Sudden Unexpected Death in Epilepsy (SUDEP)

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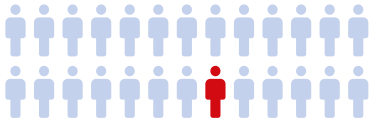
Around 50 million people worldwide live with epilepsy, making it one of the most common neurological disorders globally. The condition is associated with increased mortality risk, significant impacts on quality of life, and wide-ranging social and economic consequences for individuals, families, and healthcare systems. Despite this, public awareness of these risks remains relatively low, and there continues to be a lack of widely adopted strategies and guidelines.

50 million
people with epilepsy worldwide



1 in 26 people
will receive a diagnosis of epilepsy

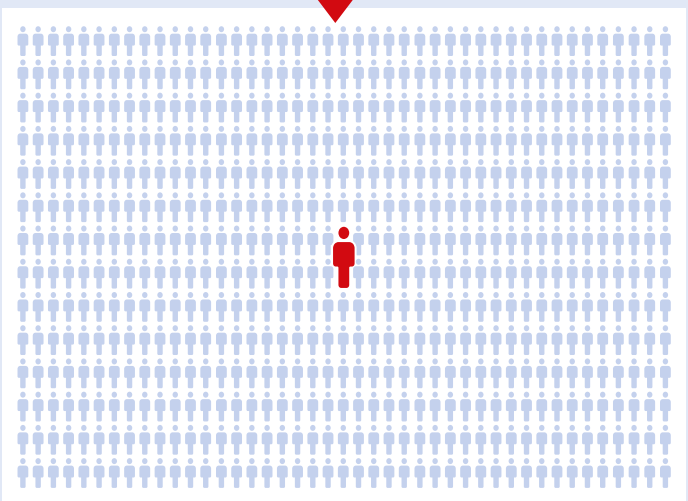
1 million
with epilepsy in the German speaking countries (DE, AT, CH)

1 in 3
people with epilepsy do not become seizure-free with anti-seizure medication

2 - 4 times
greater risk of premature death

People with epilepsy can often lead a normal life. Nevertheless, people with epilepsy, especially if they do not achieve seizure freedom through anti-seizure medications (ASM), have a significantly increased risk of premature death compared to the general population. Most studies report a mortality rate that is 2–4 times higher than in the general population. The causes include the underlying aetiology of epilepsy, immediate seizure-related complications, comorbidities, and Sudden Unexpected Death in Epilepsy (SUDEP).

1 in 1000 people with epilepsy dies from SUDEP each year



SUDEP is one of the most common causes of death related to epilepsy.
SUDEP refers to the sudden, unexpected death of a person with epilepsy that is not caused by other factors such as injury, drowning, status epilepticus, suicide or intoxication, and where no other cause of death can be identified even following an autopsy. SUDEP frequently occurs in young people, and many of those affected had no pre-existing life-threatening underlying condition. A significant proportion of these deaths are associated with identifiable risk factors, some of which can be addressed through preventive measures.

All people with epilepsy and their carers should therefore be informed, sensitively but consistently, about the risk of SUDEP and possible preventive measures.

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Epidemiology

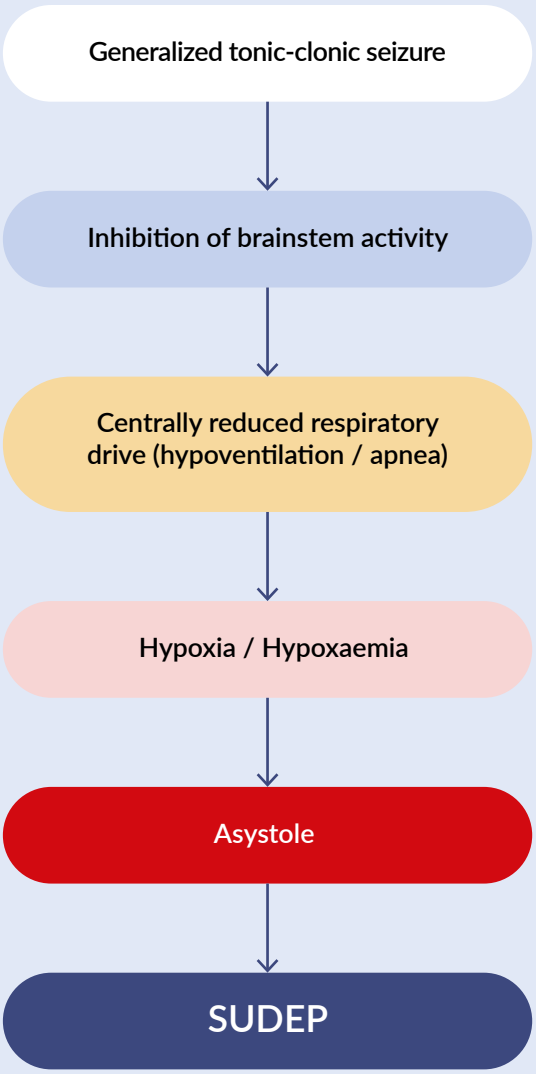
SUDEP affects around 1 in 1,000 people with epilepsy each year, making it one of the most common causes of death directly related to epilepsy. It is particularly striking that around two-thirds of SUDEP cases occur during sleep. Furthermore, a significant proportion of deaths affects young people, often under the age of 40. If epilepsy begins in childhood, the lifetime risk of SUDEP is estimated at around 7–8%.

There is a significantly increased risk among people with drug-resistant epilepsy, including children with severe, mostly genetically caused forms of epilepsy, known as Developmental and Epileptic Encephalopathies (DEE). In this particularly vulnerable group, the incidence of SUDEP is around 6.3 to 9.3 per 1,000 people affected per year, and is thus many times higher than in the general population of people with epilepsy. In Dravet syndrome, for example, around 17% of those affected die by the age of 20, with around half of these deaths attributable to SUDEP.

IMPORTANT: SUDEP does not exclusively affect people with severe or drug-resistant epilepsy.
SUDEP can also occur in forms of epilepsy previously classified as mild or 'benign', or may even be the manifestation of epilepsy itself. For example, in self-limiting epilepsy with centrotemporal spikes (SeLECTS, formerly known as Rolando's epilepsy), focal to bilateral tonic-clonic seizures frequently occur in the early hours of the morning, a circumstance which in itself is associated with an increased risk of SUDEP.

PREVENTING SUDEP:
A RISK-AWARE FAMILY IS A LIFE SAVER
STOP SUDDEN DEATH IN EPILEPSY

oskar killinger stiftung



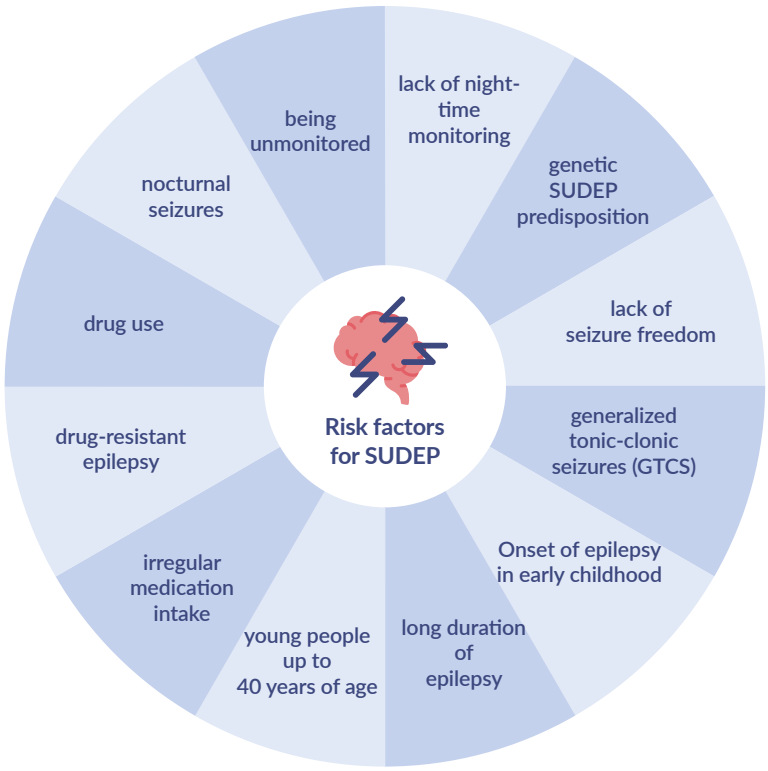
Pathogenesis

There remains a significant need for research to better understand the pathomechanisms of SUDEP, identify reliable clinical predictors and biomarkers, and develop more targeted preventive measures. Many potentially life-threatening events occur at night and go unobserved, partly because continuous night-time monitoring in the home environment, with a subsequent alarm chain, is not yet established on a widespread basis.

Various causes of SUDEP are under discussion. Based on the MORTEMUS study (Mortality in Epilepsy Monitoring Unit Study) and animal experiments, the most likely primary mechanism is considered to be suppression of brainstem function triggered by epileptic seizures, followed by hypoxia and secondary asystole during the post-ictal phase. A clear temporal link with an epileptic seizure could not be established in all SUDEP cases, suggesting that further risk factors and pathophysiological processes are involved. For example, fatal hypoventilation may occur prior to cardiac arrest, and genetic factors contributing to the dysregulation of the neurotransmitter and respiratory regulator serotonin, for instance, could play a role here.

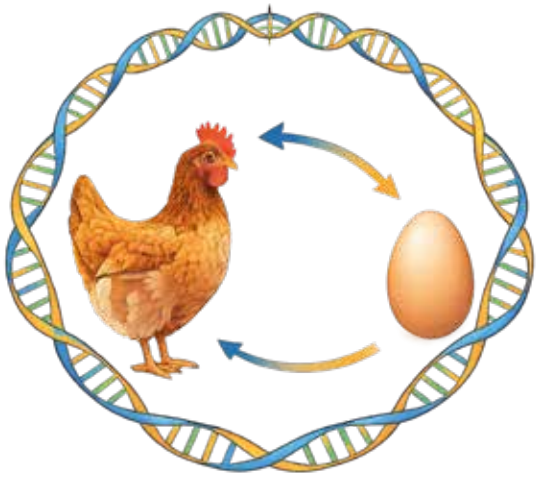
Risk factors

There are several risk factors.
The presence of focal to bilateral tonic-clonic seizures or generalised tonic-clonic seizures (GTCS) is a major risk factor for SUDEP, and the risk increases with seizure frequency.
Other risk factors include lack of seizure freedom, resistance to anti-seizure medication, poor adherence to treatment, periods of change in anti-seizure medication, the occurrence of nocturnal seizures, lack of night-time supervision (care/monitoring) or living alone, post-ictal central apnea (cessation of breathing caused by disturbances in the respiratory centre of the brain) and substance/drug misuse.



Genetic factors

Genetic factors can influence the risk of SUDEP. The precise differentiation of the causal role of a specific genetic variant, independent of the risk of associated seizures, is sometimes methodologically difficult. It is often not possible to clarify unequivocally whether genetic variants contribute directly to the development of SUDEP or act primarily via an increased seizure frequency or severity.

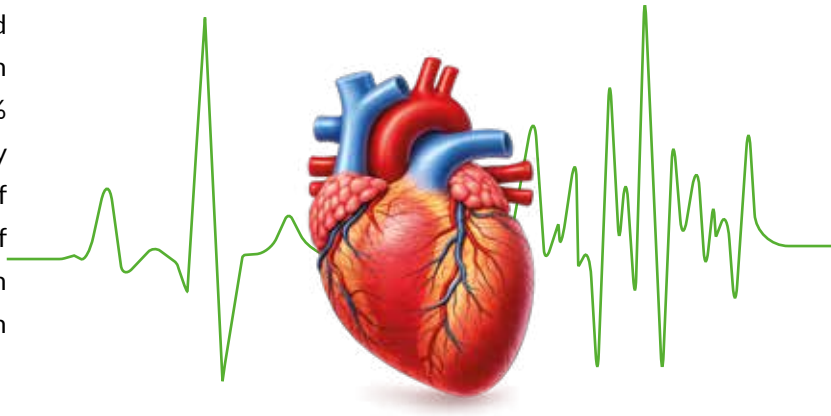


This is exemplified by Dravet syndrome, in which there is both a significantly increased risk of SUDEP and a high frequency of drug-resistant seizures, including GTCS, and it is almost impossible to distinguish the influence of the individual risk factors.

Regardless of the methodological difficulties, the presence of variants in the genes associated with an increased risk of SUDEP should be taken into account in risk assessment and also when initiating preventive measures.

The role of the heart and anti-seizure medication

People with epilepsy have a threefold increased incidence of sudden cardiac death compared to the general population, and in 66% of cases, cardiac arrest occurred without any connection to an epileptic seizure. In the context of SUDEP, primary cardiac involvement in the form of cardiac arrhythmias is also discussed, as well as an interaction between epileptic activity and changes in the cardiovascular system.



The term ‘epileptic heart’ describes the cardiac effects of long-standing epilepsy, particularly in connection with repeated rises in catecholamines, hypoxia and possible myocardial ischaemia with secondary fibrosis. In connection with seizures, ventricular fibrillation has been described in people with SUDEP and near-SUDEP.

Anti-seizure drugs such as sodium channel blockers or Gabapentin have been linked to the development of cardiac arrhythmias. In addition to measuring the QT interval in routine ECGs (electrocardiograms) for all people with epilepsy, the assessment of heart rate variability in long-term ECGs should also be considered.

A link has been postulated between sudden epileptic death and sudden cardiac death. In individuals who have died from SUDEP, genetic variants have been identified that are associated with heart disease, particularly those involving sudden cardiac death, including through lethal cardiac arrhythmias. The identification of such a finding in a SUDEP victim can have far-reaching consequences for the counselling, diagnosis and, where appropriate, treatment of the bereaved. Genetic testing should therefore also be sought in SUDEP victims, provided this has not already been carried out during their lifetime.

SUDEP prevention

There are no randomised, placebo-controlled studies that conclusively demonstrate the protective effect of individual interventions. Nevertheless, several clinical and seizure-related risk factors have been identified that can be specifically addressed within the context of care. A structured, individual risk assessment involving patients, their relatives, and treating specialists is essential in this regard.
On this basis, patient-specific preventive measures can be derived with the aim of increasing the individual's level of safety. Epilepsy should not be viewed in isolation, but should always be discussed and treated within the context of the individual's life situation, social environment and existing care structures.

Education is a key factor in preventing deaths from SUDEP, as only well-informed patients and carers can make well-considered decisions.

The absence of seizure freedom is a key risk factor for SUDEP. Consequently, an **accurate diagnosis of epilepsy** using modern diagnostic methods and the provision of optimal, individually tailored **treatment to control seizures** (treatment optimisation) are crucial. In particular, GTCS should be prevented. All treatment options should be discussed in full with patients and their carers, in person, through training sessions and with the aid of information materials: (I) drug therapy (primarily anti-seizure medication, immunomodulatory therapies, personalised precision therapies), (II) medical diets, (III) epilepsy surgery and (IV) brain stimulation procedures. All therapies aim to achieve seizure freedom whilst taking quality of life into account, or at least to reduce the frequency or severity of epileptic seizures. Accordingly, successful therapies have the potential to reduce the risk of SUDEP. For the individual, failure to recognise seizures poses a risk, as without this awareness, neither can treatment be optimised nor can carers be alerted and respond to seizures. A study in adults found that only approximately 50% of people with epilepsy correctly recognized and documented their seizures. Supervision through the presence of another person at night and/or automated ‚monitoring' of seizures at night using technical aids **(seizure monitoring)** are therefore potential ways of reducing the risk of SUDEP.

The fact that SUDEP has been linked to GTCS and occurs more frequently at night emphasises the importance of monitoring.

In addition to seizure monitoring, knowledge of the procedures to follow when an epileptic seizure occurs (**emergency plans**, Seizure Action Plan), and in the event of a resuscitation situation is crucial to having a chance of avoiding complications, including SUDEP. The MORTEMUS study reported cases in which SUDEP was prevented by initiating resuscitation measures within three minutes of the seizure ending. Caregivers of people with epilepsy should therefore be encouraged to attend resuscitation training. Particularly in the case of affected infants or young children, this should be a first-aid course with resuscitation training specifically for children, as there are significant differences, including with regard to ventilation.

For this reason, a multi-hour epilepsy education programme (MyEpiPro©) has been developed at the Charité's Epilepsy Centre for Paediatrics and Adolescent Medicine. The aim of the programme is to offer parents a concise, structured and practical training course as part of a face-to-face session lasting several hours, held every two months. Information on epilepsy, diagnosis, treatment options and complications (including SUDEP), as well as clinically tested seizure monitoring systems are provided by the medical management team in collaboration with a specialist epilepsy nurse. Training in emergency procedures, including resuscitation, is delivered by specialist staff trained in intensive care medicine. This is supplemented by a written information pack, which families receive at their first appointment, and individual consultations. The programme can receive financial support from companies. Overall, the educational programme aims to improve the information and confidence in taking action among those affected and their families.

Prof. Dr Angela Kaindl is Director of the Department of Paediatrics with a focus on Neurology and Head of the Social Paediatric Centre at Charité – Universitätsmedizin Berlin, which houses the German Epilepsy Centre for Children and Adolescents. She also heads an interdisciplinary research group on epilepsy and brain development disorders. Her scientific work focuses in particular on researching the causes and mechanisms of epilepsy and neurological developmental disorders, as well as on developing precision medicine treatment approaches. The aim is to derive targeted, individualised treatment strategies from this. A key focus for her is the prevention of complications of epilepsy, including sudden unexpected death in epilepsy (SUDEP). In this regard, she attaches great importance to educating families and maintaining open, transparent communication.

This commitment underscores her core objective: to bring about lasting improvements in the prevention, patient care and quality of life for people with epilepsy through research, education, and innovative care models.

More information about the German Epilepsy Centre for Children and Adolescents at Charité

NightWatch+ is a Class IIa medical device (EU) MDR 2017/745 and received FDA clearance (NightWatch+ US). NightWatch+ detects and alerts in the event of tonic-clonic, tonic (prolonged or serial), myoclonic (serial) and hyperkinetic epileptic seizures during sleep.

Further information
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