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Dramatic outcomes in epilepsy: depression, suicide, injuries, and mortality

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ABSTRACT

In this narrative review, we will discuss some of the significant risks and dramatic consequences that are associated with epilepsy: depression, suicide, seizure-related injuries, and mortality, both in adults and in children. Considering the high prevalence of depression among people with epilepsy (PWE), routine and periodic screening of all PWE for early detection and appropriate management of depression is recommended. PWE should be screened for suicidal ideation regularly and when needed, patients should be referred for a psychiatric evaluation and treatment. When starting an antiepileptic drug (AED) or switching from one to another AED, patients should be advised to report to their treating physician any change in their mood and existence of suicidal ideation. The risk of injuries for the general epilepsy population is increased only moderately. The risk is higher in selected populations attending epilepsy clinics and referral centers. This being said, there are PWE that may suffer frequent, severe, and sometimes even life-threatening seizure-related injuries. The most obvious way to reduce risk is to strive for improved seizure control. Finally, PWE have a 2–3 times higher mortality rate than the general population. Deaths in PWE may relate to the underlying cause of epilepsy, to seizures (including sudden unexpected death in epilepsy [SUDEP] and seizure related injuries) and to status epilepticus, as well as to other conditions that do not appear directly related to epilepsy. Improving seizure control and patient education may be the most important measures to reduce epilepsy related mortality in general and SUDEP in particular.

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1. Introduction

Epilepsy is a chronic neurological condition that affects people of all ages and has no geographic, social, or racial boundaries. It is a wide-reaching and complex illness, affecting more than 70 million people worldwide and can manifest in a variety of forms, patterns, and severities¹. Management varies by region due to the availability of diagnostic modalities and medications¹; however, antiepileptic drugs (AEDs) are the mainstay of treatment. In spite of this, AEDs fail to control seizures in about one-third of patients with epilepsy. Patients with drug-resistant epilepsy account for most of the burden of epilepsy, because of the substantial frequencies at which they experience comorbid medical and psychological conditions, and increased risk of injury and mortality, and, ultimately, a decreased life expectancy². While there is plenty of evidence that has been made available of the risks associated with epilepsy, more attention should be devoted to the severe consequences of this common condition. In this narrative review, we will discuss some of the dramatic and severe consequences that are associated with epilepsy; these

include depression, suicide, physical injuries, and mortality, both in adults and in children (Table 1). Physicians, who are taking care of patients with epilepsy, should focus not only on controlling their seizures but also on preventing these consequences.

2. Depression in people with epilepsy

Depression is prevalent in people with epilepsy (PWE). A systematic review and meta-analysis revealed a 23.1% (95% confidence interval: 20.6–28.31%)³ prevalence of active depression in PWE, which is about 4–5 times higher than that in the general population⁴ (Table 1). In a population-based study, the average lifetime and 12-month prevalence estimates of major depressive episodes were 14.6% and 5.5%, respectively in the 10 highest-income countries, and 11.1% and 5.9% in the eight countries with low- to middle-income⁴. Depression is often associated with work absenteeism, increased utilization of health care services and direct and indirect medical costs^{5,6}. In addition, depression worsens

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Table 1. Rate of depression, suicide, injuries, mortality and SUDEP in PWE compared to general population.

	Depression	Suicide	Seizure-related injuries	Mortality	SUDEP
Main features	High prevalence of depression among PWE ^{3,4}	Suicide attempts occur with increased frequency in PWE ¹⁵	Population-based studies: risk of injuries among PWE shows only a moderate increase ^{21,25}	Highest mortality rate found in PWE with epileptic encephalopathies ³⁹ intellectual disability or cerebral palsy ⁴¹	Children are equally at risk to adults for SUDEP ⁸⁴
People with epilepsy vs Controls (general population)	Prevalence of active depression is 23.1% in PWE, 4–5 times more than the general population ^{3,4}	Completed suicide among PWE is (0.5%), and among general population (0.01%) ¹⁵	1. Prevalence of severe injuries in PWE is 14.9% vs (13.3%) in the general population ²⁴ 2. Incidence of injuries in PWE is 20.6% vs 16.1% in the general population ²⁵	PWE have a 2–3 times higher mortality rate than the general population ³⁶	SUDEP most common cause of epilepsy-related death, 27-fold higher rate than in controls ⁵⁰

Abbreviations. PWE, patients with epilepsy; SUDEP, Sudden unexpected death in epilepsy.

the quality of life, is associated with subjective cognitive impairment, and may even lead to seizure aggravation (e.g. due to poor drug adherence in the affected patients)^{7–9}. Interestingly, the apparent cultural, demographic, religious, and ethnic diversity in the world has not affected this comorbidity significantly¹⁰. However, depression is often under-recognized and improperly treated in PWE¹⁰. Considering the high prevalence of depression among PWE, particularly in women, routine and periodic screening of all PWE for early detection and appropriate management of depression is recommended¹⁰.

On the other hand, people with a history of depression have a four- to seven-fold higher risk of developing epilepsy¹¹. A bidirectional relationship between depression and epilepsy has been suggested by several population-based studies and is also supported by many experimental studies¹². For instance, a marked reduction in central levels of neurosteroids has been described in patients who develop status epilepticus¹³, and among them allopregnanolone has an established role in depression¹⁴. Structural, neuropathological, and neurotransmitter disturbances associated with one condition may potentially facilitate the manifestations of the other^{11,12}. Consequently, appropriate treatment of one condition may improve the other condition¹². Selective serotonin reuptake inhibitors (SSRIs) are considered safe for the treatment of depression in PWE¹².

3. Suicide in people with epilepsy

Suicide attempts are found to occur with increased frequency in PWE (Odds ratio = 3)¹⁵. In a meta-analysis¹⁵, the pooled prevalence for suicide ideation was 23.2% (95% CI: 0.176–0.301) and for suicide attempts was 7.4% (95% CI: 0.031–0.169). The pooled rate of death due to suicide was 0.5% (95% CI: 0.002–0.016). The relationship between epilepsy and suicidality is complex. Psychiatric risk factors, epilepsy-related variables (e.g. type of epilepsy syndrome) and exposure to certain AEDs have been associated with an increased risk of suicide in PWE¹¹. The complex relationship between epilepsy and suicidality is also evident by the existence of a bidirectional relationship between these two conditions. Not only do PWE have a higher risk of suicide, but also

people with a history of suicidal ideation or behavior have a five-fold higher risk of developing epilepsy than controls¹¹. In one large population-based study¹⁶, suicide attempts and recurrent suicide attempts were associated with epilepsy even before epilepsy manifests, suggesting a common underlying neurobiological mechanism. In that study, both incident and recurrent suicide attempts were associated with incident epilepsy in the absence of AEDs and in the absence of diagnosed psychiatric disorders, further strengthening the evidence for a common underlying etiology¹⁶. In 2008, the U.S. Food and Drug Administration (FDA) issued an alert about an increased risk of suicide ideation and behavior in patients treated with AEDs¹⁷. Although some AEDs have been associated with treatment-emergent psychiatric disorders, that may lead to suicidal ideation and behavior, the actual suicidal risk seems to be very low¹⁷. Suicidality in epilepsy is multifactorial, and different variables are operant in its development. All PWE should be screened for suicidal ideation regularly and if necessary, patients should be referred for a psychiatric evaluation and treatment. Screening for suicidality and suicidal behavior in PWE is feasible using the Interactive Voice Response System CSSRS (E-CSSRS) or the Columbia Suicide Severity Rating Scale (C-SSRS) instruments¹⁸. When starting an AED or switching from one to other AED, patients should be advised to report to their treating physician any change in their mood and existence of suicidal ideation¹⁷. In addition, family members should be involved in the discussion since they might be the ones who first notice the changes.

It is noteworthy to mention that, generally, more than two-thirds of patients suffering from stress-related disorders are women, but over two-thirds of suicide completers are men. The molecular origins of this sex dimorphism are still quite obscure. However, several studies have identified many stress-related genes that are regulated by stress in a sex-specific fashion. In addition, it seems that pathways and networks in male and female individuals are not equally affected by stress exposure¹⁹. Understanding which mechanisms are more affected in men, and which in women, may lead to the identification of sex-specific approaches and treatment strategies.

4. Injuries in people with epilepsy

Intuitively, the risk of injuries appears evident in conjunction with seizures with major convulsions, falls, and loss of consciousness. Not surprisingly, such risks are also a major concern for people with epilepsy, their carers, family members and guardians, who request adequate information from health care providers concerning risks of injuries as part of routine counselling²⁰. In addition to the seizures causing injuries, people with epilepsy may suffer injuries due to their comorbidities (e.g. cerebral palsy, stroke or other disabilities), their medication (causing disturbances in balance or making patients more vulnerable to falls due to osteoporosis), or for the same reasons as people without epilepsy.

4.1. Incidence and prevalence of injuries

4.1.1. Population-based studies

Contrary to what might be expected, population-based studies have in general found that the risk of injuries among PWE is increased only moderately. A study of 247 patients with newly diagnosed epilepsy from Rochester, MN, found seizure-related injuries sufficiently serious for the patient to seek medical attention in 39 patients (16%) on 62 occasions, i.e. one injury per 44 person-years over a 10-year follow-up²¹. In a retrospective community-based study of 819 patients with epilepsy from Tasmania, 10% reported experiencing an injury in the preceding year²². In the population-based childhood onset epilepsy cohort in Nova Scotia, 52 of 472 patients (11%) reported having experienced at least one serious injury during an average follow up of 24 years²³. Among studies providing comparisons with people without epilepsy, a Canadian study based on a community health survey reported a prevalence of injuries severe enough to limit normal activities to be 14.9% among PWE compared with 13.3% in the general population over a 12-month period²⁴. A subsequent Canadian study used administrative databases to identify PWE and injuries for which medical attention was sought²⁵. The one-year incidence of injuries was 20.6% among PWE compared with 16.1% among non-epilepsy controls²⁵. In Stockholm, Sweden, 2130 patients with newly diagnosed epilepsy and 16,992 controls from the general population were followed for on average 6.3 years in administrative registries to identify injuries leading to medical consultations²⁶. The incidence of injuries was increased in PWE with a Hazard Ratio of 1.71, but this was largely related to comorbidities among PWE, as the Hazard Ratio was reduced to 1.17 in PWE without comorbidities²⁶. A population-based German study used health insurance registers to identify people with severely drug-refractory epilepsy (prescribed at least four AEDs in an 18-month period. Compared to matched controls from the general population, injury rates were higher among those with drug-refractory epilepsy (head 16% against 3%, trunk and limbs 16% against 8%)²⁷.

4.1.2. Hospital- and clinic-based studies

A large prospective European study involved 951 epilepsy referral patients and matched controls that were followed

prospectively for two years²⁸. By 24 months, 27% of the PWE and 17% of the controls had experienced at least one injury. In the epilepsy group, 24% of the injuries were seizure-related²⁸. Several other hospital/clinic-based studies have been published from different parts of the world. A retrospective questionnaire-based study of 298 patients attending an epilepsy outpatient clinic in Israel estimated that 30% had ever experienced a seizure-related injury²⁹. This translates to one injury per 21 person-years and one serious injury per 64 person-years²⁹. A retrospective study included 264 adults with epilepsy attending an epilepsy clinic in Iran and 289 healthy controls³⁰. Over a 12-month period, 47% of the patients reported having at least one injury (relative risk compared to controls 3.4), 14% a severe injury (relative risk 1.8)³⁰. In a pediatric neurology clinic and referral center in Nigeria, 125 consecutive children with epilepsy and 125 non-epilepsy controls were asked about injuries over the preceding 12 months³¹. Among children with epilepsy 46% had sustained injuries compared to 21% among controls³¹.

4.1.3. Types of injuries

Soft tissue injuries, sprains, dislocations, and fractures are the most common types of injuries among people with epilepsy as well as in the general population^{21,24–26,30}. The head and the extremities are the most common locations of the injuries, and falls are by far the most frequent mechanisms for injuries in people with epilepsy²⁶. Although far less common, the greatest increase in risk has been reported to be with drowning accidents, the risk being 6–18 times higher in PWE^{26,32}.

4.1.4. Risk factors

The risk of injuries in PWE clearly varies between different parts of the world for many different reasons including geographical, economic, and social circumstances, availability of effective treatments, workplace conditions and individual life styles. Some general epilepsy-related risk factors have, however, been identified. The most consistent findings regarding risk factors for injuries are occurrence of generalized convulsive seizures (focal to bilateral or generalized tonic-clonic seizures)^{21,22,30,33}, but atonic seizures and ictal falls have also been associated with increased risks^{21,33,34}. Intractable epilepsy, uncontrolled seizures, or high seizure frequency are also consistent risk factors for seizure-related injuries^{21–23,31,35}. Polytherapy with AEDs was reported to be associated with increased risk in a few studies^{21,31,34} although it is not clear if polytherapy is a risk factor as such or just a reflection of a more difficult to treat epilepsy with poor seizure control. Some studies have identified comorbidities as another risk factor for injuries^{21,26,30,33}.

4.1.5. Conclusion

The risk of injuries for the general epilepsy population is increased only moderately. The risk is higher in selected populations attending epilepsy clinics and referral centers. But even among people with more severe epilepsy the majority

will not sustain significant seizure-related injuries. This being said, there are PWE that suffer frequent, severe, and sometimes even life-threatening seizure-related injuries. Some risk factors have been identified and the most obvious way to reduce risks is to strive for improved seizure control. Measures that reduce the risk of seizure-related injuries, such as work place and home adjustments, should also be considered in particular for those that continue to have seizures associated with falls.

5. Mortality in people with epilepsy

People with epilepsy have a 2–3 times higher mortality rate than the general population³⁶. The standardized mortality ratio (SMR) is the most commonly used measure to describe increased mortality risk. In an early study, the SMR was 2.3 through 29 years of follow-up³⁷. The most significant increase in SMR was noted early after diagnosis³⁸. The SMR depended on seizure type and seizure control status. Generalized tonic-clonic seizures were associated with increased mortality, but absence seizures were not³⁷. A recent review of epilepsy mortality in high-income countries reported an SMR range of 1.6–3, with a weighted median SMR of 2.3 for all ages³⁹. A similar review of mortality in low- and middle-income countries found an SMR range of 1.3–7.2 with a weighted median of 2.6⁴⁰. SMR was higher in children, likely because of low expected mortality from other causes in the general pediatric population, and SMR was lower after age 60, likely related to increased expected mortality from other causes in the older age group. SMR was consistently more elevated for individuals with convulsive seizures (as compared with non-convulsive seizures) and for those with structural-metabolic causes of epilepsy (as compared with genetic or unknown etiology). The highest mortality was found in epilepsy patients with epileptic encephalopathies³⁹, and intellectual disability or cerebral palsy⁴¹. The risk of mortality was higher among those with uncontrolled seizures versus those who were seizure-free³⁹. Patients who became seizure-free after epilepsy surgery had a lower mortality rate than non-seizure-free patients⁴².

5.1. Causes of mortality

Deaths in PWE may relate to the underlying cause of epilepsy, to seizures (including sudden unexpected death in epilepsy- SUDEP) and to status epilepticus, as well as to other conditions that do not appear directly related to epilepsy⁴³. Increased mortality was seen as a result of cerebrovascular disease, pneumonia, and neoplastic disorders, even after exclusion of primary brain tumors⁴¹. In a community-based cohort with 25 years of follow-up the most common cause of death was a comorbid condition, most commonly noncerebral neoplasm, cardiovascular disease, and cerebrovascular disease, which accounted for 59% of deaths. The epilepsy etiology was the cause of death in 23%, and epilepsy-related causes accounted for 3%⁴⁴. It is likely that seizure- and epilepsy-related mortality is underestimated, largely because the role of epilepsy is ignored or other less likely causes of death

are listed on the death certificate even though criteria for SUDEP are satisfied⁴⁵. Causes of epilepsy/seizure-related mortality include drownings, suicides, and fatal unintentional injuries⁴⁵. The risk of drowning increased with an SMR of 18.7⁴⁶, and was particularly high in people with epilepsy and learning disability (SMR = 25.7), subjects in institutional care (SMR = 96.9), and in people who had a temporal lobe excision (SMR = 41.1)⁴⁶. Risk of suicide also increased with a SMR of 4.8⁴⁷. Mortality was increased by non-adherence to epilepsy treatment, with a three-fold increased risk of mortality⁴⁸. Non-adherence to medications as well as limited access to treatment may be responsible for the higher mortality in low- and middle-income countries, at least in part⁴⁰.

5.2. Sudden unexpected death in epilepsy (SUDEP)

SUDEP is defined as “sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning death, occurring in benign circumstances, in an individual with epilepsy, with or without evidence for a seizure and excluding documented status epilepticus”⁴⁹. SUDEP is the most common cause of epilepsy-related death, with a 27-fold higher rate of sudden death than in controls⁵⁰, and an annual rate of around 12 per 10,000 PWE⁴⁵. The risk of SUDEP was 1–4 times higher in male than female patients⁵¹. Definite SUDEP requires a postmortem examination showing no definite cause of death. If a postmortem examination is not performed but the definition is otherwise fulfilled, probable SUDEP can be diagnosed⁴⁹. Possible SUDEP applies to instances where there may be competing possible causes of death.

There is strong evidence that SUDEP is seizure-related⁵². When SUDEP is witnessed it is most often associated with a bilateral convulsive seizure near the time of death^{53,54}. SUDEP was primarily sleep-related and unwitnessed⁵⁵. The vast majority of unwitnessed SUDEP was associated with tongue biting or incontinence, suggesting recent tonic-clonic seizures⁵⁶. In a case-control study, supervision at night was protective when a supervising individual shared the same bedroom or when special precautions such as listening device were employed⁵⁶. Other risk factors include longer duration of epilepsy and structural-metabolic etiology⁵⁷. The frequency of bilateral tonic-clonic seizures was the prominent risk factor for SUDEP in a study⁵⁸. After adjusting for tonic-clonic seizure frequency, analysis of individual anti-seizure medications and number of antiseizure medications revealed no associated increased risk⁵⁸. In fact, antiseizure medication levels were often sub-therapeutic in SUDEP patients⁵⁹. A strong evidence that SUDEP is seizure-related came from a meta-analysis of 112 adjunctive anti-seizure medication trials⁶⁰. Rates of definite or probable SUDEP per 1000 person-years were 0.9 in patients who received efficacious antiseizure medication doses and 6.9 in those receiving adjunctive placebo. There was a strong association of SUDEP and prone position when body position was documented⁶¹, showing the similarity between SUDEP and sudden infant death syndrome. There is increasing evidence that a centrally mediated respiratory depression is involved in SUDEP. Ictal apnea and hypoxia are common, even in focal seizures that

do not progress to bilateral tonic-clonic activity⁶². Serotonin reuptake inhibitors were reported to reduce the likelihood of oxygen desaturation during focal seizures⁶³. Apnea was elicited by electrical stimulation of the amygdala⁶⁴, and ictal apnea was correlated with seizure spread to the amygdala⁶⁵. Patients who later died from SUDEP often had postictal generalized EEG suppression, thought to reflect profound cerebral dysfunction, possibly a factor in central apnea⁶⁶. The early administration of oxygen after seizure onset seemed to prevent this postictal generalized EEG suppression⁶⁷.

Improving seizure control and patient education may be the most important measures to reduce epilepsy-related mortality in general and SUDEP in particular. A recent survey of 519 Austrian, Swiss and German neurologists and neuro-pediatricians showed that premature mortality due to SUDEP or suicidality are not discussed at all with PWE by a substantial proportion of neurologists and neuropediatricians⁶⁸. Patients at risk for SUDEP need to be informed about this potential complication⁶⁹. This is particularly true for those who are not compliant with their medications and those with drug-resistant epilepsy who are excellent candidates for epilepsy surgery⁷⁰.

6. Injuries and mortality in childhood epilepsies

Injuries that may be sustained as a result of the unpredictable occurrence of convulsive seizures remain a constant source of concern to parents and carers of children, particularly those with complex epilepsy. Despite the likelihood of a higher rate of supervision, studies suggest that injuries from seizures are a serious persistent problem in childhood epilepsy. Camfield and Camfield utilized the Nova Scotia population based cohort to ask whether children had ever experienced an accident that was sufficiently concerning to lead to an emergency room visit or a visit with a family physician or a dentist. In >90% this was for a duration >10 years following the onset of epilepsy, and included individuals with all types of epilepsy except absence epilepsy. Of 595 eligible patients, 472 answered the questions, of whom 51 reported 81 such injuries²³. Such injuries included lacerations requiring suture (30%), bone fractures (19%), broken teeth (14%), concussion (10%), burns (5%) and shoulder dislocation (4%). These could occur at any period of time after the onset of the epilepsy. There did not appear to be any particular association with the type of epilepsy but there was an increased association with the presence of intellectual disability and continuing seizures. With regard to any risk and absence epilepsy (AE) this was previously examined in a similar cohort by Wirrell et al., and risk compared to a cohort with juvenile rheumatoid arthritis (JRA)⁷¹. These individuals were questioned as adults with regard to all previous accidental injuries, including nature, severity, and treatment required; those with a history of AE were additionally asked as to whether they had ever sustained injury during an absence seizure. Patients with AE had a greater number of overall accidental injuries than those with JRA ($p < .04$), but these differences were particularly marked for bicycle ($p < .003$) and car accidents ($p < .05$) and for mild head injuries

($p = .05$). Sixteen (27%) of 59 patients with AE reported accidental injury during an absence seizure, the risk was higher in absences associated with juvenile myoclonic epilepsy than in juvenile absence or childhood absence epilepsies, the risk being particularly low in the latter. A further case control study found that individuals with uncomplicated childhood epilepsy (normal IQ and neurological examination), were no more at risk of injury than sibling controls except for head injuries, and were much less likely to experience injury than individuals with complicated epilepsy (IQ <80 or abnormal neurological examination)⁷². One question that may arise however is whether there is a risk of injury in newly diagnosed or prior to the diagnosis of epilepsy; this is specifically, important when counselling for risk after a first seizure. A prospective study of newly diagnosed and untreated patients across seven centers determined 25/198 who experienced an injury before a diagnosis was established, 4 requiring medical attention, the majority in association with tonic-clonic seizures. However, none of the patients with childhood absence epilepsy reported injury⁷³.

As highlighted above, the SMR for children is higher, likely because of low expected mortality from other causes in the general pediatric population. One study combined data from four epidemiological cohorts; three prospective (Connecticut, the Netherland and Nova Scotia) and one retrospective (Rochester)⁷⁴. This revealed overall mortality rates of 2.28 per 1000 person years, but much higher rates again for complicated (7.43) compared to uncomplicated (0.36) epilepsy, suggesting comorbidities had high relevance. In a UK surveillance study where all pediatricians in the UK and Ireland were asked monthly as to whether they had seen a case over a 12-month period, of 88 confirmed cases 73/81, where data were available, had the existence of comorbidities. 51% were the result of pneumonia, sepsis or underlying genetic or metabolic conditions⁷⁵. Accidents were not listed, but reviewing from a different angle, a study of drowning fatalities and the role of pre-existing medical conditions found epilepsy to increase the relative risk of drowning in childhood, with a prevalence of 4.1% of drowning deaths compared with 0.7–1.7% among the general population. No other identified pre-existing medical condition was associated with an increased risk of drowning⁷⁶. Anti-epileptic drug association was also not listed considering adverse reactions to medication could be considered a risk. A study reviewing the causality of death in children on AEDs determined that the majority who died had underlying disorders as in other studies⁷⁷. Of 151 deaths (in 6190 subjects), 18 were epilepsy related and 5 likely (2 definite and 3 possible) related to AEDs. In addition, two status epilepticus deaths were an epilepsy-related death, data suggest that in the acute phase, death if it occurs is related to the underlying cause (e.g. bacterial meningitis)^{78,79} and in the longer term predominantly seen in those with pre-existent neurological abnormality⁸⁰.

Traditionally, there has been a belief that SUDEP is a lesser risk in childhood; the combined cohort suggested an incidence of 0.33/1000 person years⁷⁴ and the American Academy of Neurology after a systematic review of the

literature suggested an incidence of 0.22/1000 person years, quoting it affecting 1 in 4500 children per year compared to 1 in 1000 adults⁸¹. One could consider this might be the case, specifically as the risk has been suggested to be lower in supervised facilities; a study of SUDEP in a residential school revealing all deaths to occur when the pupils were not under the close supervision of the school⁸². However, two registry studies have determined incidence of definite and probable SUDEP similar to that seen in adults; the Swedish study of SUDEP in 2008 showing an incidence of 1.11/1000 person years in <16 years, and 1.13 16–50 years⁸³, and in another study of SUDEP in children <18 years the incidence was 1.1/1000 person years, rising to 1.45 after capture recapture correction⁸⁴ suggesting the risk is no different in children to adults. A recently published systematic review highlighted risk factors linked to SUDEP in children of early age at onset, high seizure frequency, intellectual impairment, multiple AED therapy and structural abnormalities on MRI scan⁸⁵. All these of course may be related to the severity or complexity of the epilepsy; certainly, the rate of SUDEP in Dravet syndrome, a specific early onset epilepsy associated with continuing seizures and intellectual impairment despite treatment has been shown to be relatively higher at 9.32/1000 person years, with overall mortality rate of 15.84/1000 person years perhaps reflecting associated comorbidities⁸⁶. Acknowledging children with a sodium channel mutation may be at increased risk for a multitude of reasons, all syndromes with continued convulsive seizures however appear to carry a risk⁸⁷. Recent evidence suggests that the appropriate involvement of tertiary specialists in pediatric care may decrease all-cause mortality. A recent study has shown where eligible patients, including those with more complex epilepsies, are seen by a pediatric neurologist there is an overall reduction in total mortality as well as mortality post transition⁸⁸.

7. Conclusion

While this review could only provide highlights and could not be comprehensive in view of its broad subject matter, we can conclude that people with epilepsy may have dramatic life experiences, such as depression, injuries, and premature mortality. Considering the high prevalence of depression among PWE, particularly in women, routine and periodic screening of all PWE for early detection and appropriate management of depression is advised. All PWE should also be screened for suicidal ideation regularly and if necessary, patients should be referred for a psychiatric evaluation and treatment. The risk of injuries for the general epilepsy population is increased only moderately. The risk is higher in selected populations attending epilepsy clinics and referral centers. This being said, there are PWE that may suffer frequent, severe, and sometimes even life-threatening seizure-related injuries. Seizure-related injuries often occur at home and therefore, simple considerations (e.g. supervised bathing, using microwave ovens instead of classical stoves, and sleeping close to the floor to avoid falling) may reduce the incidence of seizure-related injuries⁸⁹. The most obvious way to

reduce risks is to strive for improved seizure control. Finally, PWE have a higher mortality rate than the general population; children are equally at risk to adults. Improving specialist care, seizure control and patient education may be the most important measures to reduce epilepsy related mortality.

Transparency

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