Health-Related Quality of Life in Children and Adolescents With Duchenne Muscular Dystrophy

OBJECTIVES: The purpose of this study was to assess health-related quality of life (QoL) in children with Duchenne muscular dystrophy (DMD), including development and field-testing of a DMD-specific module integrated with the core Pediatric Quality of Life Inventory (PedsQL).

METHODS: The PedsQL 4.0 Generic Core and DMD Module Scales were completed by 203 families, including 200 parents and 117 boys with DMD. Scores on the PedsQL Core Scales were compared with those of matched healthy children. Relationships between PedsQL scores and patient characteristics were examined.

RESULTS: By both parent report and child self-report, mean PedsQL scores for boys with DMD were significantly lower than those for healthy children for physical and psychosocial QoL (P < .0001), with significantly impaired psychosocial QoL scores self-reported by 57%. Psychosocial QoL by self-report only, tended to be higher in the older boys (13–18 years) than in younger boys (8–12 years; P = .05) and was not significantly associated with use of mobility aids. Although parents reported higher Daily Activities scores in boys receiving steroids (P = .01), boys receiving steroids reported no difference in Daily Activities but significantly less worry (P = .004). Parent–child concordance was generally in the fair to poor range. Internal consistency reliability coefficients for PedsQL DMD module scales ranged from 0.66 to 0.86.

CONCLUSIONS: Overall, boys with DMD reported significantly lower QoL than their healthy peers. Despite decreased physical functioning, older boys seem to perceive better psychosocial QoL than perceived by their parents and by younger boys, unrelated to their need for mobility aids. Pediatrics 2012;130:e1559–e1566

WHAT’S KNOWN ON THIS SUBJECT: Medical advances have prolonged life for children and adolescents with Duchenne muscular dystrophy (DMD), the most common inherited pediatric neuromuscular disorder. Children with this progressive disease surviving to adulthood still face significant threats to their quality of life.

WHAT THIS STUDY ADDS: Self-reported psychosocial quality of life was impaired in a significant number (57%) of boys with DMD, unrelated to their need for mobility aids. Concordance between the perceptions of parents and their sons related to psychosocial functioning was fair to poor.
Health-related quality of life (QoL), a multidimensional construct that includes physical, psychological, and social functioning, has emerged as an important outcome in pediatric populations with chronic health conditions. Duchenne muscular dystrophy (DMD) is the most common inherited pediatric neuromuscular disorder with an estimated incidence of 1 in 3500 live births of male infants. Affected individuals typically lose ambulation between 8 and 12 years of age and die in their third decade as a result of cardiac or respiratory complications. Recently, the natural history of DMD has been altered with the use of chronic glucocorticosteroid therapy, improving “quality” and length of life. Studies evaluating QoL in children with DMD are few and rarely examine self-perceptions in children and adolescents. Past studies have often relied on parental report and/or are limited by small sample size or have focused predominantly on end-of-life decision-making in adults. In the absence of standardized measurements, health care providers often fail to recognize problems in patients’ health-related QoL. The purpose of this study was to assess QoL in children with DMD, including the development and field-testing of a DMD disease-specific module integrated with the core Pediatric Quality of Life Inventory (PedsQL).

**METHODS**

**Patient Population**

A convenience sample of boys with DMD, aged 6 to 18 years, and their parents were recruited from the Comprehensive Neuromuscular Care Center at our institution and from an annual meeting of Parent Project Muscular Dystrophy. The study was approved by the institutional review board, and informed consent or assent was obtained from study participants. Patients were excluded if they had another major nonneuromuscular diagnosis as determined by chart review.

**Procedures and Measures**

To assess quality of life, patients and parents completed the PedsQL. The 23-item PedsQL 4.0 Generic Core Scales encompass Physical Functioning, Emotional Functioning, Social Functioning, and School Functioning. The PedsQL scales are composed of parallel child self-report and parent proxy-report formats. Items are linearly transformed to a 0-to-100 scale, so that higher scores indicate better QoL. To create a Psychosocial Health Summary score, the mean is computed as the sum of the items divided by the number of items in the Emotional, Social, and School Functioning scales. The reliability and validity of the PedsQL Generic Core Scales have been demonstrated in healthy and patient populations. To further increase ease of use for this patient population, a computer-assisted format was developed. Parents and patients independently completed questionnaires on tablet computers with a research coordinator present to assist as needed. The initial development of the PedsQL DMD-specific module was based on methodology previously used by Varni and colleagues to develop disease-specific modules for other medical conditions. Review of the DMD-specific health-related QoL literature and discussions with health care providers formed the basis for the initial item generation. This DMD module was administered, together with the Generic Core Scales, to 30 children and parents. Focused interviews were conducted with these parents and children, using a semistructured, open-ended interview format, focusing on specific DMD- and treatment-related symptoms and problems. A content analysis of the interviews was performed to generate and revise items. The resultant PedsQL DMD module has 4 scales related to Daily Activities (5 items), Treatment Barriers (4 items), Worry (6 items), and Communication (3 items). PedsQL

**TABLE 1 PedsQL DMD Module Child Self-Report Item Content**

<table>
<thead>
<tr>
<th>DAILY ACTIVITIES (problems with….)</th>
<th>TREATMENT (problems with….)</th>
<th>COMMUNICATION (problems with….)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I have trouble eating with a fork and knife</td>
<td>1. It is hard to manage my muscle problem</td>
<td>1. It is hard for me to tell the doctors and nurses how I feel</td>
</tr>
<tr>
<td>2. It is hard to write or draw with a pen or pencil</td>
<td>2. I worry about my muscle problem</td>
<td>2. It is hard for me to ask the doctors and nurses questions</td>
</tr>
<tr>
<td>3. It is hard to put on my clothes</td>
<td>3. I worry whether my medicines are working</td>
<td>3. It is hard for me to explain my muscle problem to other people</td>
</tr>
<tr>
<td>4. My physical therapy or daily stretching hurts</td>
<td>4. I worry about my family</td>
<td>4. It is hard to use the toilet without help</td>
</tr>
<tr>
<td>5. I need more time than others to complete tasks</td>
<td>5. I worry about being treated differently from others my age</td>
<td>5. I worry about not being accepted by others</td>
</tr>
</tbody>
</table>

3.0 DMD module items are listed in Table 1. This DMD-specific module was developed simultaneously with a PedsQL 3.0 Neuromuscular Module described by Davis and colleagues with data supporting the initial feasibility, reliability, and validity of the neuromuscular module in a smaller sample of children with DMD (N = 44) and in a larger sample of children with spinal muscular atrophy.

**Statistical Analyses**

Descriptive statistics were generated for demographic and clinical variables and are reported as mean and SD values for continuous variables and frequencies/proportions for categorical variables. Mean PedsQL scale and summary scores were calculated for the DMD self- and parent-proxy reports. PedsQL Generic Core Scale scores for the DMD sample were compared with an age, gender, and race/ethnicity–matched healthy children sample from the PedsQL database.
using independent-sample t tests. Individual Psychosocial Health Summary Scores for patients with DMD were plotted to determine the frequency of scores more than 1 SD below the population sample mean, the cutoff score for clinical significance. Individual item analysis was performed to identify the most significant problems or lowest mean scores and the frequency of responses. Comparisons of PedsQL Generic Core and DMD module scale scores among age groups were performed by using analysis of variance methods with Tukey’s correction for multiple comparisons, as appropriate. Within the DMD group, PedsQL scale scores were also compared related to glucocorticosteroid therapy and use of mobility aids using independent-sample t tests. Spearman correlations were computed to assess the relationship between PedsQL Psychosocial Health Summary Scale scores and continuous variables.

For the DMD module, scale internal consistency reliability was determined by calculating Cronbach’s coefficient α. Scales with reliabilities of .70 or greater are recommended for comparing patient groups. Construct validity was determined by using the known-groups method. PedsQL Generic Core Scale scores were compared for groups differing in known health conditions (healthy children and children with DMD), using independent-sample t tests. Construct validity was also examined through an analysis of the intercorrelations between DMD module scale scores and relevant Generic Core scale scores. It was hypothesized that Daily Activities (symptoms) would be significantly correlated with Physical Functioning scores; Treatment Barriers and Worry subscales would be correlated with Psychosocial Health Summary and Emotional Functioning Scales; and Daily Activities Scale scores would be lower with advancing age. It was also hypothesized that patients with DMD who required mobility aids would have lower scores for Daily Activities and Physical Functioning. Intraclass correlation coefficients (ICCs) were calculated between patient self-report and parent proxy-report to assess parent-child agreement using variance components from random effects modeling. All statistical analyses were conducted by using SAS version 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

Patient and Family Characteristics

The PedsQL 4.0 Generic Core and DMD module scales were completed by 203 families, including 200 parents and 117 boys with DMD. Demographic characteristics of the families are shown in Table 2. Parents of 3 boys did not complete the PedsQL questionnaires but provided demographic information. Parent respondents were primarily mothers (73%). The sample was predominantly white (90%). Most parents had graduated from high school and more than half had college degrees. The majority of parents (>80%) were married. The mean age of patients was 10.4 years, including 51 children aged 5 to 7 years, 106 aged 8 to 12 years, and 46 adolescents (13–18 years old). The majority of the boys (85%) were receiving glucocorticosteroids (prednisone or deflazacort). More than half (58%) required special mobility aids, most often a wheelchair.

Comparison of QoL Scores With Population Norms

As shown in Table 3, mean scores for boys with DMD were significantly lower than those for healthy children for physical and psychosocial QoL. Comparisons of PedsQL Generic Core and DMD module scales were significant for boys 8 to 12 years old in comparison with boys aged 8 to 12 years (P < .0001). By parent proxy-report, the difference in Physical Functioning scores was significantly impaired psychosocial QoL. As reported by parents, 52% of children with DMD including all ages had Psychosocial Health Summary scores <64.38, the cutoff score for significantly impaired psychosocial QoL.

Differences in QoL Core and Module Scores Within DMD Group by Age

Mean scores for the PedsQL Generic Core Scales by age group and respondent are displayed in Table 3. By self-report, Physical Functioning Scale scores were significantly lower for boys aged 13 to 18 years in comparison with boys aged 8 to 12 years (P < .0001). By parent proxy-report, the difference in Physical Functioning scores was significantly impaired for all age groups. By self-report, 57% of all children 8 to 18 years of age had Psychosocial Health Summary scores below 66.03, the cutoff point for significantly impaired QoL in the general pediatric population. As reported by parents, 52% of children with DMD including all ages had Psychosocial Health Summary scores <64.38, the cutoff score for significantly impaired psychosocial QoL.
between these age groups was not statistically significant ($P = .27$). However, parents reported higher Physical Functioning scores for the 5- to 7-year-olds compared with the 8- to 12-year-olds ($P = .01$) and the 13- to 18-year-olds ($P < .001$). Similarly, parents reported higher Emotional Functioning scores for the 5- to 7-year-olds compared with the 8- to 12-year-olds ($P = .003$) and the 13- to 18-year-olds ($P < .001$). Older boys (13–18 years old) tended to report higher Psychosocial Health Summary scores ($P = .05$) with higher Social Functioning Scale scores ($P = .02$). This difference was not observed by parent proxy-report.

Consistent with the self-reported Physical Functioning, the mean score for Daily Activities was significantly higher for the 5- to 7-year-olds than for the 8- to 12-year-olds ($P = .002$). As shown in Table 4, parents also reported significantly lower Daily Activities scores for the 13- to 18-year-olds than for the 8- to 12-year-olds ($P < .001$) and the 5- to 7-year-olds ($P < .001$). Parents reported significantly higher Treatment Barrier scores (less barriers) and higher Worry scores (less worry) for the 5- to 7-year-olds compared with the 8- to 12-year-olds ($P < .01$) and the 13- to 18-year-olds ($P < .01$).

### Specific Concerns of the Boys With DMD

The lowest mean scores for the specific items of the PedsQL Generic Core Scales and DMD module scales and the frequency of patients reporting “often” or “almost always” experiencing a specific problem were examined. With respect to physical functioning or symptoms, the most frequently reported problems were not being able to run (68%) or walk more than 1 block (57%). In general, 14% of boys found it difficult to manage their muscle problem, including physical therapy and stretching (18%). Anger was the most frequently reported emotional problem reported by the boys (19%) and perceived by their parents (15%). In the teenage boys, 14% also reported frequently worrying about what was going to happen to them. One in 5 boys (19%) frequently worried about their family and about being treated differently from their peers (20%). Nearly one-third (32%) found it often difficult to talk to nonmedical people about their disease. With respect to Social Functioning, the most common problem was not being able to do things others their age could do (40%). While boys reported frequent problems with paying attention (13%), the most common school problem was missing school to go to the doctor or hospital (20%).

### Correlates With QoL Scores

Effects of age, parental education, use of glucocorticosteroid therapy, and use of mobility aids on QoL were examined. There was a significant negative correlation between increasing age and Physical Functioning scores ($r = -0.466$ self-report, $r = -0.347$ parent proxy-report; $P < .001$). Similarly, there
was a significant negative correlation between increasing age and the Daily Activities score ($r = -0.415$, self-report, $r = -0.554$, parent proxy-report, $P < .001$). There was no correlation between Psychosocial Summary scores and parental education. As perceived by both boys and their parents (Table 5), Psychosocial Health Summary scores were not significantly different in boys receiving steroids; however, parents reported significantly higher Daily Activities scores in boys receiving steroids ($P = .013$). While the boys receiving steroids did not report significantly higher Daily Activity scores ($P = .21$), they reported significantly higher Worry (less worry) scores ($P = .004$). Worry scores were positively correlated with Communication scores ($r = 0.391$, $P < .001$). Parents reported significantly lower Psychosocial Health Summary scores for boys using mobility aids ($P = .003$), however this relationship was not significant as reported by the boys.

**Parent–Child Concordance**

In light of observed differences between the perceptions of children and their parents, ICCs were examined for each of the Generic Core and DMD Module scales. ICCs are designated as $<0.40$, poor to fair agreement; $0.41$ to $0.60$, moderate agreement; $0.61$ to $0.80$, good agreement; and $0.81$ to $1.00$, excellent agreement. As shown in Table 6, the majority of ICCs were in the poor to fair range with the exception of the Daily Activities Scale where there was good agreement (0.681). Parent–child concordance was lowest for the Emotional Functioning Scale (0.139).

**Internal Consistency Reliability and Construct Validity of PedsQL DMD Module**

As shown in Table 7, Cronbach’s internal consistency reliability coefficients for the parent-proxy PedsQL DMD Module Scales ranged from .73 to .86. For patient self-report DMD module scales, $\alpha$ coefficients ranged from .71 to .79, with the exception of the Treatment Barriers scale (.66). Thus, the majority of the internal consistency reliability coefficients for the PedsQL DMD module scales exceeded the minimum reliability standard for group comparisons. With respect to construct validity, for every comparison, there was a statistically significant difference ($P < .001$) between PedsQL Generic Core Scale scores for healthy children and children with DMD as noted in Table 2. Construct validity of the DMD Module scales was also examined through an analysis of hypothesized correlations between DMD Module scores and relevant PedsQL 4.0 Generic Core Scale scores. Daily Activities scores were significantly correlated with self-reported Physical Functioning Scale scores ($r = 0.698$, $P < .0001$). The Worry Scale was significantly correlated with Psychosocial Health Summary Scale ($r = 0.575$, $P < .001$) and specifically Emotional Functioning scales ($r = 0.663$, $P < .0001$). Likewise, the Treatment Barriers Scale score was significantly correlated with Psychosocial Health Summary ($r = 0.547$, $P < .001$) and Emotional Functioning scores ($r = 0.475$, $P < .001$). Physical Functioning and Daily Activities Scale scores were negatively correlated with advancing age ($P < .001$) and expected disease progression. Finally, patients who required mobility aids had lower scores for Daily Activities ($P < .0001$).

**DISCUSSION**

Overall, boys with DMD reported significantly lower QoL than their healthy peers across all QoL domains, physical and psychosocial. With advancing age, boys reported decreased physical functioning and daily activities. While psychosocial functioning was impaired in a significant number of boys (57%), older patients did not tend to perceive lower psychosocial QoL despite their increased physical limitations. In fact, adolescents with DMD tended to report better psychosocial QoL than their younger counterparts, especially better social QoL, suggesting that these boys may have developed coping skills over time, allowing preserved functioning in these areas. Hendrickson and colleagues also found a trend toward improved psychosocial adjustment with advancing age as perceived by parents but recognized the possibility of an attrition/mortality bias.3

Our study findings support the findings of others17,18 that patients with more severe disease requiring mobility aids or having greater impairment of daily activities do not necessarily perceive

| Table 4 Comparison of PedsQL DMD Module Scale Scores by Age Groupa |
|-----------------------|-----------------------|-----------------------|-----------------------|
| Scale                  | Age 5–7 y             | Age 8–12 y            | Age 13–18 y           |
|                        | N  Mean  SD            | N  Mean  SD           | N  Mean  SD           |
| Child self-report      |                       |                       |                       |
| Daily Activities       | 77  77.01**           | 39  63.97             | 45  48.87             |
| Communication          | 77  63.96             | 39  67.95             | 45  66.77             |
| Treatment Barriers     | 78  70.75             | 39  70.99             | 45  19.16             |
| Worry                  | 77  72.94             | 39  68.87             | 45  19.86             |
| Parent proxy-report    |                       |                       |                       |
| Daily Activities       | 51  71.86**           | 104  65.19**          | 103  68.24            |
| Communication          | 51  60.62             | 104  60.26            | 103  70.14            |
| Treatment Barriers     | 51  82.72**           | 104  73.30            | 103  67.95            |
| Worry                  | 51  80.72**           | 104  82.72**          | 103  82.72**          |

**P < .01. — data not available.**

| **P < .001. **— significantly different than age 15–18 y.**

**a** Significantly different than age 15–18 y.

**b** Significantly different than age 8–12 y.

**c** Significantly different than age 7–8 y.
worse psychosocial QoL. Interestingly, despite the potential for emotional and behavioral side effects, patients receiving corticosteroids reported no difference in psychosocial QoL in comparison with patients not receiving steroids. Other studies have also found no significant difference in psychosocial health/adjustment associated with steroid use, despite differences in physical functioning. The finding that boys receiving steroids reported less worry may reflect greater optimism regarding slower disease progression and delayed loss of motor strength. Examination of PedsQL Generic Core and DMD module items identified specific concerns. Anger was a common emotion reported by boys with DMD, as described by children with heart disease. Hendrickson and colleagues found that psychosocial adjustment in boys with DMD was not significantly different compared with male subjects with other chronic conditions. Anger is likely multifactorial in DMD and may relate to the progressive and profound physical impairment associated with the disease. The impact of the disease on all aspects of daily living, including participation in peer activities and peer acceptance, another reported concern, as well as time required for physical therapy and the need for chronic medication, may contribute to angry feelings. Interventions that enhance access and participation in social and recreational activities, promoting and maintaining meaningful relationships, are important from both a QoL and developmental perspective. The boys in our study expressed worries about their family, about being treated differently from their peers, and older boys worried about their future. Communication with others was associated with less worry. It is especially concerning, given their worries, that 1 in 3 boys often found it difficult to talk to nonmedical people. Communication with family and friends is an important coping mechanism that is then lost to a group of boys who are already dealing with external sources of anger and stress.

Concordance between the perceptions of parents and their sons was generally fair to poor with the exception of daily activities. This is consistent with previous research in this population and others, finding that there is greater agreement for observable functioning and less for nonobservable (emotional, worry) functioning. Bray and colleagues also found moderate to poor agreement between 35 parents and their sons with DMD. In our study, boys reported more worry than was appreciated by their parents, and the boys frequently reported worrying about their family. Worry may lead to a need to protect their parents, which in turn interferes with communication and the parents’ understanding of their child’s psychosocial needs. Davis and colleagues, who also reported poor to moderate agreement between children with DMD and their parents, suggested that evaluating both perspectives be the standard because their different perspectives potentially provide unique information.
is essential to designing interventions directed at improving their psychosocial QoL.

Finally, our PedsQL DMD module provides a reliable and valid disease-specific alternative or complementary measure for assessment of QoL in children with DMD. The DMD module scales provide valuable information about the disease-specific problems and needs of boys with DMD with important clinical implications. These measures can contribute to monitoring of QoL in future research in this patient population.

This study’s strengths include the large sample size, inclusion of both parent-proxy and child self-reports, use of a reliable and validated generic instrument with healthy children comparison data, and incorporation of a disease-specific module. While the study population was a single-center convenience sample, ~50% of the patients evaluated in this clinic are from outside the local area, representing patients with DMD from across the United States, some with travel subsidized by the Muscular Dystrophy Association. Participants’ socio-economic status was not available. A potential study limitation is the lack of racial diversity (90% white) and a trend toward a higher educational status and 2-parent families, although these characteristics may have resulted in higher QoL scores for this sample, resulting in a more conservative estimate of their QoL. As previously noted, there was no significant correlation between parental education and psychosocial quality of life. Interestingly, other studies in this patient population have reported similar trends for marital status and educational level. Another potential study limitation is minimal objective data regarding disease severity.

**REFERENCES**

10. Varni JW, Seid M, Kurtin PS. The PedsQL 4.0: reliability and validity of the Pediatric


# Health-Related Quality of Life in Children and Adolescents With Duchenne Muscular Dystrophy

Karen Uzark, Eileen King, Linda Cripe, Robert Spicer, Jackie Sage, Kathleen Kinnett, Brenda Wong, Jesse Pratt and James W. Varni

*Pediatrics* 2012;130;e1559; originally published online November 5, 2012; DOI: 10.1542/peds.2012-0858

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at: /content/130/6/e1559.full.html</th>
</tr>
</thead>
<tbody>
<tr>
<td>References</td>
<td>This article cites 21 articles, 2 of which can be accessed free at: /content/130/6/e1559.full.html#ref-list-1</td>
</tr>
<tr>
<td>Citations</td>
<td>This article has been cited by 2 HighWire-hosted articles: /content/130/6/e1559.full.html#related-urls</td>
</tr>
<tr>
<td>Subspecialty Collections</td>
<td>This article, along with others on similar topics, appears in the following collection(s): Adolescent Health/Medicine /cgi/collection/adolescent_health:medicine_sub</td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: /site/misc/Permissions.xhtml</td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online: /site/misc/reprints.xhtml</td>
</tr>
</tbody>
</table>
Health-Related Quality of Life in Children and Adolescents With Duchenne Muscular Dystrophy
Karen Uzark, Eileen King, Linda Cripe, Robert Spicer, Jackie Sage, Kathleen Kinnett, Brenda Wong, Jesse Pratt and James W. Varni
Pediatrics 2012;130:e1559; originally published online November 5, 2012;
DOI: 10.1542/peds.2012-0858

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/130/6/e1559.full.html