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Predictors of Trajectories of Epilepsy-Specific Quality of Life among Children Newly Diagnosed with Epilepsy

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Abstract

Objective—To identify two year trajectories of epilepsy-specific health-related quality of life (HRQOL) among children newly diagnosed with epilepsy and to evaluate the predictive value of a comprehensive set of medical, psychosocial, and family factors.

Methods—Ninety-four children with epilepsy (8.14 ± 2.37 years of age and 63% male) and their caregivers participated in this study. Caregivers completed the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE) and measures of psychological and family functioning at one month post-diagnosis. The QOLCE was also given at eight additional time points during the subsequent two years as a part of a large observational study in children with epilepsy. Adherence data was collected via MEMS TrackCaps and medical information was collected through chart review.

Results—Unique trajectories were identified for the overall QOLCE scale, as well as the subscales. Most trajectory models for the QOLCE subscales contained at least one at-risk trajectory for children, indicating that there is a subgroup of children experiencing poor long-term HRQOL. Health-related quality of life trajectories remained predominantly stable during the two year period following treatment initiation. Number of AEDs, Internalizing Problems, and Externalizing Problems emerged as the most consistent predictors across the HRQOL domains.

Significance—Medical and psychosocial interventions, such as cognitive-behavioral strategies, should target modifiable factors (e.g., internalizing symptoms, externalizing symptoms, number of

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AEDs trialed) shortly after diagnosis to improve HRQOL for children with epilepsy over the course of their disease.

Keywords

epilepsy; quality of life; children; trajectories

1. INTRODUCTION

Health-related quality of life (HRQOL) is a widely accepted health and patient-reported outcome measure that assesses the impact of an illness and its treatment on functioning[1, 2]. Children with epilepsy are at increased risk for poor HRQOL[3, 4], particularly in the domains of emotional, behavioral, social, academic, and family functioning[5–10]. Assessing HRQOL in children with epilepsy allows healthcare professionals to have a broader conceptualization of the impact of epilepsy and antiepileptic drugs (AEDs) on the child and to make more informed decisions regarding medication, side effects, and the child's overall well-being. While many cross-sectional and longitudinal studies have been conducted examining HRQOL, few have identified the longitudinal course of HRQOL over time in children with epilepsy.

One exception is the HERQULES project, a prospective multisite study examining HRQOL and adherence in children with epilepsy at four points during the two years post-diagnosis. Ferro and colleagues[11] documented five trajectories of overall HRQOL with the majority of children being in the moderate-increasing (23%), high-increasing (32%), or high-stable (29%) trajectory groups. The remaining children were in the moderate-decreasing (12%) or low-increasing (4%) groups. Most of the children in the moderate-increasing, high-increasing, and high stable trajectory groups demonstrated clinically meaningful improvements in HRQOL over two years, while the children in the moderate-decreasing group experienced clinically significant declines in HRQOL[11]. The work by Ferro and colleagues (2013) provides important information regarding overall HRQOL trajectories over a two year period, but does not provide domain specific information. Establishing domain-specific trajectories (e.g., depression) may be more helpful in identifying at-risk patients and determining targets for intervention to improve HRQOL given that interventions target a particular domain rather than general HRQOL. Another HERQULES study examined mean scores for the domains of HRQOL (e.g., depression, behavior, stigma) and found that scores tended to be lowest at baseline and highest two years later[3]. Although Speechley and colleagues provided domain specific information, longitudinal HRQOL was examined over time by demonstrating a single, average model of HRQOL over two years, not trajectories[3]. Building from these two studies, our goal was to establish domain specific HRQOL trajectories that would allow providers to identify particular aspects of HRQOL that need to be targeted with intervention (e.g., cognitive-behavioral therapy for emotional problems vs. neuropsychological testing for neurocognitive problems). In addition, identification of the ideal timing regarding the delivery of such interventions is important.

Previous research has identified a number of predictors of HRQOL in children with epilepsy. A recent meta-analysis examined 12 risk factors for poor HRQOL in children with epilepsy

and found that more severe seizure characteristics (i.e., type, frequency, severity, duration), AED characteristics (i.e., quantity, side effects), presence of a comorbid disorder (e.g., behavior, cognitive or emotional difficulties), and family characteristics (i.e., parental anxiety, socioeconomic status) were associated with poorer HRQOL[12]. Several longitudinal studies have also documented AED side effects, AED type, seizure frequency[13], cognitive problems, family demands, and family functioning[3, 14] as predictors of HRQOL over time. Finally, the one existing study documenting overall HRQOL trajectories also found that an increased quantity of AEDs, comorbid behavior or cognitive problems, parent depression, family demands, and family functioning to be associated with less favorable HRQOL trajectories[11]. It should be noted, however, that the relative contribution of each predictor to overall HRQOL and QOLCE subscales in a combined model has not been examined.

The primary objective of this study was to identify two-year trajectories of HRQOL following pediatric epilepsy treatment initiation using the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE), an epilepsy-specific measure of HRQOL. Although previous studies have established trajectories for the Overall scale of the QOLCE and demonstrated mean models for the QOLCE subscales, no studies have established trajectories for the QOLCE subscales in a way that allows providers to identify at-risk domains of HRQOL and inform intervention type and timing. Our goal was to extend the literature by documenting trajectory groups across domains using established QOLCE subscales (e.g., physical restrictions, depression, behavior, memory, social interaction). Domain-specific HRQOL trajectories across nine time points will allow for the identification of children in need of a particular intervention at a specific time point. Our secondary aim was to examine the differential predictive value of medical, psychosocial, and family factors on domain-specific HRQOL. The recent meta-analysis[12] and existing longitudinal studies examining correlates of HRQOL[3, 15] informed the compilation of a comprehensive set of predictor variables in order to identify the most critical predictors of overall and specific domains of epilepsy-specific HRQOL.

2. METHODS

2.1 Participants and Procedures

Participants were recruited and enrolled on the day of their epilepsy diagnosis and AED initiation from the New Onset Seizure Disorder Clinic for a two-year longitudinal study examining adherence and health outcomes. Parents of children who met the following inclusion criteria were approached by a trained research assistant: 1) 2–12 years old, 2) same day epilepsy diagnosis and AED initiation, 3) no comorbid medical conditions requiring daily medication, 4) no parent reported developmental disorders, and 5) fluent in English. This study received prior approval by the hospital Institutional Review Board and caregivers provided informed consent for each patient.

Caregivers completed a demographics form and received an electronic monitor to measure adherence to AED therapy. Subsequent study visits coincided with routine clinic appointments, which occurred approximately 1, 4, 7, 10, 13, 16, 19, 22, and 25-months post diagnosis. During each visit, electronic monitored adherence data was downloaded and

caregivers completed a battery of questionnaires. The current study examined the following parent-reported variables: epilepsy-specific quality of life, socioeconomic status (SES), side effects, child externalizing and internalizing behaviors, parent fears and concerns, and general family functioning. Disease-related variables were obtained through medical chart reviews and parent-report.

2.2 Measures

2.2.1 Demographic and disease characteristics—Background information such as child age and sex was provided by each primary caregiver via a demographics form. The Duncan scoring system, an occupation-based measure, was used to compute SES[16]. Scores were calculated for each family and range from 15 to 99, with higher scores reflecting higher SES.

Disease information such as number of AEDs, seizure type, etiology, and occurrence were obtained through medical chart review. Number of AEDs signifies the total number of AEDs utilized during the two year period. Caregivers completed the 19-item Pediatric Epilepsy Side Effects Questionnaire (PESQ)[17] regarding AED side effects experienced by the child. Scores range from 0–100, with higher scores representing more side effects. The PESQ has strong internal consistency and test-retest reliability[17]. Internal consistency reliability in this sample was 0.99. Seizure probability trajectory groups indicating the likelihood of patients having a seizure over the two year study were previously identified and used a marker of seizure course in this study [18].

2.2.2 AED adherence—Adherence was assessed for the larger study utilizing a MEMS TrackCap, an electronic monitor that records the date and time the bottle was opened. Data were downloaded from the TrackCap at each study visit and those data were previously used to identify trajectories of AED adherence over the first two years. Four long-term adherence trajectory groups were identified including Severe Early Non-adherence, Variable Non-adherence, Moderate Non-adherence, and High Adherence[18] and were utilized in the current paper.

2.2.3 Epilepsy-specific quality of life—Caregivers completed the Quality of Life in Childhood Epilepsy Questionnaire (QOLCE), a 79-item parent proxy report of the child's quality of life[19]. Scaled scores, ranging from 0–100 with higher scores reflecting better QOL, were calculated for Total HRQOL and 17 subscales of the QOLCE. For ease of interpretation, QOLCE subscales are discussed in the following groups: physical domain [*Physical Restrictions (10 items, $\alpha = 0.67$), Energy/Fatigue (2 items, $\alpha = 0.63$)*], emotional domain [*Depression (4 items, $\alpha = 0.63$), Anxiety (5 items, $\alpha = 0.79$), Control/Helplessness (4 items, $\alpha = 0.67$), Self-esteem (5 items, $\alpha = 0.72$)*], behavioral domain [*Behavior (16 items, $\alpha = 0.81$), Attention/Concentration (5 items, $\alpha = 0.90$)*], neurocognitive domain [*Memory (6 items, $\alpha = 0.91$), Language (8 items, $\alpha = 0.90$), Other Cognitive (3 items, $\alpha = 0.80$)*], social domain [*Social Interaction (5 items, $\alpha = 0.35$), Social Activity (2 items, $\alpha = 0.77$), Stigma (1 item)*], and overall [*General Health (1 item), Quality of Life Item (1 item), and Overall Quality of Life (92 items, $\alpha = 0.95$)*]. The QOLCE is a well-established measure with good psychometric properties[19].

2.2.4 Psychological functioning—The Behavior Assessment System for Children-2nd Edition (BASC-2)[20] is a reliable and valid measure of behavioral and emotional difficulties. The parent-proxy version of the Internalizing (e.g., anxiety, depressive symptoms) and Externalizing (e.g., aggression, oppositional/conduct behaviors, hyperactivity) subscales were utilized in this study. Individual raw scores were compared to normative data for children of the same age and resulted in standardized *T*-scores, with *T*-scores above 65 representing at-risk functioning. Cronbach's alpha ranged from 0.88 – 0.94 for the Internalizing subscale and 0.90–0.93 for the Externalizing subscale.

2.2.5 Parent and family functioning—The 5-item Concerns and Fears subscale of the Parent Report of Psychosocial Care[21] was used to assess parental fears about the impact of the child's seizures. Higher scores indicate a greater level of worry about the child's seizures. Parents also completed the McMaster Family Assessment Device. Higher scores on the general family functioning subscale indicate a poorer level of family functioning. Internal consistency reliability for the current sample was 0.83.

2.3 Statistical Analysis

Latent class growth modeling (LCGM) analyses were implemented and missing data were handled in SAS (version 9.3; SAS Institute, Cary, NC) with the TRAJ procedure (see, e.g., [22–25]). Specifically, PROC TRAJ employs maximum likelihood estimation, and thus all available outcome data are used to obtain parameter estimates under the assumption that any missing data are missing at random (see, e.g., [26]). PROC TRAJ excludes participants from prediction models when time-invariant covariates are missing [22]. When unobserved subgroups are anticipated within a longitudinal data set, LCGM can be used to delineate these subgroups. Based on response variable patterns over time, unobserved groups are extracted and participants are assigned to one and only one of the subgroups using probabilistic estimation techniques. This approach was utilized to extract subgroups from longitudinal data from each of the QOLCE scales.

All models employed censored normal distributions for the outcome of interest. The number of groups was selected based on the Bayesian information criterion (BIC) statistic, model estimation convergence, and sufficient subgroups proportions for each outcome. In particular, quadratic models for change were analyzed starting with 1 subgroup, 2 subgroups, etc., until the number of subgroups was sufficiently large that the model did not converge within PROC TRAJ. From the available models, each with a different number of groups, a model with any subgroup proportions < .05 was not considered further. The remaining models were compared with respect to BIC to determine the optimal number of subgroups. Linear and quadratic models for change were compared via the BIC for the model with the optimal number of subgroups. In order to examine how well the subgroup solution fit the data via how definitively participants were assigned to the subgroups, average posterior probabilities were examined for the LCGMs.

After establishing the appropriate number of groups and trajectory group shapes within the LCGM for a given QOLCE subscale, trajectory group status was then predicted with an ordinal logistic regression using the LOGISTIC procedure in SAS with the following

covariates entered simultaneously: adherence group status[27], seizure group status[27], side effects, SES, number of AEDs, internalizing problems, externalizing problems, parental worries, family functioning, and seizure type. To balance Type I and Type II errors in this study of multiple outcomes and multiple covariates, statistical significance for all significance tests was defined as $p < 0.05$.

3. RESULTS

3.1 Participants

There were 111 eligible families (children with epilepsy and a parent) that were approached for study participation. Five families declined participation due to time constraints (95% recruitment rate). One participant was found to be ineligible after informed consent was obtained (due to simultaneous diagnosis of a pervasive developmental disorder). One hundred and five participants agreed to participate in our larger study, which included children 2–12 years of age. Ninety-four ($94/105 = 90\%$) of these participants completed baseline measures based on our age-eligibility (e.g. 4 years and older necessary to complete the QOLCE) for the current study. Eighty-four participants ($84/105 = 80\%$) completed the final assessment. Participants were not required to complete all time points in order to complete a final assessment. Participation rates at each assessment were as follows: 79% (4 months), 82% (7 months), 79% (10 months), 78% (13 months), 67% (16 months), 64% (19 months), 48% (22 months), and 80% (final assessment). Missing data is due to the following reasons: stopped receiving care at the NOS clinic (35%), missed appointment or did not complete measures (21%), withdrew from the study (16%), and planned missed appointment due to good clinical progress (13%).

Baseline characteristics for participants completing the initial assessment and those who completed the final assessment can be found in Table 1. Group differences were examined based on those who completed the 1 month visit ($n = 94$) vs those who completed the 25 month visit ($n = 84$). Participants who completed the final assessment were more likely to be male ($F(1, 92) = 4.36, p = .04$). No other significant differences were found with regard to demographic (e.g., age, socioeconomic status) or medical (e.g., seizure type, initial drug therapy) variables.

3.2 Determining QOLCE Trajectories

Latent class growth modeling analyses (Table 2) resulted in final subgroup growth model trajectories for each subscale and overall HRQOL. The trajectories are shown in Figure 1 and trajectory group percentages can be found in Table 2.

Trajectories were classified based on the intercept and slope of HRQOL over the 2-year period. Means and standard error of measurement (SEM) scores previously calculated for the QOLCE[3] were used to develop the trajectory labels (see Table 3 for the mean, standard deviation, and SEM of each subscale). A trajectory was labeled as “Moderate” if the intercept was within one SEM of the mean from the previous sample [3]. “High” was used if the trajectory intercept was greater than one SEM above the previous mean, while “Superior” was used if the trajectory was greater than two SEMs above the previous mean. Conversely, trajectories were labeled “Fair,” “Poor,” or “Very Poor” if the trajectory

intercept was one, two, or three SEMs below the mean, respectively. A similar naming strategy was implemented for one item scales where no SEMs were available.

Table 2 and Figure 1 provide specific information regarding trajectory analyses and percentage of children in each trajectory. For clinical purposes and ease of understanding, the percentage of at-risk children is also described in the text. While three stable trajectories emerged for *Physical Restrictions and Energy/Fatigue* (i.e., Superior/High, Moderate, Fair/Poor) trajectories of emerged, approximately 30% of children were at risk and fell in the Fair or Poor trajectory groups.

The emotional HRQOL domain subscales of *Depression, Anxiety, Control/helplessness*, and *Self-esteem* each demonstrated three to four distinct trajectories (i.e., Superior/High, Moderate, Fair/Poor). Most trajectories did not change over time, with the exception of the Poor-Moderate *Anxiety* trajectory and the High-Superior *Self-esteem* trajectory and 11–17% of children fell in the Fair or Poor trajectory groups on the emotional domain subscales.

For the more behaviorally oriented subscales (i.e., *Behavior, Attention/Concentration*), Superior, Moderate, and Poor trajectories were demonstrated consistently. The *Attention/Concentration* subscale had one additional trajectory highlighting a High level of HRQOL. The behavioral HRQOL trajectories did not significantly change over time.

Four to five trajectories were established for the Neurocognitive subscales (i.e., *Memory, Other Cognitive, Language*). Many children with epilepsy demonstrated neurocognitive difficulties with 46% in the Fair or Poor trajectories on the *Memory* subscale and 31% in the Poor or Extremely Poor trajectories for *Language*. These trajectories were persistent over time with the exception of the increasing High-Superior *Other Cognitive* (e.g., had difficulty solving problems, had difficulty making decisions) trajectory.

The social subscales of the QOLCE each produced only two trajectories. All of the participants were in a Moderate or Superior/High-superior trajectory group for *Social Activities* and *Stigma* while 79% percent of participants were in the Poor trajectory group for *Social Interaction*.

Stable Superior, High, Fair, and Poor trajectories were established for *Overall QOL* with 40% of children in the Fair or Poor trajectory. The *General Health* subscale and the *QOL Item* demonstrated consistent Superior, Moderate, and Fair trajectories. The *QOL item* demonstrated an additional Moderate-Superior trajectory.

3.3 Predictors of QOLCE Trajectories

The results for predictors of QOLCE trajectories are displayed in Table 4. Number of AEDs prescribed over the study period was a significant predictor of the physical (i.e., *Physical Restrictions, Energy/Fatigue*), emotional (i.e., *Depression, Anxiety, Control/Helplessness*), social (i.e., *Social Activity*), neurocognitive (i.e., *Memory, Other Cognitive*) and overall domains (i.e., *QOL item, General health, and Overall*). Internalizing problems significantly predicted trajectories for the physical (i.e., *Energy/Fatigue*) emotional (i.e., *Depression, Anxiety*) and overall domains (i.e., *QOL item, General health item, Overall HRQOL*). Externalizing problems was a significant predictor of physical (i.e., *Energy/Fatigue*),

emotional (i.e., *Energy/Fatigue, Self-Esteem, Depression, Control/Helplessness*), behavioral (i.e., *Attention/Concentration, Behavior*) and neurocognitive (i.e., *Memory, Other Cognitive*) domains of HRQOL. Side effects from AED treatment, seizure type, and general family functioning predicted trajectories for several subscales within the social domain. Specifically, seizure type predicted both *Social Interaction* and *Stigma* while family functioning predicted the *Social Interaction* and side effects predicted *Stigma*. Finally, AED adherence trajectories were a significant predictor on the *Depression* subscale.

4. DISCUSSION

The current study highlights the variability in HRQOL trajectories in children with newly diagnosed epilepsy over the initial two years following diagnosis and AED initiation. Establishing predictive trajectory models allows clinicians to identify children at risk for decreased HRQOL and provide recommendations regarding necessary interventions at optional time points. Across a majority of the HRQOL scales, four unique trajectories were identified, which typically included Superior, High, Moderate, and Fair/Poor courses of HRQOL. Nearly all of the subscales revealed at least one at-risk trajectory (i.e., Fair, Poor, Very poor) suggesting that a subset of children with epilepsy have decreased quality of life. Forty percent of children with epilepsy fell in at-risk trajectories for overall HRQOL and up to 78% of children were in an at-risk trajectory across subscales. Interestingly, many of the trajectories appeared stable over time. Post-hoc analyses revealed that the median number of at-risk subscales was three and that 12% of children with epilepsy were at risk on more than half of the subscales, suggesting that children with epilepsy are struggling in multiple aspects of daily functioning. When compared to the work of Ferro and colleagues establishing HRQOL trajectories for the Overall scale, our data bear some consistency[11]. Ferro et al (2013) identified five unique trajectories compared to our four trajectories and there was overlap in two of the five groups (e.g., superior/high stable and moderate increasing/fair). Although sample characteristics are quite similar (e.g., 4–12 year age range, newly diagnosed, pediatric subspecialty care), potential differences in findings could be attributed to healthcare system and usage differences between the US and Canada [28–30].

Number of AEDs was the most consistent predictor across the HRQOL domains (i.e., physical, emotional, neurocognitive, social) and of overall HRQOL. Current number of AEDs prescribed has been found to be a significant predictor of overall HRQOL in previous research[11]; however, it should be noted that in this study number of AEDs represents the quantity of AEDs trialed during the two year period, not polytherapy. Given that medications are typically only altered due to continued seizures or intolerable medication side effects, children who have trialed an increased number of AEDs likely have a more complex disease presentation. Interestingly, seizure probability trajectories and medication side effects were not significant predictors of any of the HRQOL domains (with the exception of side effects being a significant predictor of *Stigma*) when included in the model, which is contrary to previous longitudinal studies[13]. Given that number of AEDs trialed is a clinical decision variable influenced by seizure control, medical history, and medication side effects, it is possible that this variable captures the complexity of the disease in a unique way that is not captured by side effects or seizure frequency alone.

Internalizing Problems were also predictive of overall and emotional HRQOL. These findings are consistent with previous research documenting increased rates of both depression (21–26%;[7] and anxiety (5–49%)[31, 32] in children with epilepsy with subsequent negative impact on HRQOL[7]. The significant relationship between Internalizing Problems and the emotional domain of the QOLCE is not surprising given the overlapping content between the BASC-2 (utilized to assess Internalizing Problems) and the QOLCE. The identification of a modifiable factor such as Internalizing Problems that predicts HRQOL domains allows for the selection of focused psychosocial interventions. Cognitive-behavior therapy (CBT) may be one viable solution for the treatment of internalizing problems such as anxiety and depression in children with epilepsy [33, 34].

Meanwhile, Externalizing Problems predicted trajectories of emotional, behavioral, and neurocognitive domains, but not overall HRQOL. In contrast, previous studies have demonstrated a significant relationship between behavioral and cognitive comorbidities with poorer overall HRQOL[11, 12]. Differing results may be the result of using an objective validated assessment tool to assess externalizing behaviors compared to a single-item physician-reported rating of behavior or cognitive problems. This finding, however, highlights the importance of assessing for domain-specific deficits in HRQOL that may not be apparent from an overall assessment of HRQOL. Given that approximately one-third of children with epilepsy are impacted by externalizing disorders (e.g., attention-deficit/hyperactivity disorder, oppositional defiant disorder) [35] and the relationship between externalizing problems and emotional, behavioral, and neurocognitive domains of HRQOL, treatment focused on decreasing externalizing problems in the home and school settings is imperative. Evidence-based treatment for externalizing disorders includes parent-based behavioral treatment targeting behavioral principles and contingency management, age-appropriate supervision, and problem-solving skills[36, 37]. Providers should assess for behavioral and attention difficulties in children with epilepsy and recommendations for neuropsychological testing or the implementation of evidence-based interventions should be provided as soon as difficulties are noted. Obtaining a neuropsychological evaluation could provide parents and educators with information about the child's strengths and weaknesses and inform interventions to improve academic outcomes[38]. If warranted based on neuropsychological testing results, ideal interventions for externalizing behaviors may include parent training or school-based accommodations, such as 504 plans or Individualized Education Plans[39, 40].

Several other medical and family variables emerged as significant predictors of HRQOL subscales. For example, in addition to number of AEDs, side effects, seizure type, and family functioning were also predictive of group status on the social subscales. Children taking AEDs often experience significant side effects such as weight gain, fatigue, cognitive difficulties, and behavioral problems. Each of these side effects has the potential to impact a child's ability to initiate or maintain friendships. It is possible that in addition to social interference by AED side effects, children with epilepsy may not have the opportunity to engage in some social or extracurricular activities due to physical restrictions. Previous research has demonstrated that children with epilepsy have poorer social skills than healthy controls[41] and results of this study indicating that 79% percent of participants fall in the Poor trajectory group on the Social Interaction subscale support this idea. Interventions

aimed to improve family functioning or stigma-reduction interventions such as psychoeducation, cognitive restructuring, and acceptance and commitment therapies [42] may be beneficial for children with a poor social interactions trajectory.

Finally, adherence trajectory group status was also a significant predictor of Depression trajectory with children in the Early Severe Non-adherence group being more likely to have increased levels of depression than individuals in the Variable Non-adherence, Moderate Non-adherence, and High Non-adherence groups. This relationship between adherence and depression in children with epilepsy has been documented within the larger adherence literature[43, 44] and is important given that interventions such as problem-solving exist to improve medication adherence in children[45]. As noted previously, HRQOL depressive symptoms could also be addressed through Cognitive-Behavioral Therapy.

This study, however, is not without limitations. First, the significant relationships between Internalizing Problems (BASC-2) and emotional HRQOL (QOLCE) and Externalizing Problems (BASC-2) and behavior HRQOL (QOLCE) may be the result of shared variance between these scales; however, this data provides support for the convergent validity of these scales. Second, this study included children age 2–12 years and results are not generalizable to adolescents with epilepsy. Additionally, parents provided information regarding epilepsy-specific HRQOL because of the young age of study participants. Future studies may consider a larger developmental range with assessment of the child's perspective of their own HRQOL. Third, there was attrition across the course of this two-year longitudinal study, which may limit generalizability. Another limitation of the study is the poor internal consistency reliabilities on a few of the QOLCE subscales; however, many of these subscales are above the criterion generally accepted as adequate (i.e., $>.70$) [46]. Finally, we were not able to examine the predictive value of two previous established predictors of HRQOL, maternal depression and cognitive problems; however, it is a strength of this paper that behavior problems was measured with a well validated assessment tool.

5. CONCLUSIONS

This study provides a comprehensive predictive model of two-year trajectories of overall, physical, emotional, behavioral, social, and neurocognitive HRQOL for children following pediatric epilepsy treatment initiation. Results extend the literature by documenting trajectory groups across a variety of HRQOL domains and by delineating significant predictors of various domains of HRQOL. Clinicians can use these predictive trajectory models to identify children at risk for decreased HRQOL and provide recommendations regarding necessary interventions and optimal timing for the delivery of such interventions. Assessing for specific domains of HRQOL will allow for the identification of children with epilepsy who may have be at-risk in one or more HRQOL domains, but not overall HRQOL. Future research should focus on the efficacy of interventions to improve externalizing and internalizing problems and adherence in children with epilepsy and as a result improve HRQOL.

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Abbreviations

AED	antiepileptic drug
HRQOL	health-related quality of life
SES	socioeconomic status

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Highlights

- 40% of children with epilepsy fell in at-risk trajectories for overall health-related quality of life (HRQOL).
- Most subscale models contained at least one at-risk trajectory containing up to 78% of children with epilepsy.
- Many of the HRQOL trajectories appeared stable during the two years following epilepsy diagnosis and AED treatment initiation.
- Number of AEDs, Internalizing Problems, and Externalizing Problems emerged as the most consistent predictors across the HRQOL domains.
- Medical and psychosocial interventions should target modifiable factors shortly after diagnosis to improve HRQOL for children with epilepsy.

Figure 1.

Table 1

Participant Characteristics

Factor	Baseline (n = 94)		25 months ^a (n = 84)	
	<i>M</i>	<i>SD</i>		
Child age (years)	8.14	2.37	7.16	2.73
Family Duncan score ^b	53.15	19.95	55.54	20.16
	<i>n</i>	%	<i>n</i>	%
Child sex				
Male	59	63	50	59.5
Child race				
White	68	72.3	65	77.4
Black	18	19.1	13	15.5
Biracial	5	5.3	4	4.8
Other	3	3.1	2	2.4
Child epilepsy diagnosis				
Idiopathic	76	80.9	69	82.2
Localization-related	39	41.5	40	47.6
Generalized	22	23.4	17	20.2
Unclassified	15	16	12	14.3
Cryptogenic	12	12.8	11	13.1
Localization-related	6	6.4	7	8.3
Generalized	6	6.4	4	4.8
Symptomatic	6	6.4	4	
Localization-related	5	5.3	3	3.6
Generalized	1	1.1	1	2.2
Child initial antiepileptic drug therapy				
Carbamazepine	51	54.3	51	60.7
Valproic acid	43	45.7	33	39.3
Parent relationship to child				
Mother	79	84.0	70	83.3
Parent marital status				
Married	62	66.0	56	66.7

^aBaseline participant data is utilized for the 25 month assessment report to ensure comparability

^bAssociated with occupations such as property managers, physician's assistants, mail carriers, sheriffs/law enforcement, and fire prevention

Table 2

Final Trajectory Models for QOLCE overall and subscales

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
QOLCE Physical Restrictions (<i>k</i> = 3)				
Superior (8.6)	Int	84.4 (77.0 – 91.8)	22.43	<.001
	Linear	7.41 (2.71 – 12.11)	3.08	.002
	Quadratic	–0.798 (–1.390 – –0.206)	–2.64	.009
Moderate (58.6)	Int	68.2 (65.1 – 71.3)	43.20	<.001
	Linear	3.61 (1.81 – 5.41)	3.91	<.001
	Quadratic	–0.324 (–0.538 – –0.110)	–2.96	.0032
Fair (32.9)	Int	55.5 (51.3 – 59.7)	26.11	<.001
	Linear	–0.91 (–3.18 – 1.36)	–0.78	.44
	Quadratic	0.145 (–0.129 – 0.419)	1.03	.30
QOLCE Depression (<i>k</i> = 3)				
Superior (38.6)	Int	87.2 (84.4 – 90.0)	60.28	<.001
	Linear	2.21 (0.41 – 4.01)	2.41	.02
	Quadratic	–0.241 (–0.457 – –0.025)	–2.19	.03
Moderate (49.8)	Int	80.9 (78.3 – 83.5)	60.24	<.001
	Linear	–0.81 (–2.24 – 0.62)	–1.12	.26
	Quadratic	0.095 (–0.076 – 0.266)	1.09	.28
Poor (11.6)	Int	62.6 (57.1 – 68.1)	22.34	<.001
	Linear	0.01 (–2.95 – 2.97)	.01	>.99
	Quadratic	0.072 (–0.289 – 0.433)	.39	.70
QOLCE Anxiety (<i>k</i> = 4)				
Superior (11.7)	Int	94.3 (86.7 – 101.9)	24.33	<.001
	Linear	4.98 (0.16 – 9.80)	2.02	.04
	Quadratic	–0.334 (–0.951 – 0.283)	–1.06	.29
High (54.2)	Int	83.3 (79.8 – 86.8)	45.96	<.001
	Linear	–0.77 (–2.75 – 1.21)	–0.76	.44
	Quadratic	0.145 (–0.098 – 0.388)	1.18	.24
Moderate (18.4)	Int	76.8 (68.3 – 85.3)	17.74	<.001
	Linear	–2.95 (–6.73 – 0.83)	–1.53	.13
	Quadratic	0.193 (–0.332 – 0.718)	0.72	.47
Poor-Moderate (15.7)	Int	55.4 (47.4 – 63.4)	13.46	<.001
	Linear	–1.81 (–5.48 – 1.86)	–0.97	.33
	Quadratic	0.448 (–0.001 – 0.897)	1.96	.051

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
QOLCE Energy/Fatigue (<i>k</i> = 3)				
High (18.1)	Int	81.1 (71.4 – 90.8)	16.35	<.001
	Linear	4.03 (–0.79 – 8.85)	1.64	.10
	Quadratic	–0.455 (–1.008 – 0.098)	–1.62	.11
Moderate (52.6)	Int	63.8 (56.4 – 71.2)	16.99	<.001
	Linear	3.13 (0.44 – 5.82)	2.29	.02
	Quadratic	–0.306 (–0.635 – 0.023)	–1.82	.07
Poor (29.3)	Int	46.0 (39.0 – 53.0)	12.89	<.001
	Linear	0.53 (–2.80 – 3.86)	0.31	.75
	Quadratic	–0.025 (–0.436 – 0.386)	–0.12	.91
QOLCE Control/Helplessness (<i>k</i> = 4)				
Superior (15.1)	Int	85.7 (78.8 – 92.6)	24.59	<.001
	Linear	3.38 (–0.11 – 6.87)	1.90	.06
	Quadratic	–0.256 (–0.677 – 0.165)	–1.19	.24
High (37.4)	Int	76.1 (71.5 – 80.7)	32.70	<.001
	Linear	2.08 (–0.29 – 4.45)	1.72	.09
	Quadratic	–0.285 (–0.557 – –0.013)	–2.05	.04
Moderate (30.5)	Int	65.5 (60.2 – 70.8)	24.68	<.001
	Linear	–0.25 (–3.11 – 2.61)	–0.17	.87
	Quadratic	0.152 (–0.203 – 0.507)	0.84	.40
Poor (17.0)	Int	53.3 (47.6 – 59.0)	18.19	<.001
	Linear	–0.19 (–3.78 – 3.40)	–0.10	.92
	Quadratic	0.053 (–0.390 – 0.496)	0.23	.82
QOLCE Self-Esteem (<i>k</i> = 4)				
High-Superior (11.0)	Int	87.9 (81.6 – 94.2)	27.78	<.001
	Linear	5.72 (0.92 – 10.52)	2.34	.02
	Quadratic	–0.638 (–0.08 – –1.20)	–2.23	.03
High (53.1)	Int	84.7 (81.8 – 87.6)	57.67	<.001
	Linear	–0.87 (–2.56 – –.82)	–1.01	.31
	Quadratic	0.115 (–0.089 – 0.319)	1.11	.27
Moderate (25.5)	Int	70.5 (65.4 – 75.6)	26.84	<.001
	Linear	–0.79 (–3.30 – 1.72)	–0.62	.31
	Quadratic	0.116 (–0.188 – 0.420)	0.75	.27
Poor (10.4)	Int	54.8 (48.5 – 61.1)	16.86	<.001
	Linear	–0.86 (–4.66 – 2.94)	–0.44	.66
	Quadratic	0.215 (–0.259 – 0.689)	0.89	.37

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
QOLCE Behavior (<i>k</i> = 3)				
Superior (20.8)	Int	83.5 (79.4 – 87.6)	40.35	<.001
	Linear	1.06 (–1.23 – 3.35)	.91	.36
	Quadratic	–0.053 (–0.329 – 0.223)	–0.38	.71
Moderate (60.2)	Int	68.3 (65.6 – 71.0)	49.32	<.001
	Linear	0.40 (–0.99 – 1.79)	.57	.57
	Quadratic	0.015 (–0.150 – 0.180)	.17	.86
Poor (19.0)	Int	53.3 (47.2 – 59.4)	17.44	<.001
	Linear	–0.94 (–3.57 – 1.69)	–0.70	.48
	Quadratic	0.039 (–0.292 – 0.370)	0.23	.82
QOLCE Attention/Concentration (<i>k</i> = 4)				
Superior (16.9)	Int	96.4 (87.9 – 104.9)	22.21	<.001
	Linear	4.68 (–0.59 – 9.95)	1.74	.08
	Quadratic	–0.460 (–1.111 – 0.191)	–1.39	.17
High (33.0)	Int	75.8 (69.5 – 82.1)	23.46	<.001
	Linear	0.56 (–2.95 – 4.07)	.32	.76
	Quadratic	0.038 (–0.385 – 0.461)	.18	.86
Moderate (41.0)	Int	62.3 (57.3 – 67.3)	24.30	<.001
	Linear	–2.02 (–4.94 – 0.90)	–1.36	.18
	Quadratic	0.179 (–0.180 – 0.538)	.98	.33
Poor (9.1)	Int	21.7 (11.8 – 31.6)	4.33	<.001
	Linear	3.27 (–2.49 – 9.03)	1.12	.27
	Quadratic	–0.295 (–0.989 – 0.399)	–0.83	.41
QOLCE Memory (<i>k</i> = 4)				
Superior (14.1)	Int	95.1 (85.3 – 104.9)	18.94	<.001
	Linear	6.51 (1.04 – 11.98)	2.33	.02
	Quadratic	–0.704 (–1.365 – –0.043)	–2.09	.04
Moderate (39.9)	Int	76.4 (71.1 – 81.7)	28.36	<.001
	Linear	0.95 (–2.07 – 3.97)	0.62	.54
	Quadratic	–0.060 (–0.419 – 0.299)	–0.33	.74
Fair (40.0)	Int	61.2 (56.6 – 65.8)	26.12	<.001
	Linear	–1.66 (–4.54 – 1.22)	–1.13	.26
	Quadratic	0.137 (–0.222 – 0.496)	0.75	.45
Poor (6.0)	Int	43.2 (29.7 – 56.7)	6.26	<.001
	Linear	–9.28 (–16.30 – –2.26)	–2.60	.01

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
	Quadratic	1.086 (0.253 – 1.919)	2.55	.01
QOLCE Other Cognitive (<i>k</i> = 5)				
Superior (6.0)	Int	115.7 (93.9 – 137.5)	10.40	<.001
	Linear	7.71 (–4.32 – 19.74)	1.26	.21
	Quadratic	–1.318 (–2.772 – 0.136)	–1.78	.08
High (22.3)	Int	77.7 (68.8 – 86.6)	17.03	<.001
	Linear	3.33 (–1.94 – 8.60)	1.24	.22
	Quadratic	0.042 (–0.658 – 0.742)	0.12	.91
Moderate 1 (39.0)	Int	71.7 (65.9 – 77.5)	24.26	<.001
	Linear	0.73 (–2.70 – 4.16)	0.42	.67
	Quadratic	–0.108 (–0.522 – 0.306)	–0.51	.61
Moderate 2 (27.5)	Int	58.9 (51.6 – 66.2)	15.95	<.001
	Linear	–2.50 (–6.36 – 1.36)	–1.27	.20
	Quadratic	0.207 (–0.289 – 0.703)	0.82	.41
Poor (5.4)	Int	17.1 (4.9 – 29.3)	2.76	.006
	Linear	0.34 (–6.93 – 7.61)	0.09	.93
	Quadratic	–0.070 (–1.598 – 0.198)	–0.15	.88
QOLCE Language (<i>k</i> = 4)				
Superior (19.4)	Int	91.8 (83.8 – 99.8)	22.4	<.001
	Linear	4.85 (0.01 – 9.69)	1.97	.05
	Quadratic	–0.350 (–0.962 – 0.262)	–1.12	.26
Moderate (49.1)	Int	75.1 (71.0 – 79.2)	35.61	<.001
	Linear	0.00 (–2.47 – 2.47)	0.001	>.99
	Quadratic	0.145 (–0.153 – 0.443)	0.95	.34
Poor (21.8)	Int	60.7 (53.5 – 67.9)	16.65	<.001
	Linear	–1.30 (–5.06 – 2.46)	–.068	.50
	Quadratic	–0.042 (–0.501 – 0.417)	–0.18	.86
Extremely Poor (9.7)	Int	31.4 (20.9 – 41.9)	5.86	<.001
	Linear	–2.17 (–7.85 – 3.51)	–0.75	.45
	Quadratic	0.315 (–0.363 – 0.993)	0.91	0.36
QOLCE Social Interaction (<i>k</i> = 2)				
Moderate (21.2)	Int	86.2 (78.9 – 93.5)	23.10	<.001
	Linear	–1.23 (–5.60 – 3.14)	–0.55	.58
	Quadratic	0.077 (–0.462 – 0.616)	0.28	.78
Poor (78.8)	Int	63.3 (60.0 – 66.6)	37.31	<.001

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
	Linear	−0.16 (−2.02 – 1.70)	−0.17	.87
	Quadratic	−0.038 (−0.265 – 0.189)	−0.32	.75
QOLCE Social Activity (<i>k</i> = 2)				
High (47.0)	Int	101.6 (93.6 – 109.6)	24.72	<.001
	Linear	12.62 (6.39 – 18.85)	3.98	<.001
	Quadratic	−1.089 (−0.299 – −1.879)	−2.70	.007
Moderate (53.0)	Int	82.7 (75.8 – 89.6)	23.42	<.001
	Linear	0.38 (−3.58 – 4.34)	.19	.85
	Quadratic	0.077 (−0.399 – 0.553)	.32	.75
QOLCE Stigma Item (<i>k</i> = 2)				
Superior (67.3)	Int	127.5 (113.4 – 141.6)	17.62	<.001
	Linear	7.32 (−1.36 – 16.00)	1.65	.10
	Quadratic	−0.670 (−1.744 – 0.404)	−1.22	.22
Moderate (32.7)	Int	79.4 (63.5 – 95.3)	9.81	<.001
	Linear	−0.56 (−8.64 – 7.52)	−0.14	.89
	Quadratic	0.310 (−0.697 – 1.317)	0.60	.55
QOLCE General Health (<i>k</i> = 3)				
Superior (17.3)	Int	96.2 (43.9 – 148.5)	3.60	<.001
	Linear	8.04 (0.04 – 16.04)	1.97	<.05
	Quadratic	−1.1 (−2.26 – 0.15)	−1.71	.09
Moderate (49.2)	Int	67.6 (44.9 – 90.3)	5.82	<.001
	Linear	4.96 (−0.61 – 10.53)	1.74	.08
	Quadratic	−0.355 (−1.008 – 0.298)	−1.07	.29
Fair (33.5)	Int	49.5 (36.0 – 63.0)	7.18	<.001
	Linear	2.99 (−2.91 – 8.89)	.99	.32
	Quadratic	−0.202 (−0.853 – 0.449)	−.61	.54
QOLCE QOL Item (<i>k</i> = 4)				
Superior (13.6)	Int	187.5 (106.7 – 268.3)	4.55	<.001
	Linear	−29.27 (−59.73 – 1.19)	−1.88	.06
	Quadratic	2.453 (−0.326 – 5.232)	1.73	.08
Moderate to Superior (23.6)	Int	70.4 (61.2 – 79.6)	15.12	<.001
	Linear	16.86 (10.49 – 23.23)	5.19	<.001
	Quadratic	−1.534 (−2.334 – −0.734)	−3.76	<.001
Moderate (37.6)	Int	75.0 (63.4 – 86.6)	12.61	<.001
	Linear	0.77 (−4.42 – 5.96)	.29	.77

Group (%)	Parameter	Estimate (95% CI)	<i>t</i>	<i>p</i>
	Quadratic	0.016 (−0.574 – 0.606)	.05	.96
Poor (25.2)	Int	58.7 (49.5 – 67.9)	12.58	<.001
	Linear	−1.98 (−7.74 – 3.78)	−0.67	.50
	Quadratic	0.323 (−0.336 – 0.982)	0.96	.34
QOLCE Overall (<i>k</i> = 4)				
Superior (26.1)	Int	81.6 (79.4 – 83.8)	71.42	<.001
	Linear	0.99 (0.52 – 1.46)	4.19	<.001
High (33.7)	Int	77.9 (75.9 – 79.9)	75.15	<.001
	Linear	−0.13 (−0.58 – .32)	−0.57	.57
Fair (29.0)	Int	65.9 (63.9 – 67.9)	64.02	<.001
	Linear	0.32 (−0.13 – 0.77)	1.37	.17
Poor (11.1)	Int	52.7 (48.6 – 56.8)	25.06	<.001
	Linear	0.28 (−0.46 – 1.02)	.74	.46

Table 3

Baseline Means, SDs, and SEMs from current and previous samples

Subscale	Current Mean	Current SD	Previous Mean[3]	Previous SD[3]	Speechley SEM[3]
Physical Restrictions	65.00	16.12	62.53	18.48	8.24
Depression	80.83	11.78	78.03	12.47	6.71
Anxiety	77.51	16.07	70.37	16.43	7.80
Energy/Fatigue	60.11	21.08	60.43	19.26	9.33
Control/Helplessness	70.19	17.06	67.74	16.91	8.63
Self-Esteem	77.24	15.03	75.66	14.30	7.84
Behavior	69.40	13.23	67.55	14.77	5.74
Attention/Concentration	67.23	24.18	63.13	24.35	7.62
Memory	69.73	19.79	67.83	22.64	6.89
Other Cognitive	66.08	22.08	62.99	24.10	9.36
Language	69.90	22.00	70.83	22.46	5.94
Social Interaction	67.48	16.19	83.83	21.22	8.28
Social Activities	82.89	19.45	78.64	24.73	9.68
Stigma	84.51	22.19	77.16	27.78	-
General Health	62.77	24.52	61.41	26.78	-
QOL Item	71.54	20.93	72.99	22.90	-
Overall	71.44	11.07	70.24	13.87	4.01

Table 4

Results for QOLICE Scales Requiring Ordinal Logistic Regression Model

Predictors	Physical Restrictions			Depression			Anxiety			Energy/Fatigue			Control/Helplessness		
	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)
SES	0.02	.89	-	1.03	.31	-	2.11	.15	-	0.02	.90	-	1.51	.22	-
# of AEDs	7.55	.01	3.36 (1.42, 7.97)	4.73	.03	2.71 (1.10, 6.66)	6.28	.01	2.80 (1.25, 6.26)	7.07	.01	3.08 (1.34, 7.06)	6.88	.01	2.78 (1.30, 5.96)
Side Effects	0.27	.60	-	0.28	.60	-	0.21	.65	-	0.06	.81	-	0.08	.78	-
Seizures ^a	0.10	.75	-	0.10	.75	-	0.58	.45	-	0.03	.86	-	<.01	.98	-
Adherence	0.45	.93	-	8.66	.03	***	3.89	.27	-	2.66	.45	-	0.74	.86	-
Internalizing Problems	0.11	.74	-	4.56	.03	1.07 (1.01, 1.14)	6.79	.01	1.09 (1.02, 1.16)	8.01	.01	1.09 (1.03, 1.16)	2.67	.10	-
Externalizing Problems	3.79	.05	1.05 (1.00, 1.11)	4.86	.03	1.07 (1.01, 1.13)	0.70	.40	-	7.07	.03	0.94 (0.90, 0.99)	8.49	.003	1.08 (1.02, 1.13)
Parental Worry	2.06	.15	-	0.27	.60	-	0.20	.66	-	1.60	.21	-	<.01	.98	-
Family Functioning	0.20	.66	-	0.55	.46	-	2.33	.13	-	0.64	.42	-	0.18	.67	-
Seizure Type	0.27	.60	-	0.29	.42	-	0.40	.53	-	1.14	.28	-	0.35	.55	-

Predictors	Self-Esteem			Behavior			Attention/concentration			Memory			Other Cognitive		
	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)
SES	0.14	.70	-	1.67	.20	-	0.01	.91	-	0.05	.82	-	0.11	.75	-
# of AEDs	0.44	.51	-	1.29	.26	-	1.20	.27	-	5.59	.02	2.60 (1.18, 5.72)	11.92	.001	4.04 (1.83, 8.93)
Side Effects	0.54	.46	-	0.77	.38	-	0.14	.71	-	1.47	.23	-	1.88	.17	-
Seizures	0.38	.54	-	0.84	.36	-	0.79	.37	-	0.01	.91	-	0.06	.81	-
Adherence	2.29	.51	-	2.20	.53	-	4.85	.18	-	1.21	.75	-	0.92	.82	-
Internalizing Problems	0.49	.48	-	0.10	.48	-	0.12	.73	-	1.34	.25	-	0.25	.62	-
Externalizing Problems	6.44	.01	1.07 (1.02, 1.12)	17.59	.001	1.18 (1.09, 1.27)	16.26	.001	1.12 (1.06, 1.18)	4.18	.04	1.05 (1.00, 1.10)	11.19	.001	1.09 (1.04, 1.14)
Parental Worry	0.62	.43	-	0.01	.94	-	2.20	.14	-	0.85	.36	-	2.46	.12	-
Family Functioning	1.23	.27	-	0.50	.48	-	0.07	.78	-	0.20	.65	-	0.70	.40	-
Seizure Type	0.44	.51	-	0.64	.42	-	1.06	.28	-	2.04	.15	-	1.53	.22	-

Predictors	Language			Social Interaction			Social Activity			Stigma			General Health		
	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)	χ^2	P	OR (95% CI)
SES	0.09	.76	-	0.04	.84	-	2.82	.09	-	2.17	.14	-	0.02	.88	-
# of AEDs	1.15	.28	-	1.39	.24	-	4.61	.03	2.65 (1.09, 6.44)	0.02	.89	-	11.39	.001	5.38 (2.03, 14.30)
Side Effects	0.25	.62	-	1.66	.20	-	0.06	.81	-	4.55	.03	1.07 (1.01, 1.14)	0.06	.81	-
Seizures	1.65	.20	-	2.43	.12	-	0.05	.82	-	0.20	.65	-	1.23	.27	-
Adherence	4.35	.23	-	2.26	.52	-	1.20	.75	-	3.86	.28	-	4.98	.17	-
Internalizing Problems	0.19	.66	-	2.44	.12	-	<.01	.99	-	0.31	.58	-	7.50	.006	1.10 (1.03, 1.17)
Externalizing Problems	10.37	.001	1.08 (1.03, 1.14)	2.33	.13	-	0.79	.37	-	<.01	.98	-	2.93	.09	-
Parental Worry	0.02	.89	-	2.83	.09	-	0.05	.82	-	0.02	.88	-	0.63	.43	-
Family Functioning	0.11	.74	-	4.92	.03	0.05 (0.003, 0.70)	1.00	.32	-	0.97	.33	-	2.44	.12	-
Seizure Type	0.11	.74	-	8.54	.004	0.11 (0.02, 0.48)	3.42	.06	-	3.94	.05	0.40 (0.16, 0.99)	0.05	.82	-

QOL Item		Overall				
Predictors	χ^2	P	OR (95% CI)	χ^2	p	OR(95% CI)
SES	0.07	.79	-	0.08	.78	- 2.27
# of AEDs	10.81	.001	4.05 (1.76, 9.33)	4.62	.03	(1.08,4.78)
Side Effects	0.05	.82	-	0.005	.95	-
Seizures	0.03	.86	-	1.62	.20	-
Adherence	4.10	.25	-	0.43	.93	-
Internalizing Problems	8.12	.004	1.09 (1.03, 1.16)	5.00	.03	(1.01,1.12)
Externalizing Problems	2.31	.13	-	3.10	.08	-
Parental Worry	0.01	.92	-	0.01	.94	-
Family Functioning	2.87	.09	-	0.02	.90	-
Seizure Type	0.03	.87	-	1.82	.18	-

^aSeizure probability trajectory groups indicating the likelihood of patients having a seizure over the two year study were previously identified and used a marker of seizure course in this study [18]

OR (95% CI) for the Early Severe Nonadherence Group vs High Adherence Group: 26.52 (1.82, 387.54), Variable Nonadherence Group vs High Adherence Group: 0.98 (0.14, 6.84), Moderate Nonadherence Group vs High Adherence Group: 0.51 (0.12, 2.07), Severe Early Nonadherence Group vs Moderate Nonadherence Group: 52.49 (3.72, 741.23), Variable Nonadherence Group vs Moderate Nonadherence Group: 1.94 (0.35, 10.64), Group Severe Early Nonadherence vs Variable Nonadherence: 27.06 (1.66, 440.83).