Received: 7 July 2023 | Revised: 12 October 2023 | Accepted: 12 October 2023

DOI: 10.1111/epi.17799

Epilepsia

RESEARCH ARTICLE

Critical incidents, nocturnal supervision, and caregiver knowledge on SUDEP in patients with Dravet syndrome: A prospective multicenter study in Germany

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Abstract

Objective: The aim was to investigate the monitoring, interventions, and occurrence of critical, potentially life-threatening incidents in patients with Dravet syndrome (DS) and caregivers' knowledge about sudden unexpected death in epilepsy (SUDEP).

Methods: This multicenter, cross-sectional study of patients with DS and their caregivers in Germany consisted of a questionnaire and prospective diary querying the disease characteristics and demographic data of patients and caregivers.

Results: Our analysis included 108 questionnaires and 82 diaries. Patients with DS were 49.1% male ($n = 53$), with a mean age of 13.5 (SD ± 10.0 years) and primary caregivers were 92.6% ($n = 100$) female, with a mean age of 44.7 (SD ± 10.6 years). Monitoring devices were used regularly by 75.9% ($n = 82$) of caregivers, and most monitored daily/nightly. Frequently used devices were pulse oximeters (64.6%), baby monitors (64.6%), thermometers (24.1%), and Epi-Care (26.8%). Younger caregiver and patient age and history of status epilepticus were associated with increased use of monitoring, and 81% of monitor users reported having avoided a critical incident with nocturnal monitoring. The need for resuscitation due to cardiac or respiratory arrest was reported by 22 caregivers (20.4%), and most cases (72.7%) were associated with a seizure. Caregivers reported frequently performing interventions at night, including oropharyngeal suction, oxygenation, personal

Trial registration: German Clinical Trials Register (DRKS), DRKS00016967. Registered May 27, 2019, http://www.drks.de/DRKS00016967

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hygiene, and change of body position. Most caregivers were well informed about SUDEP ($n = 102$; 94%) and monitored for a lateral or supine body position; however, only 39.8% reported receiving resuscitation training, whereas 52.8% ($n = 57$) knew what to do in case the child's breathing or heart activity failed.

Significance: Critical incidents and the need for resuscitation are reported frequently by caregivers and may be related to high mortality and SUDEP rates in DS. Resuscitation training is welcomed by caregivers and should be continuously provided. Oxygen monitoring devices are frequently used and considered useful by caregivers.

KEYWORDS

encephalopathy, epilepsy, near-SUDEP, seizure

1 | INTRODUCTION

Dravet syndrome (DS) is a rare developmental and epileptic encephalopathy.[1,2] Patients experience refractory epilepsy and numerous non-epileptic manifestations, such as impaired cognition and speech and delayed motor and behavioral development. The proportion of *SCN1A* mutations in study cohorts is increasing and has recently been reported to be more than 90%.[3–5] Individuals with DS are predisposed to depressed heart rate variability, and mouse models of DS suggest prolonged ictal-onset bradycardia.[6] Frequent prolonged seizures and status epilepticus (SE) develop in the first year of life. Beyond the age of 5 years, seizure frequency begins to decrease, with a gradual transition with age to nocturnal seizures, which are the main type of seizures in adults. Nocturnal seizures are associated with challenges, including sleep disturbances for both patients and their family members.[7] Mortality in DS is high due to an increased risk of sudden unexpected death in epilepsy (SUDEP) compared with other epilepsies.[8–11] Generalized tonic–clonic seizures (GTCS) (especially nocturnal/during sleep) are a primary risk factor for SUDEP. Previous studies have indicated that caregivers use various methods to monitor their child's sleep for risk mitigation; however, there is no consistent information about the efficacy of monitoring or recommendations.[12] On one hand, caregivers believe that monitoring can prevent SUDEP, and it thus decreases their anxiety; on the other hand, frequent false alarms can result in sleep deprivation and can be frightening, which can increase anxiety and depression. Caregivers must strike a balance between completing parenting and nursing tasks, minimizing the burden on family members, and managing other psychosocial challenges.[13,14] A recent literature review suggests that the mechanism of SUDEP is a culmination of factors, such as post-ictal apnea and bradycardia, which are mostly unwitnessed and progress to terminal asystole. Watkins et al. postulated that epileptologists should discuss with caregiver's nighttime observation and other overnight monitoring techniques, including remote listening devices, to reduce the risk of SUDEP in people with frequent convulsive seizures, especially if the seizures are nocturnal. They highlighted that there is limited low-level evidence available to support the use of monitoring techniques and limited evidence of their ability to reduce SUDEP risk,[6] and there is a need to clarify the advantages and disadvantages of these techniques.[12]

Key points

- Caregivers reported a high number of critical incidents, and 20.4% indicated the need for resuscitation efforts.
- Almost all caregivers are knowledgeable about sudden unexpected death in epilepsy (SUDEP); however, there is a need for training in resuscitation.
- Monitoring devices were used regularly by 75.9% of caregivers of patients with Dravet syndrome.
- Pulse oximeters (64.6%) and baby monitors (64.6%) were frequently used, whereas licensed seizure-detection devices were used less frequently (26.8%).

To address some of these open research questions, we conducted a study focusing on nocturnal supervision among caregivers of patients with DS, the use of monitoring devices, and the occurrence of critical incidents among patients with DS.

2 | MATERIALS AND METHODS

This multicenter, cross-sectional study enrolled primary caregivers of patients with DS throughout Germany. Written informed consent was obtained from the parents or legal guardians of the patients with DS. The study obtained ethical approval from Goethe-University Frankfurt and is registered with the German Clinical Trials Register (DRKS00016967). Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were closely followed during the conduct and reporting of this study.[15]

A combined survey consisting of a previously validated retrospective questionnaire and a prospective diary[16] was administered to enrolled participants in Germany in 2019. The questionnaire consisted of questions regarding disease characteristics (seizures, medical treatment, comorbidities), demographic data of both the patients and caregivers, and details regarding nocturnal supervision (co-sleeping, monitoring and use of devices, associated costs, nightly interventions). In addition, knowledge about SUDEP and resuscitation and the occurrence of critical incidents was queried. Critical incidents were defined as a deterioration in the patient's condition that needed acute care, according to the caregiver, including stimulation by pain, artificial respiration, oxygen supply, or chest compressions. Caregivers' definitions of alarms and false alarms were also queried. The questionnaire included both closed and open-ended questions; closed questions included list-based responses, multiple-choice options, and Likert scales. The prospective diary collected data on seizures, monitoring, and emergency treatment in a 1-month period and was used to validate diurnal and nocturnal seizure frequency data reported in the retrospective questionnaire.

Statistical analysis was conducted using SPSS version 28 (IBM, Armonk, NY, USA). Variables of interest were summarized using the mean, median, range, and standard deviation (SD). The Mann–Whitney *U* test and chi-square test were used to compare predictors of the use of monitoring. A two-sided significance level of $p=.05$ was used in all statistical analyses. We did not adjust for multiple testing. The data of this study are available from the corresponding author upon reasonable request.

3 | RESULTS

3.1 | Patient and caregiver characteristics

In total, 108 questionnaires and 82 prospective diaries were collected from patients and their caregivers. Patients with DS had a mean age of 13.5 years (SD 10.0 years, median 10.8 years), and 53 (49.1%) were male. Seizure frequency was reported by caregivers at a mean of 8.5 seizure days per month (SD 9.8; median 4; range 0–30), which was comparable to the prospectively recorded mean of 8.6 seizure days per month (SD 10.8; median 3; range 0–30; $n=82$). According to the questionnaire data, nocturnal seizures were reported in 71.4% ($n=77$) of patients, with a mean frequency of 8.9 (SD 25.6; median 1; range 0–208) nocturnal seizures per month. From the diaries, 52.4% ($n=43/82$) of patients had nocturnal seizures, with a mean of 5.6 (SD 9; median 1; range 0–30; $n=82$) nocturnal seizure days per month. Patients were treated with a mean of 3.2 anti-seizure medications (ASMs; SD 1.2; median 3; range 1–5). Details are presented in Table 1.

3.2 | Use and characteristics of monitoring

Monitoring devices were used regularly by 75.9% ($n=82$) of caregivers, and they monitored for a mean of 8.2 years (SD 6.9; median 6.3; range 0.2–29.1). The use of monitoring devices was strictly defined as the use of technical equipment and did not include direct personal supervision. The caregiver's and patient's sleeping situation was assessed separately. One-third ($n=36$; 33.3%) of patients with DS slept in their parents' bedroom, of which 32 additionally used monitoring devices and 24 slept in the same bed as their primary caregiver. Twenty-six caregivers did not use any monitoring devices, of which eight slept in the same bedroom as their child. In 16.7% ($n=18$) of cases, the caregivers were supported by an ambulatory pediatric intensive care service, which provides services, for example, managing breathing function, suction, and nutrition.

Among the 82 caregivers who used monitoring devices, 87.8% ($n=72/82$) monitored daily/nightly, 3.7% ($n=3/82$) monitored several times a week, 3.7% ($n=3/82$) monitored at least once a month, and 4.9% ($n=4/82$) monitored less than once a month. When asked about the time of day of the monitoring, 89.0% ($n=73/82$) reported monitoring during sleep, 70.7% ($n=58/82$) monitored during or after seizures, 39.0% ($n=32/82$) monitored during infections, and 14.6% ($n=12/82$) monitored when the patient was awake (multiple answers were possible). The motivation for monitoring was 81.7% ($n=67/82$) from parents/caregivers and 30.5% from neuropediatricians, or a combination.

Pulse oximeters ($n=53/82$; 64.6%), baby monitors ($n=53/82$; 64.6%, 38 of these included camera functions), thermometers ($n=28/82$; 24.1%), Epi-Care ($n=22/82$; 26.8%), camera systems ($n=9/82$; 11.0%), epilepsy service dogs ($n=2/82$; 2.4%), and seizure

TABLE 1 Sociodemographic and clinical characteristics.

	All patients $n=108$
Patient characteristics	
Age, years, mean ± SD (range)	13.5 ± 10.0 (1.2–46.2)
Sex, % (n)	
Male	49.1 (53)
Female	50.9 (55)
Genetics, % (n)	
SCN1A mutation	96.3 (104)
Unknown or not available	2.8 (3)
Epilepsy characteristics	
Seizure days per month, mean ± SD (range)	8.5 ± 9.8 (0–30)
Nocturnal seizures, mean ± SD (range)	8.4 ± 25.6 (0–208)
Nocturnal seizure frequency, % (n)	
At least one per night	9.3 (10)
At least one per week	21.3 (23)
At least one per month	16.7 (18)
At least one per 6 months	11.1 (12)
At least one per year	13.0 (14)
No seizures for more than a year	25.9 (28)
GTCS frequency, % (n)	
At least one per day	4.6 (5)
At least one per week	26.9 (29)
At least one per month	25.0 (27)
At least one per 6 months	17.6 (19)
At least one per year	11.1 (12)
No seizures for more than a year	13.0 (14)
Number of ASMs, mean ± SD (range)	3.2 ± 1.2 (1–5)
Most frequently used ASM, % (n)	
Valproate	63.0 (68)
Clobazam	54.6 (59)
Bromide	43.5 (47)
Stiripentol	38.0 (41)
Topiramate	25.9 (28)
Cannabidiol	13.0 (14)
Fenfluramine	11.1 (12)
Levetiracetam	10.2 (11)
Caregiver characteristics	
Age of mother, years, mean ± SD; ($n=108$)	44.7 ± 10.6
Age of father, years, mean ± SD; ($n=108$)	47.3 ± 10.6
Use of monitoring devices, % (n)	
Yes	75.9 (82)
During sleep	67.6 (73)
During wakefulness	11.1 (12)
During/after seizures	53.7 (58)
During infection	29.6 (32)
No	24.1 (26)
Monitoring devices are used, % (n)	
Every day/night	66.7 (72)
At least once per week	2.8 (3)
At least once per month	2.8 (3)
Less than once a month	4.7 (4)

Abbreviations: ASM, anti-seizure medication; DS, Dravet syndrome; GTCS, generalized tonic–clonic seizure.

monitoring watches ($n=1/82$; 1.2%) were reported as monitoring devices. Epi-Care is available as mattress or wrist bound device to detect convulsive seizures and hence trigger an alarm.

For patients who were monitored using pulse oximeter devices, in the 0 to 5-year age group ($n=19$), the average pulse value reported at night without infection was 90 bpm (SD 14.2; range 70–120 bpm); the lower alarm threshold, on average, was set at 63 bpm (SD 9.8; range 50–85 bpm), and the upper threshold was set at 158 bpm (SD 31.3; range 125–250 bpm). In the 6- to11-year age group ($n=15$), the average pulse value at night without infection was 82 bpm (SD 17.7; range 60–115 bpm); the lower alarm threshold was set at 56 bpm (SD 8.1; range 45–75 bpm), and the upper was set at 145 bpm (SD 21.5; range 105–180 bpm). In the age group of 12 years and older ($n=10$), the average pulse value at night without infection was 73 bpm (SD 11.6; range 55–90 bpm); the lower alarm threshold was set at 58 bpm (11.7; range 50–88 bpm) and the upper threshold was set at 130 bpm (SD 18.8; range 99–150 bpm).

In the 0 to 5-year age group, the average oxygen level at night without infection was 97.4% (SD 1.6; range 94%–99%); the lower oxygen alarm threshold was set at 87.2% (SD 3.2; range 80%–93%). In the 6- to 11-year age group, the average oxygen level at night without infection was 95.6% (SD 3.3; range 85%–98%); the lower oxygen alarm threshold was set at 88.3% (SD 3.3; range 80%–92%). In the age group 12 years and older, the average oxygen level at night without infection was 97.6% (SD 1.3; range 95%–99%); the lower oxygen alarm threshold was set at 85.9% (SD 4.7; range 80%–93%).

In the group of caregivers who monitored using a pulse oximeter, 34.0% ($n=18/53$) adjusted thresholds during infections; 40.0% ($n=21/53$) based their thresholds on a neuropediatrician's recommendations, 7.5% ($n=4/53$) on a pediatrician's recommendations, and 41.5% ($n=22/53$) on their personal experience and the experiences of other caregivers.

The definition of a "false alarm" varied among caregivers. Only 25.0% ($n=27$) defined a false alarm as an alarm that did not indicate a seizure. Technical problems or incorrect sensor derivation was defined as a false alarm by 62.2% ($n=51/82$), whereas 25.6% ($n=21/82$) defined a false alarm as exceeding threshold values due to various non-seizure causes. Seizures that were missed by the monitoring method and did not trigger an alarm were defined as false alarms by 25.6% ($n=21/82$). Thirty-one caregivers ($n=31$) reported at least one (mean 8.4; median 5; SD 9.9; range 1.5–40) false alarm per week, 24 caregivers reported false alarms less than once a week, and 14 caregivers reported that they never had false alarms. Caregivers reported that false alarms led to various issues, such as brief frightening (63.4%; $n=52/82$), sleep deprivation (50.0%; $n=41/82$), and anxiety (32.9%; $n=27/82$).

3.3 | Predictors of the use and costs of monitoring

A range of factors was correlated significantly with the frequent use of monitoring. Younger parent age and younger patient age were associated with increased use of monitoring devices. Furthermore, the lifetime history of SE occurrence was related to increased use of monitoring, whereas seizure frequency was not correlated with the use of monitoring; details are provided in Table 2.

Caregivers ($n=41$) spent €174 (median 50; SD: 541.2; range €0–3500) each year on monitoring devices; only five cases received partial reimbursement from their health insurance. The caregivers reported several reasons that they considered monitoring to be important. The most frequently reported reasons were to detect seizures (84.3%), for the caregiver's reassurance (73.0%), and to detect life-threatening situations (70%) (Figure 1; multiple answers possible). Among caregivers who did not monitor their patient, 2.8% ($n=3$) would have liked to monitor but had not received a prescription from their doctor, 1.9% ($n=2$) would have liked to monitor but had not received reimbursement from health insurance, 0.9% ($n=1$) had any kind of monitoring device but did not know how to use it, and 7.4% ($n=8$) stated that the patient did not tolerate the monitoring devices. When asked about their willingness to pay for monitoring devices, 49.1% of caregivers stated that they would pay more than €300 per year

TABLE 2 Predictors of monitoring with technical devices.

	Monitoring with technical devices		Not monitoring with technical devices		
	n	Mean[a]	*n*	Mean[a]	*p*-value
Patients' characteristics					
Age (years)	82	12.46 ± 9.47	26	16.86 ± 11.1	**0.045***
Female	36		17		0.055**
Male	46		9		
Daily or weekly nocturnal seizures	25		8		0.978**
Monthly or fewer nocturnal seizures	57		18		
Daily or weekly GTCS[a]	27		7		0.562**
Monthly or less GTCS[a]	55		19		
At least one status epilepticus	80		20		**0.005****
Status epilepticus has never occurred	2		5		
More than 3 seizure days per month	36		17		**0.036****
3 or fewer seizure days per month	46		8		
2 ASMs[a]	21		7		0.894**
3 or more ASMs[a]	61		19		
Caregiver characteristics					
Age	82	44 ± 9.99	26	49 ± 11.57	**0.044***
Female	77		23		0.378**
Male	5		3		

Bold values indicate statistically significant results with a *p*-value <0.05.

Abbreviations: ASM, anti-seizure medication; GTCS, generalized tonic–clonic seizure.

[a] Mean ± standard deviation.

*Mann-Whitney *U* test, two-sided significance. **Chi-square.

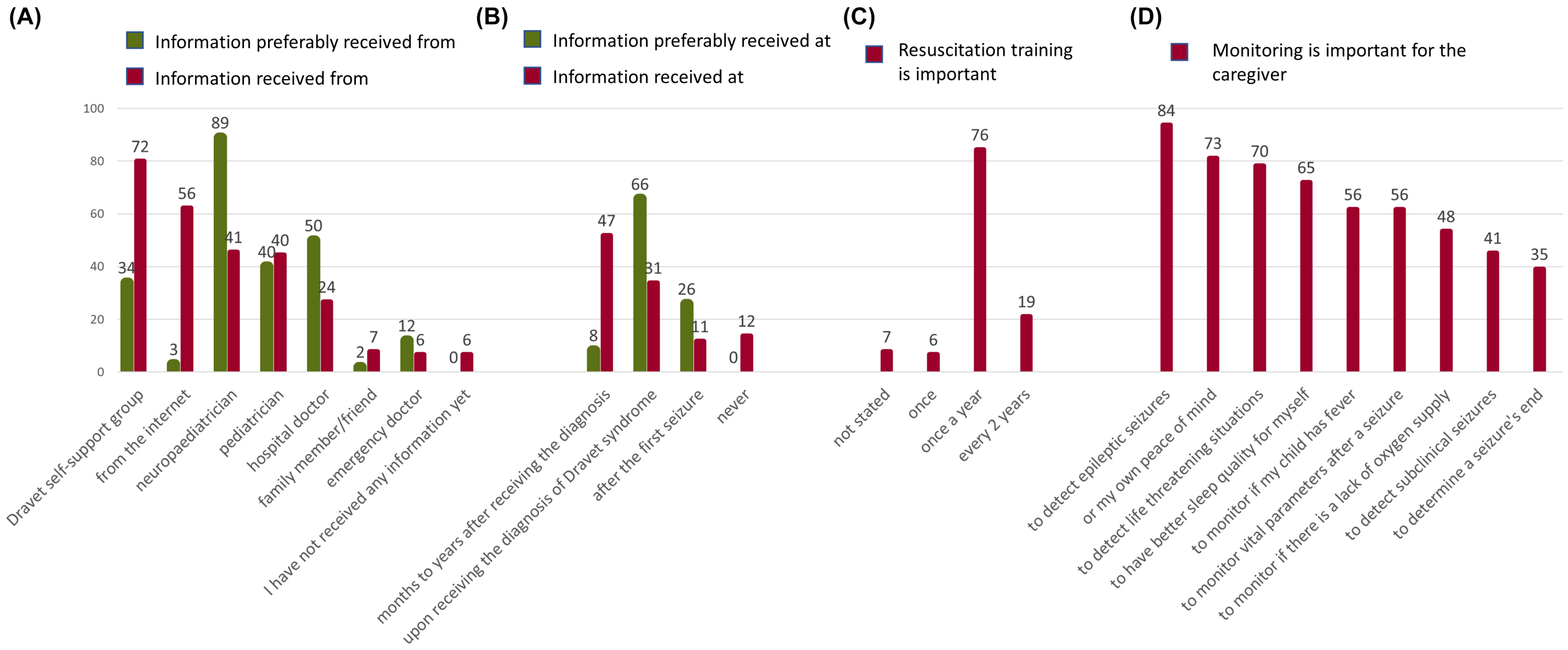

FIGURE 1 (A) Caregivers' sources of information about sudden unexpected death in epilepsy patients (SUDEP). (B) Caregivers' preference of when to receive SUDEP information. (C) Caregivers' opinions regarding the importance of resuscitation training. (D) Reasons that monitoring was important, according to the caregivers.

for better monitoring. Moreover, 47.2% of caregivers stated that they would like to have better means of monitoring their child; however, 46.3% indicated that nightly false alarms were disturbing and affected their quality of sleep and life (Figure 2).

3.4 | Critical incidents and resuscitation

Critical incidents were defined as a deterioration in the patient's condition that needed acute care, according to the caregiver, including stimulation by pain, artificial respiration, oxygen supply, or chest compressions, for details please refer to Appendix A. Of the caregivers who monitored the patients, 81% (*n* = 59/82) reported having previously averted a critical incident by nocturnal monitoring. This required stimulation by pain in 26.8% (*n* = 22/82), oxygen supply in 23.2% (*n* = 19/82), artificial respiration in 13.4% (*n* = 11/82), stimulation in 11.0% (*n* = 9/82), chest tapping in 10.8% (*n* = 8/82), chest compressions in 3.7% (*n* = 3/82), and other interventions in 18.3% (*n* = 15/82) of cases.

Critical incidents were detected by a pulse oximeter in 43.9% (*n* = 36/82) of cases, a baby monitor in 42.7% (*n* = 35/82), personal supervision in 32.9% (*n* = 27/82), a thermometer in 13.4% (*n* = 11/82), Epi-Care in 11% (*n* = 9/82), an electrocardiography (ECG) monitor in 3.7% (*n* = 3/82), an epilepsy service dog in 2.4% (*n* = 2/82), and a seizure monitoring watch in 1.2% (*n* = 1/82) of cases.

Overall, 22 caregivers (20.4%) reported that their child had to be resuscitated due to cardiac or respiratory arrest. According to the caregivers, at least 72.7% (*n* = 16/22) of the incidents were linked to a seizure (0–60 min postictal), and 4.6% (*n* = 5) did not know whether the incident was linked to a seizure. Sixteen of the caregivers reported that resuscitation was performed by health care professionals (nurses or doctors). Further information about the events indicated that they happened mostly after a prolonged seizure, infection (*n* = 3), or as a consequence of rescue medication administration (*n* = 4; clonazepam, midazolam). Single cases provided detailed information reporting actual pulselessness. Two cases reported no need for cardiac massage but for artificial respiration.

3.5 | Nightly interventions and sleeping conditions

In addition to nocturnal alarms and critical incidents, other nightly interventions were considered necessary by the caregivers. Overall, one caregiver reported the need for suction during the night, which was necessary on average 6 times per month. Oxygenation was reported by 11.0% (*n* = 9/82) of caregivers an average of 7.2 (median 3; range 1–40) times per month. Nightly interventions concerning personal hygiene (e.g., going to the toilet) were reported by 44.4% (*n* = 48) of caregivers as being necessary 17 times per month on average. Change of body position was reported by 30.6% (*n* = 33) of caregivers on average 45 times per month (median 30; range 2–300) and checking body temperature was reported by 12.3% (*n* = 13) of caregivers to occur on average 30 times per month (median 30; range 1–90). Other interventions (e.g., checking device sensors, percutaneous endoscopic gastrostomy (PEG) button care,

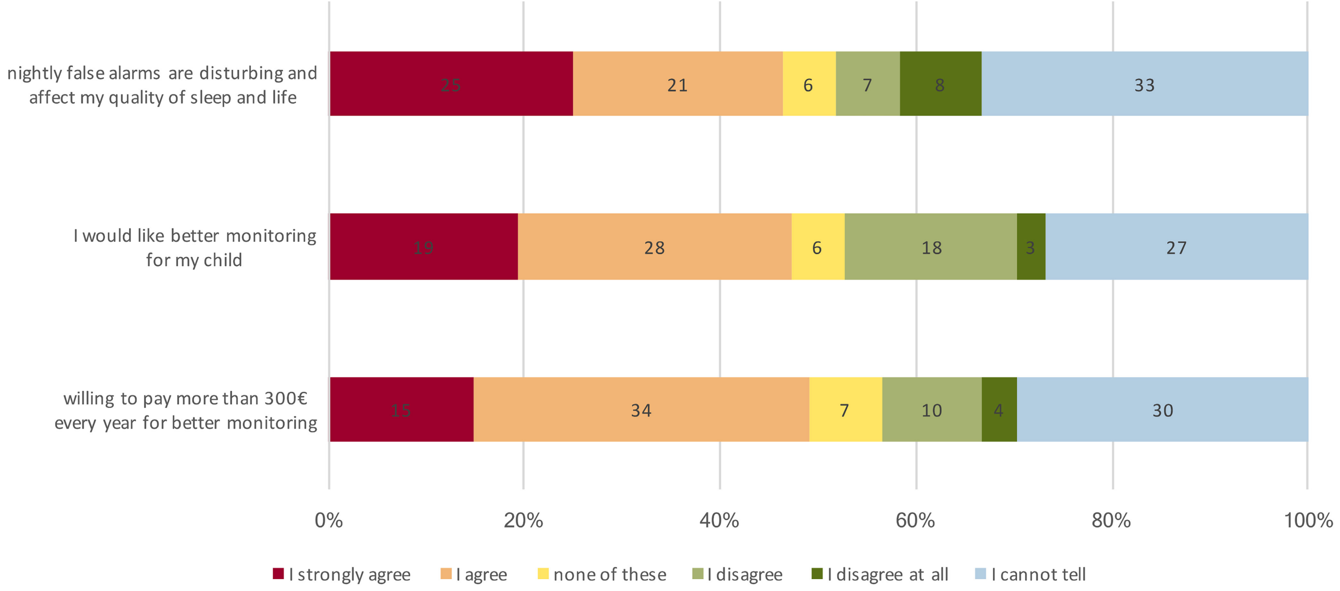

FIGURE 2 Caregivers' opinions regarding various aspects of monitoring children with Dravet syndrome.

changing clothes, and personal surveillance) were also reported.

Caregivers paid attention to the patient's sleeping position and aimed to ensure a supine position in 24% ($n=26$), lateral position in 29.6% ($n=32$), and prone position in 1.9% ($n=2$) of cases. Forty-one percent of caregivers ($n=44$) ensured that the room temperature did not exceed a certain maximum value, which was 19.8°C on average (median 20; range 16–24°C). Furthermore, 42 caregivers (38.9%) reported using special pillows and blankets, such as a flat pillow, no pillow, or a tied blanket or pillow so that it could not be pulled over the head.

3.6 | Knowledge about SUDEP and resuscitation training

In our cohort, 94% ($n=102$) of caregivers were knowledgeable about SUDEP; however, most (51.9%) obtained the information from the internet. Most of the caregivers would have preferred to be informed about SUDEP by a doctor (details provided in Figure 1). Most caregivers would have preferred to receive information at the time of diagnosis of DS; however, most received it several months or years after the diagnosis (details provided in Figure 1). Only 39.8% ($n=43$) of the caregivers reported having been trained in resuscitation, and 52.8% ($n=57$) reported being unsure of what to do in case the child's breathing or heart activity failed. Seventy percent of the caregivers considered resuscitation training as important and stated that it should be repeated once a year (Figure 1).

4 | DISCUSSION

This study provides detailed information and insights into the daily lives of patients with DS and their caregivers, highlighting the use of monitoring devices by the majority of families, the high rate of critical incidents, and the reported need for resuscitation in addition to most caregivers' adequate knowledge of SUDEP. However, the findings indicate the need for further training in resuscitation.

Annual mortality rates exceeding 5% are reported in patients with DS, which is much higher than in other types of epilepsy. SUDEP-related deaths represent 53%–61% of the reported deaths compared with 14.5% in patients with new-onset epilepsy.[11,17] A multi-institutional study involving 91 hospitals reported a mortality rate of 10.1%.[18] Critical incidents were reported by the caregiver in a high proportion of patients, and cardiac or respiratory arrest with the need for resuscitation was reported in more than 20% of patients, of which 72.7% were associated with a seizure (0–60 min postictal). These cases might comply with the term "near-SUDEP," which is often used by authors and is defined as incidents in patients with epilepsy who survive resuscitation for more than 1 h after cardiorespiratory arrest.[19] Absence of surveillance during sleep is associated with an increased risk of SUDEP,[20,21] as evidence suggests that SUDEP is primarily a sleep-related and unwitnessed event.[22] Therefore, all potentially preventive measures should be urgently evaluated. There is evidence that structured education can mitigate the risk of SUDEP. In contrast with other studies, caregivers in our cohort were largely informed about SUDEP; however, they had not received information from their preferred sources. Our findings are in line with other studies that reported that parents of patients with epilepsy desired to know more about SUDEP and that they preferred routine SUDEP counseling soon after diagnosis. Furthermore, the parents felt that the counseling should be delivered face-to-face by the treating pediatric or adult neurologist.[6,23,24] An international consensus panel consisting of experienced physicians and caregivers of patients with DS published by Wirrel et al. declared strong consensus that persons with DS are at significant risk of SUDEP, and families must be made aware of this potential risk at diagnosis (100% physicians and 100% caregivers).[25] Furthermore, 74% of the panel members stated that they would additionally support a family's request for a monitoring device and that these devices should be prescribed.

In our cohort, monitoring devices were used regularly by the majority (76%) of caregivers, and most were used every night. This is in line with a cohort of 76 parents reported by Van Nuland et al.,[26] who queried sleep-related questions. Most parents reported monitoring sleep in general (92%), especially at night (89%), during naps (61%), and only when the patient was ill (50%). The most frequently used methods were co-sleeping (59%), video monitoring (41%), SAMi movement monitor (14%), seizure dog or other animal (13%), and Embrace watch (4%). Compared with our population, they monitored sleep regardless of the child's age.[26] In line with our findings, the use of licensed seizure detection was low, whereas co-sleeping and baby monitors were frequently reported. Co-sleeping is known to lead to sleep deterioration in both patients and caregivers.[27] In contrast, no pulse oximeters were used, whereas these were the preferred and supposedly most effective methods in our cohort.

Villas et al. queried more than 235 caregivers of patients with DS about their most important concerns, and nearly one-half (46%) used a pulse oximeter, 25% used an Emfit movement monitor, 14% used a SAMi sleep activity monitor, and 3%–5% used a Smart Monitor watch or Embrace watch. However, most caregivers (85%) also used audio or video baby monitors, and 82% co-slept, a rate that was considered alarmingly high. Nocturnal seizures were reported by 77% and peaked slightly in the 16- to 25-year age group.[27]

In our cohort, nocturnal seizures were reported in 71.4% of patients in the questionnaire and 52.4% of patients in the prospective diary, which is in line with 53% in the cohort of Van Nuland et al. and 53% in the cohort of Licheni et al.[26] The latter questioned 96 caregivers of individuals with DS to determine their sleep problems. They examined a subgroup of 16 individuals with pulse oximetry during sleep and found that 88% had high oxygen desaturation indices (>3%), without indices of sleep apnea syndrome, which is considered suspicious for respiratory abnormalities.[28] Licheni et al. cautiously suggested that a high oxygen desaturation index and mean pulse rate on pulse oximetry (using a Masimo Radical 7 oximeter placed on the child's big toe) may reflect unrecognized nocturnal seizures.[28]

It is striking that many of the systems used by caregivers to monitor children with epilepsy are not intended as seizure-detection devices. Current approaches are based on detecting rhythmic movements caused by tonic–clonic seizures using sensors that are wrist-worn or on a mattress. None of these methods focuses on detecting apnea, which might be a direct predictor of SUDEP because SUDEP and near-SUDEP events may result directly from peri-ictal respiratory dysfunction with secondary effects on cardiac and cerebral function.[29] Moreover, none of these methods can detect non-convulsive seizures as effectively as they detect convulsive seizures. Therefore, systems that monitor parameters independent from movements during an epileptic seizure should be developed.

In each patient/caregiver cohort mentioned above, nocturnal seizures were an important concern, and most parents monitored their children during sleep. Video and movement monitors were the most frequently reported monitoring methods; however, pulse oximeter use was higher in our cohort than in other cohorts.[26–28]

More detailed data on pulse oxygen monitoring regarding thresholds could provide findings concerning the effective use of this method in epilepsy. Seyal et al. retrospectively analyzed data from 39 patients with 105 generalized convulsions with an epilepsy monitoring unit that used continuous digital pulse oximetry in addition to an event button and video-EEG (electroencephalography). They used a decrease in oxygen saturation (SaO_2) of below 85% as a threshold. Nursing interventions, such as administration of oxygen via a nasal cannula or face mask, oropharyngeal suction, and turning the patient to the lateral recumbent position, were associated with a shorter duration of hypoxemia and shorter duration of postictal generalized EEG suppression. They recognized a significantly shorter seizure duration and convulsion duration, with earlier intervention. The duration of postictal immobility was positively associated with lower SaO_2 nadir and longer duration of oxygen desaturation, which supports the need to monitor patients with epilepsy.[30]

In the consensus panel of physicians and caregivers of patients with DS reported by Wirrel et al., although three-fourths of physicians (74%) state that they would support a family's request for a monitoring device, 68% of physicians did not routinely recommend the use of seizure-monitoring devices for their patients. One-third (31%) of physicians reported that more than one-half of their patients already used a seizure-monitoring device, and two-thirds (67%) of caregivers reported that more than one-half of patients with DS used a seizure-monitoring device. The effectiveness of monitoring devices for seizure detection was rated by physicians ($n=15$) as 6 (interquartile range [IQR] = 5–7) and by caregivers ($n=8$) as 7 (IQR = 6–9) on a scale of 1–9, where 1 was ineffective and 9 was highly effective; however, there was no consensus among physicians or caregivers on the effectiveness of a certain monitoring device over another.[25] One of the biggest concerns of monitoring at night is that false alarms may contribute to lower sleep quality and sleep deprivation, which highlights that the disadvantages of these monitoring methods should be acknowledged critically. Our results indicate that a certain number of false alarms can be tolerated, although they undoubtedly lead to anxiety and sleep deprivation. Almost one-half (46.3%) of the caregivers in our cohort agreed that nightly false alarms were disturbing and affected their quality of sleep and life. Of note, the caregivers had varying definitions of false alarms.

Caregivers worried about both false alarms and the risk of missing a critical incident during the night. Triggered alarms result in the need to react quickly with various interventions. Most (81%) of the caregivers reported that alarms allowed them to avert a critical incident, which required a pain stimulus, oxygen supply, or even artificial respiration. However, it is difficult to predict the effectiveness of a specific method, as monitoring devices used to prevent critical incidents are redundant with those used by caregivers in general; therefore, no specific benefits could be proven. However, most caregivers (41%) are still willing to pay a significant amount of money (~€174) every year for enhanced monitoring, which indicates that more financial support is needed.

Van Nuland et al. stated that children have special needs during the night, like toileting needs or repeated checking every 15 min, which causes sleep disruption in patients and caregivers.[26] Checking and changing body position is a seemingly simple but relevant measure, as there is a statistically significant association between the prone position and SUDEP and an increased risk in those who are immobile during the postictal phase.[31,32] Advising caregivers to turn patients from this position may be an effective measure to reduce the risk of SUDEP.[33]

Limitations of this study include potential bias due to caregiver-reported data. Recruitment inter alia via self-support group (Dravet-Syndrom e.V.) indicates a study population represented by a highly motivated caregiver association. Because there is a strong caregiver concern about higher mortality rates, the number of critical incidents and resuscitation events might be overestimated.

5 | CONCLUSION

Many patients experienced critical incidents requiring acute care, including stimulation by pain, artificial respiration, oxygen supply, or chest compressions. Moreover, one-fifth of patients experienced a cardiac or respiratory arrest and had to be resuscitated, and almost three-fourths of these incidents were associated with a seizure (0–60 min postictal). Knowledge about SUDEP was adequate among our cohort; however, there is a need for resuscitation training. Monitoring devices are frequently used by caregivers. Few of the devices were developed for the detection of seizure activity. Pulse oximeters were used frequently; however, future studies are needed to demonstrate their effectiveness in detecting both convulsive and non-convulsive seizures.

AUTHOR CONTRIBUTIONS

Margarita Maltseva, Susanne Schubert-Bast, Felix Rosenow, Silke Flege, Lara Kay, and Adam Strzelczyk developed the idea for this study. Margarita Maltseva, Susanne Schubert-Bast, Markus Wolff, Sarah von Spiczak, Regina Trollmann, Steffen Syrbe, Susanne Ruf, Tilman Polster, Bernd A. Neubauer, Thomas Mayer, Julia Jacobs, Gerhard Kurlemann, Gerhard Kluger, Kerstin A. Klotz, Matthias Kieslich, Frauke Hornemann, Ulrich Bettendorf, Astrid Bertsche, Thomas Bast, and Adam Strzelczyk participated in the recruitment of patients and data collection. Adam Strzelczyk supervised the study. Margarita Maltseva and Adam Strzelczyk performed the statistical analysis, and created the charts and figures. All authors drafted the article, discussed the results, contributed to the final manuscript, and approved the final manuscript for publication.

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ACKNOWLEDGMENTS

The authors would like to thank all the patients and caregivers who contributed to this survey and the German patient advocacy group Dravet Syndrom e.V. for their help in recruiting participants. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST STATEMENT

M.M. reports grants from GW Pharmaceuticals. F.R. reports personal fees from Angelini Pharma/Arvelle Therapeutics, Eisai, GW Pharmaceuticals/Jazz Pharma, and UCB Pharma and grants from the Detlev-Wrobel-Fonds for Epilepsy Research, the Deutsche

Forschungsgemeinschaft (DFG), the Federal Ministry of Education and Research (BMBF), the LOEWE Programme of the State of Hesse, and the European Union. S.S.B. reports personal fees from Eisai, Desitin Pharma, GW Pharmaceuticals, Zogenix, UCB Pharma, and Marinus Pharma. M.W. reports personal fees from Zogenix, Desitin, and Praxis Precision Medicines. S.S. reports personal fees from Zogenix and fees from Eisai, UCB Pharma, and Nutricia paid to his department. R.T. reports personal fees from Desitin Pharma, Eisai, and Novartis. G.Ku. reports honoraria for speaking engagements from Desitin Arzneimittel, Eisai, UCB Pharma, Takeda, Shire, Zogenix, Neuraxpharm, Stada, and GW Pharmaceuticals. K.A.K. reports personal fees from Eisai, GW Pharmaceuticals, Zogenix, and Neuraxpharm. M.K. reports personal fees from Desitin Pharma, Stada Pharma, and EISAI Pharma. T.P. reports personal fees from Zogenix and Eisai. J.J. reports personal fees from Eisai, Pendopharm, UCB Pharma, and Epilog. Her research is supported by the Natural Sciences and Engineering Research Council (NSERC) and the Alberta Children's Hospital Foundation. A.B. reports grants from UCB Pharma and honoraria for speaking engagements from Biogen, Desitin Arzneimittel, Eisai GmbH, GW Pharmaceuticals, Neuraxpharm, Shire/Takeda GmbH, UCB Pharma, and ViroPharma. T.B. has received support from Bial, Desitin Arzneimittel, Eisai, GW Pharmaceuticals, Neuraxpharm, Nutricia, Shire, Takeda, UCB Pharma, and Zogenix. A.S. reports personal fees and grants from Angelini Pharma, Biocodex, Desitin Arzneimittel, Eisai, GW/Jazz Pharmaceuticals, Marinus Pharma, Precisis, Takeda, UCB Pharma, UNEEG Medical, and Zogenix. None of the other authors report conflicts of interest related to this study.

FUNDING INFORMATION

This study was supported by a LOEWE Grant from the State of Hessen for the Center for Personalized Translational Epilepsy Research (CePTER), Goethe-University Frankfurt, Frankfurt am Main, Germany.

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How to cite this article: Maltseva M, Rosenow F, Schubert-Bast S, Flege S, Wolff M, von Spiczak S, et al. Critical incidents, nocturnal supervision, and caregiver knowledge on SUDEP in patients with Dravet syndrome: A prospective multicenter study in Germany. Epilepsia. 2024;65:115–126. https://doi.org/10.1111/epi.17799

APPENDIX A

Monitoring methods used to notice critical incidents

	Pulse oximeter	ECG monitor	Thermometer	Epi-Care	Baby monitor
Stimulation by pain	14	2	2	3	12
Stimulation chest tapping	4	0	1	0	3
Artificial respiration	7	1	1	2	6
Oxygen supply	15	1	3	1	12
Chest compressions	2	1	0	1	1
Other	5	1	4	1	8