



# Decreasing SUDEP incidence in a tertiary epilepsy center between 1981 and 2016: Effects of better patient supervision<sup>☆</sup>

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## ABSTRACT

**Objective:** The objective of this study was to investigate the incidence of sudden unexpected death in epilepsy (SUDEP) in a tertiary epilepsy center in the years 1981–2016 with an emphasis on patient supervision and nursing intervention in different departments.

**Methods:** We identified 14 SUDEP cases (probable, definite, definite plus). Patient-years (PY) and incidence were calculated for the periods of six years for the general epileptology wards (adults and children) and, in addition, for the epilepsy monitoring unit (EMU) since 1990.

**Results:** The incidence of SUDEP showed a decreasing trend over time ( $r = -0.81$ ;  $p = 0.053$ , two-sided; Pearson correlation coefficient). This is especially true in children (no SUDEP occurred in pediatric general epileptology since 1992). Additionally, in the EMU (314 PY since the start of 1990), no SUDEP occurred. Sudden unexpected death in epilepsy incidence was highest (6.8/1000 PY) in the early time periods (1981–1992) and lowest (1.7/1000 PY) in the later time periods (1999–2010). In the general epileptology wards (3579 PY), the overall incidence was 3.9 per 1000 PY (95% confidence interval (CI): 2.1–6.6).

**Conclusions:** We assume that the decreased SUDEP incidence is an effect of better supervision by the use of technical means (e.g., video cameras, pulse oximeters, seizure detection systems) and rooming-in of parents or family.

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## 1. Introduction

In a recent meta-analysis, the incidence of sudden unexpected death in epilepsy (SUDEP) in children with epilepsy amounted to 0.22/1000 patient-years (PY) (95% confidence interval (CI): 0.16–0.31) and 1.2/1000 PY (95% CI: 0.64–2.33) in adults. Occurrence and frequency of generalized tonic-clonic seizures (GTCS) were a major risk factor for SUDEP whereas supervision (e.g., the presence of another individual in the bedroom) was associated with a decreased SUDEP risk [1]. In a nationwide population-based Swedish study, not included in the abovementioned meta-analysis, SUDEP incidence was 1.13 and 1.29 per 1000 PY in patients 16–50 and >50 years, respectively [2]. However, this study indicated a comparatively high SUDEP incidence in children <16 years (1.11 per 1000 PY). A recent Canadian

study affirmed a SUDEP incidence in children comparable with adults (1.17 per 1000 PY) [3].

Earlier retrospective studies found an incidence of SUDEP of 5.1/1000 PY (95% CI: 2.6–9.2) and of SUDEP or near SUDEP of 7.9 (95% CI: 4.6–12.7) in presurgical epilepsy monitoring units (EMUs) [4] and of 6.4 for patients who had been considered for epilepsy surgery [5].

The aim of our study was to investigate SUDEP incidence in the Epilepsy Centre Bethel, Mara Hospital, Bielefeld, with wards for children and adults, and for presurgical diagnosis/epilepsy surgery over 36 years (1981–2016). We hypothesize the following: 1. Overall SUDEP incidence in a tertiary epilepsy center is in the range reported for patients with medically refractory epilepsy; 2. SUDEP incidence has decreased over time, as suggested earlier [1,5]. We expected this trend because continuous monitoring permits early nursing interventions with stimulation of the patient, prevention of airway obstruction, and postictal repositioning of the patient in a supine position [6,7].

## 2. Material and methods

### 2.1. Calculation of PY

Bed occupancy days and PY were extracted from the present electronic hospital information system for the years 1994 to 2016 and

**Abbreviations:** AEDs, antiepileptic drugs; CI, confidence interval; EEG, electroencephalogram; EMU, epilepsy monitoring unit; GTCS, generalized tonic-clonic seizures; ID, intellectual disability; PY, patient-years; SUDEP, sudden unexpected death in epilepsy.

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for the EMU from 1990 to 2016. For the general epileptology wards (children and adults), bed occupancy days were estimated from 1981 to 1993 on the basis of the following five years, 1994 to 1998, with stable data. We expected the bed occupancy days to be stable in the years 1981 to 1993 because of a stable number of beds in this time period. Occupancy rate and number of patients were stable from 1994 to 2006 and then slowly increased.

The Epilepsy Centre Bethel has the status of a 'special institution' and still bills on the basis of bed occupancy days.

## 2.2. Identification and characteristics of SUDEP cases

Twelve out of 14 SUDEP cases were found by protocols of postmortem examination, which was done as a routine in unexpected deaths in the Mara Hospital. Long-standing staff members recollected 2/14 SUDEP cases without postmortem examination, which were verified in patient files. An electronic list of deaths as causes of the end of hospital stay was available for the years 2002–2016. Detailed information and classification [8] of all SUDEP cases is given in Table S1 (Supplementary material).

## 2.3. Characterization of the different wards

Details of patient supervision over the years for SUDEP prevention are given in the [Results](#) section.

### 2.3.1. General epileptology wards – children

At present, 30 beds are available, with one ward for infants and young children and another for children and youths. Two nurses make routine rounds several times per night.

### 2.3.2. General epileptology wards – adults

A total of 80 beds are available: four wards with night watches with a total of 50 beds (two wards for patients with additional handicaps, one ward for differential diagnosis including long-term electroencephalogram (EEG) without antiepileptic drug (AED) reduction, one ward for differential therapy in chronic epilepsy); another 30 beds without night watches include a ward for Behavioural and Psychotherapeutic Epileptology and a ward for young adults with epilepsy.

### 2.3.3. EMU

The EMU was established in 1990 and has 17 beds at present, 6/17 with continuous EEG/video supervision and another 11/17 with video supervision only, for patients outside the proper video-EEG monitoring period with other presurgical diagnostics, for patients immediately after surgery, and patients for follow-up controls six months and two years after surgery. About 40% of the patients are children (age: <18 years; 40.4% from 1990 to 2014). Antiepileptic drugs are often tapered within one to four days to record a sufficient number of seizures.

## 2.4. Standards of nursing intervention

A survey was carried out among the night watches (with the use of a questionnaire) and long-standing nurses (with interviews). We assessed the use of technical means over time, past and present nursing standards, and individual techniques especially for supervision during the night.

## 2.5. Statistics

The incidence of SUDEP was calculated on the basis of an estimation of total PY spent in different wards of the Mara Hospital. This calculation was done for the entire population, as well as in subgroups defined by age (adults vs. children aged <18 years).

In accordance with Ryvlin et al. [4], we calculated the 95% CI for the abovementioned incidences, first estimating the 95% CI for the number

of observed events. The denominator of the incidence rate (i.e., the number of PY) can be regarded as a nonrandom quantity whereas the number of events is a random variable that follows the Poisson distribution for rare events. The resulting CI limits were then divided by the PY spent in the epilepsy center to provide 95% CIs for incidence rates.

The Pearson correlation coefficient and nonparametric Spearman coefficient were used to describe linear and monotonic trends in SUDEP incidence over time periods. Two-sided p-values were reported.

For statistical analyses, IBM SPSS for Windows 25.0 and SAS 9.4 were used.

The study was performed in accordance with the Health Data Protection Act (GDSD NRW) of 22 February 1994. According to this act, scientific personnel may use for purposes of scientific research patient data to which they already have access due to their work in a hospital without consent of the patient. Therefore, no ethics approval was required.

## 3. Results

### 3.1. SUDEP incidence

Fourteen SUDEP cases were identified in the years 1981–2016. In the general epileptology wards (3579 PY), the overall incidence was 3.9 per 1000 PY (95% CI: 2.1–6.6); SUDEP incidence was highest (6.8/1000 PY) in the early time periods (1981–1992) and lowest (1.7/1000 PY) in the later time periods (1999–2010). [Fig. 1](#) illustrates the decreasing incidence of SUDEP over time in the general epileptology wards of our center ( $r = -0.81$ ;  $p = 0.053$ , Pearson correlation coefficient;  $r = -0.75$ ,  $p = 0.084$ , nonparametric Spearman correlation coefficient). Sudden unexpected death in epilepsy occurred in three children (incidence: 3.0/1000 PY, 95% CI: 2.1–8.8) but only in the early time periods (1981–1992). Sudden unexpected death in epilepsy incidence in adults was 4.3/1000 PY (95% CI: 2.4–7.7). After the exclusion of pediatric patients, there was still a (monotonic) decreasing tendency of SUDEP incidence ( $r = -0.69$ ,  $p = 0.126$ , Pearson correlation coefficient;  $r = -0.81$ ,  $p = 0.050$ , nonparametric Spearman correlation coefficient). Details on the number of SUDEP, PY, and SUDEP incidence are shown in Table S2 (Supplementary material). No SUDEP occurred in the EMU within 314 PY compared with 14 SUDEPs in 3579 PY in the general epileptology departments.

### 3.2. SUDEP prevention

#### 3.2.1. General epileptology wards – children

Since 1990, rooming-in of parents has been increasingly required and offered for infants and young children up to the age of 10 years and for children with intellectual disability (ID), as much as possible in limited space (rarely since 1990, as a routine since 2001 after a reorganization of the wards, and also for older children since 2006 in a new building). Later, further measures have been implemented: since 2003, pulse oximeters; since 2016, seizure detection systems for older children and video documentation (also used for supervision at night). These systems are used with patients deemed to be at risk of more severe seizures (approximately in use in 37% upon cross-sectional evaluation).

Before the use of seizure detection systems, small bells at the wrist were found very effective to signal motor seizures. Two of three SUDEP cases were detected during the last clonic jerks during the night and during the afternoon nap; the third SUDEP of a two-year-old infant occurred under the nurses' eyes in the morning. The standard situation of finding a patient dead in their bed in the morning did not happen.

#### 3.2.2. General epileptology wards – adults

Video or EEG/video documentation has been available for some patients, for later interpretation, over the entire study period. In 2000, cameras were installed in four wards for adult patients, supervising

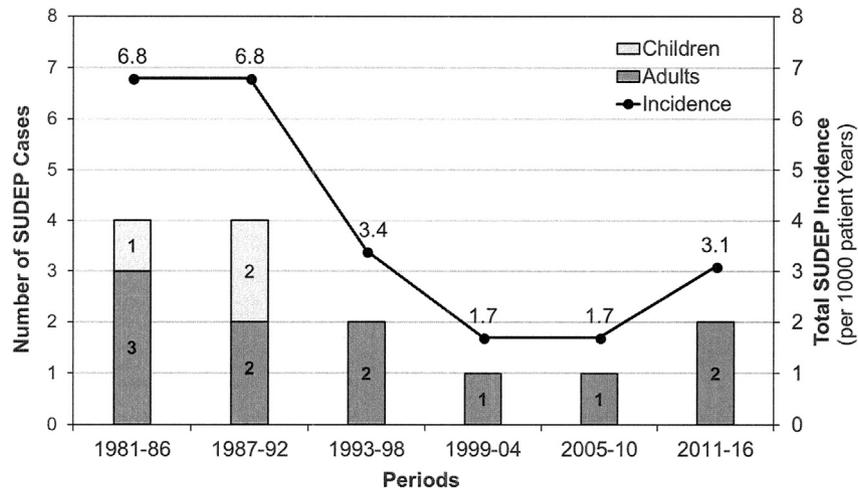


Fig. 1. Decreasing incidence of SUDEP in the general epileptology wards for children and adults.

15% of the 50 patients. In 2006, video surveillance was installed in a ward for young adults (all 18 beds). Seizures are mainly detected by chance during the day: by nurses, other patients, because of noises, and an occasional look at the monitors. At night, supervision of noises predominates. In four wards, two nurses are on duty during the night and make routine rounds in all rooms several times per night. Patients at risk are placed near the night watch's room if possible, the doors left open, and visited more frequently. There is no night watch on two wards with 30 beds; only an on-call duty is available (ward for Behavioural and Psychotherapeutic Epileptology and ward for young adults with epilepsy). Seizure detection systems have increasingly been used since 2016 (52% of the supervised beds), rarely (up to 13%) also in the previous years since 1986 (Danish Care™, later Epicare™).

### 3.2.3. EMU

From the beginning of monitoring on this ward, at least one EEG technician and one nurse are present at any time, including nights and weekends. As a routine, in GTCS, the following activation and intervention methods are used: turning on the light during the night, giving the patient a word to remember, repositioning the patient, rectal administration of diazepam (in later years, buccal administration of midazolam). The rooming-in of parents with their children is encouraged and regularly used by parents (>90% of pediatric cases).

### 3.2.4. Cardiopulmonary resuscitation

Cardiopulmonary resuscitation was attempted in seven of 14 cases, not attempted in six of 14 cases (no information for one patient). Ten SUDEPs occurred in bed during the night or during the afternoon nap; three occurred in the daytime (two out of three in the bathroom in the morning or shortly after the afternoon nap; no information for one patient).

## 4. Discussion

The reported incidence of 3.9 SUDEP cases per 1000 PY in our epilepsy center is in the range of 1.2 to 5.9 in other tertiary epilepsy centers [5]. However, there was a decreasing tendency of SUDEP incidence over time. In contrast with the reported incidence of 7.9 in the MORTEMUS study of EMUs [4], no SUDEP cases occurred in the Bethel EMU. In addition, the absence of SUDEP cases, from 1992 onwards, in the pediatric department is remarkable. The effect of supervision and increased use of technical equipment is discussed below.

### 4.1. Supervision in general epileptology – children

The absence of SUDEP in the pediatric department after 1991 argues for the influence of supervision and patient management, more so as recent studies showed the risk of SUDEP in children and adults to be similar [2,3]. Even until 1991, the standards for supervision were high and included rounds every 30 min during the night.

### 4.2. Supervision in general epileptology – adults

In comparison with the pediatric wards and the EMU, patient supervision was lower in the general epileptology wards for adults. The absence of night watches in two wards has been compensated for by video control and seizure detection systems; patients at high risk of nocturnal seizures are treated on other wards with better supervision.

### 4.3. Supervision in the EMU

Antiepileptic drugs are tapered rapidly, and the risk of GTCS is high in the EMU. For this reason, round-the-clock supervision by at least one nurse and one EEG technician was established from the beginning in 1990. The Bethel Epilepsy Centre contributed to the MORTEMUS study in June 2008 (207.5 PY at this time), with a total of 2764 PY in the whole cohort of contributors. However, in the whole cohort, the proportion of time associated with supervised monitoring during presurgical EEG/video monitoring was only 59% because of incomplete supervision during the evening and the night [4]. Data from the MORTEMUS study argue for a late detection of fatal seizures. The delay to cardiopulmonary resuscitation was 13 min at minimum in eight of 11 monitored SUDEP cases (three of 11 had no resuscitation). In contrast, the resuscitation started with a maximum delay of 3 min in seven near SUDEP cases (in 2 cases, there was an unknown delay). In all but one patient, SUDEP occurred during the time interval 19:30 and 6:00 whereas in six of seven patients, near SUDEP occurred during daytime.

### 4.4. Cardiopulmonary resuscitation and early nursing interventions (with a review of the literature)

Earlier intervention is essential to further decrease the occurrence of SUDEP. In hospitals, cardiopulmonary resuscitation might save patients. Accidental detection led to resuscitation attempts in 7/14 of our SUDEP cases. Case studies including 8 SUDEPs support the notion of late SUDEP detection in EEG/video monitoring at night: 4/8 in daytime (3/4 with successful resuscitation = near SUDEP), 3/8 at night (without

supervision or resuscitation = SUDEP), and 1/8 at unknown time of day (with successful start of resuscitation within 1–4 min = near SUDEP) [9–11]. However, some studies show that less interfering measures are also helpful. Hypoxemia is significantly shorter in patients with nursing intervention versus without nursing intervention and in early versus delayed intervention [7]. The duration of postictal immobilization and duration of postictal generalized EEG suppression are associated with severe respiratory dysfunction so that measures to interrupt postictal immobilization may contribute to reduce SUDEP risk [6]. Seizure duration correlates with earlier intervention [12]. With regard to the circumstances of SUDEP, a Swedish nationwide population-based study found definite SUDEPs more likely to occur at home, during the night, unwitnessed, in prone position, and often with a preceding seizure [13].

#### 4.5. New AEDs

A meta-analysis of placebo-controlled randomized trials showed a benefit of (adjunctive) antiepileptic treatment (as compared with adjunctive placebo) [14]. In these studies, the adjunctive antiepileptic treatment consisted of new AEDs, which might also reduce the incidence of SUDEP.

#### 4.6. Limitations

Our study has several limitations. Some ‘probable SUDEP’ cases may be lost in the years 1981–1992, in spite of a lot of long-standing personnel in our clinic who can be expected to remember such dramatic events. Thus, the incidence of (probable and definite) SUDEP may even be underestimated in this early period. Only cases with postmortem examination were entered (‘definite SUDEP’) from a study of SUDEP cases in Bethel covering the years 1981 to 1992 [15]. Some data files of one early case were lost. Some characteristics of the wards have changed over time, and the use of technical means has increased.

The number of PY in our study, especially in the EMU, is still limited from a statistical view. Multicenter studies are necessary for further evidence. On the other hand, multicenter studies like the MORTEMUS study often suffer from heterogeneous contributions. The overall number of secondarily GTCS in our hospital, as a risk factor for SUDEP and the effect of new AEDs, could not be clarified in this study. However, despite the high risk of GTCS in the EMU, no SUDEP happened with 24/7 surveillance of the patients by trained personnel.

## 5. Conclusions

The incidence of SUDEP showed a decreasing trend over time in our tertiary epilepsy center since 1981. No SUDEPs occurred in children in the past 25 years, and no SUDEP occurred in the EMU. Appropriate measures, especially 24/7 surveillance by trained personnel or by seizure detection systems, may improve SUDEP prevention. Early repositioning of the patient and, if necessary, resuscitation, are promising and easy measures for prevention of SUDEP.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2018.11.019>.

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## Conflicts of interest

R Schulz gave scientific advice to BESA (Gräfelfing, Germany).

CG Bien gave scientific advice to UCB (Monheim, Germany) and obtained honoraria for speaking engagements from Eisai (Frankfurt, Germany), UCB (Monheim, Germany), Desitin (Hamburg, Germany), Biogen (Ismaning, Germany), and Euroimmun (Lübeck, Germany). He received research support from Deutsche Forschungsgemeinschaft (Bonn, Germany), Gerd-Altenhof-Stiftung (Deutsches Stiftungszentrum, Essen, Germany), diamed (Köln, Germany), and Fresenius Medical Care (Bad Homburg, Germany). He is a consultant to the Laboratory Krone, Bad Salzflun, Germany regarding neural antibodies and therapeutic drug monitoring for antiepileptic drugs.

TW May received honoraria for speaking engagements from Eisai (Frankfurt, Germany) and Desitin (Hamburg, Germany) and received financial support from Desitin for visiting scientific meetings.

## Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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