**Treatment Factors Affecting Longitudinal Quality of Life in New Onset Pediatric Epilepsy**

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**Objectives** Recognizing the importance of patient-reported outcomes, this longitudinal, prospective study examined: Changes in health-related quality of life (HRQOL) over seven months following antiepileptic drug (AED) initiation and the relationship of seizures, AED side-effects, and AED type to HRQOL.

**Method** Parents of 124 children with newly diagnosed epilepsy completed measures of HRQOL and side-effects at each clinic visit. Treatment information was also collected. **Results** HRQOL remained stable over time; however, seizures and AED side-effects significantly affected multiple HRQOL domains. Higher seizure activity was associated with decreased Physical HRQOL. Side-effects were negatively associated with all HRQOL domains. Children taking carbamazepine who experienced higher side-effects early in therapy demonstrated declining emotional functioning compared to children experiencing no/some side-effects. **Conclusions** AED side-effects, AED type, and seizure frequency were associated with longitudinal HRQOL in children with newly-diagnosed epilepsy. Routine assessment of AED side-effects and HRQOL may be useful for clinical decision making.

**Key words** antiepileptic drugs; hierarchical linear modeling; newly diagnosed; seizures; side effects.

**Introduction**

Epilepsy, a neurological disorder characterized by repeated seizure activity, affects 325,000 children and adolescents under the age of 15 years and 1% of all youth (Zupanc, 1996). During antiepileptic drug (AED) therapy (standard treatment for pediatric epilepsy), these children are at risk for neurological/behavioral difficulties (Austin & Caplan, 2007; Loring & Meador, 2009), impairments in cognitive and social functioning (Hamiwka & Wirrell, 2009), and AED side-effects (Berg, Levy, Testa, & Shinnar, 1999). As a result, evaluation of the psychosocial impact of epilepsy and its treatment over time is critical. Many organizations, including the Food and Drug Administration, have advocated for greater use of patient-reported outcomes to measure clinical effectiveness (Food and Drug Administration, 2006). Researchers and clinicians have implemented use of health-related quality of life (HRQOL) measures to evaluate the multidimensional impact of a particular diagnosis and subsequent therapy on children’s physical, emotional, and social functioning (Varni, Burwinkle, Seid, & Skarr, 2003).

No prospective pediatric studies have longitudinally assessed changes in HRQOL in a newly diagnosed cohort of children with epilepsy. Cross-sectional studies have documented significant HRQOL impairments for children with epilepsy (Miller, Palermo, & Grewe, 2003; Modi et al., 2009) with specific factors such as increased seizure frequency (Camfield, Breau, & Camfield, 2001; Williams et al., 2003), higher seizure severity (Cramer et al., 1999; Devinsky et al., 1999), and more AED side-effects (Benavente-Aguilar, Morales-Blanquez, Rubio, & Rey, 2006; Gilliam et al., 2004) negatively associated with HRQOL. Longitudinal pediatric epilepsy studies involving children with variable disease duration and at varying points during treatment indicate that disease severity...
influences changes in HRQOL over thirty-three months of treatment (Breau, Camfield, Camfield, & Breau, 2008) while AED side-effects were adversely associated with HRQOL over a three-month time period (Jakovljevic, Jankovic, Jankovic, & Todorovic, 2008). However, no longitudinal studies using well-validated measures of both HRQOL and side-effects currently exist that examine HRQOL from AED treatment initiation. Thus, further understanding of HRQOL is needed to fully identify how disease treatment and clinical response influence changes over time. Such information will have important treatment implications (e.g., choice of AED and when to switch AED type) for healthcare professionals providing seizure management for these youth.

Using the Pediatric Quality of Life Inventory [PedsQL™ (Varni, Burwinkle, Seid, & Skarr, 2003)], the current prospective longitudinal study examined: Changes in HRQOL from diagnosis to seven months following diagnosis and the relationship of seizure presence/absence, medication side-effect severity and AED type to changes in HRQOL over time. It was hypothesized that children’s HRQOL would improve over time and the absence of seizures and less severe AED side-effects would be related to better PedsQL scores over time.

**Patients and Methods**

Potential participants were recruited from a New Onset Seizure Clinic at a Midwestern children’s hospital. Eligibility criteria included: New diagnosis of epilepsy; aged 2–12 years; no parent-reported comorbid chronic illnesses requiring routine medications (e.g., diabetes) or significant parent-reported developmental disorders (e.g., autism), no prior AED treatment, and initiation of carbamazepine or valproic acid monotherapy, which represents standard clinical practice within the New Onset Seizure Clinic. Written parental consent and assent (children 8 years and older) were obtained during their first scheduled clinic visit. During the course of the study, a change in standard clinical practice (i.e., use of the PedsQL to assess HRQOL for clinical purposes for medical and psychosocial providers) occurred and PedsQL measures became available at diagnosis; however, PedsQL scores were missing for n = 50 participants at baseline (e.g., day of diagnosis). Patients returned for routine clinical care one month later and every three months thereafter (e.g., 4- and 7-months post-diagnosis); parents completed the PedsQL at each visit. Patients and children completed several additional questionnaires as part of a larger longitudinal study examining adherence to AED therapy over two years. The study was approved by the local Institutional Review Board.

**Measures**

**Background Information Form**

Demographic information gathered at the initial visit was used to calculate the Revised Duncan (TSEI2; Stevens & Featherman, 1981), an occupation-based measure of socio-economic status (SES), where higher scores reflect higher occupational attainment. For two-caregiver households, the higher Duncan score, ranging from 15 to 97, was used.

**Pediatric Quality of Life Inventory (PedsQL™)**

Parents completed the age appropriate parent-proxy PedsQL™, a valid and reliable 23-item measure assessing generic HRQOL in children aged 2–18 years of age (Varni, Seid, & Kurtin, 2001). The PedsQL™ assesses several domains of functioning: Physical, Emotional, Social, and School and utilizes a 5-point Likert scale (from 0 = never a problem to 4 = almost always a problem). Scaled scores can be collapsed across ages due to similar item content for all versions of the PedsQL. Internal consistency coefficients at baseline ranged from 0.77 to 0.91 for the current sample. Scaled scores are standardized and range from 0 to 100, with higher scores indicating better HRQOL. Minimal clinically important difference (MCID) scores reflect the smallest difference in PedsQL domain scores that patients perceive as beneficial/detrimental and that require a change in patient care and management. The MCID scores for the parent-proxy PedsQL used were: Physical = 6.92, Emotional = 7.79, Social = 8.98, School = 9.67, and Total = 4.50 (Varni, Burwinkle, Seid, & Skarr, 2003).

**Pediatric Epilepsy Side-Effects Questionnaire (PESQ)**

The PESQ is a 44-item validated measure assessing side-effects of AEDs for youth with epilepsy. Items cover a broad range of neurological, behavioral, gastrointestinal, skin, and motor side-effects and are rated on a 6-point Likert scale from 0 (not present) to 5 (high severity). Items were summed to obtain a total side-effects severity score. The measure has demonstrated excellent reliability (Morita, Glauser, Altaye, Fordyce, & Holder, 2003) and the alpha for the current study was 0.88 at the 1-month assessment point.

**Medical History**

Information regarding seizure type, seizure presence/absence, and initiation of AEDs was obtained from medical chart review and parent interview data at each clinic visit. Since the study included children with a wide range of
seizure types and frequencies (ranging from infrequent to multiple per day) and the goal of therapy is “no seizures, no side-effects,” seizure presence/absence was dichotomized and coded as 0 = no seizure activity and 1 = any seizure activity in the time period between and proceeding clinic visits. Similar to prior studies (Mitchell, Scheier, & Baker, 2000), seizure activity was dichotomized to standardize seizure presence/absence across generalized, partial, and unclassified seizures.

Statistical Analyses

Descriptive analyses, including means, standard deviations, and frequencies, were calculated for sociodemographic variables and calculated at each time point for individual subscale and total PedsQL scores. To identify potential model covariates, Pearson correlations and independent t-tests were used to examine the relations between sociodemographic (i.e., child age, gender, minority status, family SES) and medical (i.e., seizure type) variables and PedsQL scores at the 1-month clinic visit. We chose Time 2 for analyses because the largest number of participants were included at this time point. Independent sample t-tests and chi-square tests were conducted to examine differences between patients with complete data (n = 50) versus missing data (n = 75) at any time point on sociodemographic and PedsQL data.

Longitudinal growth curve modeling (LGCM; Singer & Willett, 2003) was used to examine changes in PedsQL scores over time, controlling for significant sociodemographic variables. LGCMs with individual-specific intercepts and slopes were used to examine baseline status and change over time, respectively. Quadratic trends were also examined, but linear trends were found to provide the best fit to the data in all cases. Compared to more traditional analysis of variance methods for repeated measures, LGCM is especially advantageous because it allows for the incorporation of time-varying covariates into the model and is a more valid and efficient method for handling missing longitudinal data (Fitzmaurice, Laird, & Ware, 2004). Specifically, LGCMs are estimated with maximum likelihood estimation, an approach that allows for missing data to be missing at random (Schafer & Graham, 2002).

PedsQL subscale and total scores were included as outcome variables in separate LGCMs. Additional LGCMs examined time-varying predictors of changes in PedsQL scores. Main effects for seizure presence/absence and AED side-effect severity and their interactions with time were examined. A hierarchical approach to longitudinal model building was used (Morrell, Pearson, & Brant, 1997). For example, if a two-way interaction was statistically significant, the main effects associated with this interaction were included in the model, regardless of their p-values. Furthermore, time was controlled for in all models investigating main effects or interactions involving seizure presence/absence or AED side-effect severity. Finally, HRQOL scores were calculated to examine their relations to established PedsQL MCID scores.

The familywise type 1 error rate was set at .05 for each test (e.g., main effect of AED side-effect severity, interaction between seizure presence/absence and time) conducted on the PedsQL scores for the primary hypotheses and statistical significance was defined as p < .01 for each individual test. Confidence intervals of 99% were computed for the parameter estimates corresponding to these tests. The criterion for statistical significance for exploratory hypotheses was defined as p < .05 and 95% confidence intervals were computed. All analyses were conducted with SAS v9.1 (e.g., SAS Proc MIXED).

Results

Participants

One-hundred and thirty consecutive children with new-onset epilepsy and their parents met study inclusion/exclusion criteria. Four percent declined participation due to busy schedules and lack of interest. Demographic characteristics by time point are summarized in Table I. On average, children experienced one to twenty-one (3.4 ± 3.0, median = 3) seizures prior to their diagnosis visit (i.e., baseline) based on parent-report. Sample sizes varied across assessment points. Figure 1 represents a flow-chart and describes reasons for missingness at every time point.

Relations Between Sociodemographic Variables and Baseline HRQOL

Pearson correlations and independent t-tests revealed no significant associations between HRQOL scores at the 1-month post-diagnosis clinic visit and sociodemographic and medical predictors (i.e., partial versus generalized epilepsy), with the exception of age (r’s = −0.04–0.25). Thus, age was controlled for in all subsequent analyses.

Comparison for those with and Without Missing Data

No significant differences were noted for those with missing data at any time point (n = 75) and those with complete data (n = 49) on sociodemographic variables, with the exception of family SES (MComplete = 58.0, MMissing = 48.1, t(122) = 2.72, p = .008, d = 0.50, 95% CI of 2.7–17.1) and child race (PComplete = 17.6%, PMissing = 34.0%, χ²(1) = 4.39, p = .036). Significant differences were also
found between participants with missing data and those with complete data on the following scales by time: Time 1: Physical scale \(M_{\text{Complete}} = 87.4, M_{\text{Missing}} = 78.8, t(72) = 2.04, p = .046, d = 0.51, 95\% \text{ CI of } 0.2–17.0\); Time 1: Social scale \(M_{\text{Complete}} = 83.7, M_{\text{Missing}} = 73.1, t(72) = 2.22, p = .029, d = 0.55, 95\% \text{ CI of } 1.1–20.1\); Time 3: Social scale \(M_{\text{Complete}} = 85.4, M_{\text{Missing}} = 74.8, t(106) = 2.85, p = .005, d = 0.55, 95\% \text{ CI of } 3.2–17.8\); Time 1: Total scale \(M_{\text{Complete}} = 79.9, M_{\text{Missing}} = 71.9, t(72) = 2.10, p = .039, d = 0.52, 95\% \text{ CI of } 0.4–15.6\); Time 3: Total scale \(M_{\text{Complete}} = 79.6, M_{\text{Missing}} = 73.6, t(106) = 2.05, p = .043, d = 0.39, 95\% \text{ CI of } 0.2–11.8\).

Because our LGCMs account for missing data in the outcome variable, we did not include HRQOL as covariates in

**Table I. Demographic Characteristics of Participants by Assessment Point**

<table>
<thead>
<tr>
<th></th>
<th>M ± SD or n (%)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline*</td>
</tr>
<tr>
<td>N</td>
<td>75</td>
</tr>
<tr>
<td>Child age (years)</td>
<td>7.3 ± 2.9</td>
</tr>
<tr>
<td>Female child gender</td>
<td>28 (37.3%)</td>
</tr>
<tr>
<td>Child race</td>
<td></td>
</tr>
<tr>
<td>White (non-Hispanic)</td>
<td>61 (81.3%)</td>
</tr>
<tr>
<td>Black</td>
<td>9 (12%)</td>
</tr>
<tr>
<td>Other/biracial</td>
<td>5 (6.7%)</td>
</tr>
<tr>
<td>Child seizure type</td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td></td>
</tr>
<tr>
<td>Localization-related</td>
<td>34 (45.3%)</td>
</tr>
<tr>
<td>Generalized</td>
<td>15 (20.0%)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>13 (17.3%)</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td></td>
</tr>
<tr>
<td>Localization-related</td>
<td>5 (6.7%)</td>
</tr>
<tr>
<td>Generalized</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td></td>
</tr>
<tr>
<td>Localization-related</td>
<td>6 (8.0%)</td>
</tr>
<tr>
<td>Generalized</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Child AED</td>
<td></td>
</tr>
<tr>
<td>% on carbamazepine</td>
<td>N/A</td>
</tr>
<tr>
<td>% on valproic acid</td>
<td>N/A</td>
</tr>
<tr>
<td>% of children having seizures between clinic visits</td>
<td>N/A</td>
</tr>
<tr>
<td>Caregiver relationship to child</td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>63 (84.0%)</td>
</tr>
<tr>
<td>Father</td>
<td>9 (12.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (3.9%)</td>
</tr>
<tr>
<td>Caregiver age (years)</td>
<td>36.0 ± 6.9</td>
</tr>
<tr>
<td>Caregiver marital status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>12 (16.0%)</td>
</tr>
<tr>
<td>Married</td>
<td>50 (66.7%)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (17.3%)</td>
</tr>
<tr>
<td>Family Duncan score</td>
<td>54.1 ± 19.9</td>
</tr>
<tr>
<td>Parent-proxy PedsQL scores</td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>84.6 ± 17.3</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>71.5 ± 20.2</td>
</tr>
<tr>
<td>Social functioning</td>
<td>80.3 ± 19.7</td>
</tr>
<tr>
<td>School functioning</td>
<td>66.3 ± 23.87</td>
</tr>
<tr>
<td>Total</td>
<td>77.3 ± 15.7</td>
</tr>
<tr>
<td>PESQ Total score</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*Data reflects participant characteristics and QOL at AED treatment initiation.

**Other**: Separated, divorced, or widowed.
our models; however, we do include family SES and child’s race in all of our models to control for any possible bias due to missingness.

HRQOL Over Time
Controlling for age, family SES, and child race, no significant rates of change over time were noted for any PedsQL scaled scores with the exception of a trend for the Emotional functioning score rate of change of .51 units (99% CI from −1.17 to 1.19) per month ($t_{116} = 1.93$, $p = .056$).

Seizure Presence/Absence and HRQOL Over Time
Controlling for age, family SES and child race, LGCM analyses revealed significantly different intercepts for PedsQL Physical scores, where the intercept is 5.6 units lower (99% CI of 0.9–10.4) when seizures are present versus when they are absent ($t_{80} = -3.08$, $p = .003$). This difference was maintained across the 7-month period as the linear trend over time was not statistically significant. No significant main or interaction effects were detected for the other scales; however, a negative trend on the intercepts was noted for the PedsQL Total scores ($\beta = -3.7$, $t_{80} = -2.60$, $p = .011$, 99% CI from −7.4 to 0).

Side-Effects and HRQOL Over Time
In contrast, the intercepts were statistically significant across all PedsQL scores as a function of AED side-effect severity: Physical ($\beta = -0.43$, $t_{79} = -6.44$, $p < .0001$, 99% CI from −0.60 to −0.26), Emotional ($\beta = -0.40$, $t_{78} = -3.73$, $p < .0001$, 99% CI from −0.58 to −0.22), Social ($\beta = -0.21$, $t_{79} = -2.79$, $p = .007$, 99% CI from −0.40 to −0.02), and Total ($\beta = -0.37$, $t_{79} = -7.16$, $p < .0001$, 99% CI from −0.50 to −0.24) (see Figure 2$^1$). Specifically, children with epilepsy experiencing a higher level of side-effects

$^1$Figures used PedsQL scores implied by the LGCM results. Because of potential bias due to missing data (e.g., SES differences between patients with complete and incomplete data), the model implied scores better represent the population of interest compared to observed PedsQL scores. For illustrative purposes, the PedsQL score trajectories are graphed assuming constant values for the time-varying covariates (other than time since diagnosis) across time. While the particular trajectory an individual follows will generally change with the time-varying covariate, the figures provide a representative, but nevertheless oversimplified, account of the data. Quantitative time-varying covariates (e.g., side-effect severity) are plotted based on the $M$ and $M + 1SD$ for the sample.
demonstrated consistently lower HRQOL scores over time compared to children with no or mean level of side-effects. No rates of changes were significant nor were any significant interactions noted between side-effect severity and time for any scales.

Exploratory analyses further investigated the role of AED type and time on the AED side-effect and HRQOL relationship. The two-way interaction between AED type and side-effect severity was only statistically significant for the PedsQL Emotional Functioning Scale ($\beta = 0.30$, $t_{155} = 2.04$, $p = .043$, 95% CI of 0.01–0.59). This two-way interaction was further tested using a three-way interaction between AED type, side-effect severity, and time. The three-way interaction was statistically significant ($\beta = -0.19$, $t_{60} = -3.93$, $p < .001$, 95% CI from $-0.28$ to $-0.10$; see Figure 3 [footnote 1]). Specifically, children prescribed carbamazepine and experiencing higher initial side-effect severity (+1SD) demonstrated declining rates of change in emotional functioning over time compared to children who experienced no/some side-effects initially. In contrast, children prescribed valproic acid demonstrated steady or improving emotional functioning regardless of initial side-effect severity.

The MCID was applied to examine whether declines/improvements in PedsQL Emotional Functioning scores were clinically meaningful to patients. Children prescribed carbamazepine experiencing higher side-effect severity (+1SD)
demonstrated clinically meaningful declines on the PedsQL Emotional Functioning Scale (mean change score = −15.8 points; MCID = 7.9 points). In contrast, children prescribed valproic acid experiencing higher side-effect severity (+1SD) demonstrated clinically meaningful improvements on the PedsQL Emotional Functioning Scale (mean change score = 10.8 points; MCID = 7.9 points).

Discussion

This is the first longitudinal study to examine HRQOL over time in children newly diagnosed with epilepsy and beginning AED therapy. The current study utilized quantitative, validated measures of both HRQOL and side-effects to examine changes in HRQOL within the context of standard clinical care. Contrary to our hypothesis, HRQOL remained relatively stable from diagnosis to 7-months post-AED initiation across most scales. This is in contrast to a prior study where adults diagnosed with epilepsy demonstrated HRQOL improvements when initiated on lamotrigine (Gillham, Kane, Bryant-Comstock, & Brodie, 2000). Our study only detected a statistical trend for improvements in emotional functioning over time. This may be attributed to the fact that children and parents received extensive education regarding diagnosis, prognosis, and the benefits of AED therapy. Such education likely lessened the anxiety and fear often associated with even a single seizure (Modi et al., 2009) and receiving a diagnosis of epilepsy (Li, Ji, Qin, & Zhang, 2008; Williams et al., 2003).

The lack of significant HRQOL changes across other domains may be explained by several factors. First, physical, social, school, and total functioning remain constant over time based on group means. However, individual trajectories did vary and some patients improved while others declined over time. Although no group effects were noted, individual HRQOL data can yield patient specific clinically-relevant information for healthcare providers. Second, children with newly diagnosed epilepsy are at high risk for identification of previously undetected neurological, attentional and behavioral co-morbidities (Austin & Caplan, 2007; Loring & Meador, 2009). The assessment and identification of these comorbidities may influence how parents view their children’s overall functioning. Finally, as demonstrated by prior studies and our current analyses, several important covariates may account for individual differences in HRQOL over time, including seizure presence/absence and AED side-effects.

Overall, seizure presence/absence was differentially associated with HRQOL domains over time. Specifically, children who achieved complete seizure control over a seven-month period exhibited improvements on the PedsQL Physical Functioning Scale and a trend was noted for the PedsQL Total scale. Since physical recovery from the effects of one or more seizures is variable between patients, impairments in the Physical domain are not surprising. Furthermore, as children attain seizure control, caregivers may feel more comfortable allowing children to participate in sports/hobbies, chores, and physical activities of daily living, thereby increasing this aspect of HRQOL. Such findings are consistent with prior studies demonstrating that seizure severity/activity negatively affects HRQOL in children and adults (Bautista & Tannahill, 2009; Leidy, Elixhauser, Vickrey, Means, & Willian, 1999; Sabaz et al., 2003a). For example, it is well documented that continued seizures and intractability are associated with the worst HRQOL outcomes. These data reinforce that achieving complete seizure control must be one of the primary goals of epilepsy management.

AED side-effects were globally and negatively associated with all aspects of HRQOL. Our findings build upon prior studies in both adult (Jacoby, Snape, & Baker, 2009) and pediatric (Benavente-Aguilar et al., 2004; Jakovljevic et al., 2008) populations by demonstrating the negative relationship of side-effects starting at AED initiation and HRQOL. Common side-effects endorsed by the current sample and associated with carbamazepine and valproic acid included: Fatigue/drowsiness, hyperactivity, attention difficulties, memory problems, and headaches. Such side-effects would affect physical, emotional, social, and school functioning for children with newly diagnosed epilepsy. The persistence of side-effects relative to a discrete seizure event may play a larger role in children’s overall functioning. This has significant clinical implications as providers determine which AED to initiate and how long to maintain children on a specific AED.

Exploratory analyses revealed a three-way interaction between time, side-effects, and AED type on PedsQL Emotional functioning scores. Children prescribed carbamazepine with higher initial side-effects (+1SD) had declining emotional functioning across seven months compared to those reporting no side-effects or the mean level of side-effects initially. The decrease in HRQOL scores exceeded the MCID, suggesting that parents perceived a significant decline in their children’s emotional health. In contrast, children prescribed valproic acid demonstrated relative improvements in emotional functioning scores over time, regardless of their initial side-effects. While children on valproic acid demonstrate variable emotional HRQOL after treatment initiation, the potential mood enhancing nature of this drug appeared to affect the upward
trajectories and converging of all three side-effect groups. This implies that consideration should be given for changing AEDs in children taking carbamazepine who experience more severe side-effects initially (since the HRQOL is projected to deteriorate over time) while children prescribed valproic acid can be reassured that their HRQOL will likely improve over time. It is important to note that carbamazepine is used to primarily treat partial seizures while valproic acid is used to treat generalized and unclassified seizures; thus, these AEDs cannot be used interchangeably.

Although this is the first longitudinal study to examine HRQOL over time in a newly diagnosed cohort of children with epilepsy, there were several limitations. First, despite seven months of follow-up, this study does not address the long-term prognosis and functioning of these children; however, 7-months represent a period of time when changes in HRQOL are likely to occur due to AED treatment initiation. It is possible that a subset of children who continue to experience seizures and develop intractability will have different HRQOL trajectories one to two years following treatment compared to those who have good seizure control and minimal side effects. Thus, future studies are needed to examine the long-term (e.g., 2 years) effects of seizures and side effects on HRQOL. Second, since children had both partial and generalized seizures and variable seizure frequency, seizure presence/absence was treated as a dichotomous variable. Future studies could examine a subpopulation of children with partial epilepsy and define seizures as a continuous variable to better clarify the impact of multiple seizures on HRQOL. Third, while the PedsQL is a well-validated generic measure of HRQOL, study findings may have differed if an epilepsy-specific measure was utilized because it assesses more salient domains (e.g., cognitive functioning, behavioral symptoms). However, unlike the PedsQL measure, epilepsy-specific measures are time consuming and not feasible in a busy clinic due to length [e.g. 79 items for the United States Quality of Life in Childhood Epilepsy Questionnaire (Sabaz et al., 2003b)]. Forth, due to the age range of children in this study, only parent proxy-reported HRQOL was used. Prior literature suggests that both parent and child reports of HRQOL are correlated (Varni, Seid, & Skarr, 2001); however, children provide a unique perspective on their own functioning, especially in emotional/social functioning domains (Eiser & Morse, 2001). Use of multi-method reporting of HRQOL over time in a larger and older sample of children with epilepsy is warranted, especially given our non-random missing data (n = 49) at Time 1. Because parental functioning may also impact reporting of their child’s functioning (Janicke et al., 2007; Quittner, Davis, & Modi, 2003) and parents and children are adjusting to a new diagnosis of epilepsy (Eiser, 1993; Modi, 2009), future studies should attempt to tease apart the influence of these factors on HRQOL changes over time. Furthermore, it is possible that younger children in our sample were unable to report side effects similar to children who were older and more verbal; thus, our data may represent an underestimation of side effects. Fifth, although this study represents an initial step in examining the relations of seizures and side-effects with HRQOL of young children with epilepsy, future studies should investigate other potential correlates of HRQOL, including medical comorbidities, family functioning, and adherence to AED therapy. Finally, children were not randomized by medication type; medication was prescribed according to standard clinical practice at one institution. Children with intractable epilepsy (e.g., continued seizures and failure on two or more AEDs) or those initiated on other AEDs may experience greater/lesser adverse effects or higher/lower QOL than participants in the current study. A future, randomized trial testing medication type will help to fully clarify this issue and determine if current results generalize to other clinical settings.

The results of this study have important implications for clinical care. Although complete seizure control is a primary goal for epilepsy treatment, AED side-effects play a key role in the HRQOL of this population. Healthcare providers should provide anticipatory guidance (i.e., to help individuals know what to expect) to children and their families around the possible impact of AED side-effects; this may help patients feel more comfortable communicating whether side-effects are tolerable or intolerable. Engaging in communication around these issues will enable shared-decision making around the next steps for treatment. Healthcare professionals of children with epilepsy should routinely assess HRQOL to provide optimal therapy for their patients by ascertaining the relative impact of seizures and side-effects on their’s patient quality of life.

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References


Varni, J. W., Seid, M., & Kurtin, P. S. (2001). PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. Medical Care, 39, 800–812.
