



Epilepsy and seizure-related deaths: Mortality statistics do not tell the complete story

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ABSTRACT

Introduction: The objective of the study was to identify where epilepsy or seizures may be the underlying cause of death but not identified by the death certification process in the Australian coronial system and to better characterize such deaths.

Methods: Australian National Coronial Information System (NCIS) closed cases for the Australian Capital Territory (ACT) (population average 348,000) over 13 years were searched using cause of death, and a text search of police and autopsy reports, to identify all deaths where epilepsy or seizures were mentioned. Deaths where the underlying cause of death was not seizures or epilepsy were excluded (including suicide). The remaining cases (75) were categorized by the circumstances of death. Suspected sudden unexpected death in epilepsy (SUDEP) cases were further classified using the unified definition of SUDEP of Nashef and colleagues (2012).

Results: Of the final 75 cases, only 44 were found by the cause of death search. Key word document searches found another 31. Cases were classified as Definite SUDEP (37), Definite SUDEP Plus (10), Probable SUDEP (1), Possible SUDEP (3), Near SUDEP (4), Near SUDEP Plus (1), Asphyxia (3), Treatment-related (1), Head injury (2), Drowning (2), motor vehicle accident (MVA) (1), deaths related to a single convulsive seizure (6), and status epilepticus (SE) (4). Cases were 80% male.

Conclusions: Epilepsy and seizure-related deaths are underreported in the Australian Coronial system. Enhanced documentation of the causal chain of events leading to deaths would increase recognition. Using the unified SUDEP definition would expand SUDEP identification.

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1. Introduction

Mortality related to seizures is appropriately becoming a focus of research and community interest. However, to accurately quantify and characterize deaths where epilepsy or seizures are the underlying cause is challenging. Research suggests that such deaths are likely to be inaccurately reported, even among people with an established diagnosis of epilepsy [1,2]. Epilepsy is reputed to carry an increased mortality rate, 2–3 times higher than that of the general population [3], with the risk of sudden death in young people increased 24–28 fold [4–6]. Nevertheless, despite a known epilepsy diagnosis in a decedent, seizures are sometimes overlooked as the underlying cause of death [1]. Strategies to prevent death from seizures are urgently required; however, this research requires sharper insight into the relationship between seizures and mortality, based on a more precise reporting of seizure-related deaths [1,7].

There are inherent limitations in mortality databases that can restrict the acquisition of knowledge regarding seizure-related deaths. Mortality statistics generally code any certified epilepsy-related deaths using the *International Statistical Classification of Diseases and Health-related Problems* (ICD) [8] under the category G40. There are subcategories that can be used to distinguish between various types of epilepsy but not the specific cause of death. The ICD category R56 can be used for convulsions. If status epilepticus (SE) is nominated on the death certificate, the specific ICD code G419 can be applied. Consequently, if researching by ICD code only, without the benefit of additional information about the deaths, it is not possible to identify causal differences between epilepsy-related deaths apart from those due to SE [7].

If an epilepsy diagnosis has not been made prior to death, even where a history of seizures exists, uncertainty can lead seizures to be discounted in the cause of death reporting. If resuscitation, drowning, or head injury follows a seizure, with a subsequent death in hospital, failure to note the seizure as the underlying cause of death on the certificate will lead to alternative coding, and the death will not be identified as seizure-related in either a cause of death or a coding search [7].

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At the time a death certificate is written, if those responsible for certifying the death do not understand, or fail to recognize, the potential role of seizures as a contributing factor in some deaths such as sudden unexpected death in epilepsy (SUDEP), deaths may be certified as due to an unknown cause or due to a competing cause where some evidence of a concomitant condition exists and consequently coded as such [1,2,7].

To fully appreciate the frequency and pattern of seizure-related mortality, it is necessary to delve beyond summary mortality statistics and death certificates if possible, setting wide parameters to ensure that all potentially relevant data are identified for assessment. Seizure-related deaths occur in people who have not been given a diagnosis of epilepsy, and yet, there may be common mechanisms. Restricting research cases to only those with a formal diagnosis of epilepsy may well cause researchers to miss insights into pathophysiology that could be found through the examination of a wider spectrum of deaths associated with seizures, for example, deaths in people with seizures who have not had access to appropriate medical review, deaths following a first seizure, or deaths in children with febrile seizures [7].

This study aimed to investigate where epilepsy or seizures may be the underlying cause of death but this has not been identified by the death certification process in an Australian mortality database. Through a record review, the study also aimed to identify information that would enhance understanding of the circumstances and contributing factors in such deaths.

The study utilized the database of the Australian National Coronial Information System (NCIS) [9]. Through the NCIS, researchers can directly access key documents relating to each case that has been investigated. The database offers a valuable source of information in relation to deaths due to seizures because, whereas around 10–15% of all Australian deaths usually pass through the coronial service [10,11], in the case of epilepsy, 55% of all deaths in Australia that were coded as G40 in the 13 years of our study were handled by coroners (Australian Bureau of Statistics (ABS), email communication, September 2016).

This study aimed to identify all deaths in the NCIS database in one Australian state over a 13-year period where epilepsy or seizures might be considered as the underlying cause (including SE), regardless of the certification or coding attached to the deaths. The study sought to be inclusive in its approach, to ensure that full range of potentially epilepsy or seizure-related deaths in the study cohort might be identified. Exclusions were acute symptomatic seizures that resulted, for example, from surgery, trauma, or chemical provocation, and those where post-mortem evidence indicated that seizures were the outcome of another underlying cause. The study did not include cases of suicide in people with epilepsy.

The unified definition of SUDEP provided a tool to facilitate identification and classification of possible SUDEP deaths (Table 1) [12].

2. Material and methods

2.1. The database

The NCIS is an internet-based data storage and retrieval system for Australian and New Zealand coronial cases. It contains data about deaths reported to an Australian coroner from July 2000 (Queensland Jan 2001) and to a New Zealand coroner from July 2007 [9]. In Australia, all deaths must be reported to a coroner for investigation, if they are unexpected, unnatural, violent, occur during an anesthetic or when the person is in care or custody, and deaths where the identity of the person is unknown [10]. The police will usually be called to the scene of the death and a police report created. In most cases, an autopsy is required, and this is carried out by a doctor trained in pathology. The coroner's staff can seek out additional information if required, including a medical history; however, without a centralized medical records system in Australia, the current medical history of the patient is not always accessible. The autopsy report, police report, toxicology report, and

coroner's findings are held in the database and accessible to researchers with permission.

2.2. Case identification

This study presents a retrospective case series examination of NCIS closed cases between 2001 and 2013 (inclusive) for the Australian Capital Territory (ACT). The population average for that period was 348,800 [13]. A cause of death search was executed using the search terms 'epilep' or 'seizure' or 'convuls'. A keyword search was also performed across all documents (excluding toxicology). A stem search was not possible for the document search so a range of terms was chosen (epilepsy, epileptic, seizure/s, convulse convulsing, convulsion/s, and fit). Toxicological records were available for perusal, but they were not included in the keyword search because the information they contain means that many unrelated cases would be retrieved. Once the search was complete, duplicates were removed, and each remaining case was subject to examination and interpretation using all available information.

All material was reviewed to remove cases that were not required for the study. In the first instance, this included cases where key search terms had retrieved irrelevant cases. For example, the word seizure may have occurred in a police report with no connection to clinical matters or a report may have said that the decedent did *not* have epilepsy. The remaining cases were then reviewed to apply the clinical exclusions. For example, in an individual with epilepsy, there may have been clear evidence from the postmortem indicating an alternative underlying cause of death. In other cases, a decedent may have had a seizure noted in the autopsy or police report because it occurred following a brain trauma or myocardial infarction. The seizure therefore would not be considered as the underlying cause of death. The remaining cases were then reviewed again by both researchers, one of whom is an epileptologist, and categorized.

2.3. Categorization of cases

Potential SUDEP deaths were mapped against the unified definition of SUDEP [12] (Table 1), which provided a useful tool to assist with the categorization of complex cases. For example, the term Definite SUDEP Plus was helpful where a concomitant condition was present but may not have been responsible for the death, and the term possible SUDEP allowed for recognition of cases where an alternative cause could have been solely responsible for the death. The unified definition of SUDEP requires a diagnosis of epilepsy to be present.

Sometimes, this information is not available to an investigating team, or there has been no formal diagnosis of epilepsy, although there is an anecdotal history of possible seizures collected through the police investigation that raises suspicion of epilepsy. Because this study seeks to be inclusive and exploratory, such cases were included.

Thirteen categories were used to capture the full range of cases identified within the database. These were the following: Definite SUDEP, Definite SUDEP Plus, Probable SUDEP, Possible SUDEP, Near SUDEP, Near SUDEP Plus, Asphyxia, Treatment-related, Head injury, Drowning, motor vehicle accident (MVA), Single convulsive seizure, and SE.

Approval for the research was granted by the Justice Ethics Approval Committee and the University of Melbourne Human Ethics Committee.

3. Results

3.1. Summary

The NCIS records for the ACT between 2001 and 2013 (inclusive) held 4149 closed cases. The search yielded 395 cases. Duplicates were removed leaving 380 cases to be individually assessed (Table 2).

After review, 75 cases were retained and categorized. Of the final cases, 44 had been found by the cause of death search and 31 through

Table 1
Proposed unified definition and classification for Sudden Unexpected Death in Epilepsy (SUDEP) by Nashef et al. [12].

1. *Definite SUDEP*:^a Sudden unexpected, witnessed or unwitnessed, nontraumatic and nondrowning death, occurring in benign circumstances, in an individual with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus (seizure duration ≥ 30 min or seizures without recovery in between), in which postmortem examination does not reveal a cause of death.
- 1a. *Definite SUDEP Plus*:^a Satisfying the definition of Definite SUDEP, concomitant condition other than epilepsy is identified before or after death, if the death may have been due to the combined effect of both conditions, and if autopsy or direct observations/recordings of the terminal event did not prove the concomitant condition to be the cause of death.
2. *Probable SUDEP/Probable SUDEP Plus*:^a The same as Definite SUDEP 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.
3. *Possible SUDEP*:^a A competing cause of death is present.
4. *Near-SUDEP/Near-SUDEP Plus*: A patient with epilepsy survives resuscitation for more than 1 h after a cardiorespiratory arrest that has no structural cause identified after investigation.
5. *Not SUDEP*: A clear cause of death is known.
6. *Unclassified*: Incomplete information available; not possible to classify.

^a If a death is witnessed, an arbitrary cutoff of death within 1 h from acute collapse is suggested.

the document search (Table 2). Table 3 lists the number of cases allocated to each category and how they were identified through the search process. For the categories of Probable SUDEP, Definite SUDEP Plus, Near SUDEP Plus, Treatment-related, Head injury, Drowning, and MVA, 100% of cases were identified only through the keyword search of documents.

3.2. Definite SUDEP

Thirty-seven cases were considered appropriate for the Definite SUDEP category. Of these, 31 were found through the cause of death search (epilep or seizure or convulse). Of the 37 cases, 21 (57%) had been classified as SUDEP by the forensic pathologist. Another 13 (35%) cases had been certified using a variety of terms such as; death due to asphyxia from an epileptic fit, death due to an epileptic fit, or sudden adult death. Three cases (8%) had been certified as unascertained. Of these, one was an adult male with an anecdotal family history of occasional seizures including urinary incontinence but no formal epilepsy diagnosis. He was found dead in bed in the morning with evidence of incontinence. Because the seizures had not been medically documented, the pathologist noted that SUDEP could not be assumed. Two were children; one died overnight and was found face down in his cot. He had a history of fever that day and a past history of a prior febrile seizure. The second child had brain damage with a history of seizures under investigation and died overnight in his cot.

Table 2
Search categories used to identify cases of epilepsy or seizure-related death.

NCIS search categories	Cases identified	Duplicates removed	Review	Final cases
COD	47	0	47	44
Epilepsy	102	0	102	23
Epileptic	33	11	22	1
Seizure	67	1	66	3
Seizures	113	2	111	1
Convulse	3	1	2	0
Convulsing	7	0	7	0
Convulsion	5	0	5	1
Convulsions	2	0	2	0
Fit	16	0	16	2
Total	395	15	380	75

Abbreviations: NCIS, National Coronial Information System; COD, cause of death.

3.3. Definite SUDEP Plus

Of the 10 cases allocated to the category of Definite SUDEP Plus, all decedents had a history of seizures, although one, with a history of convulsions every 2–3 years over a long period, had not been given diagnosis of epilepsy. In all cases, there were factors apart from seizures that required assessment in deciding the cause of death.

In four cases, the cause of death was certified as unascertained. Sudden unexpected death in epilepsy was a possibility, and the evidence supporting an alternative to epilepsy was not considered to be strong enough on its own. A firm conclusion was not reached. The competing considerations were a lung condition, a minor vascular abnormality in a pregnant woman, the uncertain toxicological effect of a medication, and diabetes.

In one case, there was a medically documented history of occasional convulsive seizures over some years, but no diagnosis of epilepsy had been given. The fit elderly adult male was found prone on the floor, and the cause of death was attributed to presumed cardiac arrhythmia.

In the remaining five cases, there was uncertainty. The reports included comments such as ‘no morphological findings for death’, ‘in the absence of more specific findings death is best attributed to’, ‘determining the cause of death in this case is difficult’, and ‘can’t exclude epilepsy’ or ‘can’t confirm epilepsy’. Nevertheless, the pathologists chose to attribute the deaths according to findings that existed. The causes of death selected were ischemic heart disease (3), coronary artery disease (1), and alcoholism (1).

3.4. Probable SUDEP

One death was assigned to the Probable SUDEP category. The decedent had a 10-year history of epilepsy for which he was taking medication. He was found dead in bed following an afternoon sleep. There was no full postmortem, and the death was certified as unascertained.

3.5. Possible SUDEP

Three cases were identified where there was a competing cause that may have been solely responsible for the death. In two cases, the deaths had been certified in children as (sudden infant death syndrome). One child had a history of ‘apneic’ episodes and a family history of epilepsy. He died overnight in his cot. The second child died overnight and was reported to have had two possible seizures in the preceding months. There were also some concerns regarding developmental progress.

In the third case, the forensic pathologist noted that the evidence for ischemic heart disease was strong, but there was also a case for death due to a seizure and that death could be ascribed to either or a combination of both.

3.6. Near SUDEP and Near SUDEP Plus

Four cases were allocated to the Near SUDEP category. All died in hospital. One case was certified as cerebral hypoxia caused by an epileptic seizure. The second case was reported only as ‘hypoxic ischemic encephalopathy’. The third case was a child with a history of febrile seizures prior to the terminal event. The death certificate recorded death as due to ‘hypoxic ischemic encephalopathy’ with an antecedent cause being ‘presumed epileptic fit’. In the fourth case, the decedent had a history of epilepsy that was discussed in the postmortem. However, the cause of death was reported only as ‘global cerebral hypoxia’.

There was one case of death in hospital postcollapse in a person with epilepsy where it was considered difficult to assess the contribution of several individual factors. Death was defined as ‘cardiac arrhythmia’. This case might be best described as Near SUDEP Plus.

Table 3

NCIS cases identified as epilepsy or seizure-related and allocated to study categories by circumstance of the death.

Study categories	Search terms used to identify possible seizure-related deaths in the NCIS database							Total
	COD	Epilepsy	Epileptic	Seizure	Seizures	Convulsion	Fit	
Definite SUDEP	31	4		1		1		37
Definite SUDEP Plus		10						10
Probable SUDEP		1						1
Possible SUDEP	1	1					1	3
Near SUDEP	2	2						4
Near SUDEP Plus		1						1
Asphyxia	3							3
Treatment-related					1			1
Head injury			1				1	2
Drowning		2						2
MVA		1						1
Single seizure	3	1		2				6
Status epilepticus	4							4
Total	44	23	1	3	1	1	2	75

Abbreviations: NCIS, National Coronal Information System; COD, cause of death; SUDEP, sudden unexpected death in epilepsy; MVA, motor vehicle accident.

3.7. Asphyxia

Two cases were identified where an epileptic seizure causing marked aspiration was deemed to have caused death by asphyxiation. Minor aspiration is considered consistent with a SUDEP diagnosis, but severe aspiration itself is a cause of death [12]. These two cases were severe aspiration.

In one additional case, an epileptic seizure had led to asphyxiation as a result of body position following a fall and an object causing obstruction of the airway. All certificates made mention of an epileptic seizure in the cause of death.

3.8. Treatment-related death

One death, which occurred during the early treatment of new-onset seizures, was classified as multiorgan failure caused by hypersensitivity to phenytoin.

3.9. Head injury

Two cases of deaths through head injury related to seizures were identified. In one case, the cause was reported as a subdural hemorrhage with epileptic fit as the antecedent cause. In the other case, although there was an anecdotal history of seizures and the police report provides an account of a seizure-like event prior to the fall, the cause of death at postmortem was certified as 'closed head injury consistent with a fall'. Both cases were coded with codes unrelated to seizures.

3.10. Drowning

Two cases of death through drowning associated with seizures were identified. In one case, there was evidence of a seizure at the time of drowning in a bath in a person who had experienced one prior seizure and was under investigation for epilepsy. The case was certified as drowning. In the second case, a person with epilepsy died in hospital after drowning in a bath after a likely seizure. The death was certified as global cerebral hypoxemia due to partial drowning. Both were coded with no reference to seizures.

3.11. Motor vehicle accident

One case was identified in which a person with epilepsy died as a result of an MVA. The postmortem noted that the decedent was taking epilepsy medication but that no seizures had been reported for more than

10 years. However, the accident description suggests that a seizure-related accident could not be ruled out. The case was coded as an MVA.

3.12. Death in relation to a single convulsive seizure and no known prior history of epilepsy

Six cases were found where death was associated with a single convulsive seizure.

Four deaths were witnessed, and after investigation, two were certified as unascertained and two were certified as due to a convulsive seizure.

Two deaths were unwitnessed. One cause of death was certified as due to a probable seizure. In the other case, the cause of death was not determined at autopsy. A fatal seizure was one option put forward for consideration.

Only one of the six cases attracted a seizure-related coding.

3.13. Status epilepticus

Four cases of SE were identified in the cause of death search. One individual had a history of prior seizures, and three did not. Status epilepticus can occur for many reasons in people who have no history of epilepsy as well as those who do. In some cases, it will not be the underlying cause of death but rather, the outcome of another underlying medical condition [14]. Nevertheless, all these cases are included in the study results because SE is an oft-quoted cause of death in people with epilepsy [14], and it is of interest to note the proportion of deaths in this database that were certified as SE compared with other causes of death.

3.14. Demographics

A summary of demographic data is provided in Table 4.

The median age of death for Definite SUDEP, 42 years (1–79), and near SUDEP, 30.5 years (2–50), was younger than Definite SUDEP Plus, 53.5 years (20–80). The median age of death for the group with SE was high, 69.5 years (67–83).

Males made up 80% of the final 75 cases. Apart from the category of SE, males were the majority in all categories, ranging from 67%–100%.

3.15. Incidence of SUDEP

It is not possible to accurately estimate the incidence of SUDEP in the ACT using only the data from this study because the NCIS cohort does not represent all known SUDEP deaths in the state during the 13 years of investigation. Doctors in the community also registered 22 epilepsy deaths (G409) during this period without referral to a coroner's office

for autopsy (ABS, email communication, September 2016). Those medical records were not available to this study, and it is possible that some of these deaths were SUDEP.

For the purpose of discussion, if we were to consider only the cases identified in our study (Definite SUDEP, Definite SUDEP Plus, Probable SUDEP, Near SUDEP, and Near SUDEP Plus), but exclude possible SUDEP where there is an equally strong possible alternative cause of death, we identified a total of 53 cases within the unified diagnosis of SUDEP (albeit that some had a history of seizures without a medical diagnosis of epilepsy). Assuming an epilepsy prevalence of 7.1 per 1000 population [15] with an annual average population of 348,000, the observed annual incidence of SUDEP in the ACT would be 1.65 per 1000 person-years. If Definite SUDEP cases only were considered, the rate would be 1.15 per 1000 person-years [15].

A pooled analysis of selected population-based studies reported a rate of 1.16 per 1000 person-years [15]. However, it is acknowledged that these findings are affected by methodological differences, variations in the accepted prevalence of epilepsy, inconsistent definitions of SUDEP, and the restricted information at the time of case ascertainment. Using the combined definition of SUDEP, our observed number of SUDEP cases is higher than the expected rate, but this is a likely effect of our inclusive approach and the utilization of the combined definition of SUDEP drawing in cases that would have been excluded in other studies.

4. Discussion

Having reviewed the NCIS database for ACT cases over a 13-year period, this study identified 75 cases of deaths where epilepsy or a seizure could have been the underlying cause. However, only 44 cases could be identified through the cause of death search. The remaining cases required a full text search of key documents for all cases held in the database. The keyword search identified 333 cases from which 31 proved to be relevant. This demonstrates that there is significant underreporting of seizure-related deaths.

Furthermore, when the death recording advances on to the coding process, deaths that have not been attributed to epilepsy or seizures are unlikely to attract a seizure-related ICD code [7]. It follows that such cases will not be recognized as seizure-related deaths by the ABS, which is responsible for coding and reporting all deaths in Australia [10], and any research or public policy decisions incorporating that data will underestimate their frequency. For example, the official statistics of the ABS for the ACT during the 13-year period of our study, for deaths due to epilepsy, are based on the recording of codes G40 and G419 [10,11]. Sixty-six deaths are recorded as G40 and six as G419. Of those coded as G40, 44 were identified through the NCIS and 22 by doctors in the community (ABS, email communication, September 2016). Using broader inclusive search categories, our study identified (excluding SE) an additional 31 cases in the NDIS database where epilepsy or seizures may have been the underlying cause of death. Our retrospective study cannot definitely define the cause of all these deaths, but the results indicate that there are deaths buried in the data that need to be recognized for consideration in future research projects and public health discussions.

The majority of the deaths making up the final cases in this study were deemed to be potentially SUDEP-related, 56/75 (75%) (Definite SUDEP, Definite SUDEP Plus, Probable SUDEP, Possible SUDEP, Near SUDEP, and Near SUDEP Plus). The high proportion of such deaths in the cohort echoes an earlier Australian study in Queensland that reported 70% autopsy-confirmed SUDEP deaths in a cohort of epilepsy-related deaths with postmortem data, although the case ascertainment and SUDEP definitions used are different [16].

It was interesting to note that Definite SUDEP cases were frequently identified by the forensic pathologists who had incorporated the term into death certificates from as early as 2002. Of the 37 cases identified in this study, the forensic pathologists had recognized and certified 21

Table 4

Demographic data of cases in the study population where deaths were categorized as epilepsy or seizure-related.

	Sex		Total	Age
	Female	Male		Median age
Definite SUDEP	7	30 (77%)	37	42 (1–79)
Definite SUDEP Plus	2	8 (20%)	10	53.5 (20–80)
Probable SUDEP		1 (100%)	1	40
Possible SUDEP		3 (100%)	3	0.5 (0.25–56)
Near SUDEP		4 (100%)	4	30.5 (2–50)
Near SUDEP Plus	1 (100%)		1	48
Asphyxia		3 (100%)	3	20 (9–43)
Treatment-related		1 (100%)	1	80
Head injury		2 (100%)	2	44 (40–48)
Drowning		2 (100%)	2	28 (18–38)
MVA		1 (100%)	1	53
Status epilepticus	3	1 (25%)	4	69.5 (67–83)
Single convulsive seizure	2	4 (67%)	6	46.5 (30–65)
Total cohort	15	60 (80%)	75	43 (0.25–83)

Abbreviations: SUDEP, Sudden unexpected death in epilepsy; MVA, motor vehicle accident.

(57%). In another 13/37 cases, while SUDEP could have been an appropriate diagnosis, it was not applied. Nevertheless, the cause was still attributed to epilepsy. This study followed death certification over 13 years from 2001, and it appears that awareness and confidence in recognizing and applying the term SUDEP in Australia has increased over time, with 10 of the 13 unclassified cases occurring between 2001 and 2007 but only three cases occurring between 2008 and 2013.

Three cases of 37 Definite SUDEP cases (8%) had been certified as unascertained. These included two individuals with prior seizures and one with a prior febrile seizure, none of whom had an epilepsy diagnosis. According to the guidance on SUDEP, the classification requires a diagnosis of epilepsy [12], and this currently directs clinical decision-making for forensic pathologists. However, for the purpose of this study, these cases have been included.

The terms near Definite SUDEP Plus, Near SUDEP, and Near SUDEP Plus were not found in any of the NCIS reports that were examined. This was not surprising because the unified definition of SUDEP that proposes the use of these categories was published in 2012 and has not yet become widely adopted. However, these terms proved to be very useful in the analysis of the data, providing tools to interpret and classify some of the complex cases where, despite complicated circumstances, the potential for seizure involvement in a death needs to be recognized and has significant ramifications for the production of public health statistics.

In classifying the deaths according to the unified definition, there were challenges in distinguishing between those that should be categorized as Possible SUDEP and Definite SUDEP Plus. According to the unified definition, if competing conditions are felt to be alternate possible causes of death, such cases are to be classified as Possible SUDEP. In our study, six cases were identified where competing postmortem findings were identified and the alternate diagnosis selected instead of SUDEP. However, the nature of the findings and the lack of certainty expressed in the diagnosis implied a diagnosis of exclusion in the absence of any other direct evidence. Our study was retrospective, and when these deaths occurred, the unified definition of SUDEP was not available. It is not possible to know how the pathologists would have classified these cases had they had the benefit of the unified definitions, but retrospectively, these cases appear to agree more with the intention of the classification Definite SUDEP Plus. Nashef and colleagues write as follows:

“In some situations, evidence indicates that a preexisting condition could have contributed to the death, which otherwise is SUDEP. Examples are coronary insufficiency...in a case of sudden unexpected death associated with a habitual epileptic seizure, but autopsy fails

to reveal myocardial infarction or other structural causes of death. We propose that such a situation be designated as 'Definite SUDEP Plus' since the preexisting conditions did not clearly cause sudden death, but they may have been essential contributors to the death". [12]

They go on to say that without this category, such deaths might be placed in the Possible SUDEP category and risk exclusion from research. The key point here is whether the preexisting conditions could have *clearly caused the death*. In our six cases, the diagnosis did not appear to be confident or clear, and for this reason, they have been categorized in this study as Definite SUDEP Plus.

Two deaths occurred in children with a history of febrile seizures. Although febrile seizures have historically been classified as benign, research has identified an association between sudden unexpected deaths and febrile seizures under some circumstances [17,18]. This information has implications for the education of health professionals and parents regarding the ongoing investigation and management of children who have a febrile seizure and highlights the necessity of identifying such cases for research.

It is notable that none of the accidental deaths appeared in the cause of death search. These were only identified through the painstaking process of the full text search and individual case assessment. Lack of precision in the recording of such deaths leads to the loss of valuable information that can then no longer be retrieved from death certificates or ICD code summaries. The only path to identification would be extensive searching of any related documents.

The number of deaths certified as SE (4) was small. It is unlikely that any were missed because these deaths have their own ICD code, and the definition of SE is quite clear. They represented only 8% of the total deaths identified by the study. The median age, 69.5 years (67–83), accords with a reported increased incidence of SE in individuals aged 60 years and over [19]. Of the four cases, only one (25%) person had a history of seizures. This also aligns with published data that indicate that more than 50% of SE cases will not have a history of epilepsy [19].

The median age of the Definite SUDEP cases, 42 years (1–79), reflects the findings of previous studies [20]. The median age for Definite SUDEP Plus, 53.5 years (20–80), was higher than that of Definite SUDEP, a finding that is not surprising given that the likelihood of an autopsy revealing cardiovascular pathology or pathology in other organs is increased with age [7]. The presence of such findings can lead the investigator to form a judgment based on the positive postmortem findings rather than the circumstances of the deaths [20]. As a result, it may be, as several authors have recently suggested, that published figures represent an undercount of SUDEP in older age groups [15].

The high percentage of males identified by the study was a surprising finding. A higher incidence of male deaths has been identified in some prior studies [21], but the bias to males in this study was particularly strong in all categories apart from SE. It may represent a referral bias favoring male deaths.

Our study has limitations. The investigation was limited to data held by the NCIS only. We did not have access to information regarding the 22 deaths certified as G40 by doctors in the community during the time of our study, and therefore, we could not provide a statewide summary. Nevertheless, because of the high number of epilepsy cases that are directed to coroners in Australia, 44 deaths certified as G40 were available through the NDIS data. We had no direct access to patient medical files beyond the information available through the forensic pathology reports, and in some cases, patient history was limited. We also acknowledge that this investigation was a retrospective analysis by researchers with an interest in seizure-related death, and conclusions can be influenced by the bias of different professional perspectives. Similar reviews have noted differing conclusions where mortality data are reviewed by teams from differing medical specialties [1].

5. Conclusions

This study has demonstrated that Australian death certification processes in the coronial system lead to an underestimation of epilepsy and seizure-related deaths. Unless the causal pathway is clearly reported, the opportunity to track these deaths is diminished. Accurate and complete certification of deaths due to drowning or accidents following a seizure, deaths in hospital following resuscitation after a near SUDEP, or deaths following a single unprovoked seizure is essential. Where epilepsy is not an appropriate code for some deaths, there is an opportunity to use ICD code R56 for other unspecified convulsions.

For epilepsy-related deaths, there is a trend towards greater recognition and certification of SUDEP. The application of the unified definition of SUDEP would assist forensic pathologists to achieve a more complete ascertainment of such deaths, including deaths that occur in hospital after attempted resuscitation.

Although there is currently no specific code for a SUDEP death, when SUDEP is listed on the death certificate as the cause of death, it will facilitate identification of cases through a cause of death search in some databases. Health professionals require education [22] and encouragement to make full use of current reporting systems in order to fully capture the burden of deaths due to seizures.

Declaration of Competing Interest

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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