American Association of Physician Assistants
Annual Meeting
Nashville, TN

Premature Mortality in Epilepsy

May 20, 2023

Jeffrey R. Buchhalter MD, PhD

Phoenix, Arizona

Disclosures

- “Retired/evolved” pediatric epilepsy physician
- Partners Against Mortality in Epilepsy (PAME) Executive Committee
- Epilepsy Learning Healthcare System (Epilepsy Foundation)
- Pediatric Epilepsy Learning Healthcare System
- American Academy of Neurology Quality Committee
- Consultant: Epilepsy Foundation, Epilog, Epilepsy Study Consortium, Neurocrine, UCB

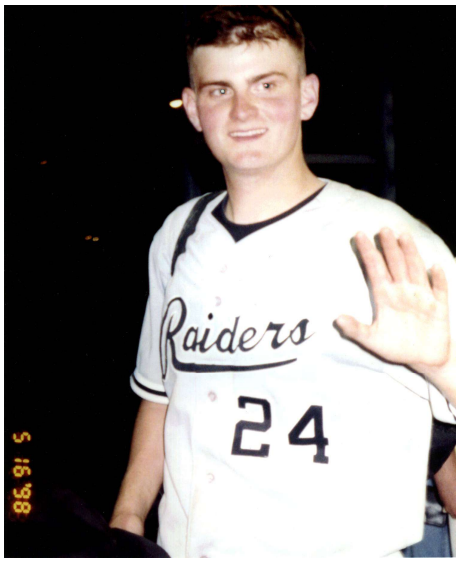
Chris Donalty

- Diagnosed with epilepsy senior in HS
  - Dilantin
  - Physician, internet, books- benign disease
- Stetson University
- Freshman year
  - Nov, April, August seizures: change to VPA
- Sophomore year
  - Depressed, AEs- lethargic
  - Dilantin & Lamictal
  - “Seizure-free”

With permission Jeanne Donalty

Chris Donalty

- Junior & senior years- continued seizures
- Died February 21, 2002; 21 years old



With permission Jeanne Donalty

Learning objectives

- Discuss the causes of premature death in epilepsy
- Identify preventative measures…..
- Discuss with patients & families the risks……

Learning objectives- revised

- Know that death can result from epilepsy
- Understand what you can do to prevent it
- Talk about it- your patients want you to

Epilepsy- the basics

- Seizures are due to too many brain neurons firing together out of control
  - Motor- tonic clonic (”grand mal”), focal
  - Impaired awareness: focal, generalized

- Epilepsy (most recent definition)
  - Two or more unprovoked seizures
  - An identified epilepsy syndrome
  - Greater than a 60% change of a second seizure

Epilepsy- the epidemiology

- Up to 10% of the population will have at least one seizure
- 1.2% of the population has active epilepsy = 3.4 million people
- Top 4 neurological disorder (headache, stroke…)

Approach, premature mortality in…

- All people with epilepsy
- Children with epilepsy
- Children with symptomatic seizures
- Children with rare (genetic) epilepsies

Causes of premature mortality related to epilepsy

- Underlying cause of seizures
- Suicide
- Drowning
- Medication overdose
- Aspiration pneumonia
- Status epilepticus
- **SUDEP**

The burden of premature mortality of epilepsy in high-income countries: A systematic review from the Mortality Task Force of the International League Against Epilepsy

Table 1. Overall mortality risk among people with epilepsy: all-age or adult-only populations

Study	Class	Locality	Population characteristic	Cohort size[a]	Follow-up (years)	SMR	95% CI
Population- or community-based studies, all ages or adults only							
Lhatoo (2001)[15]	1	England and Wales, United Kingdom	Incident cohort, all ages	792	11.8[b]	2.1	1.8–2.4
Lindsten (2000)[16]	1	Vasterbotten Co., Sweden	Incident cases, adult cohort	107	10	2.5	1.2–3.2
Hauser (1980)[14]	1	Rochester, MN, U.S.A.	Incident cases, all ages	618	13.3[b]	2.3	1.9–2.6
Benn (2008)[13]	2	Northern Manhattan, U.S.A.	Incident epilepsy or unprovoked seizures, all ages	209	2.9[b]	1.7	1.1–2.3
Cockerell (1997)[8]	2	United Kingdom	Incident cases, all ages	792	≤9	3.0	2.5–3.7
Morgan (2002)[17]	2	Cardiff and Glamorgan, United Kingdom	Prevalent cases, all ages	3,007	≤4	2.1	1.7–2.6
Olafsson (1998)[18]	2	Iceland	Incident unprovoked seizures, all ages	224	≤30	1.6	1.2–2.2
Neligan (2011)[10,c]	2	United Kingdom	Incident cases, all ages	564	22.8	2.6	2.2–3.0
Rakitin (2011)[19]	2	Estonia	Incident cases, age ≥20 years	81	12.5[b]	2.6	1.8–3.5
Population- or community-based studies, children only							
Sillanpaa (2010)[22]	1	Turku, Finland	Incident and prevalent cases, onset <16 years	245	40	6.4	5.9–7.0
Nickels (2012)[21]	1	Rochester, MN, U.S.A.	Incident cases, <18 years	467	7.9[b]	6.9	
Camfield (2002)[20]	2	Nova Scotia, Canada	Incident cases <17 years	692	13.9[b]	7.5	4.4–13.0
Clinic-based studies, all ages or adults only							
Nilsson (1997)[24]	3	Stockholm, Sweden	Previously hospitalized for epilepsy	9,061	≤17	3.6	3.5–3.7
Mohanraj (2006)[23]	3	Glasgow, United Kingdom	Incident clinic referral cases	890	7[b]	1.4	1.2–1.7
			Prevalent clinic referral cases	2,689	7[b]	2.0	1.8–2.3
Trinka (2013)[12]	3	Tyrol, Austria	Cohort of attendees of epilepsy referral clinic	3,334	≤29	2.2	2.0–2.4
Granbichler (2015)[11,d]	3	Tyrol, Austria	Cohort of adult attendees of epilepsy referral clinic	4,295	≤39	1.7	1.6–1.9
Clinic-based studies, children only							
Callenbach (2001)[26]	3	The Netherlands	Incident cases	472	5.0	7.0	2.4–11.5
Berg (2004)[25]	3	Connecticut, U.S.A.	Incident cases <16 years representative sample	613	7.9	7.5	4.4–13.0

[a]Number of persons with epilepsy followed.
[b]Median or mean follow-up period.
[c]Extended follow-up of cohort described in Cockerell et al.[8]
[d]Extended follow-up and expansion of cohort described in Trinka et al.[12]

For those living with epilepsy, the risk of dying prematurely is 1.7 – 7.5 times greater than the general population

Thurman et al. Epilepsia, 58(1):17–26, 2017 doi: 10.1111/epi.13604

The burden of premature mortality of epilepsy in high-income countries: A systematic review from the Mortality Task Force of the International League Against Epilepsy

Highest rates at younger ages

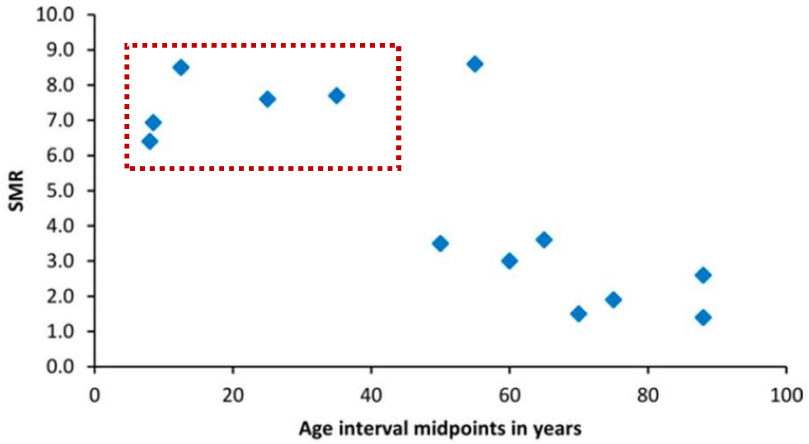


Figure 2.
Standardized mortality ratios by age: Deaths from all causes among people with epilepsy. Data points represent findings from four class I and class 2 studies.[8,14,20,22]
Epilepsia © ILAE

Highest rates sooner after diagnosis

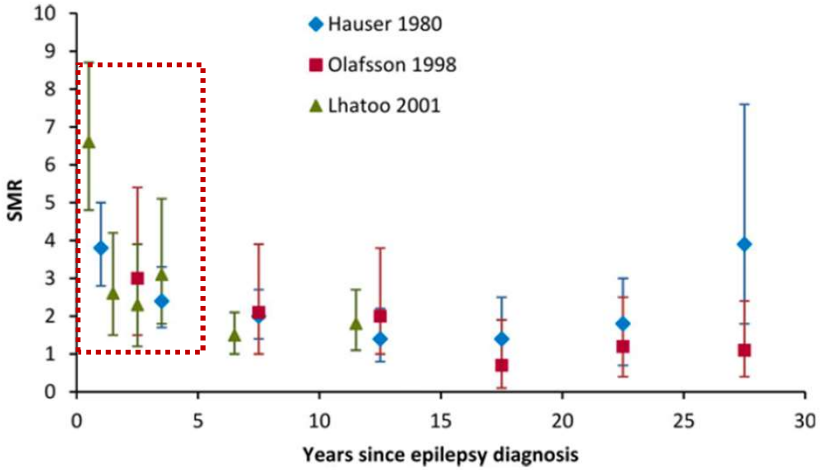


Figure 3.
Standardized mortality ratios by interval from epilepsy diagnosis.

Thurman et al. Epilepsia, 58(1):17–26, 2017 doi: 10.1111/epi.13604

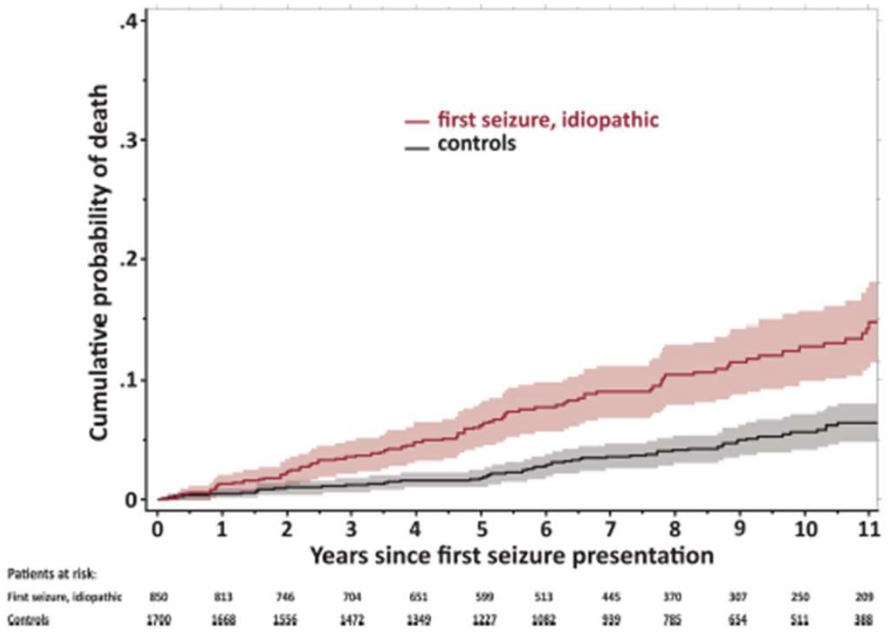
Received: 29 October 2022 | Revised: 23 February 2023 | Accepted: 28 February 2023
DOI: 10.1111/epi.17567

RESEARCH ARTICLE

Mortality after a first-ever unprovoked seizure

Elaine W. Pang[1] | Nicholas D. Lawn[1] | Judy Lee[1] | John W. Dunne[1,2]

- 3 x greater risk
- Risk factors
  - Age
  - Symptomatic cause
  - Neuro disability
  - Onset- status epilepticus
  - Anti-depressant use



Results: One thousand two hundred seventy-eight patients with a first-ever unprovoked seizure were compared to 2556 controls. Mean follow-up was 7.3 years (range = .1–20). Overall hazard ratio (HR) for death after a first unprovoked seizure compared to controls was 3.06 (95% confidence interval [CI] = 2.48–3.79), with HRs of 3.30 (95% CI = 2.26–4.82) for those without seizure recurrence and 3.21 (95% CI = 2.47–4.16) after a second seizure. Mortality was also increased in patients with normal imaging and no identified cause (HR = 2.50, 95% CI = 1.82–3.42). Multivariate predictors of mortality were increasing age, remote symptomatic causes, first seizure presentation with seizure cluster or status epilepticus, neurological disability, and antidepressant use at time of first seizure. Seizure recurrence did not influence mortality rate. The commonest CODs were neurological, most relating to the underlying cause of seizures rather than being seizure-related. Substance overdoses and suicide were more frequent CODs in patients compared to controls and were commoner than seizure-related deaths.

JAMA Neurology | Original Investigation

Risk of Unnatural Mortality in People With Epilepsy

Hayley C. Gorton, PhD; Roger T. Webb, PhD; Matthew J. Carr, PhD; Marcos DelPozo-Banos, PhD; Ann John, MD; Darren M. Ashcroft, PhD

Key Points

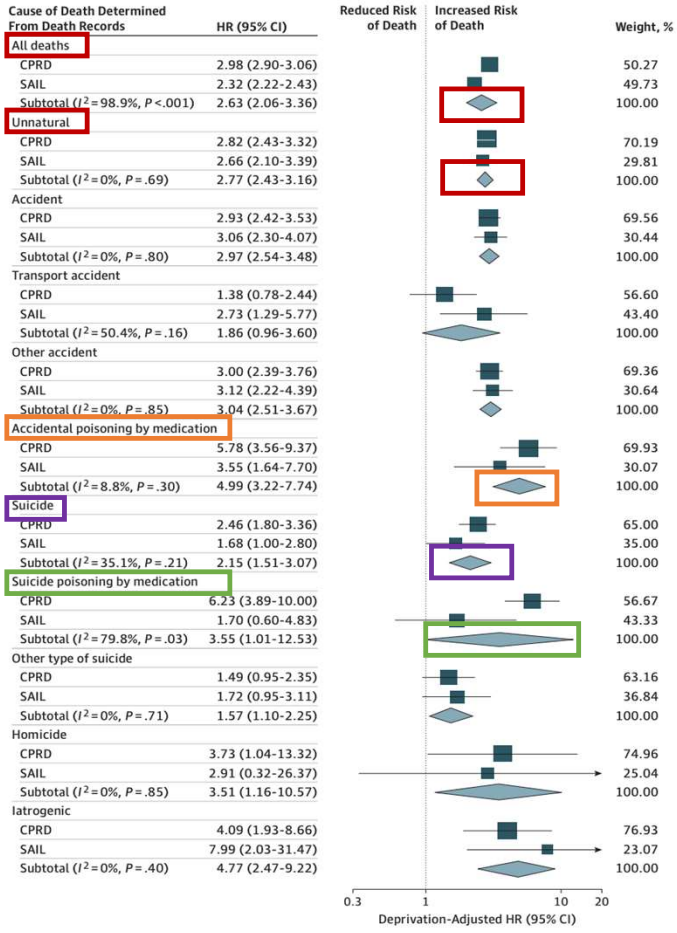
Question What is the risk and medication contribution to cause-specific unnatural mortality in people with epilepsy?

Findings In this population-based cohort study, more than 50 000 people with epilepsy and 1 million matched individuals without epilepsy were identified in 2 data sets from the general populations of England and Wales. People with epilepsy had a 3-fold increased risk of any unnatural mortality and a 5-fold increased risk of unintentional medication poisoning; psychotropic and opioid, but not antiepileptic, drugs were most commonly used in poisoning.

Meaning Clinicians should provide advice on unintentional injury and poisoning and suicide prevention and consider the toxicity of concomitant medication when prescribing drugs for people with epilepsy.

unnatural causes (unintentional injury, suicide, homicide, and iatrogenesis)

Figure 2. Forest Plot Showing Deprivation-Adjusted Hazard Ratios (HRs) for Cause-Specific Unnatural Mortality



JAMA Neurol. **2018**;75(8):929-938. doi:10.1001/jamaneurol.2018.0333

Classification of Epilepsy-related Deaths

Table 2 Classification of epilepsy-related deaths

Deaths directly due to epilepsy
Sudden unexpected death in epilepsy
Status epilepticus
Drowning
Motor vehicle accidents
Falls, burns, and other seizure-related accidents
Deaths due to acute symptomatic seizures[59]
With or without status epilepticus, occurring within 1 week of stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery
First identification of subdural hematoma or CNS infection
Active phase of multiple sclerosis or other autoimmune disorders
Deaths indirectly due to epilepsy
Aspiration pneumonia
Suicide
Cardiovascular disease that may be exacerbated or caused by antiseizure drugs
Deaths due to underlying neurologic disease
Brain tumor
Stroke
Metabolic/genetic and neurodegenerative diseases

Devinsky et al, Neurology 2015

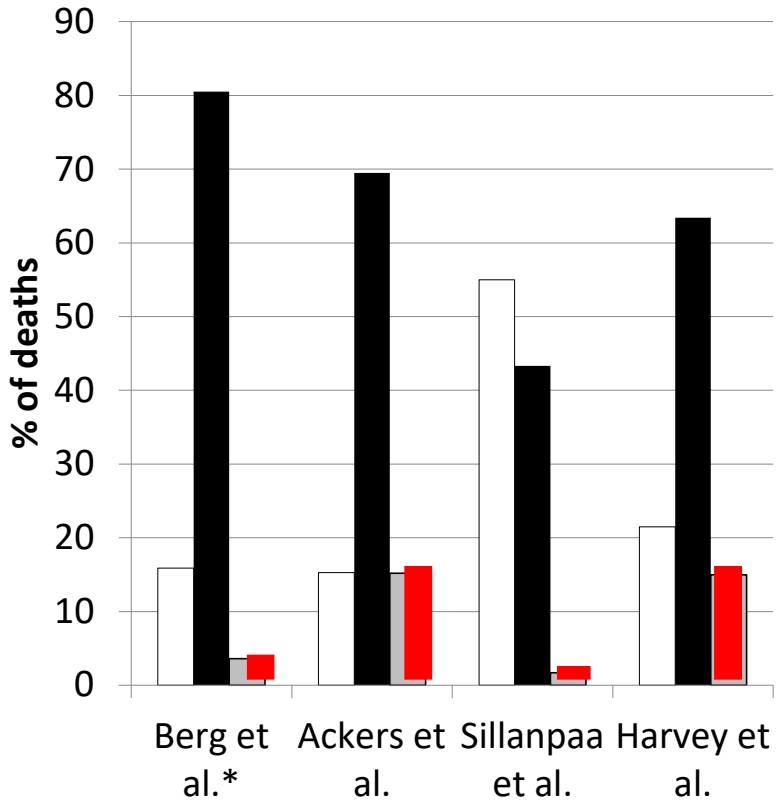
Understanding Death in Children with Epilepsy

Pediatric Neurology 70 (2017) 7-15.

Elizabeth J. Donner, Peter Camfield, Linda Brooks, Jeffrey Buchhalter, Carol Camfield, Tobias Loddenkemper, Elaine Wirrell

Causes of Death in Children with Epilepsy- all deaths

5-10 x > gen population



Status, aspiration, SUDEP complication of RX

Epilepsy-related

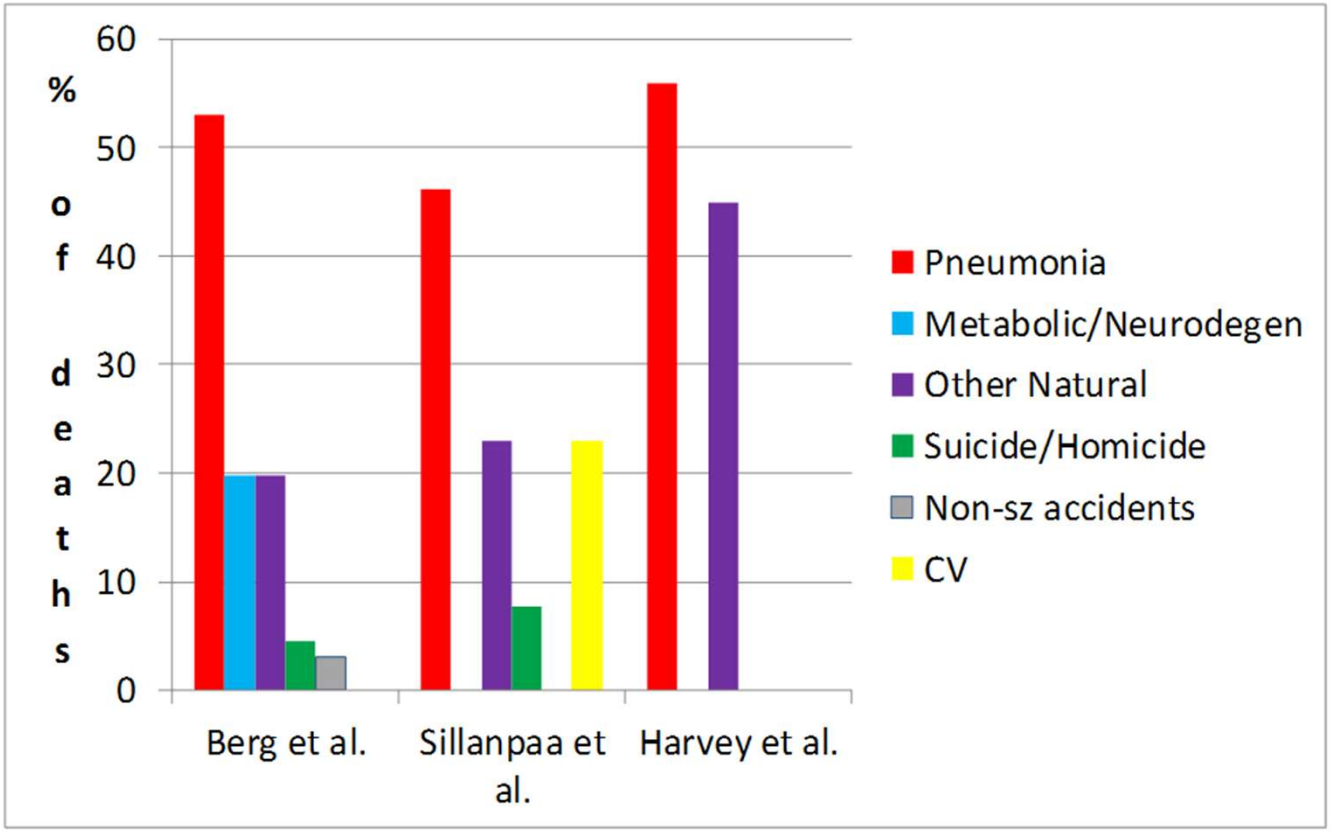
Non-epilepsy related

Uncertain

Natural- underlying neuro etiol (BT, NMD), other neuro, pneumonia
Non-natural: suicide, homicide

Donner et al….Wirrell, 2016

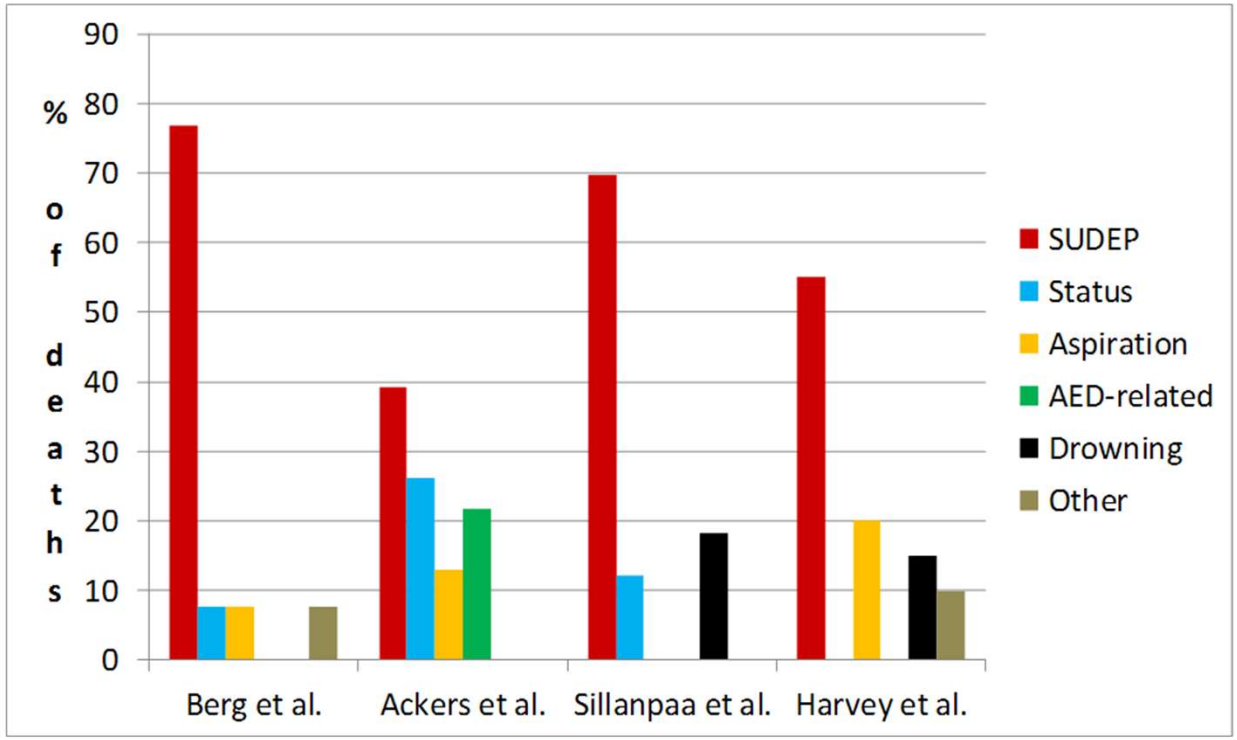
Causes of Death in Children with Epilepsy
non-epilepsy related deaths



Donner et al….Wirrell, 2016

Causes of Death in Children with Epilepsy

epilepsy related deaths



Donner et al….Wirrell, 2016

“Long-Term Mortality in Childhood-Onset Epilepsy”

- Prospective
- Population-based
- 40-year follow-up (since 1964)
- 245 individuals

Sillanpää & Shinnar. N Engl J Med 2010;363:2522-9

“Long-Term Mortality in Childhood-Onset Epilepsy”

Table 1. Mortality among Subjects with Childhood-Onset Epilepsy.*

Variable	All Subjects (N = 245)	Subjects with Idiopathic or Cryptogenic Epilepsy (N = 122)	Subjects with Epilepsy Due to Remote Symptomatic Causes (N = 123)†
Total deaths — no.	60	15	45
Age at death — yr			
Median	23	26	21
Range	1–50	11–50	1–49
No. of person-yr	8692	4638	4054
No. of deaths/1000 person-yr (95% CI)			
All	6.90 (5.3–8.9)	3.23 (1.9–5.4)	11.10 (8.3–14.9)
Men	7.33 (5.2–10.2)	2.69 (1.2–6.0)	11.63 (8.0–16.8)
Women	6.41 (4.4–9.4)	3.74 (1.9–7.2)	10.33 (6.4–16.6)
Remission status at time of death‡			
Not in remission — no./total no. of deaths (%)	51/60 (85)	11/15 (73)	40/45 (89)
In remission — no./total no. of deaths (%)	9/60 (15)	4/15 (27)	5/45 (11)
Receiving medication — no.	5	2	3
Not receiving medication — no.	4	2	2

Sillanpää & Shinnar. N Engl J Med 2010;363:2522-9

SUDEP Definitions

- A sudden, unexpected, non-traumatic death in a person with epilepsy without postmortem exam evidence of structural or toxicological cause of death
  - Definite – with autopsy, no other cause
  - Probable – no autopsy, no other cause
  - Possible – alternative cause of death, clinical data are lacking

Nashef Epilepsia 1997;38(S11):56-8

Annegers. Epilepsia 1997 (Suppl 11): S9-12

“Unifying the definitions of SUDEP”
Key Features

- Specify with or without witnessed seizure
- Specify with or without autopsy
- Include “suffocation”
- Include “dry drowning”
- Specify known competing causes
- 1 hr arbitrarily selected as time from terminal event
- “Case studies”

Nashef, So, Ryvlin, and Tomson. Epilepsia, 53(2):227–233, 2012

SUDEP Incidence

Children = Adult (until > 60 yo)

Table 2 Age- and sex-specific incidence of sudden unexpected death in epilepsy (SU

	All	
	Cases/person-years	I (95% CI)
Definite and probable SUDEP		
All ages	58/56,799	1.20 (0.93-1.52)
<16 y	7/6,310	1.11 (0.45-2.29)
16-50 y	29/25,707	1.13 (0.76-1.62)
>50 y	32/24,783	1.29 (0.88-1.82)
Definite, probable and possible SUDEP		
All ages	99/56,799	1.74 (1.42-2.12)
<16 y	9/6,310	1.43 (0.65-2.71)
16-50 y	34/25,707	1.32 (0.92-1.85)
>50 y	56/24,783	2.26 (1.71-2.93)

Abbreviation: CI = confidence interval.
Incidence rates (I) are per 1,000 person-years.
*Comparing male and female participants.

1.11

1.29

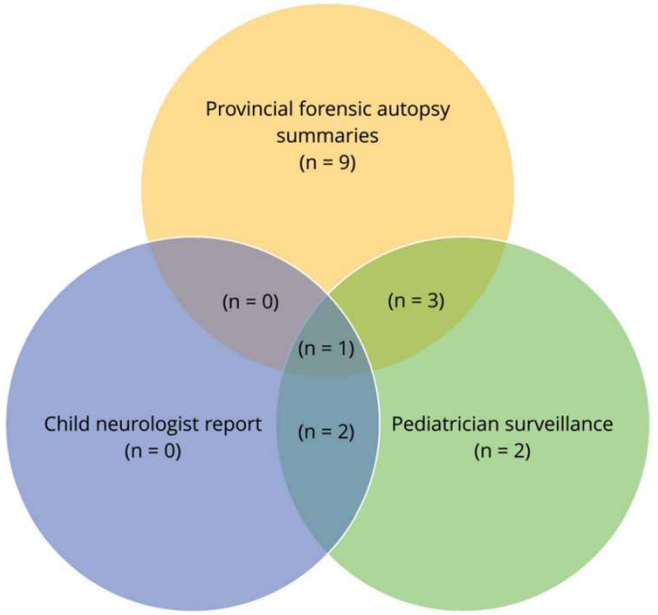
Sveinsson, 2017

Incidence of sudden unexpected death in epilepsy in children is similar to adults

Anne E. Keller, MPH, Robyn Whitney, MD, Shelly-Anne Li, MSc, Michael S. Pollanen, MD, PhD, and Elizabeth J. Donner, MD, MSc

- Ontario, Canada
- Jan 1, 2014 – Dec 31, 2015
- Sources:
  - National Pediatrics surveillance
  - Child neuro survey
  - Forensic pathology reports
- Classified: definite, definite plus, probable, possible, near
- Capture-recapture: estimates missing & adjusted definite/probable

Figure Identification of the 17 pediatric cases of sudden unexpected death in epilepsy by data source



Neurology® 2018;91:e107-e111. doi:10.1212/WNL.0000000000005762

Incidence of sudden unexpected death in epilepsy in children is similar to adults

Table Incidence of SUDEP by analysis method as compared to reported incidence in the literature

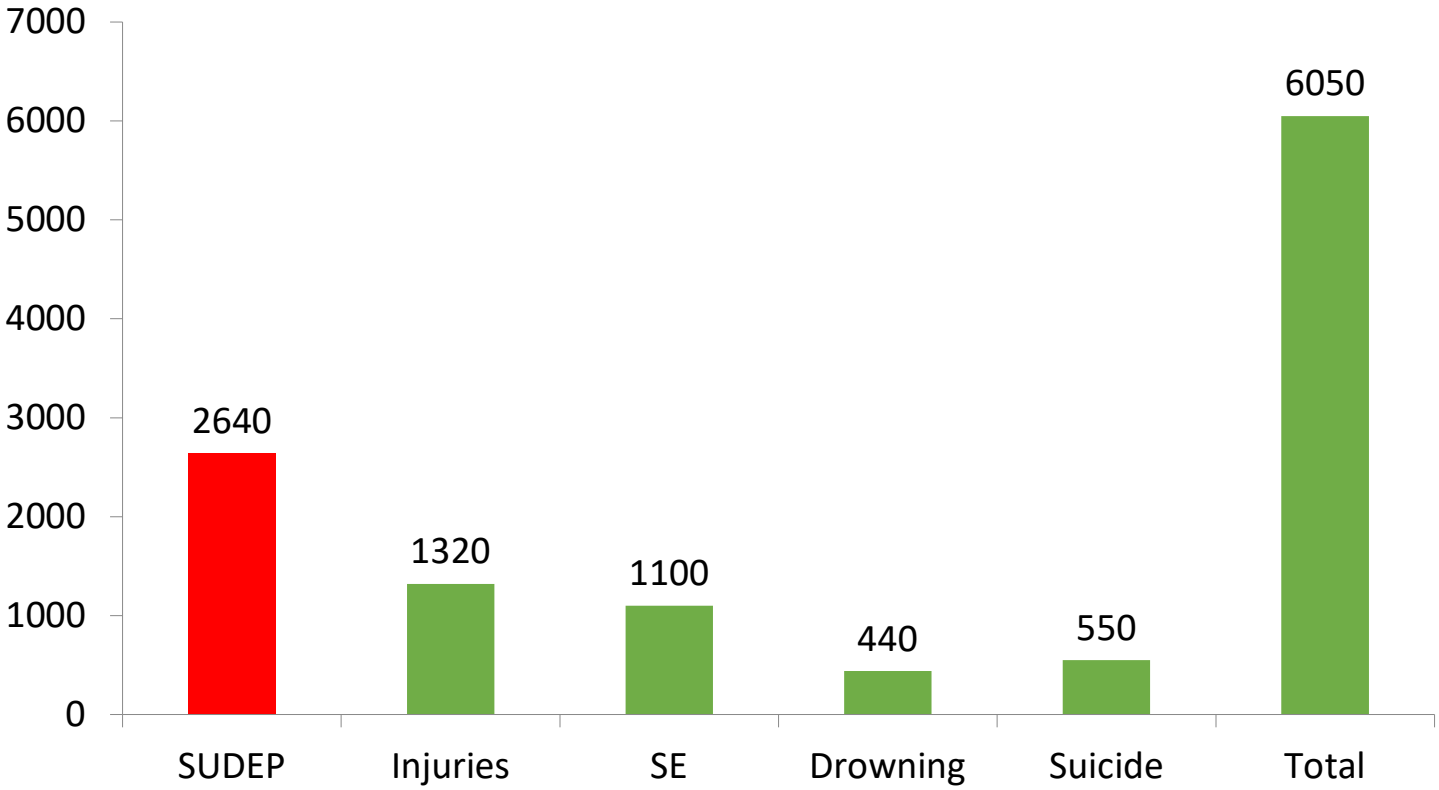
Method	Included classifications of SUDEP	No. of SUDEP cases	Epilepsy prevalence, %	Incidence (95% CI) per 1,000 patient-years
Crude analysis	All	17	0.27	1.17 (0.68–1.88)
	Definite, definite plus, probable	16	0.27	1.11 (0.63–1.79)
Sensitivity analysis	Definite, definite plus, probable	16	0.21	1.42 (0.81–2.31)
	Definite, definite plus, probable	16	0.34	0.88 (0.50–1.42)
Capture-recapture analysis	Definite, definite plus, probable	21	0.27	1.45 (0.90–2.22)

From the literature

Source	Included classifications of SUDEP	Population	Incidence (95% CI) per 1,000 patient-years
AAN guidelines[1]	Definite, definite plus,[a] probable	"Childhood"	0.22 (0.16–0.31)
	Definite, definite plus,[a] probable	"Adult"	1.22 (0.64–2.32)
Sveinsson et al.[2]	Definite, definite plus, probable	<16 y	1.11 (0.45–2.29)
	Definite, definite plus, probable	16–50 y	1.13 (0.76–1.62)
	Definite, definite plus, probable	>50 y	1.29 (0.88–1.82)

Neurology® 2018;91:e107-e111. doi:10.1212/WNL.0000000000005762

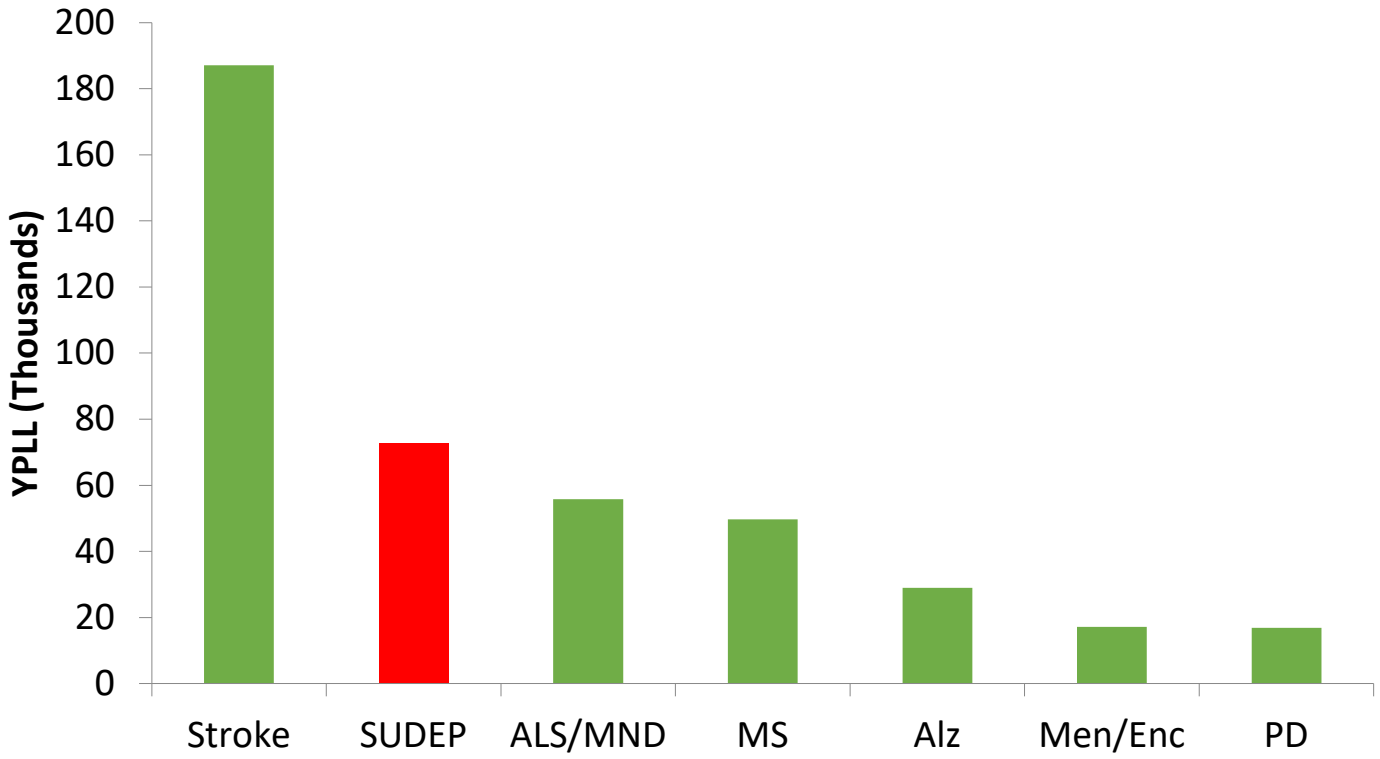
Estimated Epilepsy Deaths in the United States for 2014*



*Estimates are low due to poor surveillance data

Source: Devinsky, O, et al. Recognizing and preventing epilepsy-related mortality. Neurology 2015

Public Health Burden of SUDEP
Annual Years of Potential Life Lost



Source: Thurman, D PAME 2014 Presentation Slides

Risk Factors for SUDEP

SUDEP and Numbers of Generalized Tonic Clonic Seizures

Nilsson et al, 1999 (n=57)		Walczak et al, 2001 (n=20)	
GTCS/year	**RR (95% CI)**	**GTCS/year**	**RR (95% CI)**
0-2	**1.0 (reference)**	**0**	**1.0 (reference)**
3-12	**3.8 (1.5-9.3)**	**1-3**	**2.4 (1.8-30.5)**
13-50	**6.0 (1.9-18.7)**	**>3**	**8.1 (2.2-30.0)**
>50	**23.3 (2.1-26.2)**		
Unknown	**18.2 (7.0-47.6)**		

Modified from Tomson T, courtesy of E So

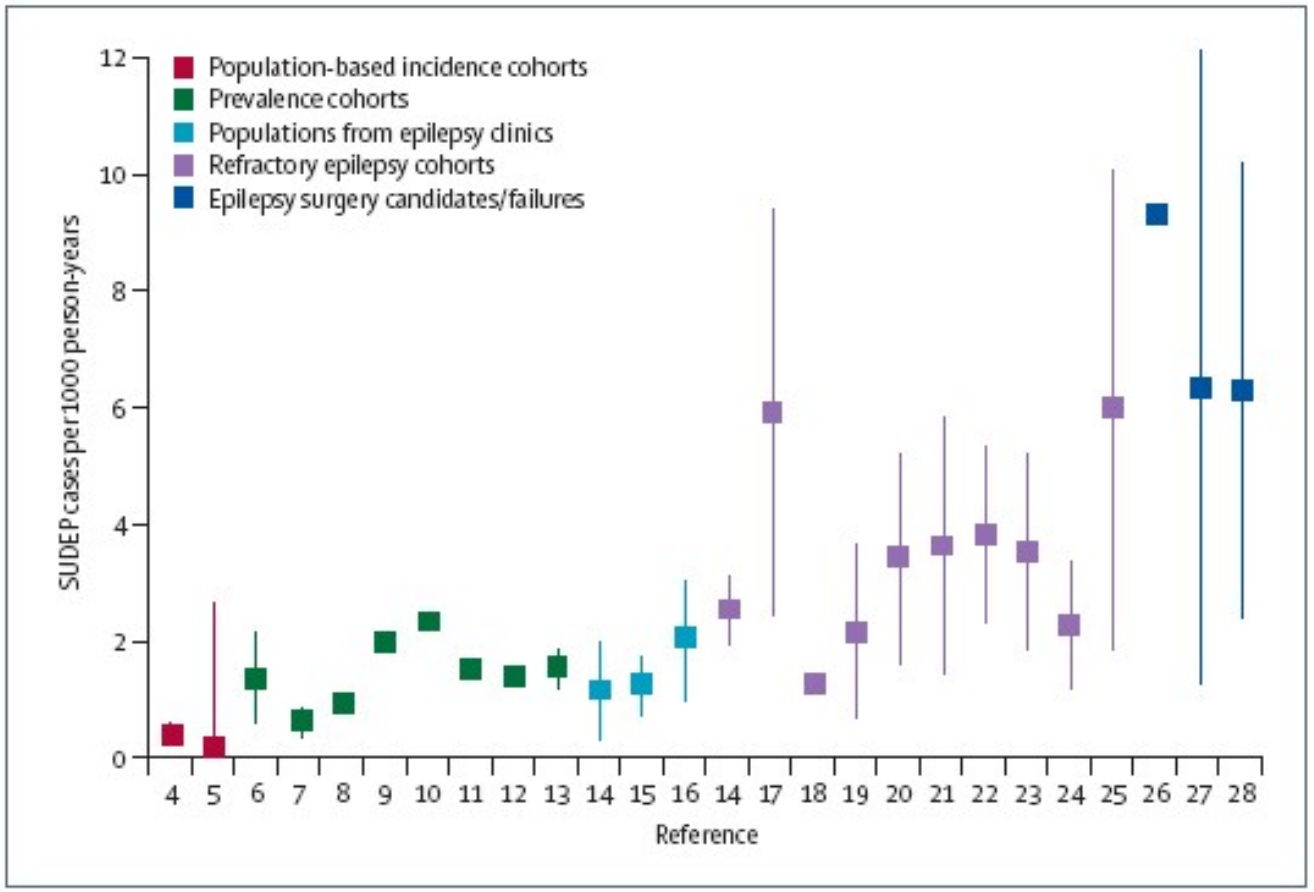


Figure 1: Incidence of SUDEP in 26 studies of different epilepsy populations
95% CIs are shown if data were available for their calculation.

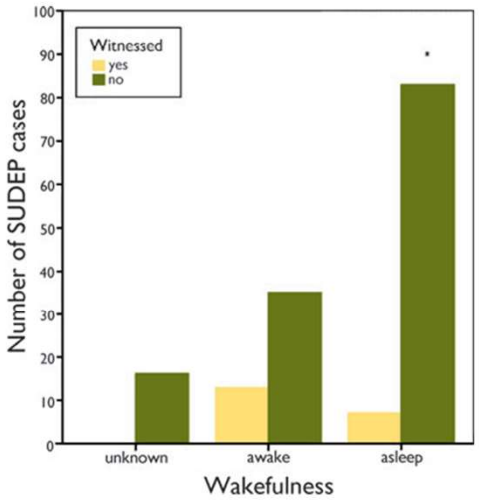
Tomson T, et al. Lancet 2008

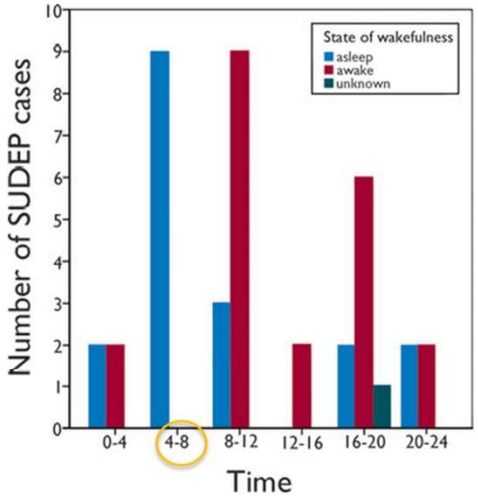
Epilepsia, 53(2):253–257, 2012

Sudden unexpected death in epilepsy: People with nocturnal seizures may be at highest risk

*Robert J. Lamberts, *Roland D. Thijs, Aoife Laffan, Yvonne Langan, and *Josemir W. Sander

Epilepsia, 53(2):253–257, 2012



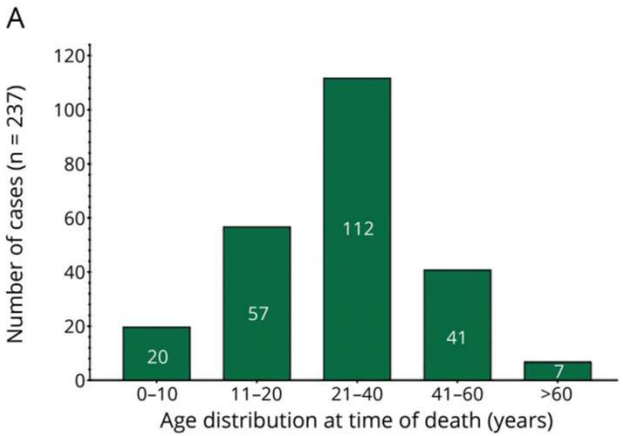


"Those who died during sleep were more likely to have a history of nocturnal seizures than those who died while awake: $v21 = 7.3$, $p < 0.01$ (OR 3.6, 95% CI 1.4–9.4)."

Clinical risk factors in SUDEP
A nationwide population-based case-control study

- 255 SUDEP cases, 1,148 matched controls
- GTCs preceding year increased risk by 27
- No increase with non-GTCs
- Nocturnal GTCs increased risk by 15
- Living alone increased risk by 5
- Not sharing bed + GTCs increased risk by 67

Sveinsson et al, Neurology® **2020**;94:e419-e429. doi:10.1212



SUDEP in the North American SUDEP Registry

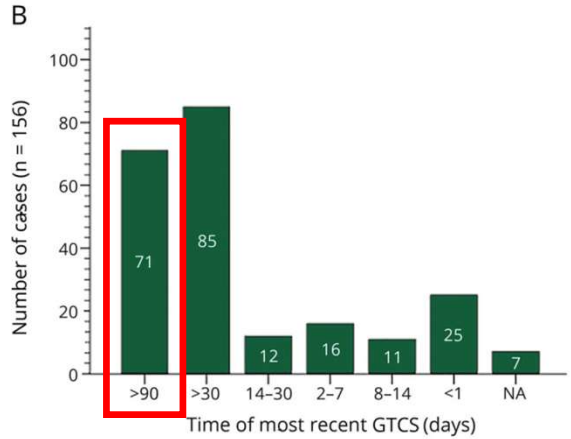
The full spectrum of epilepsies

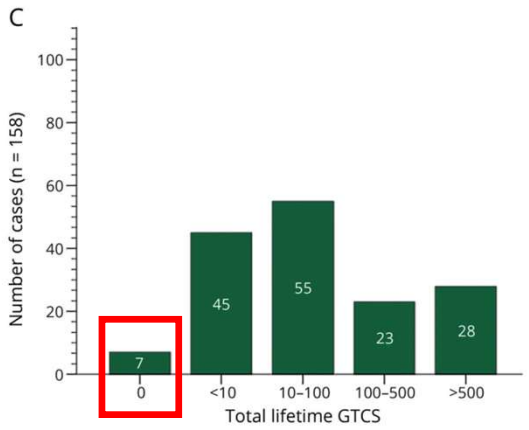
Chloe Verducci, BA, Fizza Hussain, MS, Elizabeth Donner, MD FRCP(C), Brian D. Moseley, MD, Jeffrey Buchhalter, MD, Dale Hesdorffer, PhD, Daniel Friedman, MD, MSc, and Orrin Devinsky, MD

Correspondence
Dr. Devinsky
od4@nyu.edu

Neurology® 2019;93:e1-e10. doi:10.1212/WNL.0000000000007778

- Voluntary registry, started October 2011
- Medical records, interviews, biospecimens
- 237 definite or probable SUDEP





North American SUDEP Registry

Table 1 Circumstances of death (n = 237)

Circumstance of death	n	N	%
Took last ASM dose?	66	180	37
Asleep at time of death	118	168	70
Known recent illness	30	175	17
Room sharing during sleep	57	161	35
CPR performed	108	212	51
Sleep deprived	24	157	15
Full autopsy performed	155	237	65
Found in prone position	128	186	69
Evidence of preceding seizure	123	167	74

Abbreviations: ASM = antiseizure medication; CPR = cardiopulmonary resuscitation.

Table 3 Seizure histories in cases of SUDEP with sufficient information to adjudicate (143 of 237)

Seizure history	n	N	%
Generalized	57	143	40
Tonic-clonic	46	143	32
Focal	86	143	60
Focal to bilateral	67	143	47
Preserved awareness	20	143	14
Impaired awareness	59	143	41
Unclassified	94	237	40
Both	15	143	10
Seizure-free at time of death[a]	27	182	15
Psychogenic seizures	6	166	4

Verducci et al 2019

North American SUDEP Registry- Conclusions

- SUDEP can occur
  - Seizure free
  - No tonic, clonic or tonic-clonic seizures
  - ”Benign” epilepsy syndrome
- SUDEP can occur despite
  - Taking medications
  - Co-sleeping
  - CPR
- Therefore
  - Need to discuss with <u>everyone</u>
  - Emphasize- aggressive seizure management, modifiable lifestyle factors

Verducci et al 2019

Prevention

- Anti-seizure medications
- Surgery
- Vagus Nerve Stimulator
- Nocturnal supervision
- Seizure Warning Devices
- Disclosure

Prevention- Anti Seizure Drugs

- How can this be demonstrated?
- Can't really do a trial: unethical, too long
- Look at a study to test new drugs vs baseline (+ active 'placebo')
  - If on baseline/active placebo had > 7 x chance of SUDEP

Ryvlin et al. *Lancet Neurol* 2011; 10: 961–68

Risk of sudden unexpected death in epilepsy in patients given adjunctive antiepileptic treatment for refractory seizures: a meta-analysis of placebo-controlled randomised trials

Methods We searched Medline and the Cochrane Library for randomised trials investigating any AED in the add-on treatment of drug-resistant epilepsy in adults. We extracted the number and causes of death in patients allocated to AEDs at doses that were more efficacious than placebo against seizures, AEDs at non-efficacious doses, and placebo. In our primary analysis, we compared the occurrence of definite or probable SUDEP between patients given efficacious AED doses and those given placebo…

Findings Data of 33 deaths, including 20 deemed as SUDEP, were extracted from 112 eligible randomised trials. 18 deaths were classified as definite or probable SUDEP and two as possible SUDEP. Definite or probable SUDEP, all SUDEP, and all causes of death were significantly less frequent in the efficacious AED group than in the placebo group, with odds ratios of 0·17 .., 0·17 .., and 0·37.., respectively. Rates of definite or probable SUDEP per 1000 person-years were 0·9 (95% CI0·2–2·7) in patients who received efficacious AED doses and 6·9 (3·8–11·6) in those allocated to placebo.

Interpretation Treatment with adjunctive AEDs at efficacious doses may have reduced the incidence of definite or probable SUDEP by more than seven times compared with placebo in patients with previously uncontrolled seizures.

Ryvlin et al. *Lancet Neurol* 2011; 10: 961–68

Prevention- Epilepsy Surgery

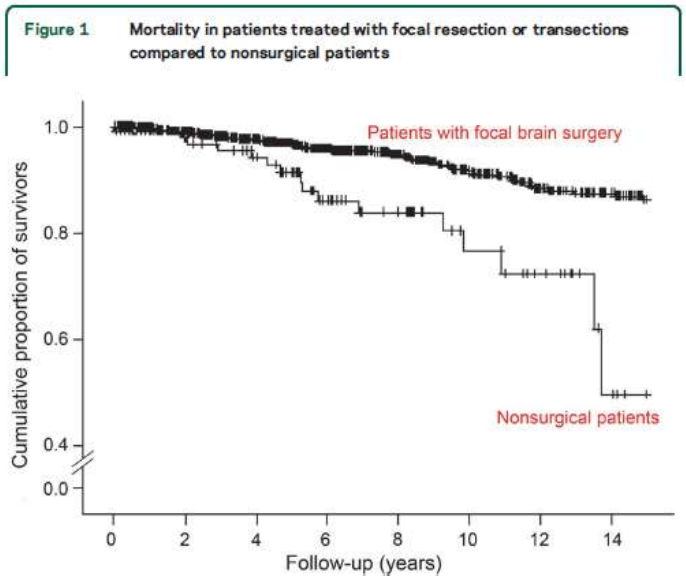
How can this be demonstrated?

- Report of SUDEP in patients who had surgery

CC excluded

Proportion Living
Most

Least



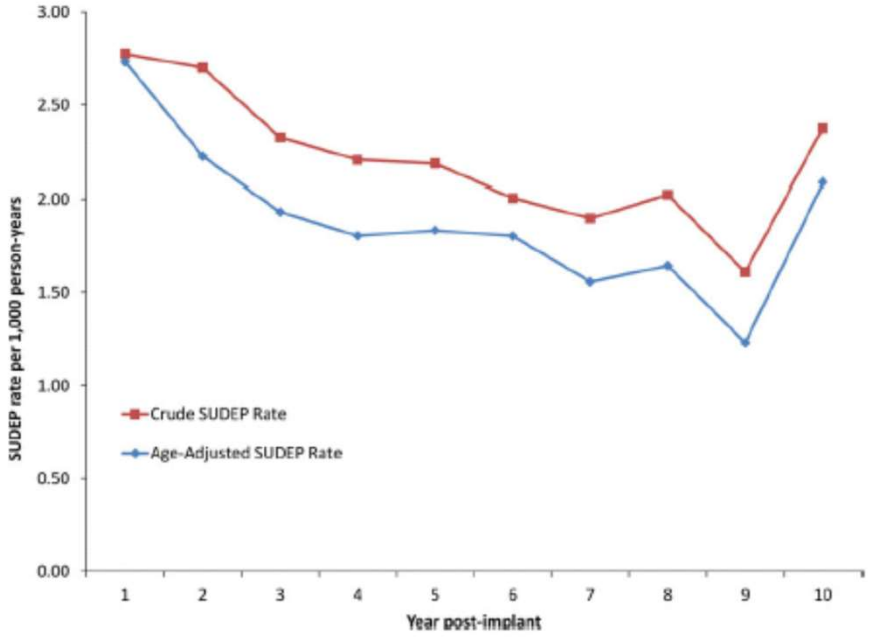
Brain surgery

No
Brain surgery

Sperling et al. Neurology 2016;86:1938–1944

Long-term surveillance of SUDEP in drug-resistant epilepsy patients treated with VNS therapy

Philippe Ryvlin[1,2] | Elson L. So[3] | Charles M. Gordon[4] | Dale C. Hesdorffer[5] | Mi
R. Sperling[6] | Orrin Devinsky[7] | Mark T. Bunker[4] | Bryan Olin[4] | Daniel Friedman[7]



- 40,443 implantations
- 3,689 deaths
- 632 SUDEP
- Only 16% definite or probable

Epilepsia, 2018;1-11

Prevention- Supervision

- In a residential school for epilepsy & LD- no deaths at school, 14 deaths occurred while on leave. Nashef et al, 1995

- Supervision at night reduced risk by 60% presence of an individual of normal intelligence and at least 10 y.o. in the same bedroom) or special precautions (regular checks through the night or a listening device Langan et al, 2005

Clinical risk factors in SUDEP
A nationwide population-based case-control study

- 255 SUDEP cases, 1,148 matched controls
- GTCs preceding year increased risk by 27
- No increase with non-GTCs
- Nocturnal GTCs increased risk by 15
- Living alone increased risk by 5
- Not sharing bedroom + GTCs increased risk by 67

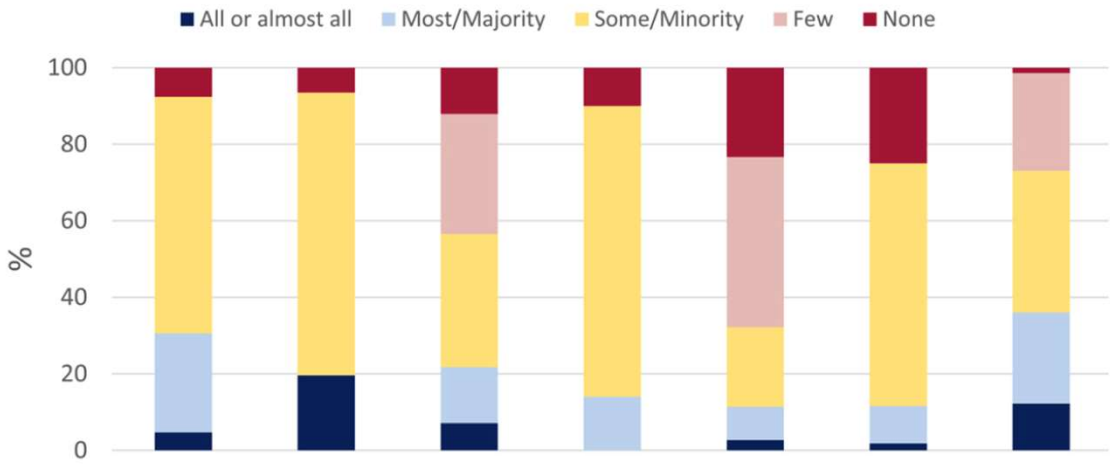
Sveinsson et al, Neurology® **2020**;94:e419-e429. doi:10.1212

Prevention- SUDEP Disclosure

- Ethics: right to know
- More than 95% of patients and caregivers **want to learn** about SUDEP
- Understanding that seizures, especially convulsive seizures seizures, can:
  - injure the brain
  - lead to cognitive and psychiatric disorders
  - lead to SUDEP
- **Patients can reduce their risk:**
  - **medication adherence,**
  - **lifestyle factors (eg, adequate sleep, avoiding excess alcohol)**
  - **Consider additional treatments**
- **Empathy**

Why child neurologists talk about SUDEP: results from two cross-sectional surveys

Authors: Anne E. Keller[1], Robyn Whitney[1,2], Elizabeth J. Donner[1,2]



Study	Morton	Gayatri	Friedman	Abdalla	Strzelczyk	Galli	Present study
Year of survey	≤2005*	≤2009*	2011	≤2013*	2014	2015	2017/18
Country	UK	UK	USA and Canada	Brazil	Austria, Germany, Switzerland	Italy	Mainly USA
N	383	46	1101	44	519	112	369

Epilepsia Open, 2020

Do people want to talk about SUDEP?

PWE C-PWE

C Wright et al, AES Annual Meeting 2012 abstract & poster

Parental and physician beliefs regarding the provision and content of written sudden unexpected death in epilepsy (SUDEP) information

*Neti A. Gayatri, †Matthew C. H. J. Morrall, ‡Vivek Jain, *Pawan Kashyape, *Karen Pysden, and *Colin Ferrie

Epilepsia 1-6, 2010

Two questionnaires

- Parents/guardians of children at pediatric epilepsy clinic

100 given- 67 (1st), 47 (2nd)

- Physicians, UK based pediatric neurologists

71 mailed, 45 (56%) returned

SPECIAL ARTICLE

Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society

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Torbjörn Tomson, MD, PhD
David Gloss, MD, MPH&TM
Jeffrey Buchhalter, MD, PhD
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Josemir W. Sander, MD, PhD, FRCP
Philippe Ryvlin, MD, PhD

ABSTRACT

Objective: To determine the incidence rates of sudden unexpected death in epilepsy (SUDEP) in different epilepsy populations and address the question of whether risk factors for SUDEP have been identified.

Methods: Systematic review of evidence; modified Grading Recommendations Assessment, Development, and Evaluation process for developing conclusions; recommendations developed by consensus.

Results: Findings for incidence rates based on 12 Class I studies include the following: SUDEP risk in children with epilepsy (aged 0–17 years) is 0.22/1,000 patient-years (95% confidence interval [CI] 0.16–0.31) (moderate confidence in evidence). SUDEP risk increases in adults to 1.2/1,000 patient-years (95% CI 0.64–2.32) (low confidence in evidence). The major risk factor for SUDEP is the occurrence of generalized tonic-clonic seizures (GTCS); the SUDEP risk increases in association with increasing frequency of GTCS occurrence (high confidence in evidence).

Recommendations: Level B: Clinicians caring for young children with epilepsy should inform parents/guardians that in 1 year, SUDEP typically affects 1 in 4,500 children; therefore, 4,499 of 4,500 children will not be affected. Clinicians should inform adult patients with epilepsy that SUDEP typically affects 1 in 1,000 adults with epilepsy per year; therefore, annually 999 of 1,000 adults will not be affected. For persons with epilepsy who continue to experience GTCS, clinicians should continue to actively manage epilepsy therapies to reduce seizures and SUDEP risk while incorporating patient preferences and weighing the risks and benefits of any new approach. Clinicians should inform persons with epilepsy that seizure freedom, particularly freedom from GTCS, is strongly associated with decreased SUDEP risk. *Neurology*® 2017;88:1674–1680

Results

"The majority (74%) of pediatric neurologists provided SUDEP information only to a select group of children with epilepsy and were uncertain about the effect such information would have upon the parent and child.

Conversely, 91% of parents expected the pediatric neurologist to provide SUDEP risk information. The provision of this information did not have a significant immediate and longer-term negative impact."

67% of parents wanted the information at the time of dx

Gayatri et al, 2010

Why child neurologists talk about SUDEP: results from two cross-sectional surveys

Authors: Anne E. Keller[1], Robyn Whitney[1,2], Elizabeth J. Donner[1,2]

Significance: Most child neurologists do not follow the current SUDEP Clinical Practice Guideline regarding SUDEP discussion. Feeling sufficiently knowledgeable and ethically obligated to discuss SUDEP were associated with increased discussion practice, suggesting an educational intervention may be effective at increasing SUDEP discussion rates.

Epilepsia Open, 2020

Learning objectives- revised

- Know that death can result from epilepsy
- Understand what you can do to prevent it
- Talk about it- your patients want you to

Prevention of Mortality

- Early diagnosis and treatment of pneumonia
- Early diagnosis and treatment of depression
- Identify etiology (more specific therapies available all the time)
- Reduce seizures to minimum possible via aggressive therapies
  - Medication (some evidence)
  - Surgery (some evidence)
  - Vagus nerve stimulation (some evidence)
  - Ketogenic diet (no evidence)
- Nocturnal supervision (some evidence)
- Seizure Warning Devices (no evidence)
- Epilepsy Learning Healthcare System(s)- diagnosis, treatment, referral, transition

What you can do

- Maintain general health, especially related to pulmonary infections
- If symptoms suggestive of depression, refer to mental health professional
- Seizure “control” means NO seizures and no/acceptable medication side effects
  - If not controlled, refer to neurologist/comprehensive epilepsy center
- Create a SEIZURE ACTION PLAN
- Talk about it
- Refer to local and national advocacy organizations

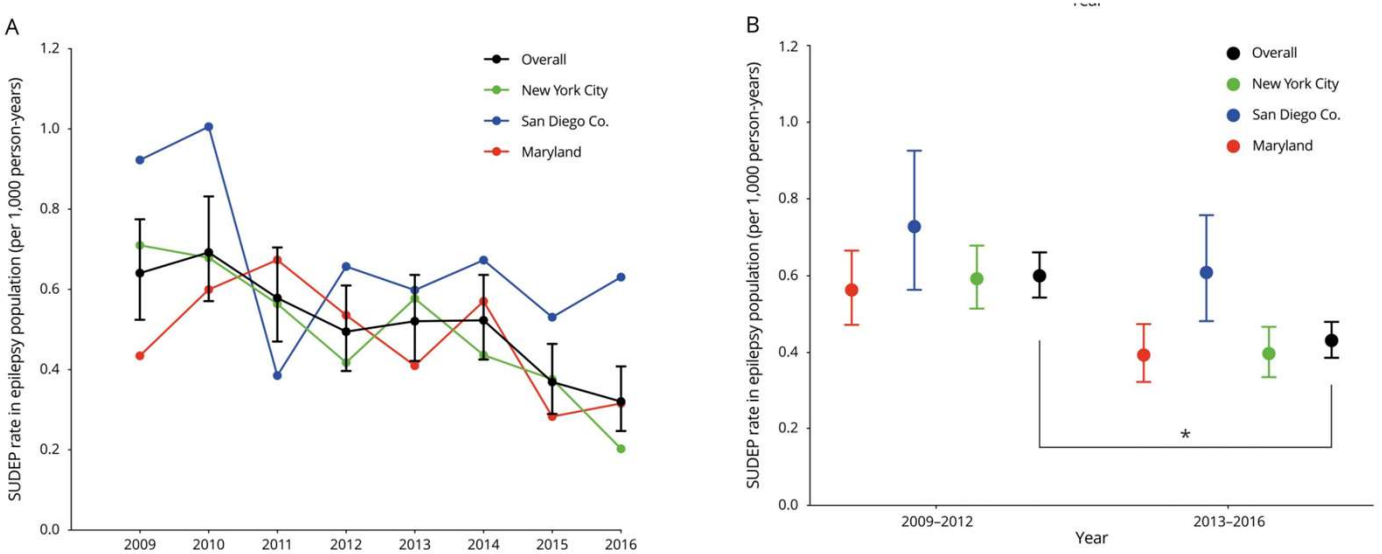
Temporal trends and autopsy findings of SUDEP based on medico-legal investigations in the United States

Esma Cihan, MD, Orrin Devinsky, MD, Dale C. Hesdorffer, PhD, Michael Brandsoy, Ling Li, MD, David R. Fowler, MB ChB, Jason K. Graham, MD, Michael W. Karlovich, Jaclyn E. Yang, Anne E. Keller, MPH, Elizabeth J. Donner, MD, and Daniel Friedman, MD, MSc

nyulangone.org

Neurology® 2020;95:e867-e877. doi:10.1212/WNL.0000000000009996

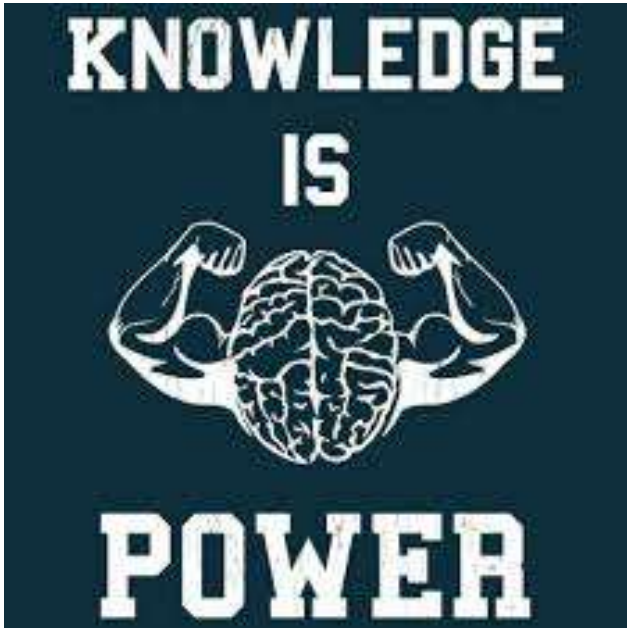
Figure 2 Temporal trends in medical examiner (ME)–investigated sudden unexpected death in epilepsy (SUDEP) incidence in 3 regions in 2009–2016



28% reduction

Reasons to discuss/treat seizures to decrease likelihood of death

- Aspiration pneumonia
- Status epilepticus
- SUDEP



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Epilepsy.com

Thanks for your attention!