View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

Seizure (2007) **16**, 1–7

SEIZURE

www.elsevier.com/locate/yseiz

REVIEW

Sudden unexpected death in epilepsy patients: Risk factors
A systematic review

C.P.J.A. Monté [a,*], J.B.A.M. Arends [b], I.Y. Tan [b], A.P. Aldenkamp [a,b], M. Limburg [a], M.C.T.F.M. de Krom [a]

[a] *University Hospital Maastricht, Department of Neurology, Maastricht, The Netherlands*
[b] *Kempenhaeghe Epilepsy Centre, Heeze, The Netherlands*

Received 16 May 2006; received in revised form 9 October 2006; accepted 23 October 2006

KEYWORDS
Epilepsy;
SUDEP;
Risk factor;
Evidence based

Summary

Introduction: Several risk factors for sudden unexplained death in epilepsy patients (SUDEP) have been proposed, but subsequent work has yielded conflicting data. The relative importance of various risk factors for SUDEP was never explored. The aim of this study is to review systematically risk factors for SUDEP and also to determine their relevance for SUDEP by calculating relative risk factor ratios.
Methods and materials: Authors performed a literature-search on "SUDEP" in Medline, the Cochrane Library and EMBASE. Studies with unknown number of SUDEP cases or with less than five SUDEP cases and reviews were excluded from further analysis. The value of each paper was assessed, based on the quality of the study and the reliability of the diagnosis of SUDEP. This value ranged from 1 (low quality) to 10 (high quality). Papers with a value below 7 were eliminated for further analysis. For each analysed factor, a risk factor ratio was determined, with a higher ratio for a stronger risk factor.
Results: A number of strong risk factors for SUDEP: young age, early onset of seizures, the presence of generalized tonic clonic seizures, male sex and being in bed. Weak risk factors for SUDEP: prone position, one or more subtherapeutic bloodlevels, being in the bedroom, a strucural brain lesion and sleeping.
Conclusions: In this study, authors have designed a quality scale to select papers. The relative importance of risk factors for SUDEP is demonstrated.
© 2006 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.

* Corresponding author.
E-mail address: cpja.monte@gmail.com (C.P.J.A. Monté).

1059-1311/$ – see front matter © 2006 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.seizure.2006.10.002

Contents

Introduction

Several potential risk factors for sudden unexpected death in epilepsy patients (SUDEP) have been investigated, but results from different studies are conflicting and the relative importance of various risk factors has not been explored in depth.[1–35] Reviewers have tried to summarise the risk factors for SUDEP but the results were not always consistent. Authors found the following factors: generalised tonic clonic seizures,[28,36–39] high seizure frequence,[28,36,37,39–41] onset of epilepsy at early age,[36,39,42] long duration of epilepsy,[36,38,40] polytherapy/high number of antiepileptic drugs (AED),[36–38,40] frequent changes of doses of AED,[36] seizure preceding death,[40] subtherapeutic AED levels,[40] young age,[28,38,40] candidates for epilepsy surgery and epilepsy referral centres,[38,40] coexisting neurological disease,[37] male sex,[28,42] poor compliance with AED,[28] history of head trauma,[38] alcohol abuse,[38] being at home,[38] being in bed,[38] seizure severity,[42] seizure etiology,[42] partial onset seizures.[42] Inconsistent and inaccurate death certification, lack of agreed definitions, different terminology, and different understanding of the same terminology hamper research into mortality in epilepsy and result in national incidence numbers that are difficult to interpret.[43] In fact, comparisons of SUDEP rates and results are nearly impossible because study variables may include different definitions of sudden unexpected death in epilepsy, group compositions or documentation requirements. In addition, the accuracy of diagnosis, the use of AED prescriptions as a marker for epilepsy, the quality of postmortem data, death certificates that may not mention epilepsy or may incorrectly state the cause of death, and selection bias, are some other factors which may also affect the accuracy of SUDEP rates in these studies.[44] None of the reviews applied a system of weighing the evidence of the different studies. The aim of this paper is to systematically review the risk factors for SUDEP and to determine the relevance of each risk factor for SUDEP by weighing the individual studies.

Methods and materials

Authors selected good quality studies analysing risk factors for SUDEP and calculated a risk factor total studies ratio (RFT) for each risk factor. The RFT is given a positive or a negative value based on the results in the studies analysing the possible risk factor and corrected for the number of included SUDEP cases in the different studies (see Table 1). Authors consider the risk factor a strong risk factor for SUDEP if RFT $\geq$ 1.0, a weak risk factor for SUDEP if RFT $\geq$ 0.5 and no risk factor for SUDEP if RFT $<$ 0.5(Tables 2 and 3).

Results

In total, 120 papers were collected (Table 4). Ninety three papers were excluded (Table 5) leaving 27 papers (908 cases of SUDEP) for further analysis (Table 6) The results of the analysis of the different factors are summarised in Fig. 1.[1–14,16–26,45,46] A number of strong risk factors for SUDEP were identified: young age, early onset of seizures, the presence of generalized tonic clonic seizures, male sex and being in bed. Weak risk factors were prone position, one or more subtherapeutic bloodlevels, being in the bedroom, a structural brain lesion and sleeping. Factors not considered to be a risk factor are summarised in Table 7.

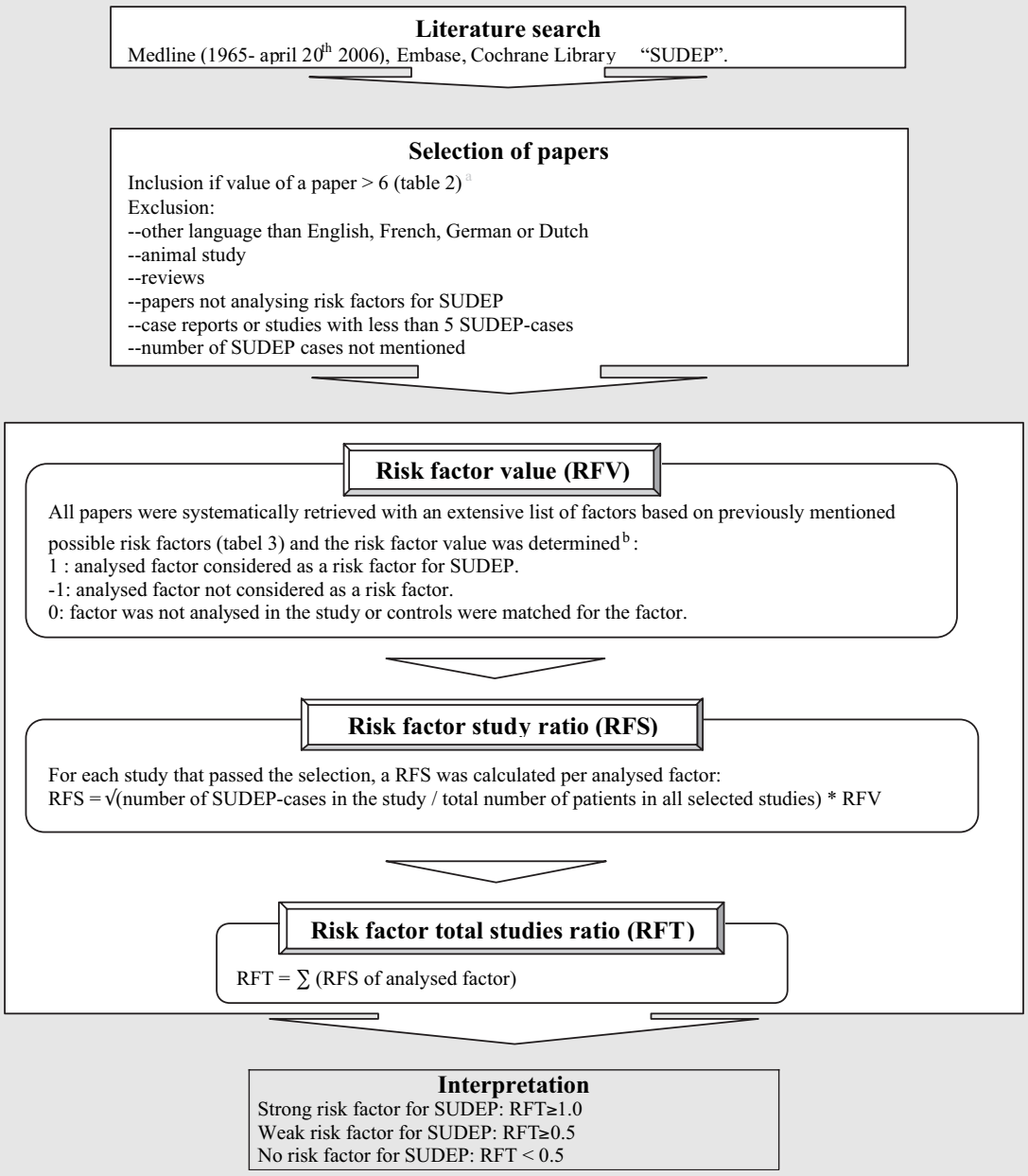
Discussion

Authors identified strong risk factors for SUDEP: young age, early onset of seizures, the presence of generalized tonic clonic seizures, male sex and being in bed. Weak risk factors were prone position, one or more subtherapeutic bloodlevels, being in the bedroom, a strucural brain lesion and sleeping.[1–14,16–26,45,46]

In another evidence-based analysis, the main risk factors were a seizure preceding death, subtherapeutic AED levels, youth (age 15–30 years), high seizure frequency (more than 15 seizures per month), high number of AED (more than two) and long duration of epilepsy (more than 15 years).[40] The different results may be explained by different definitions of the factors and by a different methodology.

Authors' methodology has various advantages. The selection of studies and the determination of

Table 1 Flowchart for analysis of possible risk factors



[a]The value of each paper was estimated, based on the quality of the study and the reliability of the diagnosis of SUDEP (Table 2). The quality of the study was expressed in a rating, and depended on the availability of a definition of the population, on the type and design of study and the number of patients included. The score ranged from 1 to 10; a higher number indicating a better quality of the study.

[b]In case an author did not decide whether a factor was or was not a risk factor for SUDEP, the authors performed the following procedure: If possible, authors used a χ^2-test. Otherwise the factor was considered a risk factor for SUDEP in the study in question if the factor was present in more than 50% of the patients under study. Inconsistencies were discussed in a panel of three authors (CM, JA, FT). In studies with an inclusion of only children or people less than 45 years of age, authors decided that the RFV of "young age" was zero.

the relevance of the risk factor are clear and transparant. Authors only included papers in which the term "SUDEP" was used. The quality of each study was expressed as a rating. Authors present a listing of risk factors by relevance. The relevance of a risk factor is based on the number of included SUDEP cases in the different studies and on a positive or a negative risk factor value, the latter allowing the authors to use a negative result in a study. In the review of Téllez–Zenteno the relevance of a risk

Table 2 Possible scores assigned to the papers based on the quality of the study and the reliability of the diagnosis of SUDEP

Item			I score	M score
Study	Definition of population	Mentioned	1	1
		Not mentioned	0	
	Study design	Cohort analysis/Case control study	1	1
		Unknown	0	
	Prospective	Prospective/premortem registration/follow-up	2	2
		Retrospective	1	
		Unknown	0	
	Number of cases	>10 cases	2	2
		≤10 cases	1	
SUDEP	Definition of SUDEP	Mentioned	1	1
		Not mentioned	0	
	Definite SUDEP/autopsy	Only definite SUDEP	2	2
		Also definite SUDEP	1	
		Only probable or possible (but no definite) SUDEP	0	
	SUDEP decided	By neurologist/coroner/team of specialists	1	1
		Unknown who decides	0	

I score: item score; M score: maximum score.

Table 3 Analysed factors for SUDEP

Category	Analysed factor
Demography	Young age, male sex, black race
Epilepsy	Generalised tonic-clonic seizures, high seizure frequency, chronic epilepsy, symptomatic epilepsy, structural brain lesion, posttraumatic epilepsy, early onset epilepsy
Psychiatry	Recent unusual stressful life event, psychiatric illness, mental retardation, psychotropic drug prescription, use of antidepressants, use of anxiolytics, use of antipsychotics, alcohol abuse
Therapy	Use of particular anti epileptic drugs (AED), the prescription of carbamazepine, the prescription of phenytoin, increasing number of AED prescribed, subtherapeutic AED levels, poor AED compliance, epilepsysurgery, vagal nerve stimulation
Circumstances of death	Lying in bed, sleeping, proneposition, being in bedroom, being outside the house
Other	Hyponatriemia, cardiovascular disease

Young age: <45 years at death; high seizure frequency: ≥1 seizure a month; chronic epilepsy: epilepsy with a duration >10 years; early onset: <45 years at diagnosis of epilepsy.

factor was based on the percentage of studies in which the factor was a positive risk factor.[40] Authors' methodology has, however, also some disadvantages. To authors' knowledge, the risk factor value method has never been validated before but this is not necessary because authors can assume that the accuracy of the study increases with the square root of the number of included patients. Papers scoring below 7 were discarded. Setting the bar at 7 was an arbitrary choice of the authors. Authors are aware that authors might forget to

Table 4 Search results for "SUDEP"

Database	Number
Medline	95
Cochrane library	0
Embase	105
Total	120

Table 5 Excluded papers

Reason for exclusion	Number
Other language	7
Animal study	6
Reviews	30
Not analysing risk factors for SUDEP	39
Number of SUDEP cases not reported	2
Case report or study with less than five cases	4
Study quality rating less than 7	5
Total	93

Table 6 Included studies (score ≥7) and number of SUDEP cases

Beran[1]	21	Walczak[10]	20	Ficker[20]	9
Nei[2]	21	Opeskin[11]	50	Langan[21]	15
Opeskin[3]	50	Annegers[12]	15	Annegers[22]	8
Nilsson[4]	10	Langan[13]	15	Nashef[23]	26
Salmo[5]	22	Opeskin[14]	44	Leestma[24]	24
Schnabel[6]	39	Henessy[16]	6	Tennis[25]	39
Donner[7]	27	Thom[17]	10	Coyle[26]	40
Nilsson[8]	57	Kloster[18]	42	Langan[45]	154
Antoniuk[9]	20	Nilsson[19]	57	Learkaul[46]	67

mention some items, but authors can expect that good studies are properly described. A clear definition of the population under study is an important methodological issue and, of course, a study without a definition of SUDEP is a bad study and will have more shortcomings. Theoretically, cases of sudden cardiac death could be included in a paper without information on the population under study. However, the authors expect that setting the limit of 7 points has minimized this risk (in fact only five studies were eventually excluded by this threshold). When determining the RFT, the authors did not distinguish between a cohort study and a case control study, while the value of the evidence from

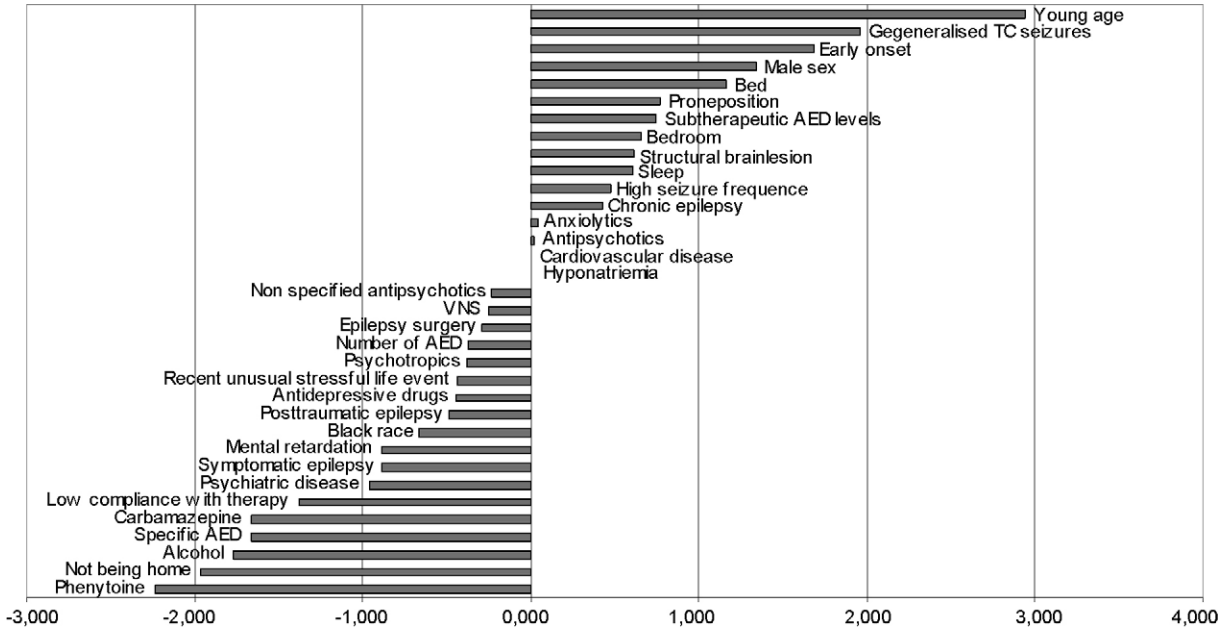


Figure 1 Risk factor total studies ratio (RFT) of possible risk factors for SUDEP. The RFT is given a positive or a negative value based on the results in the studies analysing the possible risk factor and corrected for the number of included SUDEP cases in the different studies (see Table 1). Authors consider the risk factor a strong risk factor for SUDEP if RFT ≥ 1.0, a weak risk factor for SUDEP if RFT ≥ 0.5 and no risk factor for SUDEP if RFT < 0.5. AED: anti epileptic drugs, VNS: vagal nerve stimulation, TC seizure: tonic clonic seizure is based.

Table 7 Factors considered to carry no risk for SUDEP

Category	Analysed factor
Demographic	Black race
Epilepsy	Symptomatic epilepsy, posttraumatic epilepsy, long duration of epilepsy, high frequency of seizures
Psychiatry	Recent unusual stressful life event, psychiatric illness, psychotropic drug prescription, use of antidepressants, use of anxiolytics, alcohol abuse, mental retardation
Therapy	Use of particular AED, the prescription of carbamazepine, the prescription of phenytoin, increasing number of prescribed AED, poor compliance with AED, epilepsysurgery, vagal nerve stimulation
Circumstances of death	Being outside the house
Other	Hyponatriemia, cardiovascular disease

these designs may be very different. Information on some risk factors is more easily obtained (e.g. male sex and age at death). The same study population might have been used in two or more studies. In both cases there would be a wrongful increase of the RFT.

A listing of risk factors by relevance may allow the authors to differentiate populations at higher and populations at lower risk for SUDEP. A male patient, less than 45 years old with a combination of early onset of seizures the presence of generalized tonic clonic seizures and a strucural brain lesion is at high risk for SUDEP. Being in the bedroom or in bed, prone position, sleeping and or more subtherapeutic bloodlevels are circumstantial risk factors that may increase the risk for SUDEP.

Future research on risk factors is still needed and should be based on a prospective cohort. Due to the low incidence of SUDEP, this will be a hard thing to do. More interestingly, understanding the mechanism(s) of SUDEP may allow the authors to understand which patients are or are not at high risk for SUDEP and eventually to prevent SUDEP. Different mechanisms were postulated to play a role in SUDEP including cardiac arrhytmia precipitated by seizure discharge acting via the autonomic nervous system,[47–53] respiratory arrest,[54–56] neurogenic pulmonary oedema[57] and asphyxiation.[18,23,56] It should be stressed that authors made a qualitative approximation of strength of risk factors. The more often a risk factor was considered to be important, the more likely the risk factor is of relevance. Authors have no means to estimate the (in)dependencies of the various risk factors. Most of the risk factors are unavoidable. Nevertheless, identifying groups at high risk may allow the authors to inform patients and to select patients for monitoring when admitted in epilepsy centers and may also facilitate research for pathophysiological mechanisms, which remain unclear until now.

References

1. Beran RG, Weber S, Sungaran R, Venn N, Hung A. Review of the legal obligations of the doctor to discuss sudden unexplained death in epilepsy (SUDEP)—a cohort controlled comparative cross-matched study in an outpatient epilepsy clinic. *Seizure* 2004;**13**(7):523–8.
2. Nei M, Ho RT, Abou-Khalil BW, Drislane FW, Liporace J, Romeo A, et al. EEG and ECG in sudden unexplained death in epilepsy. *Epilepsia* 2004;**45**(4):338–45.
3. Opeskin K, Berkovic SF. Risk factors for sudden unexpected death in epilepsy: a controlled prospective study based on coroners cases. *Seizure* 2003;**12**(7):456–64.
4. Nilsson L, Ahlbom A, Farahmand BY, Tomson T. Mortality in a population-based cohort of epilepsy surgery patients. *Epilepsia* 2003;**44**(4):575–81.
5. Salmo EN, Connolly CE. Mortality in epilepsy in the west of Ireland: a 10-year review. *Ir J Med Sci* 2002;**171**(4):199–201.
6. Schnabel R, Beblo M, May TW, Burmester L. Is sudden unexplained death in adult epileptic patients associated with geomagnetic disturbances at the day of death or the 4 days before? *Neurosci Lett* 2002;**329**(3):261–4.
7. Donner EJ, Smith CR, Snead OC. Sudden unexplained death in children with epilepsy. *Neurology* 2001;**57**(3):430–4.
8. Nilsson L, Bergman U, Diwan V, Farahmand BY, Persson PG, Tomson T. Antiepileptic drug therapy and its management in sudden unexpected death in epilepsy: a case-control study. *Epilepsia* 2001;**42**(5):667–73.
9. Antoniuk SA, Oliva LV, Bruck I, Malucelli M, Yabumoto S, Castellano JL. Sudden unexpected, unexplained death in epilepsy autopsied patients. *Arq Neuropsiquiatr* 2001;**59**(1):40–5.
10. Walczak TS, Leppik IE, D'Amelio M, Rarick J, So E, Ahman P, et al. Incidence and risk factors in sudden unexpected death in epilepsy: a prospective cohort study. *Neurology* 2001;**56**(4):519–25.
11. Opeskin K, Harvey AS, Cordner SM, Berkovic SF. Sudden unexpected death in epilepsy in Victoria. *J Clin Neurosci* 2000;**7**(1):34–7.
12. Annegers JF, Coan SP, Hauser WA, Leestma J. Epilepsy, vagal nerve stimulation by the NCP system, all-cause mortality, and sudden, unexpected, unexplained death. *Epilepsia* 2000;**41**(5):549–53.
13. Langan Y, Nashef L, Sander JW. Sudden unexpected death in epilepsy: a series of witnessed deaths. *J Neurol Neurosurg Psychiatry* 2000;**68**(2):211–3.
14. Opeskin K, Clarke I, Berkovic SF. Prolactin levels in sudden unexpected death in epilepsy. *Epilepsia* 2000;**41**(1):48–51.
15. Opeskin K, Burke MP, Cordner SM, Berkovic SF. Comparison of antiepileptic drug levels in sudden unexpected deaths in epilepsy with deaths from other causes.. *Epilepsia* 1999;**40**(12):1795–8.
16. Hennessy MJ, Langan Y, Elwes RD, Binnie CD, Polkey CE, Nashef L. A study of mortality after temporal lobe epilepsy surgery. *Neurology* 1999;**53**(6):1276–83.
17. Thom M, Griffin B, Sander JW, Scaravilli F. Amygdala sclerosis in sudden and unexpected death in epilepsy. *Epilepsy Res* 1999;**37**(1):53–62.
18. Kloster R, Engelskjon T. Sudden unexpected death in epilepsy (SUDEP): a clinical perspective and a search for risk factors. *J Neurol Neurosurg Psychiatry* 1999;**67**(4):439–44.
19. Nilsson L, Farahmand BY, Persson PG, Thiblin I, Tomson T. Risk factors for sudden unexpected death in epilepsy: a case-control study. *Lancet* 1999;**353**(9156):888–93.
20. Ficker DM, So EL, Shen WK, Annegers JF, O'Brien PC, Cascino GD, et al. Population-based study of the incidence of sudden unexplained death in epilepsy. *Neurology* 1998;**51**(5):1270–4.
21. Langan Y, Nolan N, Hutchinson M. The incidence of sudden unexpected death in epilepsy (SUDEP) in South Dublin and Wicklow. *Seizure* 1998;**7**(5):355–8.
22. Annegers JF, Coan SP, Hauser WA, Leestma J, Duffell W, Tarver B. Epilepsy, vagal nerve stimulation by the NCP system, mortality, and sudden, unexpected, unexplained death. *Epilepsia* 1998;**39**(2):206–12.
23. Nashef L, Garner S, Sander JW, Fish DR, Shorvon SD. Circumstances of death in sudden death in epilepsy: interviews of bereaved relatives. *J Neurol Neurosurg Psychiatry* 1998;**64**(3):349–52.
24. Leestma JE, Annegers JF, Brodie MJ, Brown S, Schraeder P, Siscovick D, et al. Sudden unexplained death in epilepsy: observations from a large clinical development program. *Epilepsia* 1997;**38**(1):47–55.

25. Tennis P, Cole TB, Annegers JF, Leestma JE, McNutt M, Rajput A. Cohort study of incidence of sudden unexplained death in persons with seizure disorder treated with antiepileptic drugs in Saskatchewan, Canada. *Epilepsia* 1995;**36**(1):29—36.
26. Coyle HP, Baker-Brian N, Brown SW. Coroners' autopsy reporting of sudden unexplained death in epilepsy (SUDEP) in the UK. *Seizure* 1994;**3**(4):247—54.
27. Black M, Graham DI. Sudden unexplained death in adults caused by intracranial pathology. *J Clin Pathol* 2002;**55**(1): 44—50.
28. Langan Y. Sudden unexpected death in epilepsy (SUDEP): risk factors and case control studies. *Seizure* 2000;**9**(3):179—83.
29. Fineschi V, Gabbrielli M, Salvinelli R. The incidence of violent mechanical asphyxia in the so-called 'sudden death' of epileptic patients. *Zacchia* 1991;**64**(4):463—78.
30. Davis GG, McGwin Jr G. Comparison of heart mass in seizure patients dying of sudden unexplained death in epilepsy to sudden death due to some other cause. *Am J Forensic Med Pathol* 2004;**25**(1):23—8.
31. Kamgno J, Pion SD, Boussinesq M. Demographic impact of epilepsy in Africa: results of a 10-year cohort study in a rural area of Cameroon. *Epilepsia* 2003;**44**(7):956—63.
32. Opeskin K, Thomas A, Berkovic SF. Does cardiac conduction pathology contribute to sudden unexpected death in epilepsy? *Epilepsy Res* 2000;**40**(1):17—24.
33. Timmings PL. Sudden unexpected death in epilepsy: is carbamazepine implicated? *Seizure* 1998;**7**(4):289—91.
34. Tavernor SJ, Brown SW, Tavernor RM, Gifford C. Electrocardiograph QT lengthening associated with epileptiform EEG discharges—a role in sudden unexplained death in epilepsy? *Seizure* 1996;**5**(1):79—83.
35. Shorvon S. Risk factors for sudden unexpected death in epilepsy. *Epilepsia* 1997;**38**(Suppl 11):S20—2.
36. Tomson T, Walczak T, Sillanpaa M, Sander JW. Sudden unexpected death in epilepsy: a review of incidence and risk factors. *Epilepsia* 2005;**46**(Suppl 11):54—61.
37. Sperling MR. Sudden unexplained death in epilepsy. *Epilepsy Curr* 2001;**1**(1):21—3.
38. McGugan EA. Sudden unexpected deaths in epileptics—a literature review. *Scott Med J* 1999;**44**(5):137—9.
39. Ficker DM. Sudden unexplained death and injury in epilepsy. *Epilepsia* 2000;**41**(Suppl 2):S7—12.
40. Téllez-Zenteno JF, Hernández Ronquillo L, Wiebe S. Sudden unexpected death in epilepsy: evidence-based analysis of incidence and risk factors. *Epilepsy Res* 2005;**65**(1—2):101—15.
41. Lhatoo SD, Sander JW. Cause-specific mortality in epilepsy. *Epilepsia* 2005;**46**(Suppl 11):36—9.
42. Annegers JF, Coan SP. SUDEP: overview of definitions and review of incidence data. *Seizure* 1999;**8**(6):347—52.
43. Nashef L. Sudden unexpected death in epilepsy: terminology and definitions.. *Epilepsia* 1997;**38**(Suppl 11):S6—8.
44. Izac SM. The phenomenon of sudden unexpected death in epilepsy (SUDEP). *Am J Electroneurodiagn Technol* 2003;**43**(1):1—12.
45. Langan Y, Nashef L, Sander JW. Case-control study of SUDEP. *Neurology* 2005;**64**(7):1131—3.
46. Lear-Kaul KC, Coughlin L, Dobersen MJ. Sudden unexpected death in epilepsy: a retrospective study. *Am J Forensic Med Pathol* 2005;**26**(1):11—7.
47. Blumhardt LD, Smith PEM, Owen L. Electrocardiographic accompaniments of temporal lobe epileptic seizures. *Lancet* 1986;**1**:1051—6.
48. Gilchrist JM. Arrhythmogenic seizures: diagnosis by simultaneous EEG/ECG recording. *Neurology* 1985;**35**:1503—6.
49. Kiok MC, Terrence CF, Fromm GH, Lavine S. Sinus arrest in epilepsy. *Neurology* 1986;**36**:115—6.
50. Lathers CM, Schraeder PL, Weiner FL. Synchronization of cardiac autonomic neural discharge with epileptogenic activity: the lockstep phenomenon. *Electroencephalogr Clin Neurophysiol* 1987;**67**:247—59.
51. Lathers CM, Schraeder PL. Autonomic dysfunction in epilepsy: characterization of autonomic cardiac neural discharge associated with pentylenetrazol-induced epileptogenic activity. *Epilepsia* 1982;**23**:633—47.
52. Lathers CM, Schraeder PL. Experience-based teaching of therapeutics and clinical pharmacology of antiepileptic drugs. Sudden unexplained death in epilepsy: do antiepileptic drugs have a role? *J Clin Pharmacol* 1995;**35**:573—87.
53. Nei M, Ho RT, Sperling MR. EKG abnormalities during partial seizures in refractory epilepsy. *Epilepsia* 2000;**41**(5):542—8.
54. Blum AS, Ives JR, Goldberger AL. Oxygen desaturations triggered by partial seizures: implications for cardiopulmonary instability in epilepsy. *Epilepsia* 2000;**41**:536—41.
55. Bird JM, Dembny KAT, Sandeman D, Butler S. Sudden unexplained death in epilepsy: an intracranially monitored case. *Epilepsia* 1997;**38**:S52—6.
56. Nashef L, Walker F, Allen P, Sander JW, Shorvon SD, Fish DR. Apnoea and bradycardia during epileptic seizures: relation to sudden death in epilepsy. *J Neurol Neurosurg Psychiatry* 1996;**60**(3):297—300.
57. Terrence CE, Rao GR, Pepper JA. Neurogenic pulmonary edema in unexpected, unexplained death in epileptic patients. *Neurology* 1981;**25**:594—5.