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Health-related quality of life and the burden of prolonged seizures in noninstitutionalized children with epilepsy

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ABSTRACT

Objective: This study aimed to provide information on the burden of illness and health-related quality of life (HRQoL) in children with epilepsy who experience prolonged acute convulsive seizures (PACS) in the community setting, and to investigate factors that may predict poor HRQoL in this population.
Methods: Noninstitutionalized children (aged 3–16 years) who had experienced at least one PACS within the past year and had currently prescribed PACS rescue medication were enrolled in a cross-sectional study in Germany, Italy, Spain, and the United Kingdom (Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3 [PERFECT-3]). Clinicians, parents/guardians, and patients completed web-based questionnaires regarding clinical characteristics, PACS frequency, and day-to-day impairment. Patients' HRQoL was rated by clinicians, parents/guardians, and patients themselves using the 5-dimension EuroQol questionnaire (EQ-5D) and summarized as a utility score. Potential predictors of poor HRQoL were tested in individual univariate generalized linear models and a global multivariable model.
Results: Enrolled children (N = 286) had experienced 1–400 PACS (median: 4) in the past year. Clinicians reported that 216/281 patients (76.9%) had learning disabilities of varying severity. Mean EQ-5D utility scores rated by clinicians (n = 279), parents (n = 277), and patients (n = 85) were 0.52 (standard deviation: 0.41), 0.51 (0.39), and 0.74 (0.29), respectively. Increasing PACS frequency, increasing severity of learning disability, and specialist school attendance were significantly associated with decreasing EQ-5D utility score. In the multivariable model, having learning disabilities was the best predictor of poor HRQoL.
Significance: Health-related quality of life was very poor in many children with epilepsy whose PACS were managed with rescue medication in the community, with learning disability being the most powerful predictor of patients' HRQoL. Mean EQ-5D utility scores were lower (worse) than published values for many other chronic disorders, indicating that optimal treatment should involve helping children and their families to manage learning disabilities and day-to-day impairments, in addition to preventing seizures.
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1. Introduction

People with epilepsy often experience poor health-related quality of life (HRQoL) [1]. Beyond controlling seizures, the ultimate goal of optimal epilepsy treatment should be to improve HRQoL [1,2]. Published information on HRQoL in children with epilepsy is limited, with most studies of the factors driving poor HRQoL in people with epilepsy conducted in adults. Comorbidities, treatment side effects, and tonic–

Abbreviations: AED, antiepileptic drug; CI, confidence interval; EQ-5D, 5-dimension EuroQol questionnaire; EQ-5D-3L, 3-level version of the EQ-5D; EQ-5D-Y, youth version of the EQ-5D; HRQoL, health-related quality of life; PACS, prolonged acute convulsive seizures; PERFECT-3, Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3; SD, standard deviation; UK, United Kingdom.

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clonic seizures were associated with poor HRQoL in adults with epilepsy in a study using both epilepsy-specific and generic measures of HRQoL [2]. Comorbidities and seizure frequency and severity were also associated with poor HRQoL in adults with epilepsy in a systematic review [1].

Adults with epilepsy have similar HRQoL impairment to those with asthma, chronic obstructive pulmonary disease, diabetes, heart failure, or stroke when compared using the 5-dimension EuroQol questionnaire (EQ-5D) [3]. The use of generic measures of HRQoL such as the EQ-5D permits comparison of HRQoL between diseases and with population norms, which are available for adults in 24 countries [4]. The EQ-5D is commonly used in Europe and North America, and is recommended by the National Institute for Health and Care Excellence in the United Kingdom (UK) for economic evaluation [5,6]. The EQ-5D has a version suitable for children and adolescents, as well as the adult version.

Here, we provide the first real-world data on HRQoL in noninstitutionalized children and adolescents with epilepsy collected using the EQ-5D. In children with epilepsy, prolonged acute convulsive seizures (PACS) are likely to progress to status epilepticus if left untreated [7], which can result in long-term consequences such as irreversible neurologic damage [8]. Practices in Emergency and Rescue medication For Epilepsy managed with Community-administered Therapy 3 (PERFECT-3) was a European retrospective observational study of noninstitutionalized children (aged 3–16 years) with epilepsy who had experienced PACS and were prescribed rescue medication.

Previously published data from PERFECT-3 showed that PACS frequency varied widely in the study population, from 1 to 400 in the 12 months before enrollment [9]. The present analyses explored the association of PACS frequency with children's schooling, functional impairment, and HRQoL, and also investigated if other factors were predictive of poor HRQoL in this population.

2. Methods

2.1. Design

The PERFECT-3 study included noninstitutionalized children and adolescents (aged 3–16 years) who had been diagnosed as having epilepsy at least 12 months before enrollment, had experienced one or more PACS in the past 12 months, and had one or more current prescriptions for PACS rescue medication. Prolonged acute convulsive seizures were defined as convulsive seizures lasting longer than 5 min [9]. Patients were not eligible for inclusion in the study if they experienced febrile seizures but had no diagnosis of epilepsy, if they had pseudo-seizures or other nonepileptic events which could be confounded with seizures, or if they were institutionalized.

Eligible patients were enrolled by physicians at 20 study centers (pediatric departments and specialist pediatric neurology centers) in Germany, Italy, Spain, and the UK by consecutive sampling of eligible patients making routine visits. A predefined algorithm was used for patient recruitment in each country to obtain a sample representative of the different age groups of interest (3–6 years, 7–12 years, and 13–16 years). The web-based system ensured that individuals could be enrolled only if the quota for their age group in that country had not been filled.

2.2. Conduct and ethics

The study was conducted from July 2013 to May 2014. Informed consent from parents/guardians and assent from patients aged 7–16 years were obtained before participation. The study was conducted in accordance with the International Conference on Harmonization of Good Clinical Practice, the principles of the Declaration of Helsinki [10], and, when applicable, local ethical and legal requirements for noninterventional studies.

2.3. Assessments

Patient demographics and baseline clinical characteristics were extracted from medical records by site staff at enrollment. Clinicians provided further information about each patient via a web-based survey comprising 13 questions. Parents (or guardians) of enrolled patients completed a 110-question web-based survey. A 35-question web-based survey was completed by patients themselves (if able and aged 13–16 years) or by a parent or guardian in conjunction with their child (if aged 3–12 years, or if aged 13–16 years and unable to complete the survey independently).

Health-related quality of life was assessed by clinicians, parents, and patients using the 3-level version of the EQ-5D (the EQ-5D-3L), which classifies health state across five domains using three possible levels of severity (no problems/some problems/severe problems). The youth version of the EQ-5D (the EQ-5D-Y) is based on the EQ-5D-3L, with the wording changed to be more suitable for children [6].

Parents and clinicians completed the EQ-5D-3L proxy version. Patients aged 13–16 years (if able) completed the EQ-5D-3L, and patients aged 7–12 years (if able) completed the EQ-5D-Y. Validated translations of all EQ-5D questionnaires were used when appropriate. Results were summarized as EQ-5D utility scores (calculated using UK-specific weightings) [11] based on a scale in which 1 is best possible health and 0 is dead [6].

2.4. Statistical analysis

This observational study had no prespecified primary endpoint. Based on the multimodal distribution of PACS frequency in the study population, patients were assigned post hoc to subgroups of low, medium, and high PACS frequencies (1–5, 6–50, and ≥51 PACS, respectively, in the 12 months before enrollment). Alternative subgroups of different PACS frequencies were also analyzed (1–5, 6–20, and ≥21 PACS in the 12 months before enrollment), which gave similar results to those presented here (data not shown). Questionnaire responses pertaining to learning disability, schooling, functional impairment, and EQ-5D utility scores were stratified by PACS frequency subgroup.

Potential predictors of EQ-5D utility score were predefined based on advice from epilepsy specialists, summarized using descriptive statistics, and analyzed using linear regression models. Predictors were as follows: PACS frequency, source of EQ-5D utility score (clinician/parent/patient), age (continuous and categorical), sex, country, route of rescue medication administration (buccal/rectal/other), formulation (prefilled syringe/other), hospitalizations in the past 3 months (continuous and yes/no), time since last seizure, schooling, and learning disability (none/mild/moderate/severe).

Potential predictors were tested individually in univariate linear regression models and were also combined into a global multivariable model using a backward selection algorithm (starting with all predictors, the predictor with the highest p value was iteratively removed from the model leaving only those that were significant at the 0.05 level). The only exception was the source of EQ-5D utility score, which was included in the final multivariable model regardless of significance level because it was considered of special interest. Univariate and multivariable analyses used generalized linear models with Gaussian family and identity link [12].

3. Results

3.1. Participants

Patient demographics, characteristics, and survey completion rates are summarized in Table 1. At the time of study entry, 96.4% of patients were receiving prescribed antiepileptic medication, with 26.3% receiving one drug, 40.2% receiving two drugs, and 29.9% taking three or more antiepileptic drugs (AEDs) [9].

Table 1
Patient demographics, characteristics, and survey completion. Abbreviations: PACS, prolonged acute convulsive seizures; SD, standard deviation.

Characteristic	Overall (N = 286)	1–5 PACS/year (n = 158)	6–50 PACS/year (n = 102)	≥51 PACS/year (n = 26)
Age, years				
Mean (SD)	8.8 (3.8)	8.6 (3.8)	9.1 (4.0)	8.8 (3.4)
Median (range)	8 (3–16)	8 (3–16)	9 (3–16)	8 (3–15)
Age groups				
3–6 years, n (%)	95 (33.2)	59 (62.1)	30 (31.6)	6 (6.3)
7–12 years, n (%)	129 (45.1)	68 (52.7)	47 (36.4)	14 (10.9)
13–16 years, n (%)	62 (21.7)	31 (50.0)	25 (40.3)	6 (9.7)
Sex				
Male, n (%)	157 (54.9)	87 (55.1)	53 (52.0)	17 (65.4)
Country				
Germany, n (%)	92 (32.2)	42 (26.6)	39 (38.2)	11 (42.3)
Italy, n (%)	75 (26.2)	46 (29.1)	26 (25.5)	3 (11.5)
Spain, n (%)	77 (26.9)	50 (31.6)	19 (18.6)	8 (30.8)
UK, n (%)	42 (14.7)	20 (12.7)	18 (17.6)	4 (15.4)
Rescue medication route of administration (n = 265)[a]				
Buccal, n (%)	76 (26.57)	40 (13.99)	29 (10.14)	7 (2.45)
Rectal, n (%)	108 (37.76)	67 (23.43)	30 (10.49)	11 (3.85)
Sublingual, n (%)	1 (0.35)	0	1 (0.35)	0
>1 route, n (%)	80 (27.97)	41 (14.34)	34 (11.89)	5 (1.75)
Number of PACS in the past 12 months				
Mean (SD)	23.6 (59.8)	2.5 (1.3)	19.0 (14.7)	169.8 (121.4)
Median (range)	4 (1–400)	2 (1–5)	12 (6–50)	100 (52–400)
Survey completion				
Clinician, n	281	156	99	26
Parent, n	258	146	88	24
Patient/proxy,[b] n	251	142	86	23

[a] Excluding missing answers (3/286), and those who answered 'do not know' (1/286) and 'other' (17/286).
[b] The survey was completed by 27/251 patients (10.8%) by themselves, with the remainder completed by proxy (a parent/guardian) in conjunction with the patient.

Overall, the median number of PACS experienced in the past 12 months was 4 (range: 1–400). The low-, medium-, and high-frequency PACS subgroups comprised of 158 (55.2%), 102 (35.7%), and 26 (9.1%) patients, respectively (Table 1). The median (range) number of PACS experienced in the past 12 months for each subgroup was 2 (1–5), 12 (6–50), and 100 (52–400), respectively. Age, sex, country of enrollment, and time since epilepsy diagnosis were generally balanced across the PACS frequency subgroups. Survey response rates were also similar among subgroups (Table 1).

3.2. Web-based questionnaires

3.2.1. Learning disability

Clinicians reported that 216/281 patients (76.9%) had learning disabilities. Of the 216 patients with learning disabilities, 61 (28.2%) had learning disabilities classed as severe (unable to attend kindergarten or mainstream school and in need of continuous care). Higher proportions of patients in the medium- and high-frequency PACS subgroups had learning disabilities (89/99 [89.9%] and 22/26 [84.6%], respectively) than in the low-frequency PACS subgroup (105/156 [67.3%]). Of the patients with learning disabilities, 22/105 in the low- (21.0%), 29/89 in the medium- (32.6%), and 10/22 in the high-frequency PACS subgroups (45.5%) had severe learning disabilities (Fig. 1A).

3.2.2. Schooling

Overall, 257 parents reported that 76 patients (29.6%) attended a specialist school. The proportion of patients who attended a specialist school rose from 32/145 (22.1%) in the low-frequency PACS subgroup to 34/88 (38.6%) in the medium- and 10/24 (41.7%) in the high-frequency PACS subgroups. According to parents, 5/258 patients (1.9%) did not attend school, kindergarten, or nursery at all, of whom three were in the high-frequency PACS subgroup (Fig. 1B).

3.2.3. Functional impairment

Clinicians reported that 148/281 children (52.7%) had functional impairment that interfered with typical day-to-day activities. The proportion of children with functional impairment increased from 64/156 (41.0%) in the low-frequency PACS subgroup to 64/99 (64.6%) in the medium- and 20/26 (76.9%) in the high-frequency PACS subgroups. Of the children with functional impairment in each of the low-, medium-, and high-frequency PACS subgroups, 19/64 (29.7%), 27/64 (42.2%), and 10/20 (50.0%), respectively, had severe impairment (Fig. 1C).

3.3. EQ-5D utility scores

3.3.1. Source of utility score

In the overall population, mean EQ-5D utility scores rated by clinicians (n = 279), parents (n = 277), and patients (n = 85) were 0.52, 0.51, and 0.74, respectively (Table 2). Five-dimension EuroQol questionnaire data were available from all three sources (clinicians, parents, and patients) for 84 patients. In this subset, the mean EQ-5D utility scores rated by clinicians, parents, and patients were 0.82, 0.74, and 0.74, respectively.

3.3.2. Descriptive analyses

Mean EQ-5D utility scores rated by clinicians, parents, and patients fell from 0.62, 0.61, and 0.82, respectively, in the low-frequency PACS subgroup, to 0.41, 0.40, and 0.62, respectively, in the medium-frequency PACS subgroup, and 0.37, 0.34, and 0.66, respectively, in the high-frequency PACS subgroup. Five-dimension EuroQol questionnaire utility score correlated weakly but significantly with PACS frequency for clinician and parent ratings ($r = -0.15$, $p = 0.013$, $n = 279$ and $r = -0.18$, $p = 0.003$, $n = 277$, respectively). Correlation of EQ-5D utility score with PACS frequency for patient ratings, although in the same direction, was not significant ($r = -0.20$, $p = 0.061$, $n = 85$).

3.3.3. Univariate modeling

Increasing PACS frequency, increasing severity of learning disability, and specialist school attendance were significantly associated with decreasing EQ-5D utility score ($p \leq 0.001$; Table 3). Patient-rated EQ-5D utility score was significantly higher than parent-rated score ($p < 0.001$), whereas clinician-rated utility score did not differ significantly from parent-rated score ($p = 0.322$). Of the other factors investigated, only country was associated with EQ-5D utility score, with patients

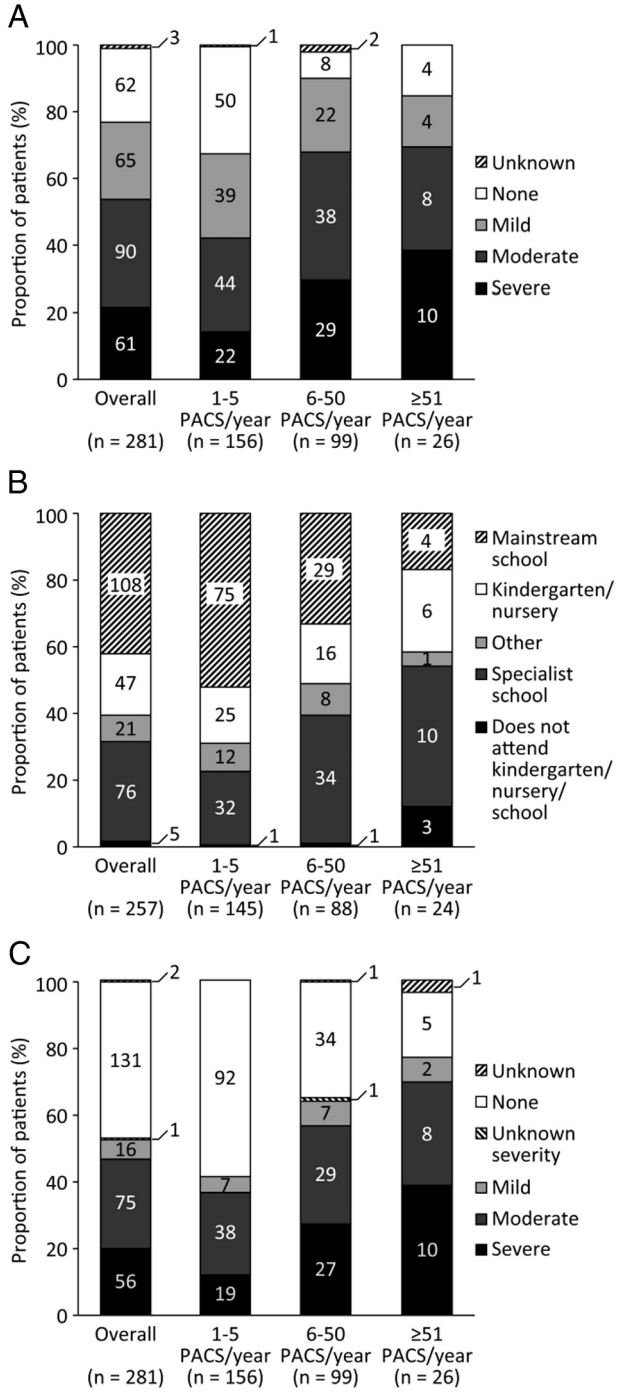

Fig. 1. A) Clinician-rated learning disability, B) parent-reported school attendance, and C) clinician-rated functional impairment. Abbreviation: PACS, prolonged acute convulsive seizures. Learning disabilities were reported by clinicians (n = 281) and classed as mild (able to attend regular kindergarten/school), moderate (attends specialist school), or severe (unable to attend specialist kindergarten/school; requires continual specialist care) (A). A parent of each child (n = 258) was asked what type of school their child attended (B). Impairments in day-to-day activities typical of the patient's age group were reported by clinicians (n = 281) (C). Proportions are based on the indicated total numbers of responses. Numbers in the bars are numbers of patients.

from Italy and Spain having better HRQoL than those from the UK (p = 0.003 and p = 0.006, respectively) (Supplementary Table S1). The number of hospitalizations in the past 3 months (both continuous and yes/no) had no significant effect on EQ-5D utility score (Supplementary Table S1).

Table 2
EQ-5D utility scores from clinician, parent, and patient ratings. Abbreviations: EQ-5D, 5-dimension EuroQol questionnaire; EQ-5D-3L, 3-level version of the EQ-5D; EQ-5D-Y, youth version of the EQ-5D-3L; SD, standard deviation.

Source	n	Mean (SD)	Median (range)
Clinician[a]	279	0.52 (0.41)	0.71 (−0.594, 1)
Parent[a]	277	0.51 (0.39)	0.69 (−0.594, 1)
Patient	85	0.74 (0.29)	0.81 (−0.166, 1)
Patient aged 7–12 years[b]	58	0.72 (0.30)	0.80 (−0.166, 1)
Patient aged 13–16 years[c]	27	0.78 (0.27)	0.85 (0.151, 1)

[a] Rated using the EQ-5D-3L proxy version.
[b] Rated using the EQ-5D-Y (3 patients aged 7–12 years filled in the EQ-5D-3L).
[c] Rated using the EQ-5D-3L (1 patient aged 13–16 years filled in the EQ-5D-Y).

3.3.4. Multivariable modeling

Learning disability, specialist school attendance, and being younger had a significant negative impact on EQ-5D utility score following iterative selection in multivariable models ($p < 0.001$, $p = 0.008$, and $p < 0.001$, respectively) (Table 4). The predictor with the greatest impact was the level of learning disability, with even mild learning disability having a significant negative effect on EQ-5D utility score. The source of utility score (clinician, parent, patient) was not a significant predictor in the multivariable model.

4. Discussion

This study revealed for the first time that HRQoL is very poor in many noninstitutionalized children with epilepsy who experience PACS. Prolonged acute convulsive seizure frequency varied widely, and children with greater PACS frequency tended to have worse disability and impairment and to need more specialist schooling. Mean parent- and clinician-rated EQ-5D utility scores for patients in the PERFECT-3 population were substantially lower, indicating worse HRQoL, than published patient-rated utility scores for adults with cancer [13], asthma, chronic obstructive pulmonary disease, diabetes, heart failure, or stroke [3].

Mean EQ-5D scores reported here by clinicians, parents, and patients were all well below the UK population norm for adults (0.51, 0.52, and 0.74 vs 0.86) (no population norm is available for children) [4,14]. In the subset of children who were able to complete the EQ-5D questionnaire themselves, HRQoL was higher than in the overall patient population (measured using the proxy questionnaires) and was similar to previously reported self-rated scores for adults with epilepsy (0.74 vs 0.76) [3]. The patient-rated EQ-5D score reported here (0.74) is lower than published values for children with cystic fibrosis (0.78), or with asthma that is not well controlled (0.82) [16,17].

For those individuals with EQ-5D assessments from all three sources (n = 84), mean EQ-5D utility scores were rated similarly by clinicians, parents, and patients. The mean EQ-5D scores in this subset were higher than for the overall population, indicating that HRQoL was higher in children and adolescents whose cognitive capacity was sufficient to enable them to complete the questionnaire compared with those who could not.

Prolonged acute convulsive seizure frequency, level of learning disability, and schooling, as well as source of EQ-5D, had a significant effect on HRQoL ($p \leq 0.001$) in univariate models. The significant effect of country (Italy $p = 0.003$ and Spain $p = 0.006$) is likely to be a result of the higher proportions of patients experiencing 1–5 PACS per year enrolled in Italy and Spain than in Germany and the UK, given that PACS frequency was a predictor of HRQoL. Route of administration of rescue medication (buccal vs rectal) did not have a significant effect on HRQoL, but it should be noted that route of administration is highly dependent on country, which may have confounded these results. For example, no patients from the UK used rectal administration, and only one patient from Italy used buccal administration at the time of the study.

Table 3
Significant predictors of EQ-5D utility score (univariate models). Abbreviations: CI, confidence interval; EQ-5D, 5-dimension EuroQol questionnaire; PACS, prolonged acute convulsive seizure.

Model covariate	Category	Coefficient	95% CI	p value
Source of EQ-5D utility score	Parent (reference)	–	–	–
	Clinician	0.011	−0.011, 0.034	0.322
	Patient	0.231	0.166, 0.296	<0.001
	Intercept	0.510	0.464, 0.556	<0.001
PACS frequency (continuous)	Per unit increase	−0.001	−0.002, −0.0003	0.010
	Intercept	0.572	0.525, 0.618	<0.001
PACS frequency (categorical)	1–5 (reference)	–	–	–
	6–10	−0.137	−0.247, −0.027	0.014
	11–20	−0.231	−0.378, 0.085	0.002
	21–50	−0.310	−0.490, −0.130	0.001
	>50	−0.247	−0.416, −0.078	0.004
	Intercept	0.643	0.588, 0.698	<0.001
Level of learning disability	None (reference)	–	–	–
	Mild	−0.168	−0.231, −0.105	<0.001
	Moderate	−0.417	−0.489, −0.344	<0.001
	Severe	−0.901	−0.964, −0.838	<0.001
	Intercept	0.896	0.854, 0.937	<0.001
Schooling	Mainstream (reference)	–	–	–
	Kindergarten/nursery	−0.233	−0.354, −0.112	<0.001
	Other	−0.214	−0.398, −0.029	0.023
	Specialist school	−0.450	−0.547, −0.354	<0.001
	Does not attend	−0.078	−0.376, 0.220	0.609
	Intercept	0.745	0.694, 0.796	<0.001

Other covariates tested are summarized in Supplementary Table S1.

Learning disability emerged as the main predictor of poor HRQoL in the multivariable model. This observation is in line with previous findings that intellectual disability led to reduced HRQoL in children with epilepsy [18,19] and that comorbidities were a significant predictor of poor HRQoL in adults with epilepsy [1,2]. Specialist schooling was also a strong predictor of poor HRQoL and presumably reflected learning disability. These findings highlight the probable impact of the underlying etiology on HRQoL being intrinsically linked to seizure frequency learning disability and functional impairment.

A key limitation of the present study was that the information collected on the etiology of patients' epilepsy and seizure type was not detailed enough for these factors to be analyzed as potential predictors of poor HRQoL. Because the interactions between underlying etiology, seizures, functional impairment, learning disability, and HRQoL are complex, it would be challenging to assess the impact of each factor independently. The contribution of each of these factors will also vary from patient to patient. For example, a patient with trisomy 21 and another with focal dysplasia could each experience 15 PACS per year, but would have very different degrees of learning disability and very different HRQoL. Nevertheless, the present study suggests that not only frequent seizures but also learning disability are key factors driving poor HRQoL in children with epilepsy as a population with a range of other disease characteristics.

Table 4
Multivariable models of potential predictors of EQ-5D utility score. Abbreviations: CI, confidence interval; EQ-5D, 5-dimension EuroQol questionnaire.

Model covariate	Category/unit	Coefficient	95% CI	p value
Level of learning disability	None (reference)	–	–	–
	Mild	−0.159	−0.223, −0.096	<0.001
	Moderate	−0.346	−0.431, −0.261	<0.001
	Severe	−0.841	−0.921, −0.761	<0.001
	Intercept	0.771	0.697, 0.845	<0.001
Schooling	Other (reference)	–	–	–
	Specialist school	−0.104	−0.180, −0.027	0.008
Age	Per 1-year increase	0.014	0.007, 0.021	<0.001
Source of EQ-5D utility score	Parent (reference)	–	–	–
	Clinician	0.002	−0.021, 0.025	0.838
	Patient	0.022	−0.022, 0.066	0.334

A further limitation is that the study did not collect sufficient information about AED treatment to enable them to be investigated as a potential predictor of HRQoL. Although a systematic review of predictors of HRQoL in adults with epilepsy did not find a clear association with AEDs [1], a more recent study showed that patients taking one or more newer AEDs (introduced from 1993) were less likely to report poor HRQoL than those on polytherapy with older AEDs (introduced before 1993) [2]. Importantly, the PACS frequency analysis was not a prespecified study outcome, and the post hoc determination of subgroups is an inherent limitation.

When interpreting the data presented here, it should also be taken into consideration that all patients in the present study had been prescribed rescue medication, which could itself negatively affect HRQoL. For example, side effects of benzodiazepines, such as midazolam and diazepam, include drowsiness, dizziness, and problems with memory and cognition [20,21].

Strengths of this study include the large, international sample of noninstitutionalized children and the assessment of HRQoL from multiple perspectives. The use of the EQ-5D rather than an epilepsy-specific HRQoL instrument enabled comparison with other diseases and with available population norms. Some HRQoL scales for children with epilepsy exclude those with severe cognitive difficulties, potentially leading to underestimation of burden compared with the present study [19]. Because this study excluded institutionalized children, however, many severe cases of epilepsy would not have been represented.

In conclusion, HRQoL was very poor in a large proportion of this population of noninstitutionalized children with epilepsy who experience PACS and are prescribed rescue medication. Severity of learning disability was a more powerful predictor of poor HRQoL than PACS frequency. These findings support previous recommendations to improve HRQoL as part of the strategy for managing epilepsy [1,2]. Here, we show that the optimal management of children with epilepsy outside specialist institutions should involve helping families to manage learning disabilities and day-to-day impairments associated with the condition, in addition to terminating seizures.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2019.04.058.

Declaration of Competing Interest

DL is an employee of BresMed Health Solutions. CLR received consulting fees for the statistical analysis of the study. TW-K is an employee of Shire, a member of the Takeda group of companies, and owns stock or stock options. The following authors have received compensation for serving as consultants or speakers for, or they or the institutions they work for have received research support or royalties from, the companies or organizations indicated: FJK (Cyberonics, Eisai, Shire [a member of the Takeda group of companies], and ViroPharma), FV (Cyberonics, Eisai, Shire [a member of the Takeda group of companies], and ViroPharma), MR-C (Shire [a member of the Takeda group of companies] and ViroPharma), BW (Shire [a member of the Takeda group of companies] and ViroPharma), and LL (Cyberonics, Eisai, Shire [a member of the Takeda group of companies], UCB, and Zogenix).

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

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Data statement

The datasets behind the results reported in this article will be available 3 months after manuscript publication, to researchers who provide a methodologically sound proposal after de-identification, in compliance with applicable privacy laws, data protection, and requirements for consent and anonymization. Data requests should follow the process outlined in the Data Sharing section on Shire's website: http://www.shiretrials.com/en/our-commitment-to-transparency/data-sharing-with-researchers and should be directed to clinicaltrialdata@shire.com.

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