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# Sudden unexpected death in epilepsy: measures to reduce risk

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## ABSTRACT

This review looks at the strategies that may help to reduce the risk of sudden unexpected death in epilepsy beyond that of trying to achieve seizure cessation, which is not possible for up to 30% of patients with epilepsy. These strategies include seizure safety checklists, mobile phone technology, telehealth and various devices currently available or in development. We highlight interventions where there is evidence of benefit, and draw attention for the need both to involve patients with epilepsy in risk reduction and to improve communication with those at risk.

## INTRODUCTION

There is nothing so tragic as a life needlessly lost.

The consequences of epilepsy are manifold. Aside from the effects it has on peoples' lives as a result of social consequences (employment, driving, schooling and sporting) and medication (side effects, contraception and pregnancy), there are medical consequences with the risk of injuries, cognitive problems and ultimately premature death. Epilepsy is the fifth highest cause of life years lost, second only to stroke as a neurological disorder, and the most common cause of death in younger people.<sup>1–3</sup>

The National Sentinel Audit of epilepsy-related deaths in 2002 recorded 1200 epilepsy-related deaths annually in the UK, of which 42% were felt to be avoidable.<sup>1</sup> In 2013 there were 1187 deaths attributed to epilepsy in England and Wales, suggesting little progress in attempting to reduce the risk.<sup>4</sup> Sudden unexpected death in epilepsy (SUDEP), defined as death not due to accidents or witnessed seizures, peaks in young adults; about 1% of young men with epilepsy die before the age of 30 years.<sup>5</sup>

Strategies to reduce the risk of SUDEP must involve not only people with

epilepsy but also their general practitioners. General practitioners have the most medical contact with people with epilepsy, not just for their epilepsy but also for other conditions that may also influence risk, such as depression and substance misuse.<sup>6–7</sup> The UK's National Institute for Health and Care Excellence epilepsy guidelines from 2004 to 2012 clearly state that the risk of death in epilepsy, in particular SUDEP, should be discussed as a priority at the time of diagnosis.<sup>8–9</sup> Its equivalent in Scotland, the Scottish Intercollegiate Guidelines Network epilepsy guidelines 2015, suggests discussion about SUDEP at an 'appropriate time'.<sup>10</sup> Despite this risk, there is a tacit avoidance of discussing the risk of death both in primary and secondary care, while the patient organisations and SUDEP Action (formerly Epilepsy Bereaved) vociferously support the patients' view that such risks should be made transparent (see box 1). This article sets out strategies that may help clinicians to improve person-centred communication when dealing with epilepsy, to reduce this risk.<sup>11</sup>

## INITIAL MEASURES TO REDUCE RISK

Reducing seizure frequency, particularly tonic-clonic seizures, may seem self-evident as a primary goal, but until a recent meta-analysis of randomised controlled trials there was little evidence that reducing seizures did reduce SUDEP risk.<sup>12</sup> Achieving this requires a cohesive approach from clinicians and teams with expertise in epilepsy. For that reason, a diagnosis of epilepsy should only be made by someone with an interest in epilepsy, be that a general neurologist or an epileptologist. The initial management should use a team approach, with the epilepsy nurse specialist (if available) being central. Information provided sensitively

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**Box 1 Quote from a patient—with permission**

The patient who has epilepsy commented: "EpSMon is just what I need to monitor my risk in between visits to doctors. It helps me take actions at all times as it measures my own particular risks of epilepsy. It can act as a safety net, being an excellent reminder of the importance of taking medication correctly and seeing my GP on a regular basis."

at an early stage empowers people with epilepsy, and we propose an early discussion about SUDEP, usually at the first follow-up after confirmation of diagnosis, as raising this issue at the diagnostic stage can be too difficult for some. In our practice, most people with epilepsy (and their families or carers) welcome the discussion of SUDEP, and find that this helps the discussion around many aspects of management.<sup>13</sup>

The choice of antiepileptic medication is important, as some may worsen certain epilepsies (eg, carbamazepine and myoclonic epilepsies). While up to 70% of patients become seizure free on their first choice for monotherapy, it is important to pay heed to reported side effects, not least because of the risk of non-concordance. Thirty per cent of people with long-term conditions in general do not take their medications regularly; epilepsy is no exception.<sup>14</sup>

Women in their fertile years require special consideration, and antiepileptic drug interactions with hormonal contraception, fears about teratogenicity, vomiting in pregnancy and blood concentration changes all demand a proactive approach. Specific clinics particularly linked to maternity services may help.<sup>15</sup>

Choosing an easy dosing regimen also helps—once daily dosing may suit some patients—and always enquire about the ease of swallow and palatability of medicines, since problems with these may reduce concordance. In people with intellectual disability and percutaneous endoscopic gastrostomy feeding, there may be formulation issues that influence absorption.

When first-line treatments fail, leaving the patient with refractory epilepsy, the clinician should consider planned sequential monotherapy or polytherapy. In one study, up to 16% of people whose epilepsy was considered refractory became seizure free or significantly improved.<sup>16</sup> People with epilepsy often respond positively to participation in clinical trials, audits and studies, and centres participating in such activities report greater patient satisfaction and better outcomes.

It is worth considering surgical interventions when medical management fails. Resective surgery remains the gold standard for selected people with epilepsy, with reported seizure freedom rates of 70% for temporal and 50% for extra-temporal procedures, although long-term data show that seizures may

recur.<sup>17</sup> Vagus nerve stimulation is often considered when resective surgery is not appropriate for various reasons, such as an unclear seizure focus, comorbidities, possible cognitive risks and so on. Many people with epilepsy prefer this option, and recent advances in device technologies now provide automated triggering, based on the heart rate changes that may accompany seizure onset.<sup>18</sup>

**DISCUSSING SUDEP**

Discussing SUDEP has been controversial and some countries still advocate a paternalistic approach on a 'need to know basis'.<sup>19</sup> A recent court judgement in Scotland supported the view that people with epilepsy and their families were entitled to be provided with such information at an early stage (see **box 2** for website links). The timing of such a discussion should be tailored to individual needs. Sometimes an early discussion is not appropriate; for example, if there is active psychiatric comorbidity or epilepsy has occurred in the setting of a malignant cerebral tumour. In patients with intellectual disability, the family and carers usually wish to know as early as possible. In our practice, we have this discussion using a structured approach and aided by the SUDEP and seizure safety checklist (**box 1**) at diagnosis in people with intellectual disability, and at the first follow-up in those without.

**SUDEP RISK CHECKLIST****The SUDEP and seizure safety checklist**

Common sense suggests anything that reduces seizure frequency should reduce mortality; hence improving concordance with medication, avoiding seizure

**Box 2 Useful websites**

[https://www.sudep.org/checklist—seizure safety checklist](https://www.sudep.org/checklist—seizure%20safety%20checklist)  
[https://www.sudep.org//epilepsy-self-monitor—epilepsy self-monitor \(EpSMon\)](https://www.sudep.org//epilepsy-self-monitor—epilepsy%20self-monitor%20(EpSMon))  
[https://www.youtube.com/watch?v=e3mECsSVgHI—EpsMon demonstration video](https://www.youtube.com/watch?v=e3mECsSVgHI—EpsMon%20demonstration%20video)  
[https://www.youtube.com/watch?v=Z9KHQvsapAc—administering seizure safety checklist](https://www.youtube.com/watch?v=Z9KHQvsapAc—administering%20seizure%20safety%20checklist)  
[http://www.who.int/patientsafety/safesurgery/checklist/en—the surgical safety checklist](http://www.who.int/patientsafety/safesurgery/checklist/en—the%20surgical%20safety%20checklist)  
[http://cdrwww.who.int/patientsafety/safesurgery/Surgical\\_Safety\\_Checklist.pdf—surgical safety checklist in use](http://cdrwww.who.int/patientsafety/safesurgery/Surgical_Safety_Checklist.pdf—surgical%20safety%20checklist%20in%20use)  
[http://qualitysafety.bmj.com/content/early/2014/07/18/bmjqs-2013-002772.full—patients' views on the surgical safety checklist](http://qualitysafety.bmj.com/content/early/2014/07/18/bmjqs-2013-002772.full—patients'views%20on%20the%20surgical%20safety%20checklist)  
[http://www.epilepsytoolkit.org.uk/—national epilepsy toolkit](http://www.epilepsytoolkit.org.uk/—national%20epilepsy%20toolkit)  
[http://www.scotland-judiciary.org.uk/10/794/Fatal-Accident-Inquiry-into-the-deaths-of-Erin-Casey-and-Christina-Fiorre-Ilia—the Scottish fatal accident enquiry](http://www.scotland-judiciary.org.uk/10/794/Fatal-Accident-Inquiry-into-the-deaths-of-Erin-Casey-and-Christina-Fiorre-Ilia—the%20Scottish%20fatal%20accident%20enquiry)

triggers and so on are all part of our routine care plans. However, the evidence basis for this common-sense approach derives only from retrospective studies. While there are common themes, there is no consensus on a standardised approach to risk reduction.

Safety checklists now form part of routine clinical practice, particularly in surgery where they reduce morbidity and mortality; both clinicians and patient groups support their use<sup>20</sup> (see [box 1](#) for website links). Creating such lists requires a detailed assessment and validation of the variables that contribute to risk.

There are numerous studies looking at the risk factors for SUDEP. An in-depth review of the literature identified 18 risk factors,<sup>7 21</sup> leading to our development of a safety checklist ([figure 1A, B](#)). Of the 18 factors, 11 were potentially modifiable, particularly non-adherence to antiepileptic medications, substance misuse, mood disorders and sleep disruption (see <https://www.sudep.org/checklist> to register, see training videos and access a copy). There is no absolute risk assigned to each item, nor to the sum of the items, but completing the list allows a discussion around risk modification. Detailed analysis and stratification of the risk factors show that some are more significant than others.<sup>22</sup> Despite initial fears that raising the issues might cause unnecessary alarm, patients tend to receive it positively<sup>13</sup> and using the checklist can modify behaviours.<sup>23</sup>

The charity 'SUDEP Action' launched the SUDEP and seizure safety checklist in the UK in 2015. There are 19 questions covering SUDEP and seizure safety risk, updated from evidence on SUDEP and fatality risk in epilepsy, and a question about the use of emergency services. Administering the checklist takes about 10 min, although discussion around the identified risks takes longer. Partners/carers of people with epilepsy are often more positive than patients about the checklist—after all, they watch the seizures and pick up the pieces afterwards.

While a clinic-led safety checklist is a step forward, it requires the patient to attend; hence we need an empowerment tool in the community. Lack of engagement with services is an identified risk. In 90% of SUDEP cases, there was deteriorating seizure control in the 3–6 months before death, and most had not had an epilepsy review for at least a year.<sup>24</sup> Thus, while simple strategies can reduce or better manage risk, these interventions also need to be positioned either in primary care or with the patients themselves.

### TELEHEALTH

Telehealth projects are well established in other disciplines, such as cardiac failure and chronic obstructive pulmonary disease. Such systems have now been piloted in epilepsy in a primary care setting using a telehealth non-clinical professional to contact people perceived to be at high risk every 3 months. Seventeen per cent of

patients had an intervention that would otherwise have not happened.<sup>23</sup> This programme is potentially cheaper than medically led interventions, seems acceptable to patients and general practitioners, has not resulted in increased referrals to secondary care and is now being developed over a larger primary care population.

### MOBILE EHEALTH (SMARTPHONES, etc)

The use of technology is often overlooked in medicine. The at-risk age group for SUDEP is smartphone savvy, and this seems an obvious aid to communication and risk assessment. There is now a mobile phone app, epilepsy self-monitor (EpSMon) based on the safety checklist ([figure 2A, B](#)), available free on iPhone and Android (see [box 1](#) for website links). It is patient driven, and reminds the user to repeat the assessment every 3 months. Risks are summarised and, if present, the app suggests a review with the general practitioner and provides relevant education. Data are stored on a secure server along with a university governance policy for research purposes (made available on application to suitable research groups). The Epilepsy Foundation (USA) is to release the app 'EpSMon USA' shortly, with evidence of its continued usability and model of delivery.<sup>25</sup> While there has been a flood of medical apps across many conditions in recent years—many unregulated, unevidenced and of doubtful benefits—the involvement of the evidence, users, charities and professionals in app development has led to EpSMon and the SUDEP and seizure safety checklist being recognised as part of the national epilepsy toolkit (see [box 1](#) for website links).

The press and social media showed considerable interest in EpSMon, and the launch of the iOS version for mobile phones featured in *The Guardian* newspaper ([figure 3](#)). This type of publicity can help to reduce the stigma of epilepsy and to spread public awareness of its risks as a lifelong condition. It gives patients a positive message that they can be 'empowered' to take charge of their condition (see [box 1](#)).

Nevertheless, a barrier to the use of the apps is the lack of awareness of risks of epilepsy, which the public generally consider as 'safe'. In addition, the 3-month gap between assessments could disengage the user. Such apps clearly need continued advertising and collaboration with patient groups and development of a seizure and medication monitoring daily diary.

Certain other factors such as bias of self-reporting are more difficult to address and felt to be a 'necessary evil' to take advantage of patient self-empowerment. The expectation is that with repeated reviews and research of growing usage data this bias could be reduced over time.

### DEVICE TECHNOLOGY

A recent systemic review into available commercial seizure detection devices showed no suitable robust seizure detection and safety technology though some

SUDEP AND SEIZURE SAFETY CHECKLIST (Adults)				Review Results		
ID	Risk Factor	Suggested Prompt	Evidence	dd/mm/yyyy	dd/mm/yyyy	dd/mm/yyyy
<b>BACKGROUND</b>						
1	Unclear seizure frequency or treatment history	Refer to patient notes. If history poor discuss with patient the benefit of regular monitoring.	Poor medical records highlighted as possible flag for risk (3, 19, 20)			
2	Duration of epilepsy more than 15 years	Refer to patient notes	Combined data from four SUDEP case-control studies found 2 fold increased risk (21)			
3	Early onset of epilepsy before aged 16	Refer to patient notes	1.7-fold increased risk of SUDEP compared to 16-60 age group (21, 22)			
4	Younger age	Refer to patient notes	Pooled data from SUDEP studies found most reported SUDEPs in age range 20-40 (4)			
5	Male sex	Refer to patient notes	Combined data from four SUDEP case-control studies found 2 fold increased risk (21)			
6	Presence of intellectual disability	Refer to patient notes. Consider patient capacity and involvement of carer in discussion.	Reported finding that people with intellectual disabilities and epilepsy do have a substantially increased risk of mortality, particularly where seizures are ongoing (23, 24)			
7	Pregnancy	Is patient of child bearing age? Has she received pre-conception counselling. If pregnant review care.	Risk in pregnancy finding from reported maternal deaths (25, 26)			
<b>RELATED RISKS</b>						
12	Lack of surveillance at night	What happens if you have a night time seizure?	Nocturnal supervision found to be protective in SUDEP study (19) Lack of supervision frequently noted when SUDEP occurred in Epilepsy Monitoring Units (29) SUDEP is frequently unwitnessed (30)	Yes	Yes	No
13	Prone position	No question to patient advised unless considered appropriate	Systematic review highlights significant association between SUDEP and prone position (31)	Unknown	Unknown	Unknown
14	Injuries or use of emergency services	Have you had any injuries or ED/999 emergency service calls?	Injuries have been identified as a risk factor for mortality (12)	Yes	No	No
15	Medicines non-adherence issues	Do you have any difficulties taking your medication as prescribed? e.g. at times forgetting to pick up a prescription; the taste of the medication is bad; at times questioning the benefits of the medication or feeling that they need more information or support to take the epilepsy medication.	Non-adherence with AED associated with a 3 fold increase in mortality (33) Not collecting scripts for 91 -192 days carried a higher mortality risk (12) Patients seizure free with AEDs showed no excess mortality (32) AEDs at efficacious doses may reduce SUDEP (34) AED hair strand levels showed greater variability in SUDEP cases (35)	Yes	Yes	No
16	Frequent AED prescribing changes	*Refer to patient notes	Frequent changes of AED dosage compared with unchanged dosage found to be a risk factor for SUDEP (19, 35)	No	No	No

**Figure 1** (A and B) Snapshots of sudden unexpected death in epilepsy and seizure safety checklist. The checklist is freely available in the UK. To access it, a request needs to be made by submitting an email. If the email is from a government department or university, no further information is required and the checklist is emailed to the requester. However, if a private email address is used (eg, john.smith@gmail.com), then a few details of who and why the checklist is being requested are asked for. There are two reasons for this: (A) The checklist risk factors are updated each year based on reviews of evidence and contact details ensure the update is emailed to all users. (B) The contact detail allows for audit and feedback processes on issues such as frequency of use, ease of use, barriers to implementation and so on.



**Figure 2** (A and B) Epilepsy self-monitor mobile phone app—poster and flier.

were clearly promising.<sup>26</sup> Most available devices detect movement and/or physiological changes that occur before or during a seizure such as altered blood oxygen levels, heart rate changes, electrical activity in muscles and changes in galvanic skin resistance. Whether we can call seizure-alert dogs a ‘device’ is debatable.

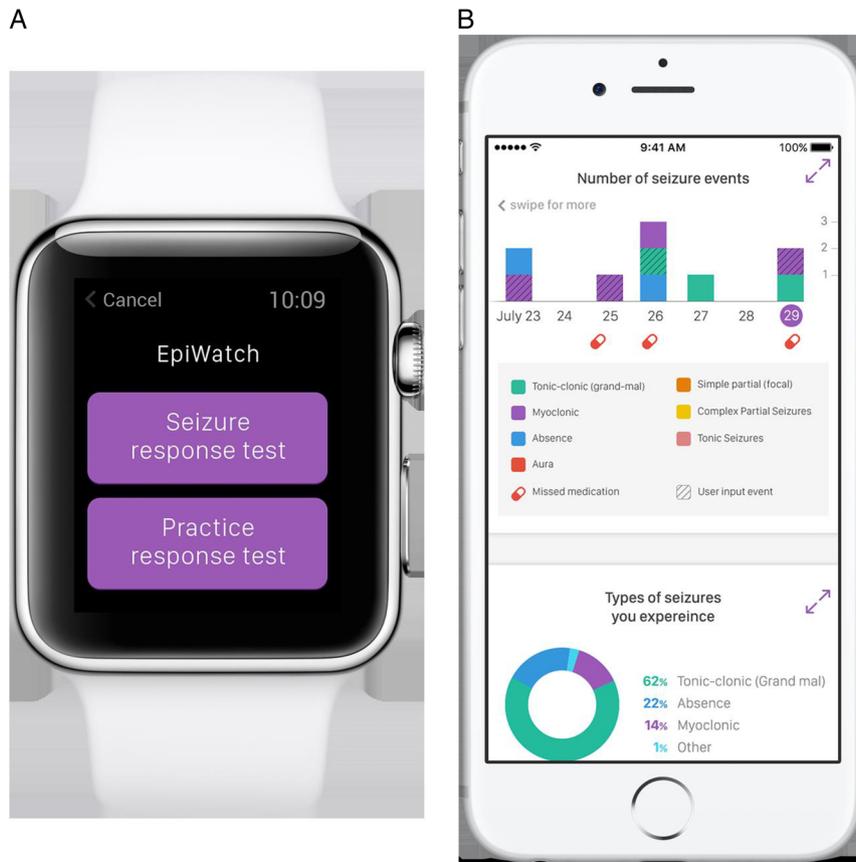
**Movement sensors**

These comprise a pressure sensor map placed under the mattress or sheets to detect an abnormal

movement and absence of movement. While weight and sleep movement adjustments can be made, seizure detection rates are variable, with the most successful devices picking up 89% of tonic-clonic seizures,<sup>27</sup> although one study failed to detect any seizures. Specificity is poor, with frequent false positives, so disrupting sleep of both carers and patients. As with all sensor devices for epilepsy, they also raise issues of individual privacy. Nonetheless, these remain the most popular among parents because of their simplicity.



**Figure 3** The Guardian newspaper review—highlighting the potential impact of technology.



**Figure 4** (A and B) Epiwatch—iWatch and iPhone link.

#### Accelerometers

These detect motion and change in velocity in two or three dimensions. Smartphones are particularly good for this. Sensitivity can be as high as 95%,<sup>28</sup> but again specificity is lower. Speed of detection in one study was a median of 17 s with all detected within 30 s.<sup>29</sup> The use of two accelerometers may improve nocturnal seizure detection.

#### Physiological changes

Seizure onset is associated with altered autonomic activity, including decreased skin resistance. When combined with an accelerometer, a galvanic device detected 94% of seizures, but with a significant false positive rate.<sup>30</sup>

Heart rate monitors in one study were 100% sensitive for tonic-clonic convulsions, and almost good for myoclonic seizures, but attempts to refine by adding breathing detectors or electromyographic analysis provided no advantage.

Apnoea devices combined with heart rate monitors are attractive in theory, but studies have not yet shown any benefits.

#### Electromyography

There are no devices for home use, but when combined with video electroencephalogram (EEG), there was 100% sensitivity within 30 s for tonic-clonic

convulsions. Thus, the assessment of a more suitable device is in progress.

#### Video and infrared devices

Video monitoring is feasible, but has not been validated by EEG support. Infrared movement monitors reliably correlate with carer-reported activity, which did not necessarily confirm seizures.<sup>31</sup> Using infrared spectroscopy to measure blood oxygen changes failed to detect seizures.

#### Seizure-alert dogs

There are numerous anecdotal reports of dogs successfully detecting seizures, but no rigorous studies.<sup>32</sup> Dogs may alert to the seizure itself but not to its onset. Dogs may also react both to non-epileptic seizures and epileptic seizures, and so are not specific. One study reported seizure reduction but our group experienced the tragedy of a patient being killed by her dog that was responding to a seizure.

#### Antisuffocation pillows

These are often purchased by families, and are advertised on epilepsy support websites, with one study on carbon dioxide retention properties showing theoretical benefits.<sup>33</sup> There is also the advantage that they are cheap and harmless.

## FUTURE DEVELOPMENTS

Refinements in safety checklists to provide semiquantified risk stratification may become more powerful in anticipating the risks of SUDEP.<sup>22</sup> The future will be in using readily available technologies with which patients are already familiar. Self-monitoring will increasingly use innovations in powerful devices such as smartphones and smartwatches. 'Embrace', a smartphone self-monitoring app based on physiological measurements (physiological stress, arousal, sleep and physical activity), is now marketed in the USA. It has a built-in accelerometer, gyroscope, electrodermal activity sensor and peripheral temperature sensor and provides a personalised insight to an individual's activity and seizures. It links to a smartphone and claims to detect convulsive seizures alerting others via a smartphone link. However, there are no available trial data to support its claims. A miniature apnoea detection device and respiratory monitor showed 100% sensitivity and specificity in detecting apnoeas, with a clinical trial now planned. 'Epiwatch', an app for the new iWatch developed by researchers at Johns Hopkins Hospital in Baltimore, Maryland, USA, offers a seizure recording and medication monitoring facility and has the potential to be linked to seizure detection devices (figure 4A, B).

## SUMMARY

People with epilepsy need a person-centred, shared-care approach, including early discussion of SUDEP. Achieving seizure freedom through a careful choice of medication and consideration of surgical interventions is all important. Only long-term studies will determine whether safety checklists, telehealth interventions and mobile technologies have an impact. We have used these approaches for several years, and have seen SUDEP in our region fall in the intellectually disabled community from 4–5/year to nil, and in the non-intellectually disabled community from 6 to 1–2/year. How much of this is from the checklist, and how much from increased awareness among clinicians, the media and people with epilepsy or from improved services in general is difficult to determine. However, these interventions do raise the profile of epilepsy mortality and may contribute to enhanced awareness. Device technology is still in its infancy, and we cannot recommend any single device particularly as none has been shown to prevent SUDEP. The ideal drug—one that suppresses all seizure activity and is free from side effects—may not be developed in our lifetime. Furthermore, clinically based interventions will not capture those individuals at high risk. Self-monitoring by people with epilepsy or carers remains important, although there will still be those whose lifestyles put them at risk. Good communication is essential, but current services are not structured with that in mind. Professionals can only do so much, leaving a service gap between the epilepsy professionals, who see a snapshot of a patient's life, and the day-to-day

experiences of people with epilepsy. Empowering people with epilepsy to take responsibility for their condition would do much to bridge that gap.

## Key points

- ▶ Sudden unexpected death in epilepsy (SUDEP) should be discussed at an early stage.
- ▶ Seizure freedom is the most important factor in preventing SUDEP; choice of medication, perseverance with medication changes and consideration of surgeries are the best ways to achieve this.
- ▶ Safety checklists, telehealth interventions and mobile technologies, such as epilepsy self-monitor, may reduce the chance of SUDEP.
- ▶ Device technologies for seizure detection have so far been disappointing.
- ▶ Patient empowerment is essential if we are to prevent SUDEP.

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**Competing interests** Epilepsy self-monitor (EpSMon) has been a joint development between SUDEP Action, Plymouth University, Cornwall Partnership NHS Foundation Trust and The Royal Cornwall Hospitals NHS Trust, to which the authors are affiliated. The SUDEP and Seizure Safety Checklist is a development of the Cornwall Partnership NHS Foundation Trust. EpSMon is provided as a free service in the UK. Any proceeds from the US version will be shared between the developing organisations in the UK and the USA.

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