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RESEARCH ARTICLE

Prospective, longitudinal, multicenter study on the provision of information regarding sudden unexpected death in epilepsy to adults with epilepsy

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Abstract

Objective: Despite increased awareness of the serious epilepsy complication sudden unexpected death in epilepsy (SUDEP), a substantial population of people with epilepsy (PWE) remain poorly informed. Physicians indicate concern that SUDEP information may adversely affect patients' health and quality of life. We examined SUDEP awareness and the immediate and long-term effects of providing SUDEP information to PWE.

Methods: Baseline knowledge and behaviors among PWE and behavioral adjustments following the provision of SUDEP information were evaluated in a prospective, multicenter survey using the following validated scales: Neurological Disorders Depression Inventory for Epilepsy for depression symptoms, the EuroQoL five-dimension scale for health-related quality of life (HRQoL), a visual analog scale for overall health, the revised Epilepsy Stigma Scale for perceived stigma, and the Seizure Worry Scale for seizure-related worries. The prospective study collected data through semiquantitative interviews before (baseline), immediately after, and 3 months after the provision of SUDEP information.

Results: In total, 236 participants (mean age = 39.3 years, range = 18–77 years, 51.7% women) were enrolled, and 205 (86.9%) completed long-term, 3-month follow-up. One patient died from SUDEP before follow-up. No worsening symptoms from baseline to 3-month follow-up were observed on any scale. At baseline, 27.5% of participants were aware of SUDEP. More than 85% of participants were satisfied with receiving SUDEP information. Three quarters of participants were not concerned by the information, and >80% of participants recommended the provision of SUDEP information to all PWE. Although most patients reported no behavioral adjustments, 24.8% reported strong behavioral adjustments at 3-month follow-up.

Clinical Trial Registration: This study was registered with the German Clinical Trials Register (DRKS00013954): http://www.drks.de/DRKS00013954

Significance: The provision of SUDEP information has no adverse effects on overall health, HRQoL, depressive symptoms, stigma, or seizure worry among PWE, who appreciate receiving information. SUDEP information provision might improve compliance among PWE and reduce but not eliminate the increased mortality risk.

KEYWORDS

counseling, depression, mortality, quality of life, SUDEP

1 | INTRODUCTION

People with epilepsy (PWE) have a higher risk of premature mortality than the general population,[1] with sudden unexpected death in epilepsy (SUDEP) representing the leading epilepsy-related cause of death.[2] The incidence of SUDEP is highest among patients with refractory epilepsy and those who are epilepsy surgery candidates, reaching as high as one in 100 patient-years.[3] Recent studies indicate that SUDEP can also occur in PWE who are considered responsive to antiseizure medications (ASMs).[4] The underlying mechanism of SUDEP remains unclear; however, generalized tonic–clonic seizures (GTCS) have been identified as the greatest risk factor. Other risk factors include young age at disease onset, long disease duration, high seizure frequency, poor seizure control, and the absence of or inadequate treatment with ASMs.[4,5] Seizure control reduces SUDEP risk.[4,6] Because most SUDEP cases occur at night, observing good sleep hygiene, avoiding prone positions, and nocturnal supervision have been suggested as strategies to lower SUDEP risk.[7,8] Studies show that knowledge of SUDEP remains poor among PWE, despite the majority of patients expressing a desire for more information.[9,10] Although SUDEP counseling is increasingly recommended in national clinical practice guidelines,[11,12] neurologists report anxiety and distress as the most frequent reactions to SUDEP disclosure among PWE.[13] Avoiding distress among PWE is stated as a predominant motivation among practitioners for not providing SUDEP information to epilepsy patients.[13,14]

The aim of this study was to clarify whether the provision of SUDEP information has immediate or long-term adverse effects among PWE. We assessed patients' knowledge of SUDEP and their responses to receiving SUDEP information, including whether they adjusted their behaviors, over a 3-month period. To detect the impacts of SUDEP information provision in areas commonly cited as major burdens among PWE,[15-17] we used validated questionnaires to assess the long-term effects on overall health, health-related quality of life (HRQoL), depressive symptoms, perceived stigma, and seizure worry.

Key Points

- Only 27.5% of participants were aware of SUDEP, and only 9.3% reported being informed of SUDEP by a neurologist.
- More than 85% of patients were satisfied or very satisfied with the provision of SUDEP information.
- No immediate or long-term adverse effects were noted for overall health, quality of life, depressive symptoms, stigma, or seizure worry.
- At 3 months after receipt of SUDEP information, >80% of participants recommended SUDEP information for all epilepsy patients.
- One patient died from SUDEP within 3 months, indicating that provision with information might reduce but not eliminate mortality risk.

2 | MATERIALS AND METHODS

2.1 | Patients

Participants were recruited consecutively at the university hospitals of Frankfurt, Greifswald, and Marburg between 2018 and 2020. Inclusion criteria for participation included a minimum age of 18 years, diagnosis of epilepsy according to the classification recommended by the latest definitions established by the International League Against Epilepsy,[18] and the ability to read and write in German. Patients with cognitive impairments who required a legal guardian were not included. Written informed consent was obtained from all participants. The study was approved by the local ethics committees at each study location. This study received ethics approval and was registered with the German Clinical Trials Register (DRKS00013954; universal trial number: U1111-1208-7283). The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were closely followed.[19]

2.2 | Procedure

We performed a series of three (baseline, post, and 3-month) sequential, questionnaire-based, one-on-one surveys to assess prior SUDEP knowledge and the reactions and emotional distress experienced upon receiving SUDEP information. Figure 1 illustrates the prospective study design. At baseline, we performed a face-to-face survey that incorporated questions regarding the patient's demographic, socioeconomic, and clinical characteristics. Patients were also interviewed regarding their knowledge of premature mortality among PWE, including SUDEP. Patients were asked to state how much information regarding mortality and SUDEP risks should be provided to PWE, at what point during the course of epilepsy information should be provided, and who should be responsible for providing this information. To identify patients with preexisting disease burdens and allow for the detection of change over time, we incorporated the following instruments into the survey: a visual analog scale (VAS) for overall health state, the EuroQoL five-dimension scale (EQ-5D) for HRQoL, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) for symptoms of depression, the Seizure Worry Scale to assess seizure worry, and the revised Epilepsy Stigma Scale (rESS) to assess disease-related stigma.

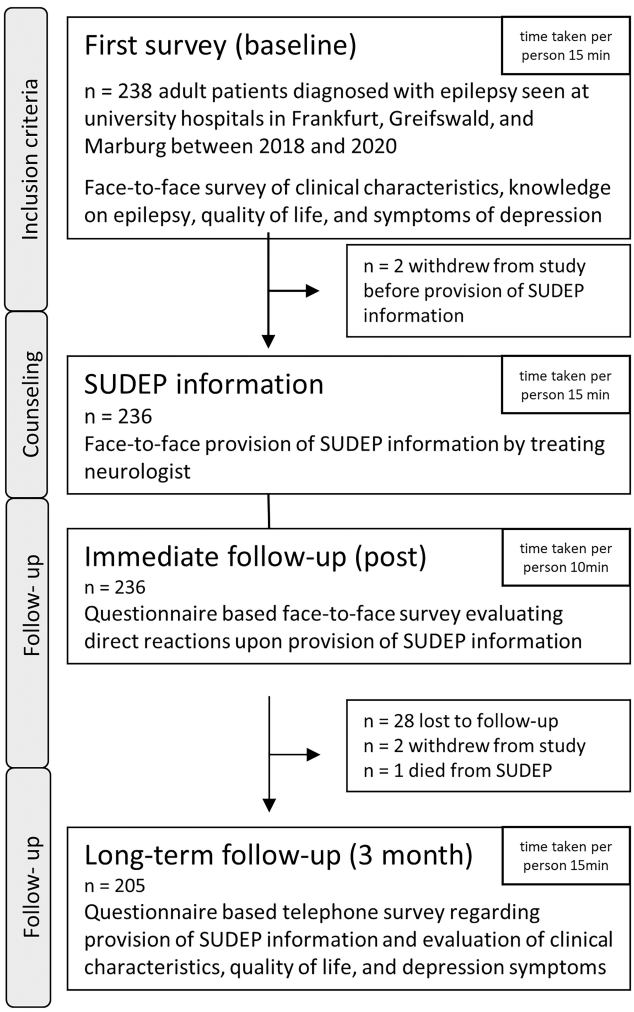

FIGURE 1 Study design, including three data collection points (baseline, post, 3-month follow-up). SUDEP, sudden unexpected death in epilepsy

In line with the clinical practice guidelines established by the American Academy of Neurology (AAN) and the American Epilepsy Society (AES),[20] patients were informed by their treating neurologist that (1) a small risk of SUDEP exists; (2) each year, SUDEP typically affects one in 1000 adults with epilepsy, indicating that 999 in 1000 adults will not be affected by SUDEP; (3) GTCS represent the primary risk factor; and (4) improved seizure control is the most effective protective factor. The neurologists at all centers were trained in providing the SUDEP information according to the AAN/AES guidance.

Immediately following the provision of SUDEP information, we conducted the first follow-up survey (post). Detailed information regarding gained knowledge, an evaluation of the provided information, assessments of increased anxiety, and information on any expected impacts or future behavioral adjustments were obtained.

Participants were interviewed again 3 months after receiving SUDEP information. The follow-up interview was conducted by phone and was supported by a questionnaire that was sent to the participants prior to the interview. To detect any changes during the 3-month interval, we incorporated the following instruments: VAS for overall health state, EQ-5D, NDDI-E, Seizure Worry Scale, and rESS. We reexamined the patients' evaluations of the provided information and the impacts of information on behavioral adjustments.

2.3 | Materials

1. The three-level EQ-5D measures generic quality of life (QoL). The EQ-5D includes a VAS (range = 0–100 units), with 100 representing the best health imaginable and 0 representing the worst health imaginable. The EQ-5D also includes five items assessed using a three-level Likert scale regarding mobility, self-care, usual activities, pain, and anxiety/depression. A single, continuous summary index is derived by transforming the EQ-5D Likert items using a "value set," which provides prespecified weights for each possible combination of answers according to country-specific population preferences. The summary index score ranges from 1 (best imaginable health) to 0 (health status equivalent to death) to negative values (health status worse than death). We derived the summary

index values using both the time-trade-off and VAS methods, using the "eq5d" index calculator for Excel (Microsoft). We report the raw VAS scores alongside the EQ-5D summary index scores.

2. The NDDI-E[21] is an externally validated instrument for assessing depression that was initially developed for a cohort of epilepsy patients. The NDDI-E features six items evaluated with a Likert scale from 1 to 4 to assess the frequency of common depressive symptoms, such as feeling guilty, frustrated, or weary of life. An aggregate value of ≥14 points (range = 6–24 points) is indicative of a depressive mood in the validated German version of the NDDI-E.[22]
3. The rESS measures disease-related stigma[23] using three questions ("I feel that some people are uncomfortable with me," "I feel some people treat me like an inferior person," and "I feel some people would prefer to avoid me"). The rESS assesses each question using a Likert scale from 0 to 3, resulting in a total score of 0–9, with 0 representing no stigma, a score of 1–6 representing mild to moderate stigma, and a score of 7–9 representing high stigma.[24]
4. The Seizure Worry Scale is a two-item instrument that uses a Likert scale from 0 to 3 to assess two questions: (1) "Are you worried about past seizures?" and (2) "Are you worried about future seizures?"[25] A total score ranging from 0 to 6 is obtained, with 0–2 representing no to mild seizure worry and 3–6 reflecting moderate to high seizure worry.

2.4 | Statistics

Descriptive analyses were conducted for sociodemographic and clinical characteristics. Sociodemographic and clinical characteristics were compared among participants at baseline, post, and 3-month follow-up using the chi-squared test and a dependent-samples *t*-test (Table 1). Mood (NDDI-E), HRQoL (EQ-5D), overall health (VAS), stigma (rESS), and seizure worry (Seizure Worry Scale) assessments were compared using the chi-squared test and the Wilcoxon test, with a Bonferroni-corrected *p*-value at alpha level of <.0083 (.05/6) considered significant. Effect sizes were reported as phi for chi-squared test and *r* for Wilcoxon test. Statistical analyses were performed using SPSS Statistics, version 28 (IBM).

TABLE 1 Demographic and clinical characteristics of patients at baseline and 3-month follow-up.

Characteristic	Complete cohort at baseline, *n* = 236	Patients completing 3-month follow-up, *n* = 205	*p*
Age, years[a]	39.3 ± 14.1	39.5 ± 14.2	.882
Age at epilepsy onset, years[a]	22.1 ± 15.6	22.0 ± 15.9	.947
Sex, *n* (%)			
Male	114 (48.3)	101 (49.3)	.840
Female	122 (51.7)	104 (50.7)	
Education ≥ 12 years, *n* (%)	166 (70.3)	152 (74.1)	.374
Epilepsy syndrome, *n* (%)			
Focal	169 (71.6)	150 (73.2)	.884
Generalized	41 (17.4)	32 (15.6)	
Other	26 (11.0)	23 (11.2)	
Treatment with ASM, *n* (%)			
1 ASM	67 (28.4)	59 (28.8)	.966
2 or more ASMs	155 (65.7)	135 (65.9)	
No/not answered	14 (5.9)	11 (5.4)	
GTCS within the past 12 months, *n* (%)			
No GTCS	106 (44.9)	88 (42.9)	.866
One GTCS or more	127 (53.8)	115 (56.1)	
Unknown	3 (1.3)	2 (1.0)	

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

[a]Mean ± SD.

3 | RESULTS

3.1 | Patient cohort

SUDEP information was provided to 236 adults with epilepsy, with a mean age of 39.3 years (SD = 14.1 years, range = 18–77 years, 122 women [51.7%]), for whom interview data were available at baseline and post. Data from the 3-month follow-up were available for 205 participants (86.9%; $n = 28$ were lost to follow-up, $n = 2$ withdrew from the study, and $n = 1$ died of probable SUDEP). Details are presented in Figure 1. No significant differences in sociodemographic or clinical characteristics were identified among participants between baseline/post and 3-month follow-up. Sociodemographic and clinical details are provided in Table 1.

3.2 | Prior knowledge of premature mortality and SUDEP among PWE (baseline)

Before the provision of SUDEP information, 46.2% ($n = 109$) of participants denied awareness of a higher risk for premature mortality among PWE, whereas 52.1% ($n = 123$) were aware of a higher risk for premature mortality. Only 27.5% of participants ($n = 65$) were aware of SUDEP, whereas 71.6% ($n = 169$) indicated that they were unfamiliar with SUDEP. Among those who were aware of SUDEP, the most frequent source for SUDEP information was the Internet ($n = 31/65$, 47.7%). One third of patients (33.8%, $n = 22/65$) aware of SUDEP received information from a neurologist, and 10 participants ($n = 10/65$, 15.4%) knew someone who had suffered from SUDEP (Figure 2).

Three quarters ($n = 183$, 77.5%) of participants indicated an interest in receiving more information regarding premature mortality risk and SUDEP. Most participants preferred that their neurologist ($n = 211$, 89.4%) act as the provider of SUDEP information, and few named the Internet ($n = 14$, 5.9%) or their general practitioner ($n = 12$, 5.1%) as their preferred source of SUDEP information. Most participants indicated that information regarding SUDEP risks should be disclosed as early as possible following an epilepsy diagnosis ($n = 131$, 55.5%) or at a second consultation following diagnosis ($n = 26$, 11.0%). Later in the course of epilepsy ($n = 32$, 13.6%) or only when seizure control fails ($n = 42$, 17.8%) were indicated as the preferred timing for disclosure by one third of participants.

3.3 | Satisfaction with and evaluation of SUDEP information

The majority of participants reported being either very satisfied ($n = 182$, 77.1%) or satisfied ($n = 34$, 14.4%) with receiving information regarding SUDEP, whereas a few patients reported being neither satisfied nor dissatisfied ($n = 18$, 7.6%) or dissatisfied ($n = 2$, .9%). No participants reported being very dissatisfied.

The majority of participants indicated that they were either not at all ($n = 147$, 62.3%) or not ($n = 31$, 13.1%) concerned with learning about SUDEP risks. Slight concern ($n = 32$, 13.5%) in response to receiving SUDEP information was experienced by some participants, whereas responses of rather much ($n = 16$, 6.8%) and very ($n = 10$, 4.2%) concerned were indicated by one in nine patients.

A statement that general SUDEP information should be provided to all epilepsy patients was endorsed by most participants ($n = 198$, 83.9%). A minority of participants ($n = 38$, 16.1%) were opposed to all patients being provided with SUDEP information. The majority of participants ($n = 140$, 59.3%) would have preferred receiving SUDEP information at the time of epilepsy diagnosis. One third ($n = 81$, 34.3%) would not have wanted to receive information earlier. A few participants ($n = 13$, 5.5%) received SUDEP information simultaneously with their first epilepsy diagnosis, and .8% ($n = 2$) did not give any answer.

3.4 | Evaluation of SUDEP information at 3-month follow-up

After 3 months, the majority of participants remained very satisfied ($n = 122$, 59.5%) or satisfied ($n = 54$, 26.3%) with having been provided with SUDEP information (Figure 3A). The number of indifferent ($n = 21$, 10.2%), dissatisfied ($n = 6$, 2.9%), and very dissatisfied ($n = 2$, 1.0%) participants increased slightly, but no significant difference was observed between post and 3-month follow-up ($p = .082$). We did not observe any worsening in the EQ-5D scores for HRQoL, the NDDI-E scores for symptoms of depression, or the rESS scores between baseline and 3-month follow-up, whereas the VAS for overall health ($p = .033$, not significant after Bonferroni correction; $Z = 2.13$; $r = .11$, low effect size) and the Seizure Worry Scale ($p = .006$; $Z = 5.65$; $r = .28$, low effect size) showed improvements (Table 2).

More than half of participants reported feeling not at all ($n = 112$, 54.6%) or not ($n = 35$, 17.1%) concerned with receiving SUDEP information, whereas one in four patients felt slightly ($n = 28$, 13.7%), rather much ($n = 23$, 11.2%), or very ($n = 5$, 2.4%) concerned (Figure 3B). Two participants (1%) did not give any answer. No significant difference was observed between post and 3-month follow-up ($p = .543$) in patients' attitudes toward the provision of SUDEP information (Figure 3C).

In a subanalysis of participants who reported being dissatisfied or very dissatisfied ($n = 10$) with receiving SUDEP information or indicating feeling rather much or

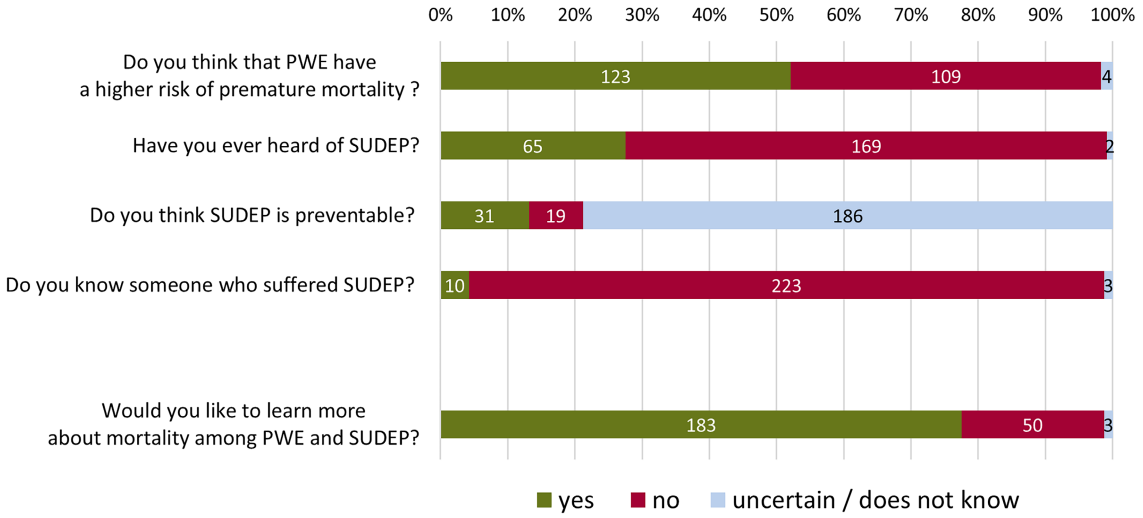

FIGURE 2 Prior knowledge among people with epilepsy (PWE) of mortality risks and sudden unexpected death in epilepsy (SUDEP).

very much concerned ($n = 48$) in response to SUDEP information at any point in our study, we failed to identify any predictors of poor response to SUDEP information, likely due to the small number of dissatisfied or concerned participants. When we evaluated whether dissatisfaction or concern with SUDEP information impacted the recommendation to provide general SUDEP information to patients diagnosed with epilepsy, we observed high levels of approval for the provision of general SUDEP information in both the dissatisfied (dissatisfied and very dissatisfied, $n = 9/10$, 90%) and concerned (concerned and very concerned, 46/48, 87%) subgroups.

The vast majority of participants ($n = 184$, 89.8%) continued to recommend the provision of SUDEP information to all epilepsy patients at 3-month follow-up, with only a few participants ($n = 19$, 9.3%) recommending against providing SUDEP information to all PWE. Two participants (1%) did not give any answer. Compared with the time point immediately after provision of SUDEP information (post), no significant difference was observed ($p = .051$).

3.5 | Behavioral adjustments in response to SUDEP information

Nearly one quarter of participants ($n = 56$, 23.7%) anticipated that they would implement strong or very strong behavioral adjustments as a consequence of having received SUDEP information. Another 30.5% of participants ($n = 72$) planned slight or some adjustments, whereas 45.7% of participants ($n = 108$) denied that receiving SUDEP information would impact their behavior.

At 3-month follow-up, a large proportion of our participants ($n = 89$, 43.4%) reported no behavioral adjustments, whereas slight or some behavioral adjustments were mentioned by nearly one third of participants ($n = 65$, 31.6%), and one quarter ($n = 51$, 24%) reported strong or very strong adjustments.

Within the group reporting behavioral adjustments, the most common adjustment was "knowledge leading to increased self-awareness" ($n = 33/116$, 28.4%), which resulted in adjustments to lifestyle, particularly "reducing stress" ($n = 31/116$, 26.7%). Behavioral adjustments associated with sleep management were reported, such as avoiding the prone position ($n = 11/116$, 9.5%) and increasing the number and regularity of sleeping hours ($n = 11/116$, 9.5%). SUDEP information was cited as a reason for ASM optimization, such as changing medications and increasing adherence ($n = 11/116$, 9.5%). "Informing relatives and caregivers" ($n = 5/116$, 4.3%) and an "increase in anxiety" ($n = 5/116$, 4.3%) were seldom mentioned as behavioral adjustments in response to SUDEP information. Two (1.7%) participants reported that SUDEP information helped during the decision-making process when opting for epilepsy surgery.

4 | DISCUSSION

This study represents the first attempt to evaluate the knowledge, response, adverse effects, and behavioral adjustments among German adult PWE following the provision of SUDEP information using a prospective, longitudinal, multicenter study design. A paucity of research exists regarding the long-term impacts of providing SUDEP information to PWE, and only a few studies have looked at different time points following the provision of SUDEP information to assess these impacts (detailed in Table 3). One study from India[26] primarily focused on ASM adherence;

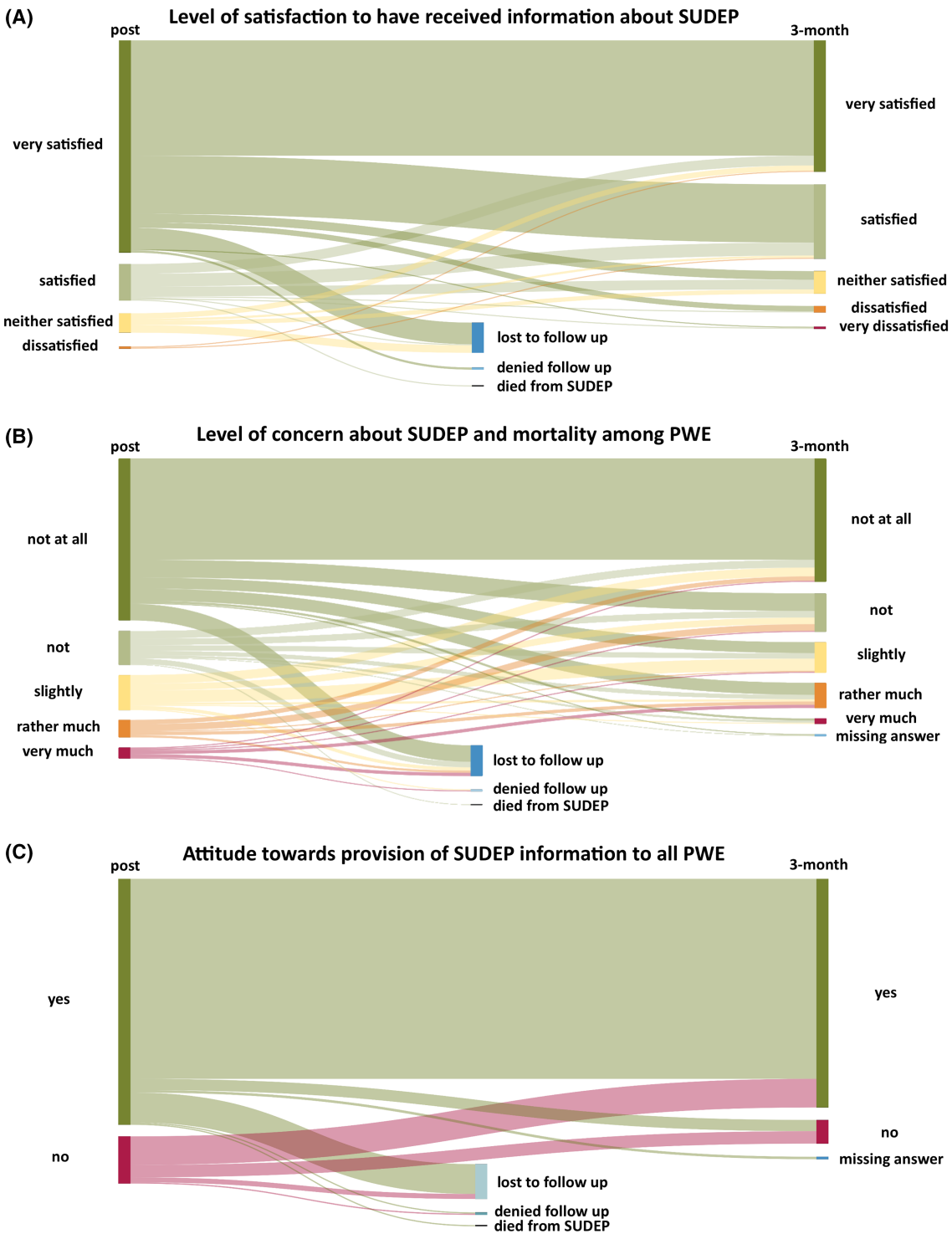

FIGURE 3 Sankey diagrams showing (A) Level of satisfaction with the decision to receive sudden unexpected death in epilepsy (SUDEP) information directly after provision of information (post) and at 3-month follow-up (3-month). (B) Level of concern among people with epilepsy (PWE) about premature mortality and SUDEP information directly at post and 3-month follow-up. (C) Attitude regarding the provision of SUDEP information to all PWE at post and 3-month follow-up.

one study from the UK focused on the use of a checklist to deliver information[27]; and one study from the United States examined the use of an animated teaching video.[28] We observed that prior SUDEP awareness was rather low (28%) among our cohort, which was surprising, because SUDEP and questions regarding the effects of discussing this issue with patients have received substantial attention, such that the number of annual publications has more than doubled in the past 10 years, based on a search for the term "SUDEP" in PubMed. In prior studies, SUDEP awareness

TABLE 2 Changes in VAS for overall health state, EQ-5D for health-related quality of life, NDDI-E for symptoms of depression, Seizure Worry Scale, and rESS between baseline and 3-month follow-up.

	Baseline		3-month follow-up		
Total, $n = 205$	**Mean ± SD**	**% (n)**	**Mean ± SD**	**% (n)**	***p* and effect sizes**
Overall health VAS	66.56 ± 18.93		69.37 ± 19.05		.033[a] $Z = 2.13$; $r = .11$
EQ-5D (TTO)	.875 ± .199		.883 ± .180		.742[a] $Z = .33$; $r = .02$
NDDI-E	12.2 ± 4.0		11.7 ± 4.2		.093[a] $Z = 1.68$; $r = .08$
Subgroup without symptoms of depression, <14		64.4 (132)		71.2 (146)	.49[b] $\varphi = -.03$
Subgroup with symptoms of depression, ≥14		29.8 (61)		28.3 (58)	
Incomplete		5.9 (12)		.5 (1)	
Seizure Worry Scale					
No or mild seizure worry, 0–2		26.8 (55)		40.0 (82)	.006[b] $Z = 5.65$; $r = .28$
Moderate or high worry, 3–6		73.2 (150)		60.0 (123)	
rESS [Jacoby Stigma Scale]					
No stigma, 0		29.4 (60)		38.7 (79)	.130[b] $\varphi = .01$
Mild or moderate stigma, 1–6		64.2 (131)		54.9 (112)	
High stigma, 7–9		6.4 (13)		6.4 (13)	
Incomplete		.5 (1)		.5 (1)	

Abbreviations: EQ-5D, EuroQoL five-dimension scale; NDDI-E, Neurological Disorders Depression Inventory for Epilepsy; rESS, revised Epilepsy Stigma Scale; TTO, time-trade-off; VAS, visual analog scale.

[a]Wilcoxon test.

[b]Chi-squared test, tested against a Bonferroni-corrected alpha level of .0083 (.05/6).

varied widely across PWE, ranging from 6% in an Indian study[26] to 67% in an Internet-based questionnaire study from the United States.[29] However, Kroner et al.[29] showed a difference in awareness between participants who responded to an Internet survey (67%) and those surveyed in clinic (29%). In our study, the Internet (47.7%) was cited as the primary source for SUDEP information, which is in line with previous studies.[29,30]

Anxiety upon provision of SUDEP information was relatively low (25%) among our cohort. In earlier studies examining the effects of receiving SUDEP information, higher anxiety rates were observed, ranging from 36% to >50%. Detailed information regarding the reactions and attitudes expressed by patients and caregivers upon the provision of SUDEP information in past studies is provided in Table 3.[26,28,29,30,31,32,33,34,35,36] These differences could be associated with the provision of SUDEP information in a written format during previous studies, whereas the treating neurologist presented SUDEP information in the current study, providing patients with an opportunity to discuss the topic immediately, which might reduce anxiety. Further research should explore these differences and provide practitioners with recommendations for how best to provide potentially distressing information to PWE. The SUDEP and Seizure Safety Checklist[37] and the AAN/AES practice guideline summary[38] are useful tools for the daily clinical routine. The AAN/AES practice guidelines[38] were referenced when informing our patients about SUDEP.

The maximum SUDEP incidence observed in high-risk patients is one in 100 patient-years.[3] In our cohort of 236 observed patients, over a period of 3 months, we observed a SUDEP rate of one per 60 patient-years. Thus, one SUDEP case in our cohort during the data collection period is in line with the known incidence rate. For us, the experience of SUDEP within our cohort further emphasizes the importance of this subject and demonstrates that providing SUDEP information might reduce the SUDEP risk but does not eliminate this risk.

Our findings contrast with neurologists' concerns,[39] indicating that the provision of SUDEP information did not increase the symptoms of depression or reduce HRQoL among adult PWE. Our data reinforce that patient education should be considered a central component of quality care. Our findings are in line with earlier findings showing that patients request that SUDEP counseling be included

TABLE 3 Attitudes toward the provision of SUDEP information among people with epilepsy in the present survey and prior studies.

Study	Wadle et al. 2023, present study	Greenlaw et al. 2021	Gutiérrez-Viedma et al. 2019	Kaddumukasa et al. 2019	Long et al. 2018
Year of survey	2018–2020	2019–2021[a]	2018	2017/2018	2016/2017
Surveyed participants	$n = 236$	$n = 52$	$n = 32$	$n = 67$	$n = 94$
Country	Germany	United States	Spain	Uganda	United States
Information given to	Patients	Patients ($n = 39$), caregivers ($n = 13$)	Patients	Patients ($n = 48$), caregivers ($n = 19$)	Adult patients ($n = 51$, 54%), caregivers ($n = 43$, 46%)
Patients' age, years	18–77	>13	>18	19–34	>18
Data collection	3 points	2 points	3 points	1 point	1 point
Follow-up period	3 months		3–5 months		
Follow-up rate	205/236 (87%)		32/32 (100%)		
Form of SUDEP information	Verbal	Animated teaching video	Verbal	No information provided	Written
Prior SUDEP awareness	65/236 (28%)	14/28 (50%)	4/32 (12.5%)	27/48 (56%)	0/94 (prior SUDEP awareness was exclusion criterion)
Satisfaction with SUDEP information	216/236 (92%)	25/25 (100%)	27/32 (84.4%)		94/94 (100%)
Anxiety caused by SUDEP information	58/236 (25%)	5/25 (20%)		2/48 (4.2%)	34/94 (36%)
Approval of provision of SUDEP information	198/236 (84%)	24/25 (96%)			89/94 (95%)
Statement that SUDEP information should be provided at point of diagnosis	157/236 (67%)		23/32 (71.9%)	10/48 (21%)	85/94 (90%)

Abbreviation: SUDEP, sudden unexpected death in epilepsy.

[a]Personal communication.

as a component of general epilepsy education and emphasize that adverse effects should not be feared. Even the small group of participants who reported dissatisfaction or concerns just after learning about SUDEP or at 3-month follow-up expressed very high levels of approval (>89% for all subgroups) for the inclusion of SUDEP counseling in standard epilepsy education.

The impacts of SUDEP disclosure on behavior remain controversial. The survey performed in India and reported by Radhakrishnan et al. indicated that SUDEP disclosure resulted in a nonsignificant increase in ASM adherence.[8,26] Data from the UK, analyzed by Tonberg et al.[33] and similar to our findings, did not reveal significant changes in ASM adherence. Among our cohort, 54.1% of participants reported never

Radhakrishnan et al. 2017	Surges et al. 2018	Tonberg et al. 2014	Kroner et al. 2014	Ramachandran Nair et al. 2016	Gayatri et al. 2010
2016/2017	2014	2014	2012/2014	2011	2005/2006[a]
$n = 231$	$n = 372$	$n = 27$	$n = 2003$	$n = 23$	$n = 67$
India	Germany	United Kingdom	United States	Canada	United Kingdom
Patients and caregivers	Adult patients (caregivers when patients <18 years)	Patients	Patients ($n = 1392$, 69.5%), caregivers ($n = 611$, 30.5%)	Patients	Parents
>15	>16	16–30	18–83	18–65	2–17
3 points	1 point	1 point, mean = 18 months (range = 0.5–58 months) after SUDEP information	1 point	1 point, several days after SUDEP information	2 points
6 months					3 month
222/231 (96%)					39/67 (58%)
Verbal and written, to the intervention group ($n = 121$) only	Written, short explanation only: "SUDEP is the very rare sudden unexpected death of people with epilepsy"	Verbal and written	Written, short explanation	Written	Written
13/231 (6%)	46/372 (12.4%)	27/27 (prior SUDEP awareness was inclusion criterion)	Internet-based: 881/1299 (67.8%), clinic-based: 27/93 (29.0%)	10/23 (43%)	23/67 (34%)
		27/27 (100%)			
No changes in Hamilton Anxiety Rating Scale			First heard about SUDEP 426/1055 (40.4%)/aware of SUDEP prior to study 511/908 (56.3%)	12/23 (52%)	34/67 (51%)
		22/27 (81%)		23/23 (100%)	61/67 (91%)
		22/27 (81%)	745/2003 (37%)	13/23 (57%)	45/61 (74%)

forgetting their medication, and one third (34.1%) reported forgetting their medication only once per month, representing a high level of adherence even before SUDEP disclosure. Nonadherence, defined as forgetting ASM at least once per week, was <10% in our cohort at all evaluated time points. Further research remains necessary to clarify the causes for differences in adherence in response to SUDEP information.

The implementation of behavioral adjustments by even a small number of PWE in response to information may well be worth the effort, particularly for SUDEP or other mortality risks. In our cohort, one quarter of participants stated an intent to change their behavior after provision of SUDEP information (23.7%), and a similar number reported (24.8%) enacting strong or very strong

behavioral adjustments at 3-month follow-up, including 12.5% ($n = 11$) who reported increased adherence to ASM or the introduction of new ASM. This finding is in line with the observed decrease in the proportion of patients without ASM, from 4.9% ($n = 10$) at baseline to 2.4% ($n = 5$) at 3-month follow-up. Two (2.3%) patients reported that the information contributed to their decision-making process in favor of epilepsy surgery, similar to the effect reported by the AES and the Epilepsy Foundation Joint Task Force.[40] Further subanalyses of which clinical factors lead to changes were not meaningful due to the limited number of patients with behavioral adjustments.

Risk communication is a complex subject,[41] requiring a solid physician–patient relationship and broad knowledge of SUDEP by the treating neurologist.[39] We conducted our study exclusively at tertiary epilepsy centers, where all involved neurologists are highly educated on SUDEP; therefore, we provided only general guidelines regarding the depth of SUDEP information that should be offered. The current practice guidelines (2017) for epilepsy treatment among adults provided by the German Neurological Society[42] do not discuss the amount of information that should be disclosed to patients to ensure a substantive but not overwhelming consultation; however, this will be changed in the 2023 update to the practice guidelines. The provision of additional written information might further improve understanding of SUDEP among PWE, and the repeated provision of SUDEP information might lead to behavioral adjustments.[27]

We aim to emphasize that the provision of SUDEP information should be a component of a good physician–patient relationship, with the aim of improving shared decision-making. SUDEP information should not be used to force PWE into any decisions, nor should SUDEP information be withheld through a paternalistic approach to caretaking. To prevent bias regarding different levels of knowledge among neurologists involved in this study, all were trained in the use of the AAN/AES guidance, and familiarized with the SUDEP and Seizure Safety Checklist. A semistructured presentation of SUDEP information with the help of brochures or online resources might be an effective method for long-term retention of information. Information should be person-centered and offered to patients multiple times, and knowledge should be queried from time to time. Future research should also look into provision of psychological support that might be provided for those who received SUDEP information. Nocturnal observation or surveillance has increased in recent years[43] and should be included as a factor in further studies of provision of SUDEP information. The recent 2022 National Institute for Health and Care Excellence guidance provides further information on nocturnal monitoring.[44]

5 | LIMITATIONS

Our prospective study had the following limitations. The study was conducted at epilepsy clinics providing tertiary services, which may have resulted in the overrepresentation of poorly controlled or complex epilepsy presentations. Furthermore, we excluded those without the ability to read and write in German, and patients with cognitive impairments who required a legal guardian. The exclusion of those with cognitive impairments due to the practicalities of study design resulted in an exclusion of a high-risk population that was characterized by the novel SUDEP-3 inventory, comprising GTCS frequency, seizure frequency, and intellectual disability.[45] Therefore, the applicability of these data to the general epilepsy population may be limited. However, the large sample size of 236 cases may minimize this shortcoming, and the baseline measurements using validated instruments resulted in findings that resembled previous findings obtained among the general population of PWE. Our cohort did not differ from previous research for measures of depression and HRQoL, and the level of depression observed in our cohort (NDDI-E score of 12.2 ±4.0) was similar to that reported by Brandt et al., who reported a mean NDDI-E score of 12.7 ±4.1.[46] As measured by the EQ-5D, our cohort reflected a moderately impaired HRQoL (.8758± .199). Similar findings (.83–.87) were reported by Zhou et al.[47] and de la Loge et al. when researching the PatientsLikeMe Online Epilepsy Community.[48] Compared with previous findings, perceived stigma was rather high in our cohort, with 70.6% reporting a perception of stigmatization at baseline and 61.3% at 3-month follow-up. In Europe, the frequency of PWE experiencing stigma has been reported to be between 31% and 69%.[23,24,49,50] Furthermore, the satisfaction with provision of SUDEP information was high, which might also reflect the satisfaction with the experience of a longer conversation with a physician in a friendly atmosphere in contrast to everyday medical practice.

6 | CONCLUSIONS

Our findings show that the provision of SUDEP counseling did not result in adverse effects on depression, QoL, stigma, seizure worry, or HRQoL among adult PWE in Germany. Furthermore, the vast majority of PWE indicated a desire for SUDEP information and recommended that SUDEP counseling be included in basic disease management. Further research remains necessary to determine the optimal method for providing SUDEP counseling, and the SUDEP-3 inventory[45] and the SUDEP and Seizure Safety Checklist[37] should be used for designing future studies. Existing teaching material on SUDEP such as videos and

the checklist should be translated into other languages, so they can be tested and modified for local use. These studies should be carried out in cooperation with people with epilepsy and also those bereaved from SUDEP.[51]

AUTHOR CONTRIBUTIONS

Nora-Elena Wadle, Christina Schwab, Carola Seifart, and Adam Strzelczyk developed the idea for this study. Nora-Elena Wadle and Christina Schwab acquired the data. Felix von Podewils, Susanne Knake, and Adam Strzelczyk supervised the study at each study center. Nora-Elena Wadle and Adam Strzelczyk conceived the paper and performed statistical analysis. Nora-Elena Wadle, Laurent M. Willems, and Adam Strzelczyk created the charts and figures. All authors wrote the paper, discussed the results, contributed to the final manuscript, and approved the final manuscript for publication.

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CONFLICT OF INTEREST

F.v.P. reports personal fees from Bial, Eisai, GW Pharmaceuticals, Angelini Pharma, Zogenix, and UCB Pharma. K.M. reports speaker honoraria from Boehringer Ingelheim. F.R. reports personal fees from Angelini Pharma, Eisai, GW Pharmaceuticals/Jazz Pharmaceuticals, Novartis, Roche Pharma, and Zogenix, and grants from Desitin Arzneimittel, the Detlev-Wrobel Fund for Epilepsy Research, the Chaja Foundation Frankfurt, the Deutsche Forschungsgemeinschaft, the LOEWE Program of the State of Hessen, and the European Union. A.S. reports personal fees and grants from Angelini Pharma, Desitin Arzneimittel, Eisai, GW/Jazz Pharmaceuticals, Marinus Pharma, Precisis, Takeda, UCB Pharma/Zogenix, and UNEEG medical. The other authors declare that they have no competing interests. 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.

DATA AVAILABILITY STATEMENT

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

PATIENT CONSENT

All participants provided written informed consent.

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