Sudden Unexpected Death in Epilepsy:

Risk stratification, Prevention, and Communication with Families

EST 30th ANNIVERSARY ANNUAL MEETING

SUDEP: Risk Stratification, Prevention, and Communication with Families

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Disclosures

- No conflicts of interest with regard to this presentation

Overview

- Key facts of Sudden Unexpected Eealth in Epilepsy (SUDEP)
- Risk stratification & Preventive strategies

Causes of Death in Epilepsy patients

- Standardized Mortality Ratio (SMR): 2.2-2.6
- SMR higher for children: 5.3-9.0
- Predictors of mortality:
    1. Active epilepsy
    2. Symptomatic epilepsy
    3. ASM adherence
    4. Medical intractability

"sudden death is 24-34X more likely in young PWE[1,4]"

40-year follow-up of childhood-onset epilepsy: 30% mortality[3]

- Deaths related to epilepsy: direct/indirect, SUDEP
- Deaths related to the cause of epilepsy
- Deaths unrelated to epilepsy

Table 2. Causes of Death.

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
Death related to epilepsy — no./total no. of deaths (%)	33/60 (55)	9/15 (60)	24/45 (53)
Witnessed seizure — no.	6	0	6
Status epilepticus — no.	4	0	4
Probable seizure — no.	3	2	1
Drowning — no.	6	0	6
Sudden, unexplained death — no.	18	7	11
Death not related to epilepsy — no./total no. of deaths (%)	26 (43)	6 (40)	20 (44)
Pneumonia — no.	12	0	12
Cardiovascular disease — no.	8	2	6
Suicide — no.	2	2	0
Other cause of death — no.	4	2	2
Cause of death unknown — no.	1	0	1

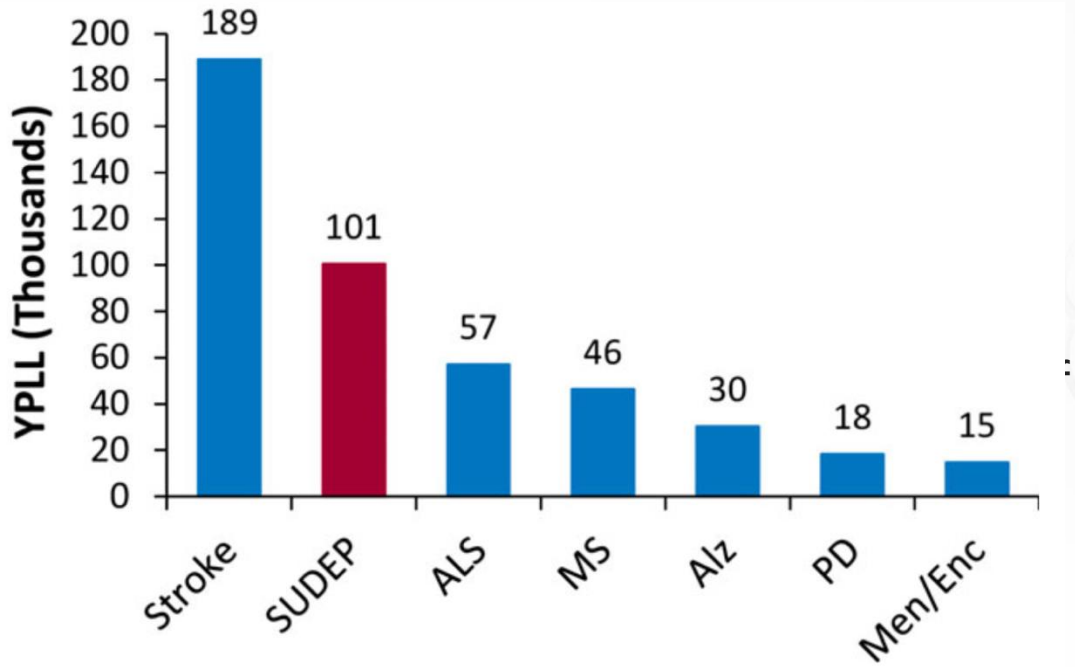
* A remote symptomatic cause of epilepsy indicates epilepsy associated with a major neurologic abnormality or insult.

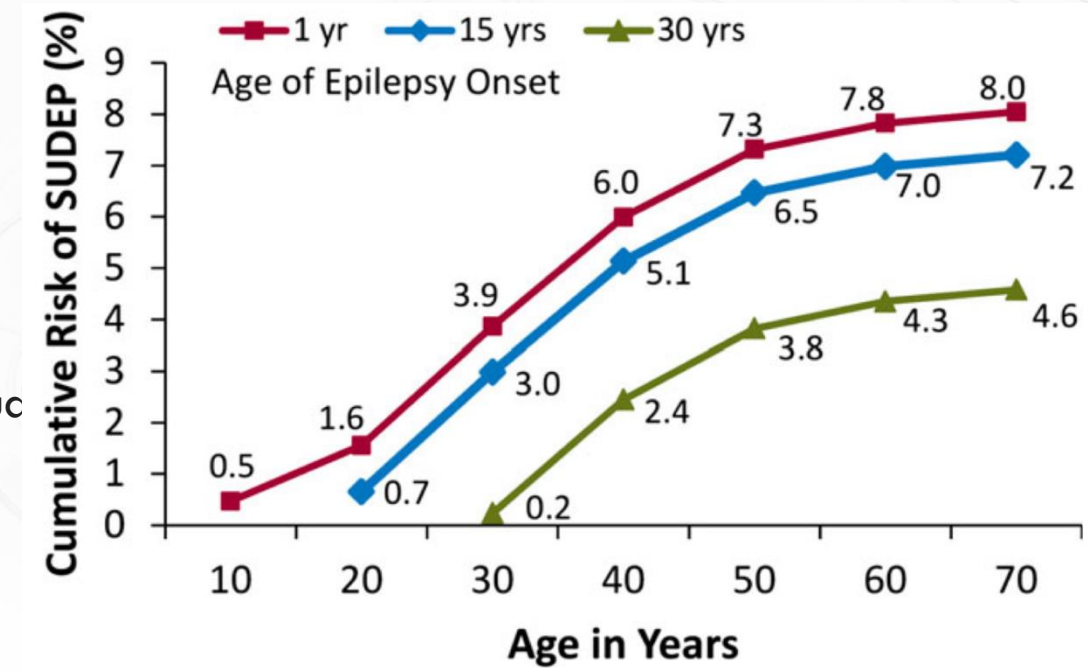
1. Ficker et al. Neurology 1998; 2. Ficker. Epilepsia 2000; 3. Sillapaa & Shinnar. N Engl J Med 2010; 4. Klovgaard et al. Epilepsia 2021

Sudden unexpected death in epilepsy: Assessing the public health burden

*David J. Thurman, †Dale C. Hesdorffer, and ‡Jacqueline A. French

Systematic search for epidemiologic studies of sudden death in epilepsy





- ✓ SUDEP ranks second only to stroke in term of years of potential life lost (YPLL)
- ✓ Lifetime risk of 4.6-8% by age 70

Thurman et al. Epilepsia 2014

SUDEP is a diagnosis of exclusion

- ✓ Has epilepsy, death was sudden and unexpected, in benign circumstances
- ✓ NOT a consequence of trauma, drowning, or status epilepticus
- May be witness or unwitnessed ; evidence of a preceding seizure is NOT required
- Postmortem exam: NOT reveal cause of death = Definite SUDEP
- Without autopsy = Probable SUDEP; a competing cause of death = Possible SUDEP
- Survives resuscitation >1 h = Near-SUDEP
- A clear cause of death is known = **NOT** SUDEP

Nashef et al. Epilepsia 2012

Risk of SUDEP varies within the epilepsy population

- Newly diagnosed epilepsy: 0.09 per 1000 patient-years
- Candidates for epilepsy surgery: 9 per 1000 patient-years

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)
Canada	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)
Sweden	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)

Keller et al. Neurology 2018

A major risk factor is the presence & frequency of GTCS

SPECIAL ARTICLE

AMERICAN ACADEMY OF NEUROLOGY

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

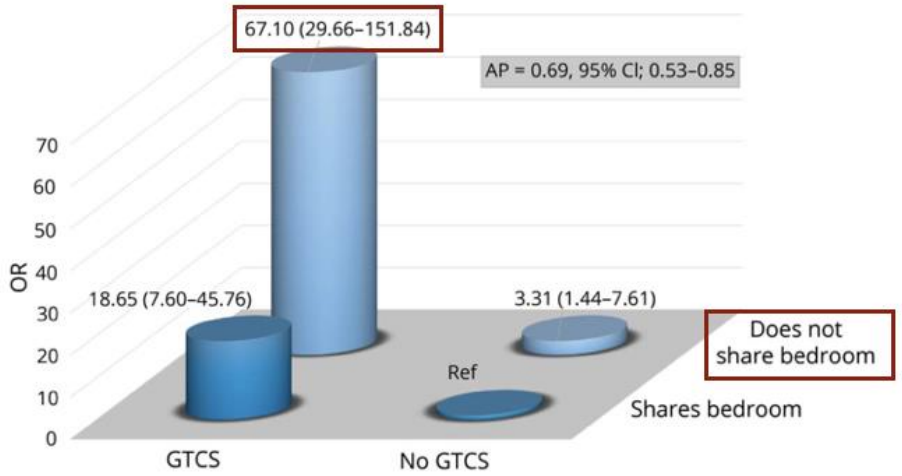
Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society

Factor	Odds ratio (CI)	Confidence level
Presence of GTCS vs lack of GTCS	10 (7–14)	Moderate
Frequency of GTCS	OR 5.07 (2.94–8.76) for 1–2 GTCS per y, and OR 15.46 (9.92–24.10) for >3 GTCS per y	High
Not being seizure free for 1–5 y	4.7 (1.4–16)	Moderate
Not adding an AED when patients are medically refractory	6 (2–20)	Moderate
Nocturnal supervision (risk reduction)	0.4 (0.2–0.8)	Moderate
Use of nocturnal listening device (risk reduction)	0.1 (0.0–0.3)	Moderate

Clinical risk factors in SUDEP

A nationwide population-based case-control study

	OR (95% CI)
GTCS during the preceding year	26.8 (14.9-48.4)
Nocturnal GTCS during last year	15.31 (9.6-24.5)
Living alone	5.0 (2.9-8.6)
Sharing household, not bedroom	2.3 (1.1-4.6)



AAN/AES Joint Guideline 2017; Sveinsson et al. Neurology 2020

SUDEP in the North American SUDEP Registry

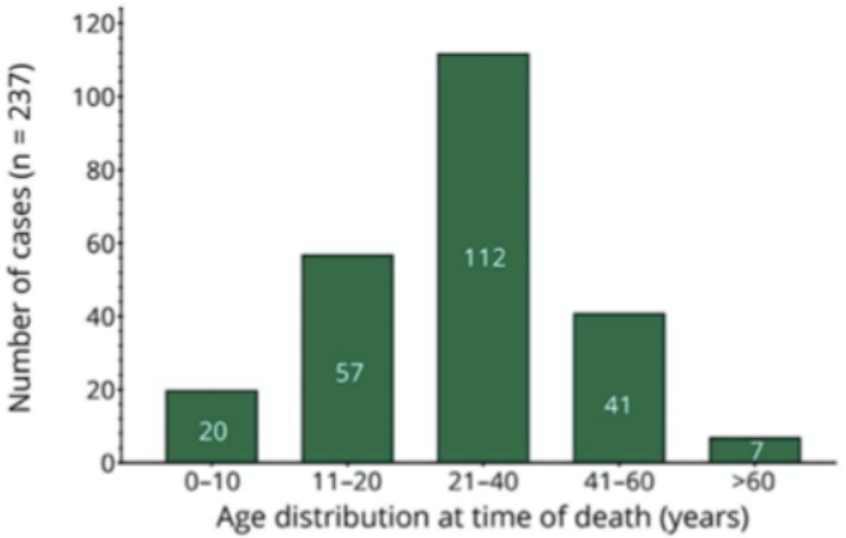
The full spectrum of epilepsies

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

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

Young adult, during apparent sleep, were prone



median age: 26 y (1-70)

- Low rate of witnessed death 7%
- Only 16% of next of kin had heard about SUDEP before their relatives' death

Verducci et al. Neurology 2019

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

- GGE are also at risk
- SUDEP affects the full spectrum of epilepsies
- SUDEP risk is NOT limited to frequent GTCS

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

JME, 9 (4%)

BECTS, 4 (1%)

LGS, 5 (3%)

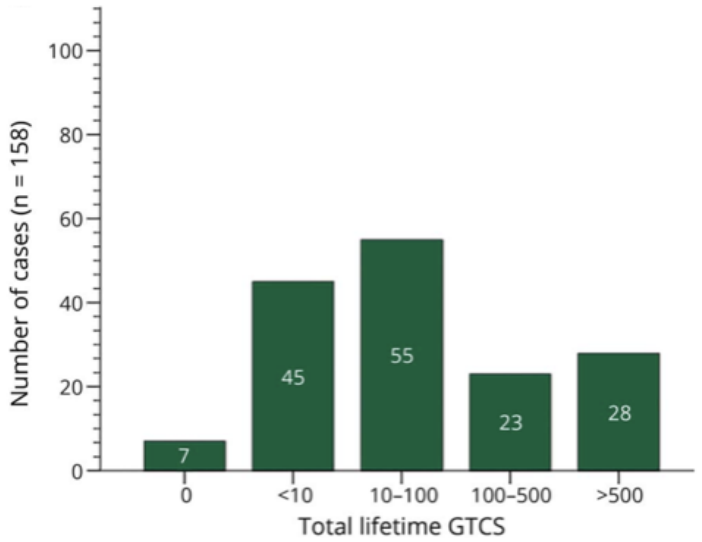
Febrile Sz plus, 7 (3%)

Dravet syndrome, 13 (5%)

Dup15q chromosome, 9 (4%)

Epilepsy surgery 42 (18%)

Neurostimulation 32 (14%)



Verducci et al. Neurology 2019

How does SUDEP happen?

Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study

- Study pooled cardiorespiratory arrests during video-EEG admissions worldwide (147 units)
- 16 SUDEP, 9 near-SUDEP

Time to CPR: SUDEP 13-180 min; near-SUDEP ≤3 min

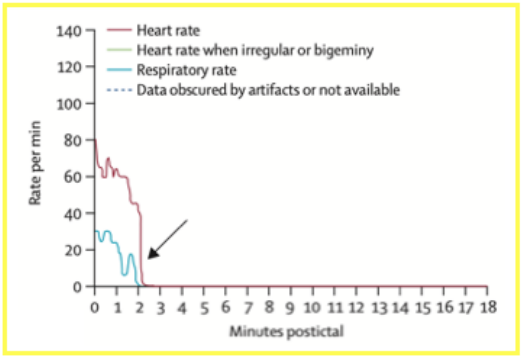
Secondary generalized tonic-clonic seizure

Post-ictal hyperventilation, HR varied

Post-ictal generalized EEG suppression (all cases)

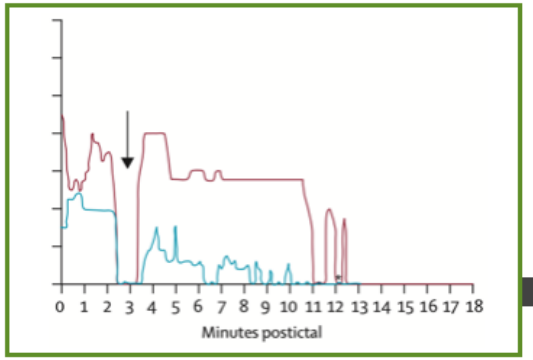
during the first 3 min

Central apnea, bradycardia/asystole



Terminal (n = 3)

Transient (n = 6)



(n = 6)

Terminal apnea

Terminal asystole

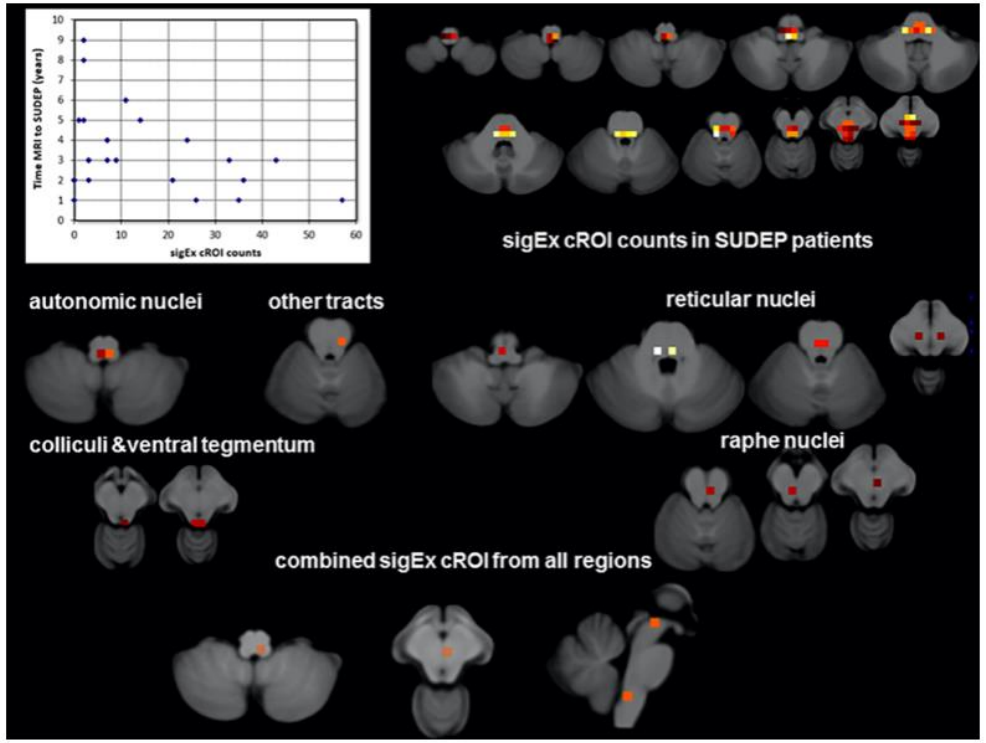
Ryvlin et al. Lancet Neurol 2013

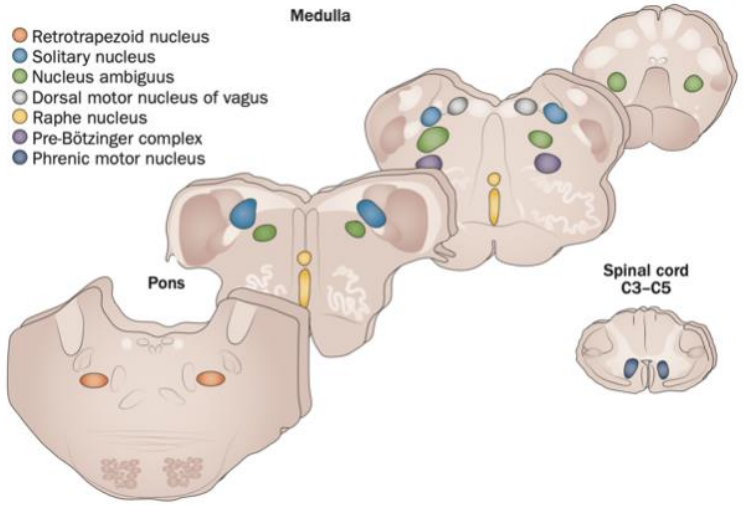
Brainstem network disruption: A pathway to sudden unexplained death in epilepsy?

Susanne G. Mueller[1] | Maromi Nei[2] | Lisa M. Bateman[3] | Robert Knowlton[4] | Kenneth D. Laxer[5] | Daniel Friedman[6] | Orrin Devinsky[6] | Alica M. Goldman[7]

Hum Brain Mapp *2018*: 39:

Two population: 18 focal epilepsy vs 11 controls; 26 SUDEP patients





- Volume loss in brainstem regions was correlates w/ autonomic dysfunction (HRV) in epilepsy patients
- Patients who died of SUDEP had widespread brainstem volume loss in their last MR exam
- More extensive damage correlated with shorter survival time

Mueller et al. Hum Brain Mapp 2018

Selected gene mutations that increase SUDEP risk

Genetic

- Genetic epilepsies with increased SUDEP risk
- Cardiac arrhythmia genes (7-15%)
- Respiratory genes

Cause of death in 177 Dravet syndrome cases

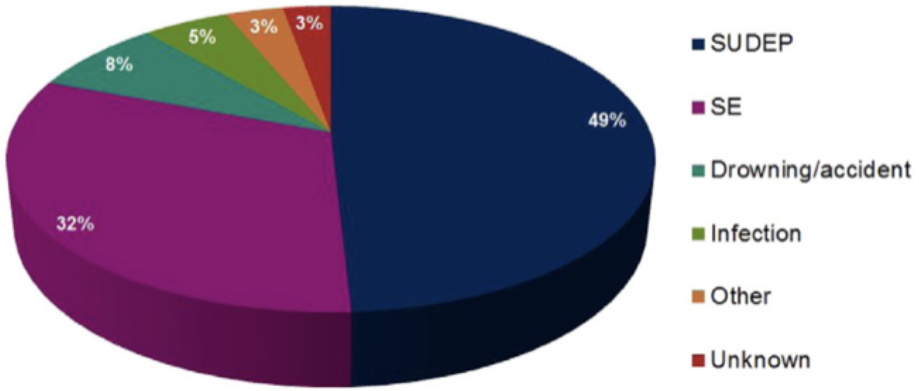


Table 1 | Selected gene mutations that increase the risk of SUDEP

Gene	Protein	Associated human disease	Human disease manifestations	Mouse model phenotype	SUDEP	Reference
SCN1A	$Na_v1.1$	Dravet syndrome	Febrile seizures in children; refractory seizures in adults; psychomotor regression; ataxia; sleep disturbance; cognitive impairment; premature death	Interictal heart rate variability; atropine-sensitive ictal bradycardia; premature death	Yes	Kalume (2013)[80] Kalume *et al.* (2013)[88] Auerbach *et al.* (2013)[127]
*SCN5A**	$Na_v1.5$	Brugada syndrome	ST-segment elevation in V1–V3 on electrocardiogram; syncope; seizure; disrupted sleep; premature death	Ventricular tachycardia; cardiac abnormalities	Possibly	Hedley *et al.* (2009)[128] Martin *et al.* (2012)[129] Derangeon *et al.* (2012)[130]
SCN5A‡	$Na_v1.5$	Long QT syndrome type 3	Delayed repolarization; torsades de pointes; sudden death; palpitations; syncope; gastrointestinal symptoms	QT prolongation, ventricular tachycardia and early afterdepolarization *in vitro*	Possibly	Aurlien *et al.* (2009)[131] Johnson *et al.* (2009)[132]
KCNA1	$K_v1.1$	NA	Episodes of ataxia with continuous inter-attack myokymia; partial epilepsy in some cases	Severe epilepsy; atrioventricular conduction block; bradycardia; premature ventricular contractions; premature death	Yes	Glasscock *et al.* (2010)[79] Zuberi *et al.* (1999)[133]
KCNH2	$K_v11.1$	Long QT syndrome type 2	Delayed repolarization of the heart; torsades de pointes; heart palpitations; syncope; sudden death; long QT events triggered by auditory stimuli	*Kcnh2*$^{-/-}$ genotype is embryonic lethal	Yes	Anderson *et al.* (2014)[74] Johnson *et al.* (2009)[132] Tu *et al.* (2011)[134]
KCNQ1	$K_v7.1$	Long QT syndrome type 1	Delayed repolarization of the heart; torsades de pointes; palpitations; syncope; sudden death; hearing loss; long QT events during swimming	Impaired neuronal repolarization; seizures; dysregulated autonomic control of heart	Yes	Goldenberg & Moss (2008)[71] Goldman *et al.* (2009)[77]
HTR2C	$5\text{-}HT_{2C}$	NA	NA	Epilepsy; respiratory arrest; cardiac monitoring not completed	Yes	Tecott *et al.* (1995)[23]
RYR2	RyR2	Catecholaminergic polymorphic ventricular tachycardia	Tachycardia due to catecholamine release during exercise; dizziness; syncope; seizures; premature death	Exercise-induced ventricular arrhythmias; generalized tonic–clonic seizures; sudden cardiac death	Yes	Derangeon *et al.* (2012)[129] Lehnart *et al.* (2008)[135] Napolitano *et al.* (1993)[136]

*Loss-of-function mutation. ‡Gain-of-function mutation. Abbreviations: NA, not applicable; SUDEP, sudden unexpected death in epilepsy.

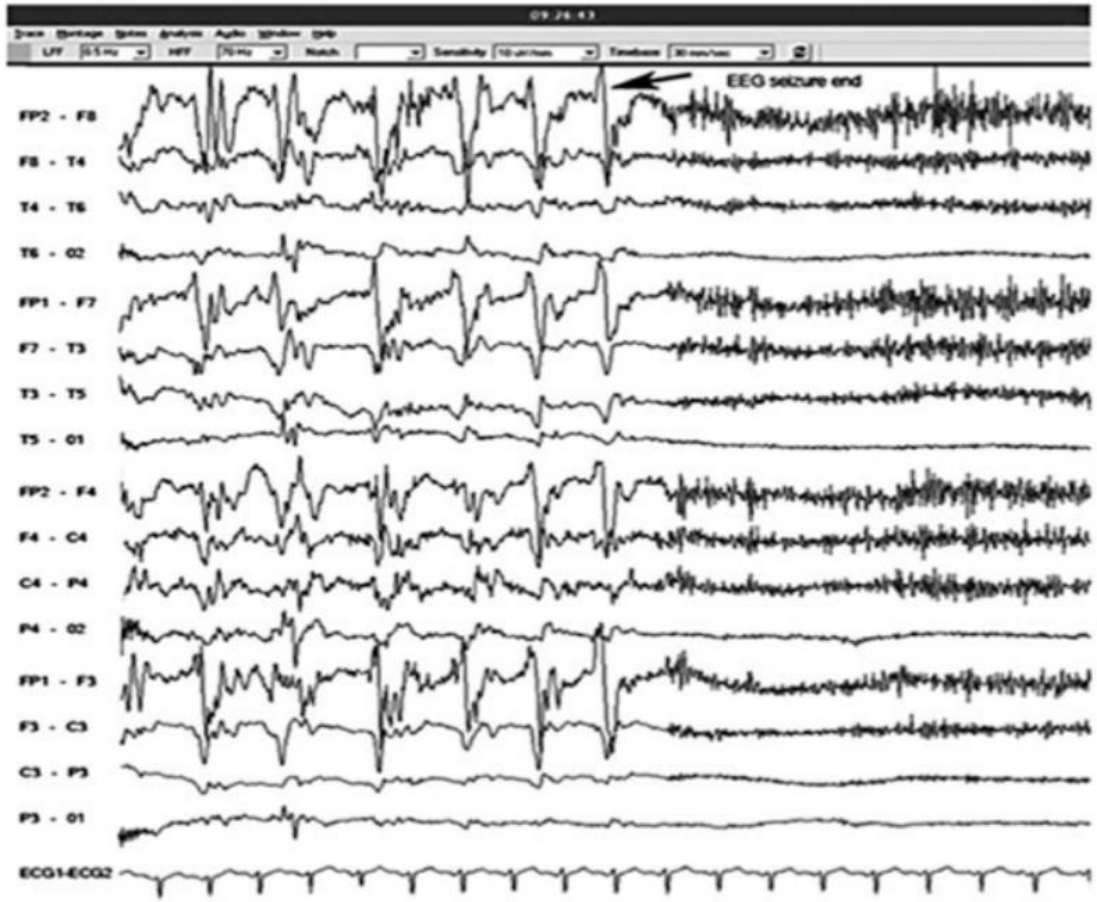
Massey CA et al. Nat Rev Neurol 2014; Shmuely et al. Epilepsy Behav 2016

Whether PGES is an independent marker of SUDEP is unknown

- ☑ Yes:
  - All SUDEP cases in MORTEMUS were preceded by PGES
  - 10 SUDEP cases and 30 controls (US): PGES >50 sec associated with increased risk (OR 5.22)
- ○ No:
  - 17 SUDEP cases and 19 controls (UK): PGES presence or duration did not differ between both groups
  - Prior studies examine PGES and SUDEP risk have been small and single center

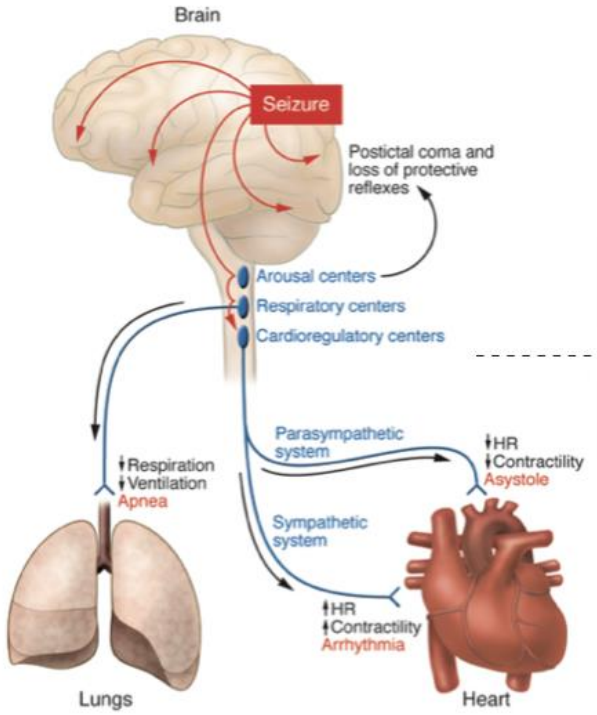
Post-ictal generalized EEG suppression (PGES)

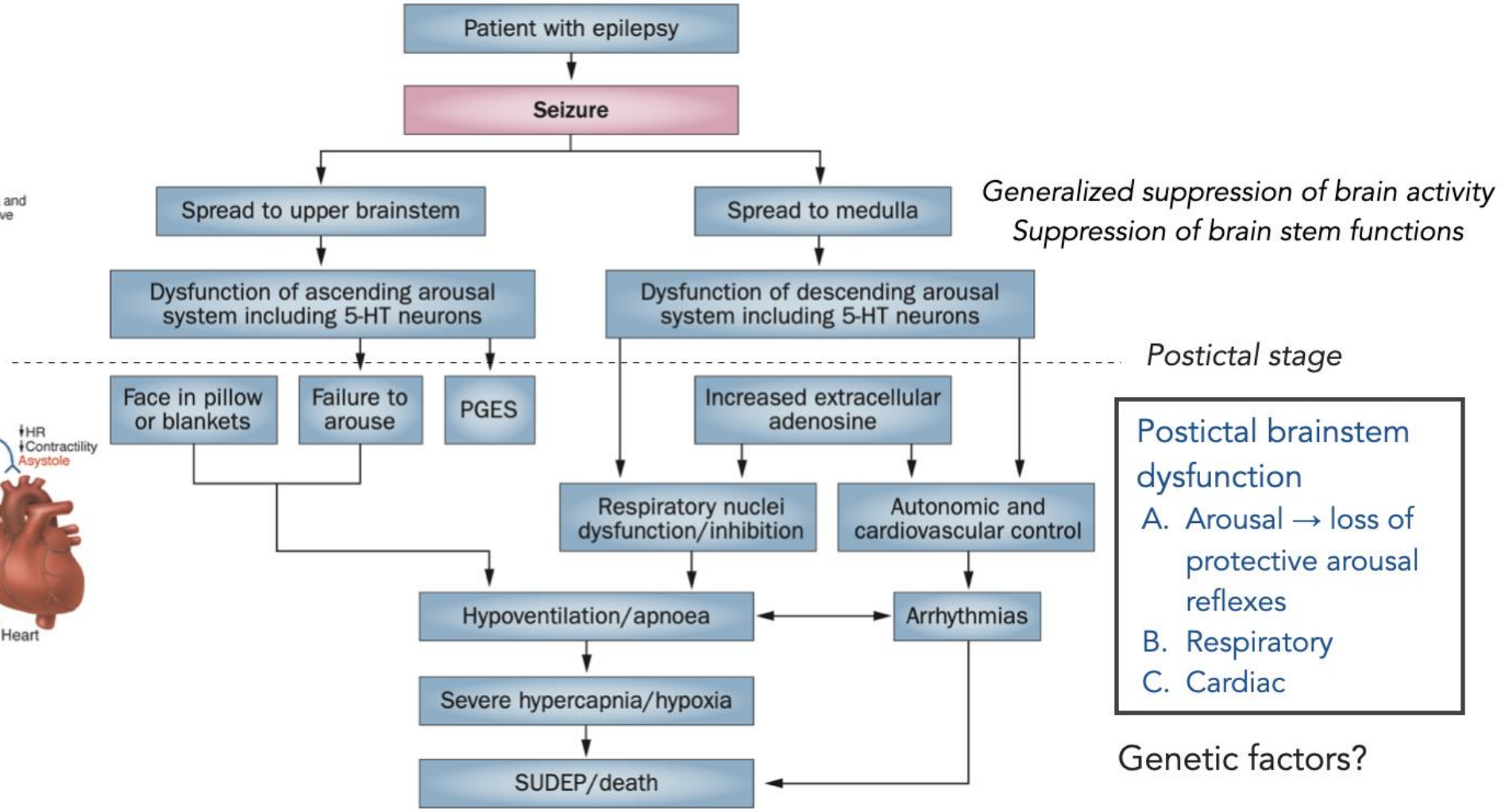
- *<10 mV, >1 sec, within 30 sec of seizure cessation*
- *40-60% of those who had GTCS*



Lhatoo et al. Ann Neurol 2010; Surges et al. Epilepsy Behav 2011

No single mechanism established





Friedman et al. J Clin Invest 2013; modified from Massey et al. Nat Rev Neurol 2014

SUDEP risk stratification

Risk factor	SUDEP-7	Revised SUDEP-7
GCTS in the past 12 months	0 seizures → 0 points 1-3 seizures → 1 point ≥4 seizures → 3 points	0 seizures → 0 points 1-3 seizures → 1 point ≥4 seizures → 2 points
Any seizure, frequency per month in the past 12 months	0 seizures → 0 points 1-49 seizures → 1 point >50 seizures → 3 points	0 seizures → 0 points 1-49 seizures → 1 point >50 seizures → 2 points
Epilepsy duration	0-29 y → 0 points ≥30 y → 3 points	
Number of AEDs	0-2 drugs → 0 points ≥3 drugs → 1 point	
Cognitive impairment	IQ ≥ 70 → 0 points IQ < 70 → 2 points	
Total score	12 points	10 points

SUDEP risk factors	SUDEP–3 weighting	OR (95% CI)
GTC seizure frequency >3 in last year	0 or 1	2.7 (0.9-7.7)
Seizure of any type >0 in last year	0 or 2	8.4 (1.0-71.1)
Intellectual disability	0 or 1	3.1 (0.7-13.4)
Total SUDEP-3 score	0 to 4	

SUDEP inventory

SUDEP-7 → revised SUDEP-7 → SUDEP-3

2010 2015 2021

SUDEP-CARE 2022: drug-resistant focal epilepsy

Risk factors	Point(s) if yes
Generalized tonic–clonic seizure frequency in the last year	
<1 per year	0
Between 1 per month and 1 per year	1
>1 per month	2
Presence of intellectual disability	1
Current or past depressive disorder	1
Respiratory symptoms during or after seizure	1
Sleep-related or nocturnal seizures	2
Able to alert someone of an oncoming seizure	−1
Seizure-related falls	1
	Total score (sum)

DeGiorgio et al. Epilepsy Behave 2010; Novak et al. Front Neurol 2015; Rasekhi et al. Epilepsia 2021; Serrand et al. Eur J Neurol 2023

Can we prevent SUDEP?

Cochrane Library

Cochrane Database of Systematic Reviews

Treatments for the prevention of Sudden Unexpected Death in Epilepsy (SUDEP) (Review)

Maguire MJ, Jackson CF, Marson AG, Nevitt SJ

We included one cohort study and three case-control studies of serious to critical risk of bias. The 6-month prospective cohort study observed no significant effect of providing patients with SUDEP information on drug compliance and quality of life, anxiety and depression levels. The study was too short and with no deaths observed in either group to determine a protective effect. Two case control studies reported a protective effect for nocturnal supervision against SUDEP. However due to significant heterogeneity, the results could not be combined in meta-analysis. One study of 154 SUDEP cases and 616 controls reported an unadjusted odds ratio (OR) of 0.34 (95% CI 0.22 to 0.53; P < 0.0001). The same study demonstrated the protective effect was independent of seizure control, suggesting that nocturnal supervision is not just a surrogate marker of seizure control. The second case-control study of 48 SUDEP cases and 220 controls reported

Authors' conclusions

adjusted OR 0.4 (0.2-0.8)

We found limited, very low-certainty evidence that supervision at night reduces the incidence of SUDEP. Further research is required to identify the effectiveness of other current interventions — for example seizure detection devices, safety pillows, SSRIs, early surgical evaluation, educational programmes, and opiate and adenosine antagonists — in preventing SUDEP in people with epilepsy.

Maguire et al. Cochrane Database Syst Rev 2020

Approaches to SUDEP prevention

1. Optimizing epilepsy care: target GTCS and FBTCS
   - Optimize medical therapy: efficacious adjective ASM, 0.9 vs 6.9 per 1000 person-years
   - Timely referral for non-medical therapy:
     - 2 large studies have shown lower SUDEP and all-cause mortality in epilepsy surgery groups, 10.4 vs 5.2 and 4.6 vs 1.9 per 1000 person-years
     - VNS, RNS studies suggest SUDEP rates lower in treated patients
2. Early cardiopulmonary resuscitation, recommend first-aid course to relative
3. Nocturnal supervision, seizure detection devices, sharing household

Ryvlin et al. Epilepsia 2011; Sperling et al. Neurology 2016; Devinsky et al. Epilepsia 2018; Casadei et al. Epilepsy Behav 2020

EST 30th ANNIVERSARY ANNUAL MEETING

Sudden Unexplained Death in Epilepsy (SUDEP): Risk Stratification, Prevention, and Communication with Families

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EST 30th ANNIVERSARY ANNUAL MEETING

Talking about SUDEP with Patients with Epilepsy (PWE) and Caregivers

Practice Guideline Summary: AAN 2017

- Recommend counselling on SUDEP risks to children and young adults with epilepsy and their cargivers

- 1 in 1,000 adults with epilepsy

- 1 in 4,500 children with epilepsy

- 9 in 1,000 with Dravet syndrome

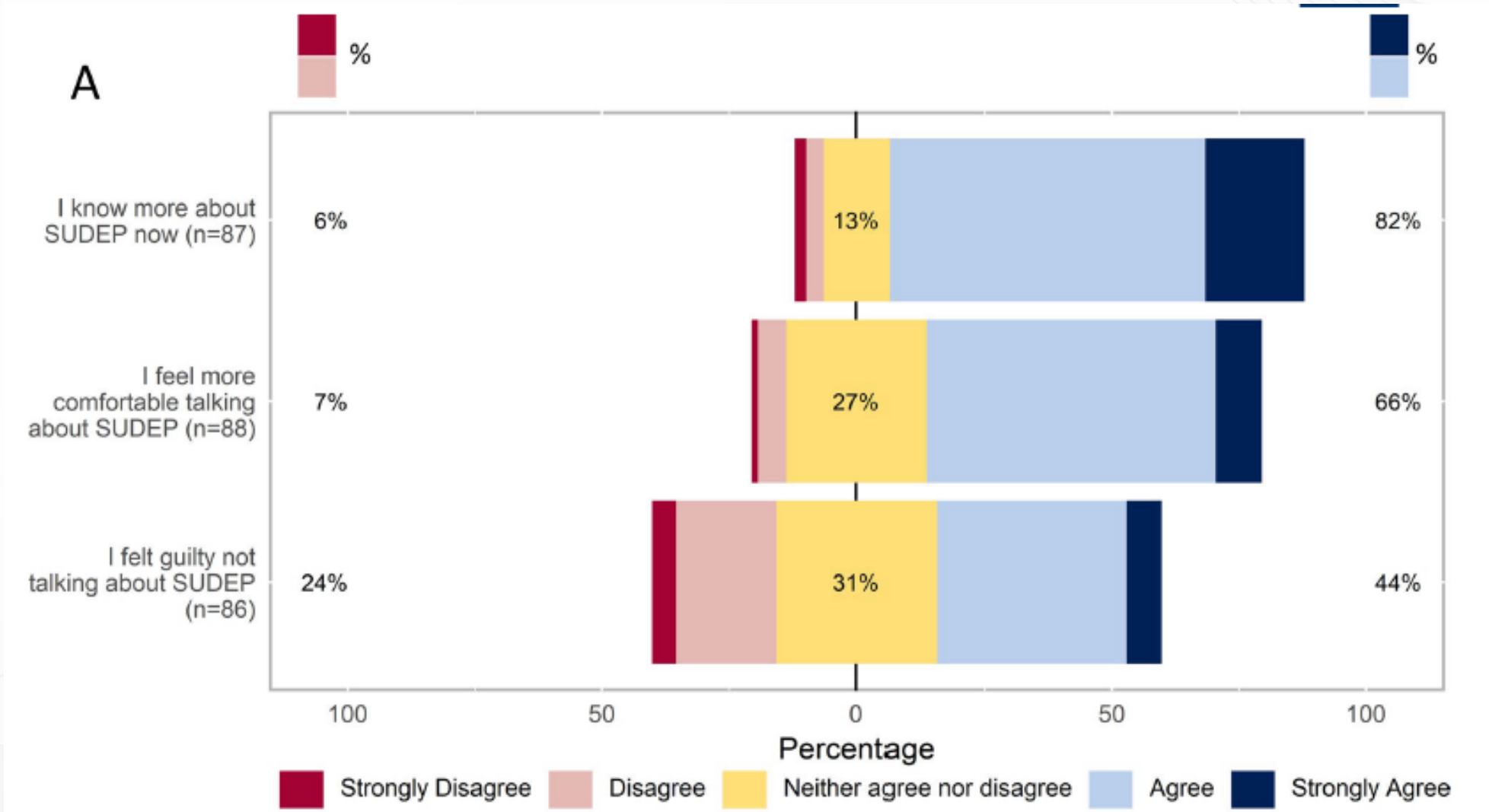
Harden C, AAN 2017

Neurologists Perspective

- 12% of child neurologists discussed SUDEP with most of patients
- 54.8% of 1123 neurologists from 27 countries never or rarely discuss SUDEP with patients and/or caregivers
- May provoke excess anxiety or worry among family members
- Barriers: time constraints, a lack of modifiable factors, poor evidence basis of risk mitigation
- Clinical experience and environment appear to impact SUDEP discussion

Vasiliadis A, Epilepsia 2026, Asadi-Pooya, Epilepsy Behav 2022

Themes for Changing SUDEP Discussion Practice



Keller A, Epilepsia Open 2020

PwE and Caregivers Persecptive

- 71% of PWE want to hear about SUDEP
- 79% patients/caregivers expected neurologist to discuss SUDEP
- 70% bereaved family members were unaware of SUDEP
- PwE have a right to know about SUDEP

Cooper K, Seizure 2020

Discussing SUDEP with PwE and parents/carers

- Some discordance between carers'/family members' and healthcare professionals on discussing the risk of SUDEP
  - Only 3.4% neurologists discussed SUDEP
  - Awareness lessens trauma, grief, and guilt for parents whose children died of SUDEP
  - SUDEP counseling motivated changes > 2 epilepy-related childcare behaviors and practices in 84% of parents
  - Adult PwE reported that SUDEP awareness motivated better medication adherence and risk-reducing lifestyle modifications (88%)

Knowing better than not knowing

Shankar R, Eur J Neurol 2018, Long L, Epilepsy Behav 2018, Kumari S, Epilepsy Res 2022

Discussing SUDEP with PwE and parents/carers

- Consideration on timing and who should be present during SUDEP discussions
  - Face-to-face delivery, with supporting written information
  - By a suitably knowledgable healthcare professionals whom the caregivers/PwE feels comfortable
  - Appropriate time at or close to diagnosis

Cooper K, Seizure 2020

Discussing SUDEP with PwE and parents/carers

- SUDEP information should include prevalence, risk factors, and risk reduction
  - Balanced counselling
  - Basic information is sufficient
  - Risk reduction methods relative to individual concerned

Cooper K, Seizure 2020, Harden C, AAN 2017

What can be done?

- Educate yourself:
  - https://aesnet.org/about/about-aes/position-statements/position-statement-on-sudep-counseling
- Known the risk factors for SUDEP
  - GTC seizures, particular > 3/y
  - Non-adherence to ASMs
  - Failure to escalate treatment in DRE patients
  - Nocturnal GTC seizures
  - Living alone
  - Early age at seizure

Vasiliadis A, Epilepsia 2026

Frame the Discussion

Received: 29 April 2026 | Revised: 27 June 2026 | Accepted: 29 June 2026

DOI: 10.1002/epi.70387

Epilepsia®

COMMENTARY

A practical framework for discussing sudden unexpected death in epilepsy with patients and families: Resolving the communication gap

Anne Q. Vasiliadis[1] | Gazelle Zerafati-Jahromi[1] | William D. Gaillard[1] | Dewi F. Depositario-Cabacar[1] | Gardiner Lapham[2] | Howard P. Goodkin[3] | Madison M. Berl[4] | Nathan T. Cohen[1]

- Say the words
- Benchmark the risk in understandable terms
- Focus on modifiable risks

Vasiliadis A, Epilepsia 2026

Say the words

- Make SUDEP part of your risk counselling at the initial diagnosis
- A direct and frank discussion of SUDEP (Do not be vague)
- Discussion should not be limited to the first visit
- The discussion should be revisited, especially when there is an escalation in GTC seizures or concerns about ASMs adherence

Benchmark the risk in understandable terms

- “There is a rare risk of SUDEP”
- “In 1 year, SUDEP typically affects 1 in 4,500 children with epilepsy; in other words, annually, 4,499 of 4,500 children will NOT be affected by SUDEP”
- “In 1 year, SUDEP typically affects 1 in 1,000 adults with epilepsy; in other words, annually, 999 of 1,000 adults will NOT be affected by SUDEP”
- The annual risk of dying in a motor vehicle collision is about 1:8500

Vasiliadis A, Epilepsia 2026

Focus on modifiable risks

- Emphasize ASM adherence
- Recommend co-sleeping
- Recommend nocturnal seizure monitoring devices
- Emphasize the benefits of early epilepsy surgery

The SPIKES Protocol

- Setting: a comfortable and private space
- Perception: assess the caregiver baseline knowledge
- Invitation: Ask directly about how much and what kind of information will be helpful for them
- Knowledge: Share your knowledge about SUDEP in a clear, direct, and comprehensive manner
- Empathy: Acknowledge and respond to caregiver emotions
- Summarize: Summarize the information by using lay language

Maney K, Pediatr Neurol 2025

A 9-year-old male

- Drug resistant epilepsy, CP (GMFCS V), hydrocephalus underwent VP shunt on home ventilator with tracheostomy
- First seizure: 4 month with fever and status epilepticus -> *S. pneumoniae* meningitis
- Current seizure frquency
- Epileptic spasms occurred at 10 months of age, frequency: daily
- GTC seizures occurred since 2 year of age, frequency: 3/day
- Current medication: VPA, VGB, CNZ, Propranolol
- Came to follow up regularly every 6 months

Next week later

- Parents came back to inform that he passed away peacefully

Conclusions

- Caregivers and PwE emphasize the value of SUDEP risk counselling
- Although, there is a lack of evidence on “how” to impact this sensitive information, neurologists should educate caregivers about SUDEP in an empathic manner
- Adequate control of GTC seizures using medical and surgical therapies, lifestyle changes, and possibly nocturnal supervision aare the main preventive strategy