A large proportion of patients were not employed at the time of death (73 patients, 44%); 55 patients (33%) were working or retired; 44 patients (27%) were beneficiaries; 18 patients (11%) were children or students, five patients (3%) were home makers and work status was not available for 15 patients (9%) (Figure 5).

Discussion

By definition, SUDEP is always sudden and unexpected, and it causes enormous grief to families. It is a tragic cause of early loss of life. In this study 67% of patients were under the age of 46 years at the time of their death, and 36% were younger than 31 years.

Figure 5: Employment status.



As with previous studies, we found a higher proportion of male deaths than female deaths.

Our findings are similar to those reported recently from the North American SUDEP registry (NASR).[10] The authors identified 237 definite and probable cases of SUDEP. The median age at death was 26 (range 1–70), and 62% were male. Most (93%) SUDEPs were unwitnessed; 70% occurred during apparent sleep; and 69% of patients were prone when discovered.

AED non-compliance has previously been considered a contributing factor for SUDEP. In the NASR study, only 37% of cases of SUDEP took their last dose of anti-seizure medications (ASMs).[10] We could not determine whether patients had taken their most recent dose of ASM, but the majority of patients in our study had at least one anti-epileptic detected by toxicology.

Unemployment rates in our cohort (73 patients, 44%) are far higher than in the general population. This may indicate that these patients had particularly severe epilepsy, but it also indicates serious social disadvantage in this group.

This retrospective study, based on coroners' reports, and post-mortem and toxicology reports, has confirmed that SUDEP is a major cause of premature mortality in people with epilepsy in New Zealand. However, there is much that we still do not know. For example, the type of epilepsy and the aetiology was only documented in one-third of cases in this series, and information about seizure frequency and duration of epilepsy was not consistently reported. It is likely that this study underestimated the number of patients who died due to SUDEP. A recent meta-analysis of SUDEP, noted that previous studies were likely to underestimate the true incidence of SUDEP.[6] The incidence of epilepsy in New Zealand is uncertain, but most Western countries report a prevalence of approximately 0.7%.[11] If this is true for New Zealand, we would expect approximately 33,500 people to have epilepsy. If the incidence of SUDEP in New Zealand is 1.2 per 1,000 people with epilepsy per year,[6] we would expect that approximately 40 people with epilepsy will die annually from SUDEP. However, in this study, the number of deaths per year ranged from 11 to 26. It is possible that the incidence of SUDEP is declining, but we suspect that not all cases were identified.

We are now planning to conduct a prospective study to determine the true incidence of SUDEP in New Zealand. This study is being performed in conjunction with the chief coroner, Judge Marshall, and the Neurological Association of New Zealand. The study is being funded by the Neurological Foundation of New Zealand and the Auckland Medical Research Foundation. During this study we will also gather information about possible risk factors for SUDEP. All coroners will be made aware of the study, as will forensic and coronial pathologists. We would like to hear about cases from multiple sources, and we would therefore request that all neurologists, paediatric neurologists, general physicians, paediatricians and general practitioners notify the research group of all deaths in patients with epilepsy, so that we can be sure that we identify all SUDEP cases.

We hope that this future study will provide valuable information about this tragic condition.

Competing interests:
Nil.
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