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The PedsQL™ in Pediatric Patients with Spinal Muscular Atrophy: Feasibility, Reliability, and Validity of the Pediatric Quality of Life Inventory™ Generic Core Scales and Neuromuscular Module

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Abstract

For Phase II and III clinical trials in children with Spinal Muscular Atrophy (SMA), reliable and valid outcome measures are necessary. Since 2000, the American Spinal Muscular Atrophy Randomized Trials (AmSMART) group has established reliability and validity for measures of strength, lung function, and motor function in the population from age 2 years to 18 years. The PedsQL™ (Pediatric Quality of Life Inventory™) Measurement Model was designed to integrate the relative merits of generic and disease-specific approaches, with disease-specific modules. The PedsQL™ 3.0 Neuromuscular Module was designed to measure HRQOL dimensions specific to children ages 2 to 18 years with neuromuscular disorders, including SMA. One hundred seventy-six children with SMA and their parents completed the PedsQL™ 4.0 Generic Core Scales and PedsQL™ 3.0 Neuromuscular Module. The PedsQL™ demonstrated feasibility, reliability and validity in the SMA population. Consistent with the conceptualization of disease-specific symptoms as causal indicators of generic HRQOL, the majority of intercorrelations among the Neuromuscular Module Scales and the Generic Core Scales were in the medium to large range, supporting construct validity. For the purposes of a clinical trial, the PedsQL™ Neuromuscular Module and Generic Core

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Competing Interests: Dr. Varni holds the copyright and the trademark for the PedsQL™ and receives financial compensation from the Mapi Research Trust, which is a nonprofit research institute that charges distribution fees to for-profit companies that use the Pediatric Quality of Life Inventory™.

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Scales provide an integrated measurement model with the advantages of both generic and condition-specific instruments.

INTRODUCTION

Spinal muscular atrophy (SMA) is a genetic disease of the anterior horn cell with a frequency of 8 per 100,000 live births [1,²]. In 1995, the disease gene SMN1 was identified with a disease modifying gene, SMN2[3]. This discovery has brought about some understanding of disease mechanism and several hypotheses for treatment strategies[4]. Pilot studies as well as Phase I and II clinical trials were undertaken on the basis of these hypotheses. Although no effective treatment has been found to date, much has been learned in terms of conducting clinical trials in the SMA pediatric population[5].

For Phase II and III clinical trials, reliable and valid outcome measures are necessary[6]. In 2000, the American Spinal Muscular Atrophy Randomized Trials (AmSMART) group was formed in order to develop clinical outcome measures for children with SMA. AmSMART established reliability and validity for measures of strength, lung function, and motor function in the population from age 2 years to 18 years[7–10]. Biological markers of disease progression are currently under investigation.

Health-related quality of life measurement has been increasingly acknowledged as an essential health outcome measure in clinical trials involving children with neuromuscular disorders[7–12]. The Food and Drug Administration (FDA) has strongly recommended the inclusion of health-related quality of life (HRQOL) assessment as an endpoint in clinical trials regardless of the age of the patient. A sensitive and specific HRQOL instrument must address factors unique to a particular disease and age group. Although generic HRQOL instruments have been developed for use in pediatric populations, there are few disease-specific measures available.

HRQOL is a multidimensional construct, consisting at the minimum of physical, psychological (including emotional and cognitive), and social health dimensions delineated by the World Health Organization[13,¹⁴]. HRQOL has emerged as the most appropriate term for quality of life dimensions that represent a patient's perceptions of the impact of an illness and its treatment on their own functioning and well-being and which are within the scope of healthcare services and medical products[14,¹⁵]. Generic HRQOL measurement instruments enable comparisons across pediatric populations and facilitate benchmarking with healthy population norms, while disease-specific measures enhance measurement sensitivity for health domains germane to a particular chronic health condition. There is an emerging perspective that for pediatric chronic health conditions, both generic and disease-specific HRQOL measures should be administered in order to gain a comprehensive evaluation of the patient's HRQOL[16,¹⁷].

The PedsQL™ (Pediatric Quality of Life Inventory™) Measurement Model was designed to integrate the relative merits of a generic core instrument with disease-specific modules[18–23]. It has been an explicit goal of the PedsQL™ Measurement Model to develop and test brief measures for the broadest age group empirically feasible, specifically including child self-report for the youngest children possible[24]. The PedsQL™ 4.0 Generic Core Scales was specifically designed for application in both healthy and patient populations[25] and has been utilized with over 35,000 healthy children and children with numerous pediatric chronic health conditions internationally[26], including children with neuromuscular disorders[12]. Findings have been reported in over 350 peer-reviewed journal articles since 2001 (A full listing of the updated peer-reviewed journal publications is available at www.pedsq.org). The PedsQL™ 4.0 Generic Core Scales, however, is not a disease specific instrument and cannot provide detailed information on the specific factors that influence HRQOL in pediatric patients with neuromuscular disorders. Consequently, during the past decade we have developed the

PedsQL™ 3.0 Neuromuscular Module to measure HRQOL dimensions specific to children ages 2 to 18 years with neuromuscular disorders, in particular, SMA. The aim of the current study was to investigate the feasibility, reliability, and validity of the PedsQL™ 3.0 Neuromuscular Module and the PedsQL™ 4.0 Generic Core Scales in children with SMA.

PATIENTS AND METHODS

Spinal Muscular Atrophy Sample

A total of 176 children with SMA were accrued overall for the field test of the PedsQL™ 3.0 Neuromuscular Module. Table 1 provides information for the 13 centers from which participants were recruited. Participants were approached during routinely scheduled clinic visits. SMA diagnosis was confirmed by mutation analysis for all children. The average age of the 76 boys (43.2 %) and 91 girls (51.7 %; Missing Gender = 9, 5.1%) was 8.53 years (SD = 4.75). With respect to ethnicity, the sample contained 19 (10.8%) Hispanic or Latino, 143 (81.3%) Not Hispanic or Latino, and 14 (8.0%) Unknown. In terms of race, the sample consisted of 8 (4.5%) Black or African American, 138 (78.4%) White, 8 (4.5%) Asian, 2 (1.1%) Native Hawaiian or Other Pacific Islander, 7 (4.0%) More than One Race, and 13 (7.4%) Unknown. Mean socioeconomic status (SES) was unavailable for this sample. Our sample is representative of the underlying population of children with SMA in the United States[27].

Healthy Children Sample

The healthy children sample was derived from the previously conducted PedsQL™ 4.0 initial field test[25] and a State's Children's Health Insurance Program(SCHIP) evaluation in California[28]. The healthy children sample was selected and matched for age, gender, and race/ethnicity to the SMA sample utilizing the SPSS Version 15.0 statistical software random sample case selection command[29]. This command allows the percentage of children in the healthy sample to be matched to the SMA sample on the targeted demographic characteristic (age, gender, race/ethnicity). Children were assessed either in physicians' offices during well-child visits, by telephone, or via a statewide mailing. The average age of the 531 boys (46.8 %) and 603 girls (53.2 %) was 9.73 years (SD = 3.28). With respect to race/ethnicity, the sample contained 806 (71.7 %) White non-Hispanic, 149 (13.1 %) Hispanic, 74 (6.5 %) Black non-Hispanic, 74 (6.5 %) Asian/Pacific Islander, and 31 (2.8%) Other. Mean socioeconomic status (SES) was unavailable for this sample, although the statewide SCHIP sample was representative of low-income families (<250% of the federal poverty level).

Measures

PedsQL™ 3.0 Neuromuscular Module—The 25-item PedsQL™ 3.0 Neuromuscular Module encompasses 3 Scales: 1) About My/My Child's Neuromuscular Disease (17 items related to the disease process and associated symptomatology), 2) Communication (3 items related to the patient's ability to communicate with health care providers and others about his/her illness), and 3) About Our Family Resources (5 items related to family financial and social support systems). The PedsQL™ Neuromuscular Module Scales are comprised of parallel child self-report and parent proxy-report formats for children ages 5 to 18 years, and a parent proxy-report format for children ages 2 to 4 years. The format, instructions, Likert response scale, and scoring method for the PedsQL™ 3.0 Neuromuscular Module are identical to the PedsQL™ 4.0 Generic Core Scales, including child self-report formats for ages 5–7, 8–12, and 13–18 and parent proxy-report formats for ages 2–4, 5–7, 8–12, and 13–18. The young child form (ages 5–7 years) does not contain the Communication and About Our Family Resources Scales since in the present field test we found Cronbach's coefficient alphas on these two scales to be in the unacceptable range for children ages 5–7 years. Items are linearly transformed to a 0 to 100 scale (0=100, 1=75, 2=50, 3=25, and 4=0) so that higher scores indicate better

HRQOL. Scale scores are computed as the sum of the items divided by the number of items which were answered.

The PedsQL™ 3.0 Neuromuscular Module was developed using the authors' research and clinical experiences with neuromuscular disorders, such as SMA and Duchenne Muscular Dystrophy (DMD), and other chronic conditions, and by employing the methodology documented by Varni [24] that has been used to create PedsQL™ disease-specific modules for asthma, arthritis, diabetes, cancer, cerebral palsy, and heart disease[18,^{20–23},30] and the instrument development literature[31–33].

We reviewed the neuromuscular disease HRQOL literature related to DMD and SMA and generated feedback from pediatric neurology healthcare providers (HCP) about issues faced by patients and families with SMA, DMD, and other neuromuscular diseases.

Our literature search and the HCP feedback, including physicians, nurses, physical therapists, and psychologists, obtained from 1998 to 2000, formed the basis for topics addressed in semi-structured, open-ended interviews, or focus groups, with 7 neuromuscular patients, diagnosed with either SMA or DMD, 12 parents, and one sibling at Texas Scottish Rite Hospital for Children. The purpose of these interviews was to elicit neuromuscular-specific treatment-related symptoms and problems. Children ages 5 to 7 were interviewed with their parents, while those ages 8–18 years were interviewed separately from their parents to obtain patient-perceived symptoms and problems. Interview sessions were tape-recorded with patient and parental consent. Content was transcribed and independently evaluated by two raters (RB and AM), in consultation with the principal developer of the PedsQL™ Measurement Model (JV), who each generated a list of pertinent content areas, or domains, using content analysis. Discrepancies between raters were clarified through consensus. Repeated themes were identified and each of the disease and treatment-related symptoms/problems/concerns were then placed into eight preliminary content domains and a preliminary list of 50 items was generated, with each one placed in the appropriate domain. HCP from the SMA Research Team (AmSMART) then provided feedback on the domains in July, 2000, rating the importance of each for the patient's health condition. None of the domains/items were changed based on feedback from the SMA Research Team.

In August, 2000, a list of the eight domains was mailed to 50 patient families for feedback regarding their importance, with 13% returning the ratings. Parents were asked to rate each domain on a 5-point Likert scale from "Not at all Important" to "Very Important." The eight domains were: Family Resources, School, Information, Disease/Treatment, Activities of Daily Living, Mobility, Social, and Emotional. Each item was placed in the appropriate content, or domain, area.

Cognitive interviews were then conducted at Texas Scottish Rite Hospital for Children for the purpose of obtaining feedback for the items and scales from this preliminary PedsQL™ Neuromuscular Module from two patients, ages 9 and 11, and eight parents. Probing questions were posed following each item response. These interviews were audio-taped and transcribed, then used to detect any problems regarding lack of clarity of questions or response options. Scales and items were then revised based on feedback from HCP and cognitive interviews, and the preliminary PedsQL™ Neuromuscular Module was constructed of 34 items, in 7 domains, which consisted of Family Resources (5 items), School (3 items), Information (2 items), Disease/Treatment (8 items), Activities of Daily Living (9 items), Social (3 items), Emotional (4 items). The resulting questionnaire was administered to two parents and one patient, age 12, and they were asked to rate how much of a problem each item had been for the past month, using a Likert scale of 1 to 5. Follow-up questions were also posed.

Based upon the previous content analysis and feedback from this cohort regarding the disease-relevance of our content areas, we developed a 34-item disease-specific questionnaire for patients and parents, with three domains, “About My Neuromuscular Disease,” “About My Family Resources,” and “About Me.” Each item asked how much of a problem that item had been during the past month for the affected child. The initial field testing was conducted in October, 2000, with 15 patient-parent dyads (11 in clinic, 4 mailings), using patients with neuromuscular diseases ranging from 5 to 17 years of age. Feedback was also collected from this cohort regarding clarity, content, and relevance of the items. Using feedback from the mailing, the field testing, cognitive interviews, and consultation with the PedsQL™ principal developer (JV), the preliminary PedsQL™ Neuromuscular Module was further revised for clarity and content. Specifically, the “About Me” domain was eliminated since it overlapped with items on the PedsQL™ 4.0 Generic Core Scales and the “Communication” domain was added to be consistent with other PedsQL™ disease-specific modules. The resulting PedsQL™ 3.0 Neuromuscular Module is a 25-item, 3-domain instrument which is the focus of the present study.

The PedsQL™ 4.0 Generic Core Scales—The 23-item PedsQL™ 4.0 Generic Core Scales encompass: 1) Physical Functioning (8 items), 2) Emotional Functioning (5 items), 3) Social Functioning (5 items), and 4) School Functioning (5 items)[24,25]. To create the Psychosocial Health Summary Score, the mean is computed as the sum of the items divided by the number of items answered in the Emotional, Social, and School Functioning Scales.

Procedures

Participants were children ages 5 to 18 years with SMA and parents of children ages 2 to 18 years with SMA at 13 clinical centers (Table 1). The SMA diagnosis was confirmed by mutation analysis for all children. Participants completed the PedsQL™ 4.0 Generic Core Scales and the PedsQL™ 3.0 Neuromuscular Module during a routinely scheduled clinic visit. For test-retest reliability, a subset of participants (n = 60) completed the PedsQL™ measures a second time during a routinely scheduled clinic visit if they had suffered no adverse events since the first visit. The human subject institutional review boards at each center approved the study, and written parental informed consent and child assent were obtained prior to enrollment.

Paper-and-pencil questionnaires were self-administered for parents and for children ages 8 to 18 years and interview-administered for children ages 5 to 7 years. If a child was unable to read or write, as a consequence of either physical or cognitive impairment, a Research Assistant interviewer administered the questionnaire verbally and recorded the results. Parents and children completed the instruments separately. The PedsQL™ was typically completed in the waiting room or in the clinic exam room. A Research Assistant was on hand to answer any study subject questions about the PedsQL™. All pediatric patients were English speakers and completed English versions of the PedsQL™ instruments. All but 13 patients (Spanish, n = 6; Urdu, n = 1; Tamil, n = 1; Persian, n = 1; French, n = 1; German, n = 2; Indonesian, n = 1) were indicated as having English as their native language. All parents of pediatric patients completed English versions of the PedsQL™ instruments without the help of a translator except 2 parents who completed Spanish versions with a translator and 1 parent who completed English versions with a translator (Persian).

Statistical Methods

Feasibility was determined from the percentage of missing values[34]. The extent to which individual items correlated with their hypothesized scale construct rather than with other scales was determined [35]. Multitrait scaling analyses were summarized via tests of individual item scaling success, defined as the percentage of items correlating equal to or higher with their hypothesized scale construct rather than with another scale using adjusted total scores when

the item was a part of the score [34]. Scale internal consistency reliability was determined by calculating Cronbach's coefficient alpha[36]. Scales with reliabilities of 0.70 or greater are recommended for comparing patient groups, while a reliability criterion of 0.90 is recommended for analyzing individual patient scores[37,38]. Test-retest reliability was assessed for a subset of the sample (n = 60) using Intraclass Correlation Coefficients (ICCs) [39]. Patients and their parents were assessed on average 29.85 days (SD = 8.38) after baseline. ICCs are designated as ≤ 0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.81–1.00 excellent agreement[40,41].

Construct validity for the Generic Core Scales was determined utilizing the known-groups method[42], which compares scale scores across groups known to differ in the health construct being investigated. Generic Core Scales scores in groups differing in known health condition (healthy children and children with SMA) were computed using independent samples t-tests. To determine the magnitude of the differences, effect sizes were calculated[43]. Effect size as utilized in these analyses was calculated by taking the difference between the healthy sample mean and the SMA sample mean, divided by the pooled standard deviation. Effect sizes for differences in means are designated as small (.20–.49), medium (.50–.79), and large (.80 and above) in magnitude[43].

Construct validity for the Neuromuscular Module was examined through an analysis of the intercorrelations among the Generic Core Scales and Summary Scores with the Neuromuscular Module Scale Scores. Computing the intercorrelations among scales provides initial information on the construct validity of an instrument[37]. We hypothesized greater disease-specific symptoms or problems would correlate with lower overall generic HRQOL based on the conceptualization of disease-specific symptoms as causal indicators of generic HRQOL [44]. Pearson Product Moment Correlation coefficients are designated as small (.10–.29), medium (.30–.49), and large ($\geq .50$)[43].

Construct validity was further assessed by comparing mobility groups (non-sitter, sitter, and walker) across the PedsQL™ Generic Core Scales and Neuromuscular Module. Since age is known to influence the mobility status of SMA patients, age was included as a covariate for all models. If age was a significant covariate in the model ($p < 0.05$), the means and standard deviations were evaluated at the mean of the covariate. We hypothesized that the PedsQL™ 4.0 Generic Core Physical Functioning Scale and Neuromuscular Module About My Neuromuscular Disease Scale would be related to mobility status with the average for non-sitter the lowest and walker the highest.

Agreement between child self-report and parent proxy-report was determined through Intraclass Correlation Coefficients (ICCs)[45]. The ICC offers an index of absolute agreement as it takes into account the ratio between subject variability and total variability[45,46]. Statistical analyses were conducted utilizing SPSS Version 15.0 for Windows[29].

RESULTS

Feasibility: Missing Item Responses

For child self-report and parent proxy-report on the PedsQL™ 3.0 Neuromuscular Module, the percentage of missing item responses was 0.8% and 1.0%, respectively, for all scales. For child self-report and parent proxy-report on the PedsQL™ 4.0 Generic Core Scales, the percentage of missing item responses was 1.3% and 1.3%, respectively, for all scales. On the PedsQL™ Neuromuscular Module, 46.7% of the items across all forms had no missing responses; the highest percentage of missing responses for any single item on the Neuromuscular Module was 4.7% for child self-report and 4.0% for parent proxy-report.

Across all child self-report and parent proxy-report forms on the PedsQL™ 4.0 Generic Core Scales, the percentage of missing responses for any single item was < 5%.

Item Scaling Tests

For patient self-report scales, scaling success for “About My Neuromuscular Disease” was 76.5%, “Communication” was 100%, and “About Our Family Resources” was 80.0%. For parent proxy-report scales, scaling success was 94.1% for “About My Neuromuscular Disease”, 100% for “Communication”, and 80.0% for “About Our Family Resources”.

Internal Consistency Reliability

Internal consistency reliability coefficients for the Generic Core Scales are presented in Table 2. Overall, child self-report and parent proxy-report scales on the Generic Core approach or exceed the minimum reliability standard of 0.70 required for group comparisons. Internal consistency reliability coefficients for the Neuromuscular Module are presented in Table 3. All child self-report and parent proxy-report scales on the Neuromuscular Module exceed the minimum reliability standard of 0.70 required for group comparisons.

Test-Retest Reliability

Intraclass Correlation Coefficients (ICCs) for test-retest reliability for child self-report and parent proxy-report are presented in Table 4. The majority of these ICCs are in the good to excellent reliability range.

Construct Validity

Table 2 demonstrates the differences between healthy children and children with SMA. For each Generic Core Scale and Summary Score, children with SMA and their parents report statistically significant lower HRQOL than healthy children. All effect sizes (with the exception of Emotional Functioning for child self-report) are in the large range, supporting discriminant validity. The greatest effect sizes were demonstrated on the Physical Functioning Scale for both child self-report and parent proxy-report.

The intercorrelations between the Generic Core Scales and Summary Scores with the Neuromuscular Module are shown in Table 5. The majority of intercorrelations are in the medium to large range, supporting construct validity.

Table 6 provides the results comparing mobility groups (non-sitter, sitter, and walker) for parent proxy-report and child self-report on the PedsQL™ Generic Core and Neuromuscular Module. The a priori hypothesis that the PedsQL™ Physical Functioning Scale and About My Neuromuscular Disease Scale would be significantly related to mobility was confirmed for both child self-report and parent proxy-report. In addition, the parent proxy-report Total Score and About Our Family Resources Scale are significantly related to mobility. The means increase from non-sitter, sitter, to walker for all the PedsQL™ Neuromuscular Module scores except for child self-report Communication.

Parent/Child Agreement

ICCs between child and parent report are presented in Table 4. ICCs are in the moderate agreement range for 6 out of 10 of the PedsQL™ Scales, and in the poor to fair agreement range for 4 out of 10 of the PedsQL™ Scales. The greatest overall agreement is found on Total Generic Core (0.49) and About My Neuromuscular Disease (0.48).

DISCUSSION

These data support the feasibility, reliability, and validity of the PedsQL™ 3.0 Neuromuscular Module and the PedsQL™ 4.0 Generic Core Scales in pediatric patients with SMA. The Generic Core Scales distinguished HRQOL between children with SMA and a matched sample of healthy children, with most effect sizes in the large range. Consistent with previous findings with children with neuromuscular disorders[12], the greatest deficits on the PedsQL™ 4.0 Generic Core Scales were seen in physical function as reported by both children and parents. PedsQL™ 4.0 Generic Core Scale scores of children with SMA in the present sample were comparable to PedsQL™ scores of children with a chronic clinically significant physical impairment, that is, children with cerebral palsy[20]. There were minimal missing item responses on the PedsQL™ 3.0 Neuromuscular Module and the PedsQL™ 4.0 Generic Core Scales, indicating that children and their parents were able to provide good quality data regarding the child's HRQOL.

Internal consistency reliabilities on the PedsQL™ 3.0 Neuromuscular Module exceeded the minimum alpha coefficient standard of 0.70 required for group comparisons for all child self-report and parent proxy-report scales. The PedsQL™ 4.0 Generic Core Scales internal consistency reliabilities generally exceeded or approached the minimum alpha coefficient standard of 0.70. Although Cronbach's alpha represents the lower bound of the reliability of a measurement instrument, and is a conservative estimate of actual reliability[47], scales that did not meet the 0.70 standard should be used only for descriptive analyses. Overall, responses on the Neuromuscular Module and Generic Core Scales were in the good to excellent agreement range across a 30 day period and were significantly correlated, supporting test-retest reliability.

Consistent with the conceptualization of disease-specific symptoms as causal indicators of generic HRQOL, the majority of intercorrelations among the Neuromuscular Module Scales and the Generic Core Scales were in the medium to large range, supporting construct validity. The finding that children with neuromuscular disorders and their parents showed poor to moderate agreement is consistent with both the adult and pediatric literature, suggesting information provided by proxy-respondents is not equivalent to that reported by the patient [48, 49]. Imperfect agreement between self-report and proxy-report has been consistently documented in the HRQOL measurement of children with and without chronic illness[50, 51], particularly for less observable or internal symptoms. Taken together, the data suggest that evaluating both children's and parents' perspectives regarding HRQOL should be the standard for routine assessment in clinical practice and clinical trials for children with neuromuscular disorders since their different perspectives potentially provide unique information. Given the potential differences between patient and proxy reports, we recommend that the primary patient-reported outcome should be pediatric patient self-report while parent proxy-report should also be collected as a secondary patient-reported outcome.

The present findings have a number of potential limitations. Information on nonparticipants and participants' socioeconomic status was not available; such information could affect our findings. We were not able to perform a factor analysis given the sample size. Factor analysis helps to explore further the construct validity and dimensionality of an instrument. Comrey and Lee indicate as a guide for factor analysis that a sample size of 50 is very poor, 100 is poor, 200 is fair, 300 is good, 500 is very good, and 1000 is excellent[52]. Correlation coefficients from a factor analysis tend to be less reliable when estimated from small samples sizes[53]. Future research with large samples will provide the opportunity to conduct factor analysis with this population. Additionally, a translator was utilized for 3 parents, and the use of a translator introduces heterogeneity in the methods that may impact the findings. While the PedsQL™ 3.0 Neuromuscular Module was developed to measure HRQOL dimensions specific to children with neuromuscular disorders, the present study examined feasibility, reliability, and validity

in a sample of children with SMA. Further validation work is being conducted with children with other neuromuscular disorders, in particular, pediatric patients with Duchenne Muscular Dystrophy. Finally, responsiveness to change was not evaluated for the PedsQL™ 3.0 Neuromuscular Module and should be formally tested in future longitudinal studies.

There is an emerging perspective that for pediatric chronic health conditions, both generic and disease-specific HRQOL measures should be administered so as to gain a more thorough evaluation of the patient's HRQOL[54]. For the purposes of a clinical trial, it is recommended that the PedsQL™ Neuromuscular Module be administered with the PedsQL™ 4.0 Generic Core Scales in order to obtain a comprehensive and integrated assessment of HRQOL in children with neuromuscular disorders.

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Table 1

Participants by Center and Gender

	Gender			
Center	Male	Female	Unknown	Total
Dallas TX	11	12		23
Cincinnati OH	10	9		19
Portland OR	9	5		14
Richmond VA	4	2		6
St. Paul MN	3	3		6
Salt Lake City UT	5	9		14
Philadelphia PA	7	11		18
Toronto ONTARIO	3	0		3
St. Louis MO	7	12		19
Washington DC	2	0		2
Rochester MN	2	4		6
New York NY	8	11	8	27
Boston MA	5	13	1	19
Total	76	91	9	176

Table 2

PedsQL™ 4.0 Generic Core Scales Scores and Reliability for Parent Proxy-Report and Child Self-Report for Spinal Muscular Atrophy Sample and Comparisons with Healthy Children Scores

Scale	Number of Items	Spinal Muscular Atrophy			Healthy			Difference	Effect Size
		n	α	Mean	SD	n	Mean		
Parent Proxy-Report									
Total Score	23	174	0.85	53.35	14.19	1133	84.67	31.32*	2.39
Physical Health	8	172	0.85	36.30	24.60	1134	87.73	51.43*	3.02
Psychosocial Health	15	174	0.86	62.94	14.44	1133	83.02	20.08*	1.48
Emotional Functioning	5	173	0.77	67.17	17.61	1133	81.39	14.22*	0.87
Social Functioning	5	174	0.64	57.36	17.37	1131	86.74	29.38*	1.75
School Functioning	5	154	0.75	63.79	19.95	1111	80.85	17.06*	1.00
Child Self-Report									
Total Score	23	125	0.81	58.71	14.36	1134	84.78	26.07*	2.07
Physical Health	8	123	0.72	43.43	21.13	1130	88.81	45.38*	3.26
Psychosocial Health	15	125	0.81	66.57	16.30	1130	82.69	16.12*	1.13
Emotional Functioning	5	125	0.68	67.40	23.00	1132	80.88	13.48*	0.74
Social Functioning	5	125	0.64	66.13	19.54	1129	85.81	19.68*	1.15
School Functioning	5	124	0.68	66.20	20.91	1107	81.32	15.12*	0.89

Note: All differences are statistically significant at $p < 0.001$ based on independent samples t-tests.

Higher values equal better health-related quality of life.

Effect sizes designated as small (0.20), medium (0.50), and large (0.80).

α equals Cronbach's coefficient alpha. SD equals standard deviation.

Table 3
Reliability and Descriptive Statistics for the PedsQL™ 3.0 Neuromuscular Module Scores for Parent Proxy-Report and Child Self-Report

Scale	Number of Items	n	α	Mean	SD
Parent Proxy-Report					
Total Score	25	172	0.89	59.74	16.75
About My Child's Neuromuscular Disease	17	176	0.87	58.82	17.70
Communication	3	172	0.91	67.01	31.09
About Our Family Resources	5	176	0.77	59.58	22.16
Child Self-Report					
Total Score	17/25	123	0.88	67.54	15.57
About My Neuromuscular Disease	17	123	0.81	65.95	16.54
Communication	3	80	0.77	70.83	23.64
About Our Family Resources	5	80	0.82	74.66	21.73

Note: Higher values equal better health-related quality of life.

α equals Cronbach's coefficient alpha. SD equals standard deviation.

Communication and About Our Family Resources scales include child self-report ages 8–18 only. Total Mean Score for child self-report includes only About My Neuromuscular Disease Scale for ages 5–7. Cronbach's coefficient alpha for Total Score for child self-report includes 25 items completed by ages 8–18.

Table 4

Intraclass Correlations (ICC) between Child Self-Report and Parent Proxy-Report on the PedsQL™ 4.0 Generic Core Scales and the PedsQL™ 3.0 Neuromuscular Module and Test-Retest Reliability for the Spinal Muscular Atrophy Sample

Scale	Parent-Child Agreement ICC	Child Self-Report Test-Retest Reliability ICC	Parent Proxy-Report Test-Retest Reliability ICC
PedsQL™ Generic Core Scales			
Total Generic Core	0.49*	0.84*	0.60*
Physical Health	0.40*	0.78*	0.34*
Psychosocial Health	0.44*	0.78*	0.79*
Emotional Functioning	0.37*	0.73*	0.78*
Social Functioning	0.36*	0.73*	0.61*
School Functioning	0.41*	0.72*	0.59*
PedsQL™ Neuromuscular Module			
Total Neuromuscular Module	0.45*	0.81*	0.89*
About My Neuromuscular Disease	0.48*	0.84*	0.90*
Communication	0.41*	0.63*	0.82*
About Our Family Resources	0.33*	0.58*	0.80*

ICC: Intraclass Correlation

All ICCs are statistically significant at $p < 0.001$.

ICCs are designated as ≤ 0.40 poor to fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 good agreement, and 0.81–1.00 excellent agreement. Communication and About Our Family Resources scales include child self-report ages 8–18 only.

Total Neuromuscular Score for child self-report includes only About My Neuromuscular Disease Scale for ages 5–7.

Table 5

Pearson's Product Moment Correlations among PedsQL™ Scales for Child Self-Report (Above Diagonal) and Parent Proxy-Report (Below Diagonal) for Spinal Muscular Atrophy Sample

Scale	TG	PH	PsyH	EF	SF	SchF	TN	AN	C	FR
PedsQL™ Generic Core Scales										
Total Generic Core (TG)	=====	0.69	0.87	0.69	0.72	0.67	0.79	0.75	<i>0.34^a</i>	0.69
Physical Health (PH)	0.83	=====	<i>0.25^a</i>	<i>0.20^b</i>	<i>0.21^b</i>	<i>0.19^b</i>	0.50	0.55	<i>0.01^{ns}</i>	0.55
Psychosocial Health (PsyH)	0.80	<i>0.23^a</i>	=====	0.79	0.82	0.78	0.73	0.65	0.50	0.62
Emotional Functioning (EF)	0.62	<i>0.19^b</i>	0.80	=====	<i>0.49</i>	<i>0.38</i>	0.54	<i>0.47</i>	0.50	0.53
Social Functioning (SF)	0.64	<i>0.16^b</i>	0.81	<i>0.47</i>	=====	<i>0.48</i>	0.55	<i>0.48</i>	0.52	0.50
School Functioning (SchF)	0.63	<i>0.16^{ns}</i>	0.78	<i>0.41</i>	<i>0.46</i>	=====	0.64	0.60	<i>0.22^{ns}</i>	0.51
PedsQL™ Neuromuscular Module										
Total Neuromuscular Module (TN)	0.61	<i>0.47</i>	<i>0.49</i>	<i>0.48</i>	<i>0.38</i>	<i>0.43</i>	=====	0.96	<i>0.42</i>	0.78
About My Neuromuscular Disease (AN)	0.62	0.50	<i>0.48</i>	<i>0.43</i>	<i>0.29</i>	<i>0.42</i>	0.94	=====	<i>0.19^{ns}</i>	0.59
Communication (C)	<i>0.25^a</i>	<i>0.09^{ns}</i>	<i>0.27</i>	<i>0.19</i>	<i>0.32</i>	<i>0.12^{ns}</i>	<i>0.41</i>	<i>0.14^{ns}</i>	=====	<i>0.32^a</i>
About Our Family Resources (FR)	0.53	<i>0.33</i>	<i>0.49</i>	<i>0.45</i>	<i>0.34</i>	<i>0.36</i>	0.85	0.71	<i>0.31</i>	=====

Note: Pearson's product moment correlations for child self-report are presented above the diagonal. Pearson's product moment correlations for parent proxy-report are presented below diagonal. Pearson's product moment correlations are designated as small (0.10), medium (0.30), and large (0.50).

All values are statistically significant at $p < .001$ except for superscript "a," which is statistically significant at $p < .01$, and superscript "b," which is statistically significant at $p < .05$, or unless otherwise indicated ns (not significant).

Small effect sizes are in plain text, medium effect sizes are in italics, and large effect sizes are in bold.

TG equals Total Generic Core. PH equals Physical Health. PsyH equals Psychosocial Health. EF equals Emotional Functioning. SF equals Social Functioning. SchF equals School Functioning. TN equals Total Neuromuscular Module. AN equals About My Neuromuscular Disease. C equals Communication. FR equals About Our Family Resources.

Communication and About Our Family Resources scales include child self-report ages 8–18 only.

Total Neuromuscular Score for child self-report includes only About My Neuromuscular Disease Scale for ages 5–7.

Table 6

Analysis of covariance comparing the 3 mobility groups and the Scale Scores on the PedsQL™ Scales for Child Self-Report and Parent Proxy-Report

Scale Scores	Non-Sitter		Sitter		Walker		Mobility Main Effect	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	p-value	
Parent Proxy-Report								
Generic Core Total Score	23	55.24 ± 13.62	82	55.34 ± 13.57	43	57.29 ± 13.55	0.7238 ^a	
Physical Functioning	23	31.93 ± 23.91	80	34.66 ± 23.82	43	44.65 ± 23.80	0.0469 ^b	
Psychosocial Health	23	64.36 ± 12.28	82	62.50 ± 13.89	43	61.61 ± 17.85	0.7749	
Emotional Functioning	23	69.04 ± 17.53	82	67.46 ± 17.45	42	64.06 ± 17.44	0.4685 ^c	
Social Functioning	23	57.52 ± 18.22	82	58.17 ± 16.97	43	54.23 ± 19.21	0.4969	
School Functioning	14	66.43 ± 17.65	75	60.89 ± 19.44	40	66.60 ± 22.28	0.2944	
Neuromuscular Module Total Score	23	52.39 ± 19.43	83	59.43 ± 15.65	43	70.33 ± 17.91	0.0001	
About My Neuromuscular Disease	23	49.12 ± 15.55	83	55.01 ± 15.49	43	69.8 ± 15.48	<0.0001 ^d	
Communication	23	55.90 ± 30.84	81	68.36 ± 30.67	41	68.2 ± 30.66	0.2135 ^e	
About Our Family Resources	23	53.83 ± 17.65	83	54.52 ± 21.32	43	72.79 ± 19.83	<0.0001	
Child Self-Report								
Generic Core Total Score	11	58.45 ± 14.52	60	59.23 ± 12.81	35	64.77 ± 17.93	0.1852	
Physical Functioning	9	35.00 ± 19.82	60	40.77 ± 19.79	35	50.82 ± 19.88	0.0275 ^f	
Psychosocial Health	11	64.69 ± 14.72	59	65.51 ± 14.83	35	68.90 ± 19.41	0.5825	
Emotional Functioning	11	65.91 ± 19.47	60	65.08 ± 19.32	35	70.43 ± 25.76	0.5059	
Social Functioning	11	62.29 ± 19.79	60	66.67 ± 19.71	35	67.17 ± 19.83	0.7655 ^g	
School Functioning	11	64.91 ± 11.79	59	64.83 ± 18.45	35	70.00 ± 24.43	0.4684	
Neuromuscular Module Total Score	11	63.45 ± 16.22	59	67.42 ± 13.04	34	71.79 ± 19.55	0.2414	
About My Neuromuscular Disease	11	58.36 ± 17.59	59	62.20 ± 15.27	34	72.85 ± 17.14	0.0040	
Communication	10	70.01 ± 22.45	38	73.57 ± 22.8	22	60.97 ± 22.91	0.1363 ^h	
About Our Family Resources	10	61.00 ± 22.34	38	72.58 ± 20.61	22	78.86 ± 24.00	0.1098	

Note: Communication and About Our Family Resources scales include child self-report ages 8–18 only.

Total Mean Score for child self-report includes only About My Neuromuscular Disease Scale for ages 5–7.

^aCovariate age significant, $p = 0.0182$.

^bCovariate age significant, $p = 0.0040$.

^c Covariate age significant, $p = 0.0121$.

^d Covariate age significant, $p = 0.0003$.

^e Covariate age significant, $p = 0.0004$.

^f Covariate age significant, $p = 0.0002$.

^g Covariate age significant, $p = 0.0284$.

^h Covariate age significant, $p = 0.0319$.