

Epilepsy Common Data Elements: Quality of Life Recommendations of the Quality of Life Subcommittee

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Purpose:

To evaluate disease-specific and generic instruments for measuring health-related quality of life (HRQOL) in children and adults with epilepsy and make recommendations for:

- A. epilepsy-specific quality of life instrument for pediatrics
- B. epilepsy-specific quality of life instrument for adults
- C. generic quality of life instruments for pediatrics and adults

Methods:

MEDLINE and CINAHL databases were searched to identify epilepsy-specific quality of life instruments for children or adults with epilepsy that were published in the past 10 years. Search terms included the following: children or adults, epilepsy, and health-related quality of life. Articles were reviewed to identify the most commonly used instruments and any new instruments that had been developed. Evaluation criteria included: clinical relevance of domains, availability in English, breadth and depth of psychometric properties, respondent burden, child age range, and availability of the scale.

A. Epilepsy-Specific Quality of life Instrument for Children and Adolescents

Rationale:

A search of the literature in the past 10 years for pediatric epilepsy identified that the most commonly used instrument was Quality of Life in Childhood Epilepsy (QOLCE) (Sabaz et al., 2000). The original QOLCE, which was developed in Australia in 2000, has 76 items, is parent completed, and takes approximately 30 minutes to complete. In 2003, a US version of the QOLCE was developed that has 79 items and 16 subscales (Sabaz et al., 2003). A 55-item version of the QOLCE (i.e., QOLCE – 55) was developed in 2015 (Goodwin et al., 2015) by investigators at the Advancing Research in Children’s Health Laboratory in Canada. The QOLCE-55 addressed the weaknesses of the original QOLCE (e.g., large number of items and subscales) and retained its strengths of having clinically relevant domains, excellent psychometric properties, applicability to a wide age range of children, and availability. It was the most recent version, QOLCE-55, that was recommended by the committee for an epilepsy-specific quality of life instrument for pediatric epilepsy.

Instrument Recommended: QOLCE-55: Quality of Life in Childhood Epilepsy

Description:

The QOLCE-55 is a parent-completed 55-item instrument that measures four dimensions of quality of life: Cognitive (22 items), Emotional (17 items), Social (7 items), and Physical (9 items). For Cognitive, Social, and Physical domains, parents respond to items about how often their child displayed the described behavior on 5-point scales: (Very Often, Fairly Often, Sometimes, Almost Never, and Never) during the past 4 weeks. For the Emotional domain, parents respond to how much of the time that their child displayed the described emotions on 5-point scales (All the time, Most of the time, Some of the time, A little of the time, and None of the time) during the past 4 weeks. Parents are also able to respond with Not Applicable for all items. The total score ranges between 0 and 100 with a higher score reflecting a higher well-being. Time required to complete the scale is approximately 12-14 minutes.

Psychometric Properties:

The four dimensions were confirmed by factor analysis. Internal consistency reliability (Cronbach's alpha) for the four dimensions and total scale were: Cognitive (.97), Emotional (.88), Social (.89), Physical (.82), and Total (.96). Validity was supported when QOLCE-55 subscale scores were strongly correlated with similar subscales and weakly correlated with dissimilar subscales on the Child Health Questionnaire in a sample of children with new-onset epilepsy. Measurement equivalence was demonstrated when a sample of children with new-onset epilepsy was stratified by age (4-7 years vs 8-12 years), sex (male vs. female), and time (diagnosis vs. 24 months later). Support for the factor structure, internal consistency reliability, and validity was also found in a sample of children with drug-resistant epilepsy. Information on test-retest reliability and sensitivity to change have not been reported.

Relationships with Other Variables:

Predictors of better quality of life were related to absence of cognitive problems, better family functioning, and fewer family demands.

Weaknesses:

Because there is no child report version available, there is no opportunity to obtain children's perceptions with this instrument. Although respondent burden is less than for the original QOLCE, the QOLCE-55 is still a relatively long instrument for parents to complete. Tests of measurement equivalence across groups stratified by clinical characteristics of epilepsy (e.g., IQ level, comorbidities, seizure severity) have not been reported.

Sources for Materials and Permissions:

The QOLCE-55 measure is freely available and can be accessed online at <http://archlab.ca/qolce-55-available-for-download/>. Scoring instructions and relevant publications on its development are also included on the website.

Primary Reference:

Goodwin, SW, Lambrinos, AI, Ferro, MA, Sabaz, M. & Speechley, KN. Development and assessment of a shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55). *Epilepsia*. 2015;56(6): 864–872.

Selected References:

Conway L, Widjaja E, Smith ML, Speechley KN, Ferro M. Validating the shortened Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) in a sample of children with drug-resistant epilepsy. *Epilepsia*. 2017;58(4):646–656.

Ferro MA, Goodwin SW, Sabaz M, Speechley KN. Measurement equivalence of the newly developed Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55). *Epilepsia*. 2016;57(3):427–435.

Sabaz M, Cairns D, Lawson J, Nheu N, Bleasel A, Bye A. Validation of a new quality of life measure for children with epilepsy, *Epilepsia*. 2000;41(6):765–774.

Sabaz M, Lawson JA., Cairns DR, Duchowny MS, Resnick TJ, Dean PM, Bye, AME. Validation of the quality of life in childhood epilepsy questionnaire in American epilepsy patients. *Epilepsy Behav*. 2003;4(6):680–691.

Other Epilepsy-Specific Instruments of Note:

If investigators desire to have children (ages 8 – 15 years) complete an epilepsy-specific instrument, the committee recommended the *Childhood Quality of Life in Epilepsy (CHEQOL)* (Ronen et al., 2003). Children are asked to respond twice to 25 items to how true the statement is for them. There are 5 subscales: Interpersonal/Social Consequences; Worries and Concerns; Intrapersonal/Emotional; Secrecy and Concealment; and Quest for Normality. There is also a parent proxy scale available. Psychometric properties are excellent.

It is also important to mention that a new epilepsy-specific scale for children ages 5 to 18 years, the PedsQL™ Epilepsy Module, is being developed (Follansbee-Junger, et al., 2016). This 29-item instrument has five subscales: Impact, Cognitive, Sleep, Executive Functioning, and Mood/Behavior. There is a parent proxy scale.

Psychometric properties are very strong in early testing. The process to develop the scale followed that of the generic PedsQL, and Dr. Varni (the creator of the original PedsQL) was involved in the design of the epilepsy-specific module to ensure that rigorous methodology was followed related to the development of HRQOL measures (e.g., focus groups, expert review, cognitive testing, full scale validation). The PedsQL-Epilepsy module can be administered along with the generic PedsQL.

References:

Ronen GM, Streiner DL, Rosenbaum P; Canadian Pediatric Epilepsy Network. Health-related Quality of Life in Children with Epilepsy: Development and Validation of Self-report and Parent Proxy Measures. *Epilepsia*. 2003;44(4):598–612.

Modi AC, Junger KF, Mara C, Kellermann T, Barrett L, Wagner J, Mucci GA, Bailey L, Guilfoyle SM, Urso L, Hater B, Hustzi H, Smith G, Hermann B, Perry S, Zupance M, Varni, J. Validation of the PedsQL™ Epilepsy Module: A pediatric epilepsy-specific health-related quality of life measure. *Epilepsia*. 2017;58(11):1920–1930.

Follansbee-Junger KW, Mann KA, Guilfoyle SM, Morita DA, Varni JW, Modi AC. Development of the PedsQL™ Epilepsy Module: Focus Group and Cognitive Interviews. *Epilepsy Behav*. 2016;62:115–120.

B. Epilepsy-Specific Quality of life Instrument for Adults

Rationale:

A search of the literature in the past 10 years identified the most commonly used instrument to measure quality of life in adults with epilepsy was the 31-Item Quality of Life in Epilepsy Inventory (QOLIE-31; 1998). This tool was one of the instruments recommended for use in the original Common Data Elements for quality of life in epilepsy.

The QOLIE-31 was developed by eliminating many of the generic QOLIE-89 items and adding other items reflecting concerns of persons with epilepsy, based on expert panel review. Approximately half the QOLIE-31 items are taken from the QOLIE-89. The others were developed specifically for this instrument and are not included in the QOLIE-89. The QOLIE-31 now contains 31 items assessing the 7 domains of Seizure worry (5 items), Overall QOL (2 items), Emotional well-being (5 items), Energy-Fatigue (4 items), Cognitive functioning (6 items), Medication effects (3 items), Social functioning (5 items) and Overall health (1).

Instrument Recommended: The 31-Item Quality of Life in Epilepsy Inventory (QOLIE-31; 1998)

Description:

The QOLIE-31 was originally “designed to serve as an epilepsy-specific instrument for rapid evaluation of the major HRQOL domains of concerns of adults with epilepsy.” (Borghs, et al., 2012; Cramer, et al., 1998). It covers the time frame of the previous 4-week period for 19 questions; the future 4 weeks in 2 questions; and is unspecified for 10 questions. There are several questions related to each of the epilepsy specific concerns. Completion takes approximately 5-15 minutes.

Cross-cultural translations and validation studies have been done. Translations are now available in Danish, Dutch, German, Canadian French, French, Italian, Spanish, Swedish, UK English, Greek, Thai, Czech, Brazilian Portuguese and Chinese. Validation studies have been performed in Spanish, Chinese, Greek, Thai, Italian, French, Czech, Brazilian Portuguese, and German. Additionally, there are recent published studies using the QOLIE-31 in Bhutan, Bulgaria, India, Malaysia, Nigeria, Persia, Russia, Serbia, Turkey and Uganda.

Psychometric Properties:

Scoring is 0 – 100 points with higher scores indicating better quality of life. Sub-scale and total scores can be calculated.

Reliability – .89 overall; subscales ranged from .77-.85. Test–retest demonstrated good reliability with range: $r = 0.64 - 0.85$.

Validity – Known-groups validity has been established for seizure frequency and severity, employment, polytherapy, health care utilization, economic status, age and epilepsy onset. QOLIE-31 scales correlate with measures of mood, depression, and AED toxicity.

Responsiveness to Change – has been shown to be sensitive to the effects of changing to a novel AED, participating in a disease management program, and surgery to control seizures.

Weaknesses: This questionnaire is not intended for use in intellectually impaired persons. Respondents must be able to read and comprehend the questions at a 10 to 12-year-old level.

Source for Materials and Permissions: Joyce Cramer (Joyce.Cramer@gmail.com)

References:

Primary References:

Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. *Epilepsia* 1998;39:81–88.

Borghs S, de la Loge C, Cramer JA. Defining minimally important change in QOLIE-31 scores: estimates from three placebo-controlled lacosamide trials in patients with partial-onset seizures. *Epilepsy Behav.* 2012;23(3):230–234.

Secondary References:

Blond BN, Detyniecki K, Hirsch LJ. Assessment of treatment side effects and quality of life in people with epilepsy. *Neuro Clin.* 2016;34:395–410.

Leone NA, Beghi E, Righini C, Apolone G, Mosconi P. Epilepsy and quality of life in adults: A review of instruments. *Epilepsy Res.* 2005;66:23–44.

Saadi A, Patenaude MA, Mateen FJ. Quality of life in epilepsy-31 inventory (QOLIE-31) scores: A global comparison. *Epilepsy Behav.* 2016;65:13–17.

C. Generic Quality of life Instrument for Adults and Children

Rationale:

Neuro-QoL (Quality of Life in Neurological Disorders) is a set of health-related quality of life (HRQoL) measures for use with adults (18+) and children (ages 8-17) who have a neurological condition or disorder, including epilepsy. While Neuro-QoL has not been widely used in epilepsy, uptake is increasing, and the committee recommended it as a generic HRQoL measure for the reasons described below. Neuro-QoL development was funded by NINDS with the goal of providing a set of standard measures that could be used across a variety of neurological conditions and in both neurology clinical research and clinical practice. Neuro-QoL is appropriate for both within-disease and cross-disease comparisons. Recent work linking individual Neuro-QoL instruments to generic measures included in the Patient Reported Outcomes Measurement Information System (PROMIS) also allows comparisons to non-neurological conditions.

Development utilized state-of-the art qualitative and quantitative methods (including item response theory [IRT]) consistent with FDA guidance regarding Patient Reported Outcomes. Domains (constructs) were selected and items refined based on

patient, caregiver, and expert input. Most of the measures were constructed as item banks, which confers several advantages. The item banks enable assessment using either a variety of fixed-length short forms (SFs) or computer adaptive tests (CAT). CATs, computerized tests that select the most informative items to present based on the participant’s previous response, can shorten assessments while maintaining measurement precision. Any or all items within a bank can be used for assessment, with scores comparable no matter which item or subset of items are used. Thus, users can create their own “custom” short forms that best meet their measurement needs.

Instruments Recommended: Neuro-QoL Measurement System

Description:

The Neuro-QoL system assesses important domains (symptoms, concerns, and issues) of physical, mental and social health that are relevant across disorders (generic measures) along with instruments that assess areas most relevant for specific patient populations (targeted). These domains and available adult and pediatric measures are shown in Table 1. Neuro-QoL domains that are not typically found in epilepsy-specific HRQoL instruments include Stigma, Sleep Disturbance, Emotional and Behavioral Dyscontrol and Positive Affect & Well-being.

Table 1. Neuro-QoL Domains and Measures		Adult	Pediatric
Physical	Function/Health		
	Upper Extremity Function – Fine Motor, ADL	x	x
	Lower Extremity Function – Mobility	x	x
	Symptoms		
	Fatigue	x	x
	Sleep Disturbance	x	
	Pain		x
Mental	Emotional Health		
	Depression	x	x
	Anxiety	x	x
	Stigma	x	x
	Anger		x
	Positive Affect and Well-Being	x	
	Emotional and Behavioral Dyscontrol	x	
	Cognitive Health		
	Cognitive Function	x	x
Communication (Scale)	x		
Social	Ability to Participate in Social Roles and Activities	x	
	Satisfaction with Social Roles and Activities	x	

	Social Relations – Interaction with Peers		x
	Social Relations – Interaction with Adults		x

Length. Standard Neuro-QoL Short Forms are generally 8 items long. Neuro-QoL CATs are typically ~6 items. On average, adult respondents can answer 5 questions and pediatric respondents able to answer 4 questions per minute. Thus, it takes adults ~1 to 1.5 minutes and children ~1.5 to 2 minutes to complete Neuro-QoL measures, depending on which format they are administered in.

Reference period. “In the past 7 days” is the reference period for all items in the adult Neuro-QoL except for Cognitive Function (some items use “currently”), Physical Function (no recall period) and Stigma and Positive Affect and Well-Being, which begin items with “Lately...” Pediatric measures use a 7-day recall period except for Stigma (items begin with “Lately...”) and Cognitive Function (no recall period).

Scores. Neuro-QoL scores are on a T-score metric (mean = 50 and standard deviation = 10) with higher scores indicating more of what is being measured. Short forms can be hand scored using look-up tables. Short forms (standard or custom) and CATs can be automatically scored using one of the available data collection software systems or a free scoring service.

Available translations. Neuro-QoL measures are available in English and Spanish. Individual measures have been translated into other languages. A list of available translations can be found at: <http://www.healthmeasures.net/explore-measurement-systems/neuro-qol/intro-to-neuro-qol/available-translations>

Source for Materials and Permissions: Neuro-QoL is currently distributed through HealthMeasures. Free, administration-ready PDFs can be downloaded from the HealthMeasures website (www.healthmeasures.net).

Psychometric Properties:

Adult Neuro-QoL Short Forms

Reliability – internal consistency of individual instruments ranged from 0.86- 0.96. One-week test-retest range = 0.57- 0.89.

Validity – Neuro-QoL measures correlated in expected directions (convergent and discriminant validity) with generic and epilepsy-specific (e.g., QOLIE-31) legacy measures. However, while correlated with other measures of self-reported cognition, Neuro-QoL cognition was not significantly associated with performance-based measures of cognitive function. Neuro-QoL measures successfully discriminated between different levels of seizure severity.

Responsiveness to Change – Measures showed sensitivity to self-reported change in health status.

Weaknesses: Responsiveness has not been evaluated in intervention or other trials designed to produce change. Neuro-QoL measures do not have caregiver-report versions, limiting their use in adults with cognitive or other deficits that prevent self-report.

Pediatric Neuro-QoL Short Forms

Reliability – internal consistency (ICCs) of individual instruments ranged from 0.44 for Stigma to 0.94 for Upper Extremity Function. Except for Stigma, all measures had ICCs greater than .62. Test-retest reliability (Cronbach's alpha) ranged from 0.76- 0.87.

Validity – Neuro-QoL measures correlated in expected directions with generic and epilepsy-specific measures of similar domains (convergent validity). Anxiety and Cognitive Function discriminated amongst participants with different seizure severity levels. All pediatric Neuro-QoL measures except Cognitive Function and Upper Extremity Function discriminated participants with different levels of quality of life.

Responsiveness to Change – Neuro-QoL did not show sensitivity to self-reported change over time. This finding may have been due to lack of change in the sample, as the primary legacy measure (PedsQL) also failed to demonstrate responsiveness.

Weaknesses: The measures do not have parent-report versions and therefore are not appropriate for use with children younger than 8 years of age. Responsiveness to change has yet to be evaluated in studies where change is to be expected.

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Cella D, Nowinski C, Peterman A, Victorson D, Miller D, Lai JS, Moy C. The neurology quality-of-life measurement initiative. Arch Phys Med Rehabil. 2011;92(10 Suppl):S28–36.

Lai JS, Nowinski C, Victorson D, Bode R, Podrabsky T, McKinney N, Straube D, Holmes GL, McDonald CM, Henricson E, Abresch RT, Moy CS, Cella D. Quality-of-life measures in children with neurological conditions: pediatric Neuro-QoL. Neurorehabil Neural Repair. 2012 Jan;26(1):36-47.

Victorson D, Cavazos JE, Holmes GL, Reder AT, Wojna V, Nowinski C, Miller D, Buono S, Mueller A, Moy C, Cella D. Validity of the Neurology Quality-of-Life (Neuro-QoL) measurement system in adult epilepsy. Epilepsy Behav. 2014;31:77–84.

Lai JS, Nowinski CJ, Zelko F, Wortman K, Burns J, Nordli DR, Cella D. Validation of the Neuro-QoL measurement system in children with epilepsy. *Epilepsy Behav.* 2015;46:209–214.

Correia H, Pérez B, Arnold B, Wong AW, Lai JS, Kallen M, Cella D. Spanish Translation and Linguistic Validation of the Quality of Life in Neurological Disorders (Neuro-QoL) Measurement System. *Qual Life Res.* 2015;24(3):753–756.