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Risk Factors for Sudden Unexpected Death in Epilepsy (SUDEP) and Their Mitigation

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Abstract

Purpose of review People with epilepsy have an increased risk of mortality when compared to the general population. Sudden unexpected death in epilepsy (SUDEP) is the most common cause of epilepsy-related death in children and adults. The purpose of this review is to discuss SUDEP, with an emphasis on SUDEP risk factors, their mitigation and prevention.

Recent findings SUDEP affects approximately 1 in 1000 people with epilepsy each year. Recent studies suggest that the incidence in children is similar to that of adults. The most important risk factor for SUDEP is the presence and frequency of generalized tonic-clonic seizures. The presence of nocturnal supervision may decrease risk along with the use of nocturnal listening devices. Underlying genetic influences, both cardiac and epilepsy-related may further alter risk. Risk mitigation strategies include reducing seizure frequency, optimizing therapy, and the use of nocturnal supervision/seizure detection devices.

Summary Risk factors for SUDEP are well established; however, pediatric specific risk factors have not been identified. Current prevention strategies are focused on reduction of risk factors and the possible role of seizure detection devices. More research is needed to better understand the varied underlying pathological mechanisms and develop targeted prevention strategies. Further understanding the genetic factors that influence SUDEP risk may potentially aid in understanding the underlying pathophysiology of SUDEP.

Introduction

Epilepsy is a common neurological disorder, often with onset in childhood. Epilepsy affects 0.5–1% of all children and adults and the incidence of epilepsy peaks in the first year of life [1, 2]. In the pediatric population, the incidence of epilepsy ranges from 41 to 187/ 100,000 and declines over the first decade and approaches that of adults [1, 2]. A second peak occurs in the elderly population [1]. Although the majority of adults and children with epilepsy achieve seizure freedom when treated with anti-epileptic medication (AED), approximately 30% develop medically refractory seizures, defined as failure to achieve sustained seizure freedom with adequate trials of two tolerated, appropriately chosen, and used antiepileptic drugs [3]. The effects of living with epilepsy are profound, even more so when the epilepsy is deemed to be medically refractory and include social, cognitive, neurologic, and psychological comorbidities as well as an increased risk of mortality.

Mortality in epilepsy

When compared to the general population, individuals with epilepsy have a two to three times increased risk of premature death [4, 5]. The risk of sudden death is 24 times more likely in individuals with epilepsy than without [6]. Further, the risk of mortality in children with epilepsy is increased compared to that of adults, and the increased risk of mortality associated with childhood-onset epilepsy persists even into adulthood [5]. Berg et al. (2013) examined mortality in pediatric epilepsy by combining four pediatric epilepsy mortality cohort studies [7–12]. The overall death rate in children with epilepsy was reported as 228 per 100,000 person-years, which is 5–10 times greater than the age-matched death rate in the general population [7–12]. The death rate in pediatric epilepsy was observed to be markedly increased in those with complicated epilepsy (i.e., with associated neurodisability or brain lesion), 743 per 100,000 person-years, compared to those with uncomplicated epilepsy, 36 per 100,000 person-years [7–12]. The higher mortality rate in children is felt to reflect the increased mortality among children with neurodisability and epilepsy, whom often die of complications related to their underlying disease [4, 12]. Children with uncomplicated epilepsy do not have a significant risk of mortality when compared with the general pediatric population [12].

Etiology of mortality in epilepsy

Mortality in epilepsy includes both epilepsy-related and not epilepsy-related causes. In children with epilepsy, most deaths are not epilepsy-related including natural causes such as deaths secondary to complications of an underlying neurodegenerative disorder, respiratory complications, cardiovascular disease and infection, as well as non-natural causes such as suicide, trauma, or accidents [5, 12, 13•]. Epilepsy or seizure-related causes include deaths secondary to drowning, status epilepticus, aspiration secondary to seizures, seizure-related accidents, and sudden unexpected death in epilepsy (SUDEP) [13•]. In the pooled cohort study, Berg et al. (2013) observed that 70% of deaths in children with epilepsy were due to non-epilepsy-related natural causes and 19% were epilepsy-related, 77% of which were SUDEP. Sillanpaa et al. (2010) followed a Finnish cohort of 245 children with epilepsy over 40 years into adulthood, reported on deaths that occurred during childhood and adulthood and found

that epilepsy-related causes were more common, 55% versus 43%, than non-epilepsy-related causes [5]. SUDEP was the most common cause of epilepsy-related death (55%). Individuals who were not in 5-year terminal remission at the time of last follow-up and those with symptomatic etiologies had increased risk of mortality. In both studies, pneumonia was the most common non-epilepsy-related cause of death [5, 12]. After pneumonia, cardiac-related causes of death were also commonly observed in the Finnish cohort, accounting for 31% of all non-epilepsy-related deaths [5].

Sudden unexpected death in epilepsy

SUDEP refers to the sudden unexpected death of a person living with epilepsy. The death may be witnessed or unwitnessed, with or without evidence of a preceding seizure and the death is not secondary to trauma, drowning, or documented status epilepticus. Autopsy does not reveal an anatomical or toxicological cause of death (refer to Table 1) [14]. The term definite SUDEP is used when the aforementioned criteria are met. The term definite SUDEP plus is used when the death satisfies the criteria for definite SUDEP, but there is a concomitant condition (i.e. long QT syndrome), which may have also contributed to death. Cases, which fulfill all criteria, but lack an autopsy, are referred to as probable SUDEP. The term possible SUDEP is used when a competing cause of death is present. While the term near SUDEP is reserved for when a patient survives resuscitation for more than 1 h and near SUDEP plus, when a concomitant condition is also present [14].

SUDEP is the most common epilepsy-related cause of death in children and adults [5, 12, 13•, 15, 16••, 17, 18•, 19••]. When compared to other neurological conditions, SUDEP is second to stroke in the number of potential years of life lost [15, 19••].

SUDEP incidence

Determining the incidence of SUDEP has been hampered by poor awareness of this category of death, difficulties with case identification and subsequent under-estimates [15, 19••, 20, 21••, 22•]. Decreased recognition of SUDEP by coroners and pathologists and differences in terminology or SUDEP criteria may also affect case identification [20, 21••]. Obtaining incomplete death records and differences among study methodology may also affect the accuracy of estimating the true incidence of SUDEP [15, 19••, 20, 21••, 22•]. Moreover, in some cases, the role of epilepsy may be under recognized in determining the

Table 1. Definition of SUDEP

SUDEP Nashef Definition[14]:
• Refers to the sudden unexpected death of a person living with epilepsy
• Death may be witnessed or unwitnessed
• With or without evidence of a preceding seizure
• Death is not secondary to documented status epilepticus, drowning, or trauma
• Autopsy does not reveal an anatomical or toxicological cause of death

cause of death and more weight may be given to other findings on autopsy [23••]. Given the aforementioned challenges in SUDEP identification, a position paper was recently published on the recommendations for investigating death in individuals with epilepsy [24••].

In 2017, the American Academy of Neurology (AAN) and American Epilepsy Society (AES) published a clinical practice parameter guideline on SUDEP which included information related to the incidence of SUDEP and its risk factors [25••]. The incidence of SUDEP was reported as 1.2 per 1000 person-years in adults and 0.22 in children per 1000 person-years [25••]. The guideline concluded that occurrence of SUDEP was uncommon in adults and rare in children [25••].

Although the AAN/AES guideline concluded that the risk of SUDEP was lower in the pediatric population, two recent studies have challenged this finding. Keller et al. (2018) reported the overall incidence of pediatric SUDEP as 1.17 per 1000 person-years in the province of Ontario, Canada and concluded that pediatric SUDEP may be more common than previously reported [26••]. Similarly, Sveinsson et al. (2017), using linked records from the Swedish National Patient Registry and National Cause of Death Registry, reported the incidence of SUDEP to be similar across all age groups: 1.1 per 1000 person-years in children < 16 years and in adults 1.13 (age 16–50 years) and 1.29 (age > 50 years), respectively [21••]. The incidence in children and adults over 50 years was higher than previously reported [21••]. In both studies, a more comprehensive study design that used multiple data sources was employed to screen for cases of SUDEP. As a result, it is plausible that this led to more complete case identification and a more accurate estimate of SUDEP incidence.

Risk factors for SUDEP

The identification of risk factors is imperative to help identify individuals at risk, potentially help understand the underlying pathophysiology of SUDEP, and to help identify how risk can be mitigated and SUDEP prevented. A number of studies have been published with the aim of understanding SUDEP risk factors. However, these studies have varied with regard to the populations studied, methodology, and study design as well as the results and identified risk factors for SUDEP [27]. The majority of studies to date have focused on SUDEP risk in adults and therefore pediatric specific risk factors for SUDEP are not as well understood.

In 2011, the International League Against Epilepsy (ILAE) published a combined analysis of four case control studies to identify SUDEP risk factors [27–31]. The study included 289 cases of SUDEP and 958 controls. The factors associated with a statistically significant risk of SUDEP were increased frequency of generalized tonic-clonic seizures, duration of epilepsy > 15 years, young age at onset, symptomatic epilepsy, and male gender [27–31]. When stratified by age of onset of epilepsy (age younger < 16 years and age > 16 years), the same risk factors persisted. In the initial analysis and publication, polytherapy and GTCs were believed to result in a steady increase in SUDEP risk [27]. However, a follow-up study, which aimed to examine whether increased risk of SUDEP was associated with AED polytherapy, GTC frequency, or both, or with a specific AED refuted this finding [32]. It was concluded that GTC frequency remained

an important risk factor for SUDEP; however, when adjusting for the number of GTCs, there was no increased risk associated with single drug treatment, polytherapy, or any specific AED studied [32].

In the 2017 AAN/AES guideline, the risk factor analysis included a systematic review in which six class I and 16 class II articles were included [25••]. The presence and frequency of GTCs were cited as the most important risk factors for SUDEP, similar to the ILAE analysis. Other factors associated with heightened SUDEP risk were not being seizure free for 1–5 years (OR 4.7) and not adding an AED when patients are medically refractory (OR 6); the presence of nocturnal supervision was found to reduce SUDEP risk (OR 0.4), as did the use of a nocturnal listening device (OR 0.1); refer to Table 2. Although the combined ILAE analysis referenced early onset of epilepsy, specific AED use, polytherapy, duration of epilepsy, and symptomatic etiology as risk factors for SUDEP, the AAN/AES concluded that the evidence was low (i.e., male gender, specific AED) or very low/conflicting to make any recommendations regarding these factors specifically (i.e., etiology, polytherapy, age of onset, duration of epilepsy) [25••].

The presence, and most importantly the frequency of GTCs are the most significant risk factor for SUDEP [25••]. Failure to achieve seizure freedom, particularly from GTCs, is associated with increased SUDEP risk. The presence of GTCs alone is associated with increased SUDEP risk (OR 10) and the risk of SUDEP is observed to increase with the number of GTCs per year: 1–2 GTCs per year (OR 5.07), 3 or more GTCs per year (OR 15.46) [25••, 27–31].

Table 2. Risk factors for SUDEP and their mitigation

Established risk factors for SUDEP[25]:

- The presence of generalized tonic-clonic seizures (OR: 10)
- The frequency of generalized tonic-clonic seizures; 3 or more generalized tonic-clonic seizures per year (OR: 15.46)
- Failure to add an additional anti-epileptic medication when patients are refractory (OR: 6)
- Not being seizure free for 1–5 years (OR: 4.7)

SUDEP risk reduction[25]:

- The use of nocturnal listening devices (OR 0.1)
- The presence of nocturnal supervision (OR 0.4)

SUDEP mitigation strategies:

- Inform/educate patients and their families about SUDEP and its risk factors
- Reduce the frequency of generalized tonic-clonic seizures
- Avoid seizure triggers (i.e., sleep deprivation, missed medication, alcohol)
- Attend regular appointments with a health care professional
- Optimize medication compliance
- Add an additional anti-epileptic medication when patients are refractory
- Consider additional treatment strategies when patients are refractory (i.e., epilepsy surgery, dietary therapy, vagal nerve stimulation)
- Consider the use of nocturnal listening devices and nocturnal supervision
- Provide appropriate intervention (i.e., stimulation, change position, resuscitation) promptly when needed following a seizure

Reprinted from: Harden C, Tomson T, Gloss D, Buchhalter J, Cross JH, Donner E, et al. 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. Neurology 2017 Apr 25; 88(17):1674–1680, with permission from Wolters Kluwer Health, Inc. [25••]

When individual AEDs were examined in the combined ILAE study, lamotrigine therapy was found to be associated with increased risk of SUDEP in individuals with idiopathic generalized epilepsy, however after adjusting for GTC frequency, no increased SUDEP risk was associated with any AED as monotherapy or polytherapy. The incidence of SUDEP was also observed to be significantly higher in a cohort of woman with epilepsy from Norway who were treated with lamotrigine therapy [33]. Prior studies had also suggested that carbamazepine therapy, or high therapeutic drug levels (carbamazepine level > 40 μmol/L) in patients receiving polytherapy or with frequent dose changes were associated with increased risk of SUDEP [34, 35]. In contrast, others have found no risk associated with specific AEDs and SUDEP [28, 36].

The finding that specific AEDs are associated with heightened SUDEP risk has been challenged from the results of recent studies, including the follow-up ILAE study as discussed [32, 37, 38]. Tomson et al. (2012) examined the risk of SUDEP with lamotrigine therapy compared to placebo and comparators and found no difference in the rate of SUDEP between lamotrigine and comparator groups [38]. Both the AAN/AES concluded that the evidence was low or low/conflicting for specific AED use and polytherapy, respectively, for SUDEP risk [25••]. Failure to control for confounding factors like seizure frequency, duration of epilepsy and polytherapy have been sighted criticisms of studies that have looked at the association between specific AED therapy and SUDEP risk [37, 38].

Furthermore, there is evidence that optimization of AED therapy may reduce SUDEP risk. In individuals with refractory epilepsy, the risk of SUDEP is increased when an AED is not added to the treatment regimen [25••]. Ryvlin et al. (2011) conducted a meta-analysis of randomized placebo-controlled trials in individuals with refractory epilepsy, to determine the occurrence of definite/probable SUDEP in patients given efficacious AED doses compared to those given placebo [39]. The study targeted randomized trials investigating AED add-on therapy in individuals with treatment resistant epilepsy. There were 33 deaths, from a total of 112 eligible randomized trials and 18 of these deaths were secondary to SUDEP [39]. The rate of definite or probable SUDEP was decreased in those who received efficacious add-on AED doses, 0.9 per 1000 person-years, compared to 6.9 per 1000 person-years in those allocated to placebo [39]. Taken together, these findings further emphasize the importance of treatment optimization in reducing the risk of SUDEP.

In most cases, SUDEP deaths are unwitnessed and occur at nighttime from sleep [13•, 16••, 27, 31, 40–42]. Thus, it is not unexpected that the presence of nocturnal seizures may be associated with increased SUDEP risk as well that a lack of nocturnal supervision may accentuate risk [25••, 40–42]. Nocturnal seizures alone have been reported to be an independent risk factor for SUDEP [41]. The presence of nocturnal supervision, defined by the presence in the bedroom of an individual of normal intelligence and at least 10 years old, has been found to be protective (OR 0.4), in addition to the use of nocturnal listening devices (OR 0.1) [25••, 31]. In the MORTEMUS study, all 16 SUDEP deaths that occurred in an epilepsy-monitoring unit (EMU) were preceded by a GTC. In 11 of the 16 cases that had EEG monitoring at the time of death, GTCs were followed by increased respiratory rate, and subsequently apnea, bradycardia, and eventual cardiac arrest with concomitant generalized EEG suppression. When cardiopulmonary resuscitation (CPR) was initiated within a short time frame of 3 min, the patients were successfully resuscitated [42]. The

aforementioned suggests that the presence of an individual in the room may be able to detect the seizure and provide sufficient respiratory stimulation/intervention prior to cardiac arrest [25••].

Certain genetic and epilepsy syndromes are also associated with increased risk of SUDEP. Individuals with Dravet syndrome (DS), an infantile onset epileptic encephalopathy most often secondary to mutations in the SCN1A gene, are at increased risk of SUDEP and premature mortality [13•, 43•, 44•, 45]. SUDEP is responsible for nearly 50% of deaths in DS [44•]. Individuals with mutations in SCN8A, a severe epileptic encephalopathy of infantile onset, may also be at increased risk of SUDEP [46], although a recent review of all-cause mortality in SCN8A has suggested otherwise [47•]. Three cases of SUDEP in boys with Benign Childhood Epilepsy with Centrotemporal Spikes—all with nocturnal seizures, GTC, and not on an AED at the time of death—highlight the spectrum of children who die from SUDEP [48•]. SUDEP risk is also heightened in individuals with isodicentric chromosome 15 syndrome and those with severe neurological dysfunction are most at risk [49•]. Several other genes have been found to be associated with SUDEP including epilepsy-related genes such as, but not limited to, SCN2A and DEPDC5 and long QT syndrome genes such as KCNQ1, KCNH2, and SCN5A [50••].

While certain pediatric-onset epilepsy/genetic syndromes are associated with increased SUDEP risk, other pediatric specific SUDEP risk factors that exist have not been well defined. The majority of pediatric SUDEP studies to date have varied in methodology, number of SUDEP cases, and their results. In the largest pediatric SUDEP cohort published to date (27 cases), Donner et al. (2001) reported that the majority of children who died of SUDEP had GTCs (23/23 cases where seizure information was available) and 52% had a symptomatic etiology, but neither polytherapy nor AED serum levels were associated with increased SUDEP risk [51]. SUDEP was more common in boys (63%), similar to Sveinsson et al. (2017) who reported all SUDEP cases under the age of 16 occurred in boys [21••, 51]. Although an interesting finding, it remains unknown how sex may modify SUDEP risk.

Several other SUDEP case series have included children. Weber et al. (2005) reported four cases of pediatric SUDEP, all had GTCs, refractory epilepsy, required polytherapy, had a cryptogenic etiology, and were developmentally delayed [52]. Gronberg et al. (2014) identified six cases of pediatric SUDEP, all had GTCs, intellectual disability, and a cryptogenic/symptomatic etiology and all but one had uncontrolled epilepsy requiring polytherapy [53]. Similarly, in a cohort of children and young adults with epilepsy in a residential school, all those who died of SUDEP had GTCs and all deaths occurred when students were not under close nocturnal supervision of the school setting [54]. GTCs and secondary GTCs were the most common seizure type found in Vlooswijks' cohort of seven children (2007), although when compared to controls, this factor was not statistically significant [55]. In comparison to the controls, those who died of SUDEP were younger and had earlier age of epilepsy onset [55]. McGregor et al. (2006) reported 10 cases of SUDEP in children, all had GTC, most had developmental delay/borderline intellectual disability, and most died in sleep. There was no relationship found between certain AEDs and SUDEP [56]. Ackers (2011) reported nine cases of SUDEP in children, four had no underlying neurological condition, and three were on monotherapy, highlighting the spectrum of children lost to SUDEP [57], while Terra et al. (2009) reported that chronic uncontrolled epilepsy was associated SUDEP in 12 children [58].

Although the findings regarding pediatric SUDEP risk are heterogeneous, it appears that the presence of GTCs is associated with SUDEP in children [51–56]. Most SUDEP deaths in children are unwitnessed and occurred in sleep [51–56]. Some studies suggested a relationship between polytherapy and SUDEP [52, 53], but not all, and specific AED use did not appear to be associated with SUDEP risk [51, 55, 56]. Further, the reports of SUDEP deaths in children with Benign Childhood Epilepsy with Centrotemporal Spikes who were not treated with an AED and the observation in some pediatric SUDEP cohorts that uncontrolled seizures/refractory epilepsy increase risk highlight the need for careful treatment to reduce seizure frequency in pediatric epilepsy [48•, 52, 53]. The role of epilepsy etiology in determining pediatric SUDEP risk is imprecise with some cohorts reporting more symptomatic/cryptogenic etiologies and/or developmental delay [51–53, 56]. Ultimately, further investigation is needed to better understand the factors that place children with epilepsy at risk of sudden death.

Mitigation of SUDEP risk

Understanding the risk factors associated with SUDEP is imperative to help identify individuals at risk and to determine how risk can be mitigated and SUDEP prevented (refer to Table 2). As discussed, the most important risk factor for SUDEP is the presence and frequency of GTCs. Therefore, gaining adequate control of GTCs is crucial [25••]. Counseling individuals with epilepsy about SUDEP, the importance of avoiding seizure triggers and medication compliance is important. The AAN/AES guideline recommends that clinicians caring for children and adults with epilepsy should inform their patients of the risk of SUDEP. Furthermore, patients with epilepsy clearly want to be informed of the risk of SUDEP [25••, 59•, 60–62]. In individuals with refractory epilepsy, the risk of SUDEP is increased when an AED is not added to the treatment regimen, thus optimizing AED therapy should be a treatment goal. When medications are not adequate to control seizures, other epilepsy treatments should be considered, as epilepsy surgery, vagal nerve stimulation (VNS), responsive neurostimulation (RNS), and the ketogenic diet.

Epilepsy surgery has been associated with lower mortality rates in surgically treated patients when compared to non-surgically treated patients [63••]. Mortality after epilepsy surgery is related to seizure control, and those that remain uncontrolled have higher rates of mortality than those who achieve seizure control [63••, 64]. The persistence of GTCs after epilepsy surgery has also been associated with increased mortality, and thus, every effort should be made to decrease GTCs [63••]. In addition to epilepsy surgery, the risk of SUDEP has also been shown to decrease over time with VNS therapy [65••, 66]. Ryvlin et al. (2017) demonstrated that in individuals with medically refractory epilepsy, VNS therapy was associated with a decrease risk of SUDEP over time [65••]. Other studies, however, have not shown lower SUDEP rates in individuals receiving VNS therapy, although a trend toward a lower mortality rate has been seen [67]. Similar to epilepsy surgery and VNS, RNS has also been shown to reduce seizure frequency and may in turn reduce SUDEP risk [68••].

Nocturnal seizures alone have been reported to be an independent risk factor for SUDEP, and the presence of nocturnal supervision and use of

nocturnal listening devices may be protective [25••, 40–42, 54, 69••]. In accordance with the AAN/AES guideline, for individuals with frequent GTCs and nocturnal seizures, clinicians may advise on an individualized basis to use nocturnal supervision/listening devices [25••]. Nocturnal listening devices/supervision can help to alert caregivers of a seizure so that interventions such as the administration of a rescue medication, tactile stimulation, or cardiorespiratory resuscitation can be performed [70]. An alerted caregiver may also turn the patient from prone to the recovery position—which may help prevent further respiratory compromise [70, 71]. Enhanced supervision within the EMU is also required and includes measures such as constant supervision by a health care provider and/or the use of oxygen saturation or electrocardiogram monitoring to mitigate SUDEP risk [42, 70]. Early nursing intervention in the EMU following generalized seizures has been shown to be associated with decreased duration of respiratory dysfunction and post-ictal generalized EEG suppression [72]. Therefore, education of EMU health care providers regarding SUDEP risk and the need for prompt intervention in the face of cardiovascular compromise is crucial [70].

People who die of SUDEP are often found in the prone position and an association between prone positioning and SUDEP has been suggested [16••, 42, 56, 73, 74]. In the MORTEMUS study, 14 out of 16 patients in the EMU were found in the prone position at the time of cardiac arrest. Sveinsson et al. (2018) documented prone positioning in 70% of SUDEP cases and similarly Kloster et al. (1999) observed it in 71% of cases [16••, 73]. A recent systematic review of 253 cases of SUDEP found a significant difference between positioning in SUDEP deaths, 73.3% died in the prone position, versus 26.7% in the non-prone position [74]. Although prone positioning has been observed to be more common in some SUDEP cohorts, its contribution to SUDEP risk remains unclear; specifically, the role of the initial sleep position and the role of the prone position after a GTC [25••]. Further, it remains undetermined whether counseling individuals with epilepsy to sleep on their back would mitigate risk—as natural turning occurs throughout the night or may occur secondary to seizure activity [75].

Finally, with advances in technology, a growing number of devices have been developed to help detect seizures. Devices can be divided into two categories, EEG-based systems (i.e. video EEG, ambulatory EEG, neurostimulation devices-RNS, VNS) and non-EEG systems [76•]. Non-EEG devices employ several different technologies including accelerometry (ACM) (which measures change in velocity direction during seizures), electrodermal activity (EDA) or skin resistance/conductance, mattress devices (which detect motion), near-infrared spectroscopy (measures cerebral oxygen saturation), electrocardiogram, electromyogram, and video monitoring [76•]. Multimodal detection systems, such as those combining movement and heart rate detectors, are believed to be superior for seizure detection [76•, 77•]. Although several devices exist, their sensitivity for seizure detection is highly variable, ranging from as low as 2% (bed sensor alarm) to as high as 100% (accelerometry), in addition to their ability to detect different seizure types [76•, 77•]. The specificity of devices is also highly variable and false alarm rates (FAR) per hour also vary depending on the device used [76•, 77•, 78•]. A higher number of FAR can be disruptive/distressing to individuals with epilepsy and their caregivers and limit their utility [76•, 77•, 78•].

Early seizure detection via use of the aforementioned devices could provide caregivers with the opportunity to intervene and provide appropriate intervention (i.e., stimulation, change in positioning, resuscitation) when needed. However, whether the use of such devices can actually prevent SUDEP remains to be proven, as highlighted in a recent case study [79••]. Devinsky et al. (2017) documented a case of probable SUDEP that was recorded via a 3-axis ACM and EDA device (Empatica smartwatch) [79••]. Although the device successfully detected the seizure, resuscitation was delayed—performed 15 min after seizure onset, highlighting the need for prompt intervention to minimize the risk of SUDEP occurrence [78•]. Ultimately, more investigation regarding the use of seizure detection devices is needed, including their effectiveness and possible role in SUDEP prevention.

Conclusion

Among epilepsy-related deaths, SUDEP remains the most common cause of mortality in both children and adults living with epilepsy. Although risk factors for SUDEP have been well documented, pediatric specific risk factors are less well understood. More research is needed to better understand the factors that place children with epilepsy at risk of SUDEP. It is clear that in both populations that the presence and frequency of GTCs is the most important risk factor for SUDEP. The presence of nocturnal supervision and the use of nocturnal listening devices may be associated with decreased risk. How SUDEP risk can be mitigated and deaths prevented remains an important focus of ongoing inquiry. Reducing the frequency of GTCs and providing education around seizure triggers and medication compliance is crucial. Considering alternative therapies when seizures are refractory may help mitigate SUDEP risk. Understanding genetic factors that influence SUDEP risk is also important and may help elucidate the pathophysiological mechanisms involved in SUDEP. Finally, although an increasing number of seizure detection devices are reported, more exploration is needed to understand and compare their efficacy and clarify their role in SUDEP risk mitigation and prevention.

Compliance with Ethical Standards

Conflict of Interest
Elizabeth J. Donner reports personal fees from Eisai, personal fees from UCB, outside the submitted work. Robyn Whitney declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

Publisher's Note

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Papers of particular interest, published recently, have been highlighted as:

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- •• Of major importance

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