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Counseling about sudden unexpected death in epilepsy (SUDEP): A global survey of neurologists' opinions

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ABSTRACT

Objective: To investigate the opinions and attitudes of neurologists on the counseling about sudden unexpected death in epilepsy (SUDEP) worldwide.
Methods: Practicing neurologists from around the world were invited to participate in an online survey. On February 18th, 2021, we emailed an invitation including a questionnaire (using Google-forms) to the lead neurologists from 50 countries. The survey anonymously collected the demographic data of the participants and answers to the questions about their opinions and attitudes toward counseling about SUDEP.
Results: In total, 1123 neurologists from 27 countries participated; 41.5% of the respondents reported they discuss the risk of SUDEP with patients and their care-givers only rarely. Specific subgroups of patients who should especially be told about this condition were considered to be those with poor antiseizure medication (ASM) adherence, frequent tonic-clonic seizures, or with drug-resistant epilepsy. The propensity to tell all patients with epilepsy (PWE) about SUDEP was higher among those with epilepsy fellowship. Having an epilepsy fellowship and working in an academic setting were factors associated with a comfortable discussion about SUDEP. There were significant differences between the world regions.
Conclusion: Neurologists often do not discuss SUDEP with patients and their care-givers. While the results of this study may not be representative of practitioners in each country, it seems that there is a severe dissociation between the clinical significance of SUDEP and the amount of attention that is devoted to this matter in daily practice by many neurologists around the world.

1. Introduction

Epilepsies are common chronic neurological disorders affecting about 70 million people worldwide [1]. Patients with epilepsy (PWE) may die unexpectedly without a clear structural or pathological etiology. This condition is called sudden unexpected death in epilepsy (SUDEP), and it accounts for a large proportion of deaths among PWE. Sudden unexpected death in epilepsy incidence rates vary with the study designs, ranging from 0.35 per 1000 person-years in the population-based studies to 9.3 per 1000 person-years in the studies investigating patients with drug-resistant epilepsy [2]. A systematic review and meta-analysis of the incidence rate of sudden death in epilepsy showed that the pooled estimated incidence rate for SUDEP was 1.4 per 1000 patient-years; its incidence rate was 23 times the incidence rate of sudden death in the total population of the same age [3]. There are also data indicating similar incidence rates in children [4]. As many PWE are between 20 and 40 years of age when dying suddenly, SUDEP leads to a considerable loss of potential life-years [5–7]. The most important risk factors for SUDEP are nocturnal and tonic-clonic seizures; therefore, supervision and effective seizure control are the key elements for SUDEP prevention [1,5].

While SUDEP is a universal phenomenon, there are global variations (e.g., resources, challenges in the diagnosis of SUDEP, etc.) in the approach to this condition by healthcare professionals around the world. In a global survey, the authors scrutinized the investigative practices into sudden death in epilepsy [8]. Only 13% of the participants had a high level of confidence in the accuracy of the cause of death in PWE. Sixty-six percent of the responders were not aware of published or unpublished research or audits on sudden death in epilepsy in their country in the last decade [8].

Knowledge and education of healthcare professionals, PWE, and their care-givers about SUDEP is very important to deliver and apply appropriate preventive measures; however, this is still widely a neglected mission [5]. It is important to empower neurologists to provide better informed person-centered advice on SUDEP to PWE in order to help reduce their risk of premature death [9]. However, the first step toward such a goal is to be informed about attitudes and opinions of the neurologists toward counseling about SUDEP in different parts of the world.

The purpose of this international survey was to inquire about the opinions and attitudes of physicians (pediatric and adult neurologists and epileptologists) on the issue of counseling about SUDEP for PWE. This information may provide useful guidance for authorities involved in education to contemplate well-designed and goal-oriented educational strategies to empower neurologists with appropriate knowledge and improve their attitudes in providing such a counseling for patients and their care-givers.

2. Materials and methods

Practicing neurologists (pediatric and adult) from around the world were invited to participate in an online survey. On February 18th, 2021, we (AAP, ET, and FB) emailed an invitation including a link to a free online tool with a (Google-forms) questionnaire to lead neurologists (based on the number of their publications in epilepsy) from 50 countries around the world. The invited countries were from all the continents and the invitation was based on the number of their publications in epilepsy and also our previous experiences with the colleagues in those nations. We asked the lead neurologists to share the survey with as many of their colleagues as possible in their corresponding nations. A reminder was sent every week. The study was closed on June 1st, 2021. Only nations with 20 or more participants were included in the analysis (except for the countries with less than 5 million population, for which the limit was 15 participants). The survey anonymously collected data about the participants [demographics, years in practice, discipline [adult neurology, pediatric neurology, fellowship in epilepsy (in training or trained)], country, work setting (university, hospital or private clinic) and work location (urban, rural)], and answers to the questions about their opinions/attitudes toward

counseling about SUDEP (Appendix 1). The survey was designed and developed as follows: we conducted a literature review; we developed the items; we conducted an expert validation (to assess how clear and relevant the items were with regard to the construct of interest). Residents were not included. There was no compensation for participation. The survey was conducted in English and German languages.

We descriptively summarized the demographic variables and responses from the whole cohort. Logistic regression analyses were performed to explore the associations between the baseline characteristics of the survey participants and their responses to the selected questions ('Should all patients with epilepsy be told about SUDEP?', 'Are you comfortable with discussing SUDEP with your patients?', and 'Do you have concerns about patients' emotional reaction upon discussion of SUDEP?'); baseline predictors included sex, years in practice (< or ≥10 years), their highest training (adult neurologist, pediatric neurologist, epilepsy fellowship), their work setting (academic or not academic), location of their work (urban or rural), the number of PWE seen per month (<5, 5–19, 20–49, 50–100, >100), and the number of cases of SUDEP they have encountered during their practice (1–5, 6–10, >10). Odds ratios (OR) and 95% confidence intervals (CI) were estimated. Results were considered significant for p values <0.05 (two-sided). Data analyses were performed using STATA/IC 13.1 (StataCorp LP, College Station, TX, USA).

2.1. Standard protocol approvals and consents

The Shiraz University of Medical Sciences Institutional Review Board approved this study (24686). The ethical institutional review board at each participating center approved the study when it was required. Participation was voluntarily and anonymity was reinforced and assured.

2.2. Data availability statement

The data are confidential and will not be shared.

3. Results

In total, 1123 respondents from all over the world (27 countries) took part in the study; their demographic and general characteristics are reported in Table 1. It is not possible to calculate a response rate, as we do not know how many people received the survey. The median age of the respondents was 42 years, and slightly more of the participants were women (55.3%). The majority of respondents were active as adult neurologists (65.5%), had a clinical experience of at least 10 years (64.3%), and came from urban (94.9%) and non-academic (65.8%) settings. Most participants (58%) reported to visit 5–49 PWE per month. Answers to each survey question are summarized in Table 2.

Approximately, half of the participants (49.2%) had encountered one to five cases of SUDEP, and only 7% had encountered six or more cases during their practice. Many respondents (41.5%) reported to discuss the risk of SUDEP with patients and their care-givers only rarely or only with some patients (by 29.5%). The majority of the participants (72.4%) favored to verbally discuss SUDEP with patients and care-givers, rather than to provide a written "epilepsy information pack" to patients. Many respondents (49.2%) believed that the best time to discussing SUDEP with the patients and care-givers was after having established a trusting relationship with them. In children (6–11 years of age), most respondents reported to discuss SUDEP only with the care-givers (67.0%). Conversely, in adolescents (12–18 years of age) and adults, most participants discussed this topic with both the patients and their care-givers and family members. The most frequent reasons to counsel on SUDEP were to prevent it from happening or to prevent the legal consequences should it happen. In response to the question "Should all patients with epilepsy be told about sudden unexpected death in epilepsy?", 384 people (34%) answered "Yes". There were significant differences between the world regions [Africa: 13/70 (18.6%); Middle-East: 71/272 (26.1%); Asia: 15/49 (30.6%); Europe: 96/311 (30.9%); Former Union of Soviet Socialist Republics: 47/130 (36.2%); South America: 99/197 (50.3%); North America: 43/68 (63.2%); 26 missing values] (Table 3). In general, specific subgroups of patients who should especially be told about this condition were considered to be those with poor drug adherence, frequent tonic-clonic seizures, or with drug-resistant epilepsy. The main reasons for refraining from discussing about

Table 1
Baseline characteristics of participants.

Number of participants	1123
Age, years	
median (IQR)	42 (36–53)
Sex	
Male	497 (44.7%)
Female	616 (55.3%)
Highest training	
Adult neurologist	736 (65.5%)
Pediatric neurologist	218 (19.4%)
Epilepsy fellowship	169 (15.1%)
Years in practice	
<10 years	392 (35.7%)
≥10 years	707 (64.3%)
World regions*	
Europe (Austria, France, Germany, Italy, Sweden)	313 (28.3%)
Africa (Egypt, Morocco, South Africa, Tunisia)	70 (6.3%)
Asia (India, Taiwan)	50 (4.5%)
Middle East (Iran, Iraq, Kuwait, Oman, Qatar, UAE)	273 (24.7%)
North America (USA)	68 (6.2%)
South America (Argentina, Brazil, Colombia, Venezuela)	201 (18.2%)
Former Union of Soviet Socialist Republics (Armenia, Georgia, Kazakhstan, Kyrgyzstan, Russia)	130 (11.8%)
Work setting	
Not academic	738 (65.8%)
Academic	383 (34.2%)
Location of work	
Urban	1063 (94.9%)
Rural	57 (5.1%)
Patients with epilepsy seen per month	
<5	103 (9.2%)
5–19	332 (29.7%)
20–49	316 (28.3%)
50–100	257 (23.0%)
More than 100	110 (9.8%)

* 23 countries with no or few responses: China, Japan, South Korea, Indonesia, Malaysia, Thailand, Saudi Arabia, Turkey, Spain, UK, Ireland, Switzerland, Belgium, Denmark, Norway, Ukraine, Canada, Mexico, Chile, Ecuador, Nigeria, Australia, New Zealand.

Table 2
Answers to the survey questions.

Cases of SUDEP encountered	
None	489 (43.8%)
1–5	550 (49.2%)
6–10	50 (4.5%)
>10 cases	28 (2.5%)
With what proportion of your patients, do you discuss the risk of SUDEP?	
Never	149 (13.3%)
Rarely (1–9%)	465 (41.5%)
Some (10–49%)	330 (29.5%)
Most (50–90%)	134 (12.0%)
All (>90%)	42 (3.7%)
What is the best strategy to discussing SUDEP with patients/care-givers?	
Providing a written "epilepsy information pack" to patients including some information on SUDEP	307 (27.6%)
To verbally discussing SUDEP with patients/care-givers	804 (72.4%)
When is the best time to discussing SUDEP with the patients/care-givers?	
At the first visit	92 (8.2%)
After I have established a trusting relationship with the patient	549 (49.2%)
If the patient has poor drug adherence or bad life styles	342 (30.6%)
If the patient is a candidate for epilepsy surgery	29 (2.6%)
Only when they ask for the information	105 (9.4%)
In children (6–11 years) with no intellectual disability, with whom you discuss SUDEP?	
Only the patient	12 (1.1%)
Only the caregivers	716 (67.0%)
Both the patient and their care-givers	219 (20.5%)
It is not necessary to discuss SUDEP in this age group	122 (11.4%)
In adolescents (12–18 years) with no intellectual disability, with whom you discuss SUDEP?	
Only the patient	19 (1.7%)
Only the caregivers	276 (25.3%)
Both the patient and their care-givers	715 (65.5%)
It is not necessary to discuss SUDEP in this age group	82 (7.5%)
In adult patients with no intellectual disability, with whom you discuss SUDEP?	
Only the patient	208 (19.3%)
Only the family members	109 (10.1%)
Both the patient and their family members	697 (64.7%)
It is not necessary to discuss SUDEP in this age group	64 (5.9%)
Why do you counsel on SUDEP?	
To prevent it from happening	365 (33.6%)
To prevent the legal consequences should it happen	84 (7.7%)
Both	548 (50.4%)
Others	90 (8.3%)
[a]**If not all patients with epilepsy should be told about SUDEP, which patients should be told about it?**	
New onset patients	57 (5.1%)
Drug-resistant patients	396 (35.3%)
Patients with frequent tonic–clonic seizures	394 (35.1%)
Patients on antiepileptic drug polypharmacy	282 (25.1%)
Patients with poor drug adherence	407 (36.2%)
In candidates for epilepsy surgery	155 (13.8%)
Adults	146 (13.0%)
Children	67 (6.0%)
Only those who ask for the information	150 (13.4%)
[a]**Why not all patients with epilepsy should be told about SUDEP?**	
I do not have sufficient time to discuss SUDEP during an office visit	53 (4.7%)
If the patient does not actively seek the information on SUDEP, we should not start the conversation	99 (8.82%)
It causes undue anxiety for patients and their care-givers	478 (42.6%)
It is a rare phenomenon in people with well-controlled seizures	377 (33.6%)
The knowledge of mortality does not significantly alter the management process	145 (12.9%)
There is no proven way to prevent SUDEP	153 (13.6%)

[a] More individual answers were allowed.

SUDEP in all patients were that it may cause undue anxiety for patients and their care-givers and that it is a rare phenomenon in people with well-controlled seizures.

Associations between the baseline characteristics of the survey participants and their responses to the selected questions are reported in Table 4. The propensity to tell all PWE about SUDEP was higher among women and those with epilepsy fellowship. The propensity to tell all PWE about SUDEP increased according to the number of SUDEP cases encountered during the practice years of the participants. Having an epilepsy fellowship and working in an academic setting were factors associated with physicians feeling comfortable discussing SUDEP with patients and their care-

Table 3
The world regions.

Should all patients with epilepsy be told about SUDEP?		
The world region[a]	***OR (95% CI)***	***p value***
Africa	0.51 (0.27–0.98)	**0.042**
Asia	0.99 (0.51–1.90)	0.971
The Middle-East	0.79 (0.55–1.14)	0.205
North America	3.85 (2.23–6.67)	**< 0.001**
South America	2.26 (1.56–3.27)	**< 0.001**
Former Union of Soviet Socialist Republics	1.27 (0.82–1.95)	0.280

The significant *p* values are in bold. Odds ratio (OR); confidence interval (CI).
[a] Reference is Europe.

givers/family members. The degree of comfort in discussing this topic with patients was inversely associated with a female sex and increased according to the number of SUDEP cases encountered. Females were more strongly of the view that SUDEP should be discussed with all patients, but they were less comfortable doing so. Having an epilepsy fellowship and having seen more than 10 SUDEP cases were associated with lower concerns about patients' emotional reactions upon discussion of SUDEP.

4. Discussion

In this global survey of physicians' opinions on the issue of counseling patients and their care-givers about SUDEP, we observed that many respondents reported to discuss the risk of SUDEP with patients and their care-givers only rarely. Furthermore, the best time to discussing SUDEP with the patients and care-givers was reported to be after having established a trusting relationship with them by many. Most respondents reported to discuss SUDEP only with the care-givers in pediatric patients and with both the patients and their care-givers in adolescents and adults. Many respondents believed that patients and their care-givers should be told about SUDEP when they have poor drug adherence, frequent tonic-clonic seizures, or drug-resistant epilepsy, to prevent SUDEP from happening. Otherwise, they believed that one should refrain from discussing about SUDEP to prevent causing undue anxiety for patients and their care-givers. There were significant differences between the world regions.

It is controversial whether all PWE and their care-givers should be informed and counseled about SUDEP [10,11]. While some experts believe that all PWE should be counseled about SUDEP as part of an essential education about their disorder [10–12], in view of the very low risk in individuals with well-controlled epilepsy, others feel that discussing SUDEP in such cases is not only inappropriate, but in certain situations may be harmful [11,13]. This controversy was evident among the neurologists in different places in the world in the current study. However, experts in the field believe that patients with poor drug adherence, those with frequent tonic-clonic seizures, and people with drug-resistant epilepsy (i.e., high risk patients for SUDEP) should definitely receive such information and counseling about the risks of SUDEP [11]. Most of the participants in the current study had similar opinions as above, but opposite to that, more than two-fifths of the participants reported to discuss the risk of SUDEP with their patients only rarely. This is in spite of the observations that non-adherence rates to antiseizure medications (ASMs) reported to be 25–66% in previous studies [14], some patients suffer from frequent tonic-clonic seizures, and about one-fourth of PWE have drug-resistant epileptic seizures [15]. It seems that there is a severe dissociation between the clinical significance of SUDEP on one side and the

Table 4
Logistic regression analyses of the whole participants.

Should all patients with epilepsy be told about SUDEP?		
Variable	***OR (95% CI)***	***p value***
Female	1.43 (1.10–1.88)	**0.008**
Years in practice ≥ 10	0.73 (0.55–0.96)	**0.026**
[a]Highest training		
Pediatric neurologist	1.12 (0.80–1.58)	0.515
Epilepsy fellowship	1.57 (1.07–2.30)	**0.02**
Academic setting	1.21 (0.91–1.59)	0.186
Rural location of work	1.20 (0.65–2.21)	0.557
[b]Patients with epilepsy seen per month		
5–19	1.02 (0.63–1.65)	0.943
20–49	1.03 (0.62–1.68)	0.922
50–100	0.79 (0.46–1.34)	0.382
More than 100	0.71 (0.38–1.34)	0.289
[c]Cases of SUDEP encountered		
1 to 5	1.40 (1.04–1.87)	**0.027**
6 to 10	2.27 (1.18–4.36)	**0.014**
>10 cases	4.10 (1.74–9.66)	**0.001**
Are you comfortable with discussing SUDEP with your patients?		
Variable	***OR (95% CI)***	***P value***
Female	0.50 (0.38–0.65)	**< 0.001**
Years in practice ≥ 10	0.83 (0.63–1.11)	0.214
[a]Highest training		
Pediatric neurologist	0.71 (0.50–1.00)	0.051
Epilepsy fellow	2.17 (1.43–3.28)	**< 0.001**
Academic setting	1.37 (1.04–1.82)	**0.027**
Rural area of work	0.78 (0.42.1.46)	0.434
[b]Patients with epilepsy seen per month		
5–19	1.00 (0.61–1.63)	0.995
20–49	1.28 (0.78–2.11)	0.336
50–100	1.96 (1.15–3.34)	**0.014**
More than 100	1.45 (0.77–2.72)	0.25
[c]Cases of SUDEP encountered		
1 to 5	2.19 (1.64–2.92)	**< 0.001**
6 to 10	2.06 (1.05–4.03)	**0.035**
>10 cases	4.02 (1.49–10.86)	**0.006**
Do you have concerns about patients' emotional reaction upon discussion of SUDEP?		
Variable	***OR (95% CI)***	***P value***
Female	1.36 (0.96–1.92)	0.084
Years in practice ≥ 10	1.06 (0.73–1.53)	0.773
[a]Highest training		
Pediatric neurologist	0.74 (0.47–1.16)	0.187
Epilepsy fellow	0.50 (0.32–0.81)	**0.004**
Academic setting	0.96 (0.67–1.39)	0.83
Rural location of work	0.70 (0.34–1.45)	0.34
[b]Patients with epilepsy seen per month		
5–19	0.62 (0.32–1.21)	0.158
20–49	1.11 (0.54–2.26)	0.781
50–100	1.04 (0.49–2.20)	0.914
More than 100	0.72 (0.31–1.64)	0.43
[c]Cases of SUDEP encountered		
1–5	0.97 (0.66–1.43)	0.878
6–10	1.70 (0.62–4.67)	0.307
>10 cases	0.39 (0.16–0.99)	**0.048**

The significant *p* values are in bold. Odds ratio (OR); confidence interval (CI).
[a] Reference is adult neurology.
[b] Reference is less than 5.
[c] Reference is none.

opinions of healthcare professionals on the other and the amount of attention that is devoted to this matter in daily practice by many healthcare professionals around the world.

Receiving a diagnosis of epilepsy by itself can be associated with undue anxiety in PWE and their care-givers [16]. Therefore, it seems appropriate to discuss the risk of SUDEP only when the treating physician has established a trusting relationship with them. Of course, this discussion should not be delayed for long in high risk patients. On the other hand, some of the authors of the current study favored discussing the SUDEP risk at the time of the first diagnosis or at early follow-up visits for several reasons; first, SUDEP can occur even early in the disease course or in "benign" epilepsies, as previously reported [17,18]. Second, a survey among patients and care-givers revealed that more than one-third desired to be informed about SUDEP at the time of the diagnosis and 50% of the participants preferred the follow-up visits [19]. Third, it might be difficult to estimate whether a patient is at high risk or not early after the diagnosis, given the fact that even tonic-clonic seizures remain unreported or unobserved, especially when they occur during night [20]. Finally, many persons with newly diagnosed epilepsy may come across SUDEP when they search the web for information on epilepsy. Physicians who do not bring up the topic may jeopardize the patients' trust. After all, patient empowerment is the most important step to prevent SUDEP from happening. While most respondents in the current study favored to verbally discuss SUDEP with patients and care-givers, rather than to provide a written "epilepsy information pack" to patients, some experts prefer the latter approach [11]. In a previous descriptive qualitative study of 23 PWE, there was consensus among all the participants that all PWE should be informed about SUDEP. Many participants believed that the best time to be told about SUDEP was at the diagnosis. The majority of participants suggested that the discussion about SUDEP should take place face to face (i.e., verbal discussion), followed by written information pack to take home [21]. The advantages and disadvantages of either approaches (first visit *vs.* follow-up visits and verbal *vs.* written Information) should be investigated in future studies.

The most frequent reasons for the participants in the current study to counsel on SUDEP were to prevent it from happening or to prevent the legal consequences should it happen. The underlying mechanisms of SUDEP remain unclear; however, tonic-clonic seizures have been identified as the greatest risk factor [2,22]. Seizure control reduces the risk of SUDEP [21]; so far, there are no other prevention strategies with proven efficacy [10]. Therefore, any measure that helps with seizure control may help reduce the risk of SUDEP. These measures may include advice on good drug-adherence in all PWE and timely epilepsy surgery in people with drug-resistant epilepsy, among others. One previous study showed that brain surgery is associated with a reduction in mortality rate in drug-resistant epilepsy, both when seizures are abolished and when it results in a significant palliation of tonic-clonic seizure frequency [22]. With regard to legal implications, duty of care dictates an open and frank discussion with those seeking the information and healthcare professionals are advised to document the discussion around SUDEP [13].

Knowledge of the variables that are associated with the opinions and attitudes of healthcare professionals may provide useful guidance for authorities involved in education to contemplate well-designed and goal-oriented educational strategies to empower neurologists with appropriate knowledge and improve their attitudes in providing appropriate counseling on SUDEP for PWE and their care-givers. For example, we observed that having an epilepsy fellowship and having seen more than 10 SUDEP cases were associated with lower concerns about patients' emotional reactions upon discussion of SUDEP. It seems that physicians with more training and also more experienced neurologists were less likely to encounter negative reactions, suggesting that there may be ways to frame the discussion that minimizes the patient/care-giver distress [23]. Among the variables that had associations with the opinions and attitudes of the participants in the current study, having a better education (i.e., epilepsy fellowship) was consistently associated with more favorable attitudes (e.g., discussion with more patients, having a comfortable discussion about SUDEP with patients and their care-givers, and having lower concerns about patients' emotional reactions upon such a discussion); and, it is a modifiable variable (variables such as gender, work setting, etc. are not modifiable). A recent survey of SUDEP education among the U.S. and international neurology trainees showed that approximately, half of the U.S. (49%) and international (54%) trainees rarely or never counseled patients on SUDEP. Less than half of the U.S. (44%) and international (41%) trainees were educated about SUDEP [24]. Ideally, efforts to increase SUDEP counseling should especially focus on junior clinicians [25]. In our survey, there were striking regional differences in the attitudes to counsel on SUDEP, with lowest rates in Africa (18.6%) and the highest rate in North America (63.2%). The reasons for this more than three-fold difference should be further investigated in future studies. The training and education, ethical, psychosocial and spiritual attitudes, resources, as well as legal frameworks in the respective healthcare systems might have played roles in this significant difference between the world regions. For example, a previous study showed significant disparities in the investigation into the cause of sudden death in epilepsy across countries [8].

5. Limitations

This study has some limitations. The actual representativeness of the participants for each country is not known and it is possible that physicians with a positive attitude about counseling on SUDEP were more likely to participate in such a survey. Socio-cultural issues may also add to the risk of bias in this study. Furthermore, the physicians that have been included do not reflect either the distribution of the world's population or the neurologists/epileptologists. For example, in many parts of the world management of epilepsy is led by other healthcare professions (not neurologists). Furthermore, (while invited) lack of response from some countries (e.g., the UK, Australia, Japan and Denmark) with a significant history of SUDEP research (and publications) was an important limitation. In addition, the structure and language of the survey might have influenced the results. If re-visited in a few years, this research should be done considering and improving these limitations.

6. Conclusion

Similar to other surveys [10,22,24], albeit with a significantly higher number and a larger geographical distribution of the participants, we observed that neurologists often do not discuss SUDEP with PWE and their care-givers. Furthermore, we observed a severe dissociation between the clinical significance of SUDEP on one side and the opinions of neurologists on the other and the amount of attention that is devoted to this matter in daily practice by many neurologists around the world. There were significant geographic variations in the attitudes of the physicians to counsel patients on SUDEP, with the lowest rates in Africa and the highest in North America. It is necessary that educational policy makers incorporate better educational materials in the curriculum of all medical education programs (at the undergraduate and postgraduate levels, where appropriate), considering the significance of SUDEP. Improving the self-esteem of healthcare professionals by training appropriate communication skills should be a cornerstone of such

educational programs. It may be beneficial to incorporating local expertise on legislation, culture, and social issues in the development of educational programs that are tailored to the need of the specific target regions. Finally, it would be very helpful if scientific bodies, such as the International League Against Epilepsy (ILAE), the International Bureau for Epilepsy (IBE), the World Federation of Neurology (WFN), and others, develop and share resources digitally accessible in multiple languages for patients and healthcare professionals around the world.

Authors' contributions

Ali A. Asadi-Pooya, Eugen Trinka, Francesco Brigo, and Simona Lattanzi: study design, data collection, statistical analyses, and manuscript preparation.

Others: data collection and manuscript preparation.

The authors conducted the statistical analyses.

Conflict of interest

Ali A. Asadi-Pooya: Honoraria from Cobel Daruo, Tekaje, Sanofi, Actoverco, and RaymandRad; Royalty: Oxford University Press (Book publication); Grant from the National Institute for Medical Research Development.

Simona Lattanzi has received speaker's or consultancy fees from Eisai, UCB Pharma, and GW Pharmaceuticals and has served on the advisory board for GW Pharmaceuticals.

Vicente Villanueva has participated in advisory boards or pharmaceutical industry-sponsored symposia by Arvelle, BIAL, EISAI, GW pharma, Newbridge, Novartis, UCB.

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Appendix A. Supplementary data

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References

[1] Singh A, Trevick S. The Epidemiology of Global Epilepsy. Neurol Clin 2016;34:837–47.
[2] Asadi-Pooya AA, Sperling MR. Clinical features of sudden unexpected death in epilepsy. J Clin Neurophysiol 2009;26:297–301.
[3] Saetre E, Abdelnoor M. Incidence rate of sudden death in epilepsy: A systematic review and meta-analysis. Epilepsy Behav 2018;86:193–9.
[4] Keller AE, Whitney R, Li SA, Pollanen MS, Donner EJ. Incidence of sudden unexpected death in epilepsy in children is similar to adults. Neurology 2018;91:e107–11.
[5] Pensel MC, Nass RD, Taubøll E, Aurlien D, Surges R. Prevention of sudden unexpected death in epilepsy: current status and future perspectives. Expert Rev Neurother 2020;20:497–508.
[6] Granbichler CA, Zimmermann G, Oberaigner W, Kuchukhidze G, Ndayisaba J-P, Taylor A, et al. Potential years lost and life expectancy in adults with newly diagnosed epilepsy. Epilepsia 2017;58:1939–45.
[7] Thurman DJ, Hesdorffer DC, French JA. Sudden unexpected death in epilepsy: assessing the public health burden. Epilepsia 2014;55:1479–85.
[8] Kinney MO, McCluskey G, Friedman D, Walker MC, Sander JW, Shankar R. Investigative practice into sudden death in epilepsy: A global survey. Acta Neurol Scand 2019;139:476–82.
[9] Shankar R, Donner EJ, McLean B, Nashef L, Tomson T. Sudden unexpected death in epilepsy (SUDEP): what every neurologist should know. Epileptic Disord 2017;19:1–9.
[10] Strzelczyk A, Zschebek G, Bauer S, Baumgartner C, Grond M, Hermsen A, et al. Predictors of and attitudes toward counseling about SUDEP and other epilepsy risk factors among Austrian, German, and Swiss neurologists and neuropediatricians. Epilepsia 2016;57:612–20.
[11] Brodie MJ, Holmes GL. Should all patients be told about sudden unexpected death in epilepsy (SUDEP)? Pros and Cons. Epilepsia 2008;49(Suppl 9):99–101.
[12] National Institute for Health and Care Excellence (NICE). The Epilepsies: The Diagnosis and Management. NICE clinical guideline [CG137], Published: 11 January 2012, Last updated: 12 May 2021, http://guidance. nice.org.uk/cg137. Accessed September 4, 2021.
[13] Beran RG, Weber S, Sungaran R, Venn N, Hung A. Review of the legal obligations of the doctor to discuss Sudden Unexplained Death in Epilepsy (SUDEP)–a cohort controlled comparative cross-matched study in an outpatient epilepsy clinic. Seizure 2004;13:523–8.
[14] Farrukh MJ, Makmor-Bakry M, Hatah E, Tan HJ. Use of complementary and alternative medicine and adherence to antiepileptic drug therapy among epilepsy patients: a systematic review. Patient Prefer Adherence 2018;12:2111–21.
[15] Sultana B, Panzini M-A, Veilleux Carpentier A, Comtois J, Rioux B, Gore G, et al. Incidence and prevalence of drug-resistant epilepsy: A systematic review and meta-analysis. Neurology 2021;96:805–17.
[16] Kobau R, Gilliam F, Thurman DJ. Prevalence of self-reported epilepsy or seizure disorder and its associations with self-reported depression and anxiety: results from the 2004 HealthStyles Survey. Epilepsia 2006;47:1915–21.
[17] Verducci C, Hussain F, Donner E, Moseley BD, Buchhalter J, Hesdorffer D, et al. SUDEP in the North American SUDEP Registry: The full spectrum of epilepsies. Neurology 2019;93:e227–36.
[18] Hebel JM, Surges R, Stodieck SRG, Lanz M. SUDEP following the second seizure in new-onset epilepsy due to limbic encephalitis. Seizure 2018;62:124–6.
[19] Kroner BL, Wright C, Friedman D, Macher K, Preiss L, Misajon J, et al. Characteristics of epilepsy patients and caregivers who either have or have not heard of SUDEP. Epilepsia 2014;55:1486–94.
[20] Hoppe C, Poepel A, Elger CE. Epilepsy: accuracy of patient seizure counts. Arch Neurol 2007;64:1595–9.
[21] RamachandranNair R, Jack SM. SUDEP: What do adult patients want to know? Epilepsy Behav 2016;64:195–9.
[22] Sperling MR, Barshow S, Nei M, Asadi-Pooya AA. A reappraisal of mortality after epilepsy surgery. Neurology 2016;86:1938–44.
[23] Friedman D, Donner EJ, Stephens D, Wright C, Devinsky O. Sudden unexpected death in epilepsy: knowledge and experience among U.S. and Canadian neurologists. Epilepsy Behav 2014;35:13–8.
[24] Nascimento FA, Laze J, Friedman D, Lam A, Devinsky O. SUDEP education among U.S. and international neurology trainees. Epilepsy Behav 2021;121:108098.
[25] Barbour K, Yozawitz EG, McGoldrick PE, Wolf S, Nelson A, Grinspan ZM. Predictors of SUDEP counseling and implications for designing interventions. Epilepsy Behav 2021;117:107828.