SUDEP: From Prediction to Prevention

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Disclosure:	The author has declared no conflicts of interest.
Received:	06.07.26
Accepted:	21.07.26
Keywords:	Epilepsy mortality, prediction, prevention, sudden unexpected death in epilepsy (SUDEP).
Citation:	EMJ Neurol. 2026;14[1]:80-83. https://doi.org/10.33590/emjneurol/S3X7U7GL

INTRODUCTION

Sudden unexpected death in epilepsy (SUDEP) remains the leading directly epilepsy-related cause of death. It is predominantly nocturnal and unwitnessed, and most of those who die are found prone in bed.[1,2] Overall annual incidence is approximately 1.2 per 1,000 patient-years in people with epilepsy, rising to 2.6–4.8 per 1,000 in drug-resistant cohorts,[3] and it occurs throughout the lifespan, most frequently in the third and fourth decades. A single generalised tonic–clonic seizure (GTCS) can prove fatal in an otherwise well young adult.

The only prevention measure with randomised support is indirect. A meta-analysis of placebo-controlled trials found that adjunctive antiseizure medication, through reducing seizures, lowered the incidence of seizure-related mortality roughly sevenfold, though these trials were not designed to measure SUDEP.[4] Reducing seizures is therefore the only measure that we can state with confidence prevents SUDEP, albeit at the population rather than the individual level. No intervention has yet been tested in a trial designed to prevent SUDEP, and we cannot say whether recommended measures have lowered its incidence.[5] Prevention has two components: identifying those at risk and acting to reduce that risk, and interrupting the fatal process once it begins. As this commentary argues, each is challenging for different reasons.

HOW THE TARGET HAS CHANGED

The understanding of what makes a seizure fatal has shifted over time. Early attention focused on seizure-induced cardiac arrhythmia, then on postictal brainstem failure, impaired arousal, blunted responses to rising carbon dioxide, and depressed respiratory drive. Video-EEG recordings of patients who died in monitoring units captured a stereotyped terminal cascade: hyperventilation, then central apnoea, bradycardia, and asystole.[1] In the last decade, emphasis has settled on an integrated failure of brain, heart, and respiration.[6]

SUDEP is not a single mechanism but a family of them: positional asphyxia, failure of respiratory drive and arousal, cardiac arrhythmia, and autonomic dysfunction.[6] An intervention works only if it matches the mechanism: repositioning for asphyxia, stimulation and rescue for failure of arousal, and a cardiac-directed approach for arrhythmia. No single strategy can protect everyone.

PREDICTION AND INTERRUPTION

These two problems are difficult for different reasons. Prediction, identifying who will die and when, is limited by the rarity of SUDEP, its mechanistic heterogeneity, and biomarkers whose group-level associations have so far translated poorly to the individual. Postictal generalised EEG suppression (PGES) illustrates this gap: associated with SUDEP across cohorts,[7] it is nonetheless inconsistent within the same person from seizure to seizure, and is unreliable as a predictor for individuals.[8] Interruption, arresting the cascade once it has begun, faces different obstacles: a window of minutes, usually in someone unobserved; an effective action that differs by mechanism and may not be identifiable at the time; and an event that cannot ethically be left unattended to randomise a rescue.

Sudden arrhythmic death shows that interruption can be operationalised once the mechanism is defined and an effective rescue device exists. Cardiac arrhythmia is common in epilepsy, and patients do receive pacemakers;[9] chronic epilepsy itself can remodel the heart, adding a further arrhythmic substrate.[10] Even so, the chain to lives saved in people with epilepsy is unproven: pacing prevents syncope but has not been shown to prevent SUDEP, and ictal asystole is usually self-limiting.[11] The cardiac field is nonetheless decades ahead with a deployable rescue for a defined mechanism. For the respiratory and positional mechanisms behind most SUDEP, we are earlier still: whether the cascade can be interrupted at all, by what, and within what window, is largely unknown. One rodent model has given us hope for feasibility: transient diaphragmatic pacing reduced postictal mortality, though it did not always restore breathing (likely reflecting coexistent laryngospasm).[12]

WHAT WE CAN DO NOW

Two recent prospective studies used video-EEG to test peri-ictal biomarkers against subsequent SUDEP. In the REPO$_2$MSE study (1,074 adults with drug-resistant focal epilepsy), the pre-specified endpoint of oxygen desaturation below 80% did not separate those who died from controls, and the number of antiseizure medications was not associated with risk.[13] A larger cohort found peri-ictal central apnoea associated with SUDEP (a link that weakened after adjustment), while living alone and frequent convulsions persisted as known risks.[14] Both cohorts came from monitoring units, with few deaths and wide uncertainty, and the association with apnoea was not significant with exclusion of possible and near-SUDEP cases.

A caution is needed here: a biomarker that correlates with death is not necessarily a target that saves lives when modified. In the Cardiac Arrhythmia Suppression Trial, drugs that suppressed the surrogate (ventricular ectopy) increased mortality.[15] Prevention requires evidence that changing a marker changes the outcome, which for SUDEP currently holds for no peri-ictal variable. With that caveat, four measures can be appraised. Seizure prevention acts furthest upstream; supervision and detection serve prediction, or enable a further rescue; and only repositioning would interrupt the cascade directly (this remains untested).

Medication Adherence and Seizure Prevention

Non-adherence is a recognised modifiable risk factor, and subtherapeutic drug levels are common at post-mortem, though confounded by redistribution. Recent prospective data found no association between the number of antiseizure medications and SUDEP.[13] Adherence matters not because a drug level is protective but because it maintains seizure control. It is also among the few SUDEP relevant factors measurable in life, through drug levels, refill records, or possession ratio. Supporting seizure control, including timely medication changes and specialist or surgical referral where seizures remain refractory, is deliverable prevention.

Nocturnal Supervision and Detection

Nocturnal supervision carries a protective signal, though evidence is observational and

guidelines endorse it only weakly. Sharing a bedroom or using a listening device is associated with reduced risk, apparently independent of seizure control, yet the most recent systematic review judged the certainty very low and found no adequate evidence for detection devices.[5] Supervision is, moreover, least deliverable to those at highest risk: younger adults with refractory convulsions, often living alone. Wearable devices detect convulsions with high sensitivity; however, it is unknown whether these alarms improve outcomes.[16] Detection, though, is not prevention. A device that senses a seizure must also summon someone who can reach the patient and intervene in a way that interrupts the SUDEP process. The first step is established; the second is not. Conversely, firm evidence that supervision reduced mortality would itself show the cascade can be interrupted.

Body Position

About 73% of SUDEP cases are found prone, with the proportion being higher in younger decedents.[2,17] These data come from observations after death, invariably without knowing the position before the terminal seizure. The implied mechanism is logical but unproven: positional airway obstruction and reduced ventilatory drive prevents recovery and the resultant hypoxia impairs self-rescue, as in sudden infant death syndrome; this pattern was seen in 11 of 13 patients with positional data in MORTEMUS.[1] Advising against prone sleeping addresses only part of the problem, since in monitored cases prone position arose nearly as often from the convulsion itself as from sleeping posture.[1] Prevention must instead focus on postictal repositioning.

Postictal Repositioning

Here the evidence is weakest. No study has causally tested whether turning a patient from prone to lateral after a seizure prevents SUDEP. The supporting data are indirect and almost entirely from video-EEG: early peri-ictal intervention (repositioning, airway clearance, oxygen, stimulation) shortens respiratory dysfunction and PGES, and postictal immobility tracks the depth of respiratory compromise.[18] No one has quantified prospectively how often repositioning occurs, how fast, and whether speed matters. Video-EEG suits that first step, relating repositioning latency to the duration of apnoea, desaturation, and PGES. A definitive trial would move into the community, where most SUDEP occurs, and could not be designed until data showed which surrogate to target.

Communication

Underlying all of these is engagement. The risks described here are modifiable (even if their impact on SUDEP is unestablished), but only by the person with epilepsy. Taking medication reliably, reporting seizures accurately, adjusting sleeping arrangements, and heeding nocturnal events are acts the patient must choose to undertake, none of which follows from a clinic letter alone. Informed discussion is therefore not an adjunct to prevention but how every measure above is delivered. And because risk runs across the whole epilepsy population, that conversation should be routine, not only for those labelled high-risk.

WHAT WE MUST STILL ESTABLISH

We understand how people die of SUDEP far better than how to prevent it. Several answerable questions block the path from plausible to proven. Which seizures are fatal, and which, of hundreds, are survived? In an individual, which mechanism will prove lethal, positional, respiratory, or cardiac, and can it be identified in advance? Does earlier repositioning shorten the at-risk window? Can trials be designed not to identify risk but to reduce it?

The epilepsy monitoring unit can begin to answer several of these. It records physiology and is where the phenotypes of the operative mechanism can be defined. Yet, while apnoea and EEG suppression are increasingly captured, the two variables most needed for the positional mechanism are often missing: body position, time-stamped through the event, and the latency and nature of repositioning. The video holds both, but neither is routinely coded in a form usable for research. Coding

them to a common standard, alongside the parameters that established cohorts already capture, would give every recorded convulsion a minimum peri-ictal dataset. SUDEP is too rare in monitored patients for mortality to be a feasible endpoint, but the unit can answer the question on which any prevention trial depends: whether the cascade is interruptible, and within what window. The one randomised attempt to improve postictal recovery, naloxone administration during monitored seizures, did not improve oxygenation, a measure of how early this work remains.[19]

While SUDEP risk can be stratified across groups, it cannot yet be predicted in the individual. Novel respiratory, sleep, electroclinical, and anatomical markers are improving mechanistic understanding, though most require external validation and assessment of clinical utility. Despite this, prevention should not await a perfect predictive model. The current priorities are clear and can be delivered now: reduction of convulsive seizures, timely management of drug resistance, and honest and proportionate communication around appropriate nocturnal supervision and seizure first aid.

References

1. Ryvlin P et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. Lancet Neurol. 2013;12(10):966-77.
2. Grundmann A et al. The epilepsy deaths register: third-party reports of SUDEP in adults and older adolescents. Seizure. 2025;132:20-9.
3. Harden C et al. Practice guideline summary: sudden unexpecteddeath in epilepsy incidence rates and risk factors. Neurology. 2017;88(17): 1674-80.
4. Ryvlin P et al. Risk of sudden unexpected death in epilepsy in patients given adjunctive antiepileptic treatment for refractory seizures: a meta-analysis of placebo-controlled randomised trials. Lancet Neurol. 2011;10(11):961-8.
5. Maguire MJ et al. Treatments for the prevention of sudden unexpected death in epilepsy (SUDEP). Cochrane Database Syst Rev. 2020;4:CD011792.
6. Devinsky O et al. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. Lancet Neurol. 2016;15(10):1075-88.
7. Lhatoo SD et al. An electroclinical case-control study of sudden unexpected death in epilepsy. Ann Neurol. 2010;68(6):787-96.
8. Lamberts RJ et al. Postictal generalized EEG suppression: an inconsistent finding in people with multiple seizures. Neurology. 2013;81(14):1252-6.
9. Rugg-Gunn FJ et al. Cardiac arrhythmias in focal epilepsy: a prospective long-term study. Lancet. 2004;364(9452):2212-9.
10. Verrier RL et al. The epileptic heart: concept and clinical evidence. Epilepsy Behav. 2020;105:106946.
11. Tényi D et al. Ictal asystole: a systematic review. Epilepsia. 2017;58(3):356-62.
12. Purnell BS et al. Diaphragmatic pacing for the prevention of sudden unexpected death in epilepsy. Brain Commun. 2022;4(5):fcac232.
13. Ryvlin P et al. Seizure-related biomarkers of sudden unexpected death in epilepsy (SUDEP) in drug-resistant focal epilepsy (REPO2MSE): a prospective, multicentre case–control study. Lancet Neurol. 2026;25(1): 50-60.
14. Ochoa-Urrea M et al. Risk markers for sudden unexpected death in epilepsy: an observational, prospective, multicentre cohort study. Lancet. 2025;406(10511):1497-507.
15. Echt DS et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med. 1991;324(12):781-8.
16. Beniczky S et al. Automated seizure detection using wearable devices: a clinical practice guideline of the International League Against Epilepsy and the International Federation of Clinical Neurophysiology. Epilepsia. 2021;62(3):632-46.
17. Liebenthal JA et al. Association of prone position with sudden unexpected death in epilepsy. Neurology. 2015;84(7):703-9.
18. Seyal M et al. Impact of periictal interventions on respiratory dysfunction, postictal EEG suppression, and postictal immobility. Epilepsia. 2013;54(2):377-82.
19. Rheims S et al. Efficacy of naloxone in reducing hypoxemia and duration of immobility following focal to bilateral tonic-clonic seizures. Epilepsia Open. 2025;10(3):880-93.