

Health-related quality of life (HRQoL) associated with Duchenne muscular dystrophy (DMD): A study using the Health Utilities Index (HUI)

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BACKGROUND

- DMD is a rare X-linked neuromuscular disorder caused by mutations in the gene for dystrophin.^{1,2}
 - Progression in DMD leads to loss of ambulation (LOA) in the early teenage years, cardiomyopathy and respiratory insufficiency by early adulthood, and early mortality from late teens into the third decade of life.³⁻⁵
- Due to its severity, it is not surprising that the progression of DMD dramatically affects the HRQoL of patients and their caregivers.
- Utility scores, values anchored between 0 (dead) and 1 (full health), reflect preferences for the HRQoL implications of specific health states; these are required inputs in the cost-effectiveness evaluations of new therapies.
- Published utility values for DMD are relatively scarce and are available for only a few health states.⁶
- As existing utility data derive from cross-sectional surveys, longitudinal estimates from clinically well-characterized samples are unavailable.

OBJECTIVE

- To estimate health state utility values by age, ambulatory status and over time among boys with DMD.

METHODS

- Data from placebo-treated ambulant boys with DMD with exon 51 skip amenable mutations, recruited under NCT01254019 (provided by BioMarin Pharmaceuticals Inc), were included.
- Patients were followed over 48 weeks and North Star Ambulatory Assessment (NSAA), timed rising from floor (RFF) and 10-meter walk/run (10MWR) tests were performed at baseline and every 12 weeks.
- Family members serving as proxy respondents also completed the 15-item HUI questionnaire, a preference-based utility measure, at baseline, week 24, and week 48.
 - The HUI3 system considers eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain.

METHODS, CONT.

- The HUI2 system includes seven attributes: sensation, mobility, emotion, cognition, selfcare, pain, and optionally, fertility (not assessed).
- In terms of analysis
 - Baseline characteristics of the sample were summarized.
 - Mean (standard deviation [SD]) HUI3 and HUI2 utility values were calculated at baseline and 48 weeks; and presented according to ambulatory status and age.
 - Among patients with LOA, mean (SD) utility values were calculated across patient-visits post-LOA
 - Factors associated with changes in utility were explored by comparing mean attribute scores at baseline vs. after LOA.

RESULTS

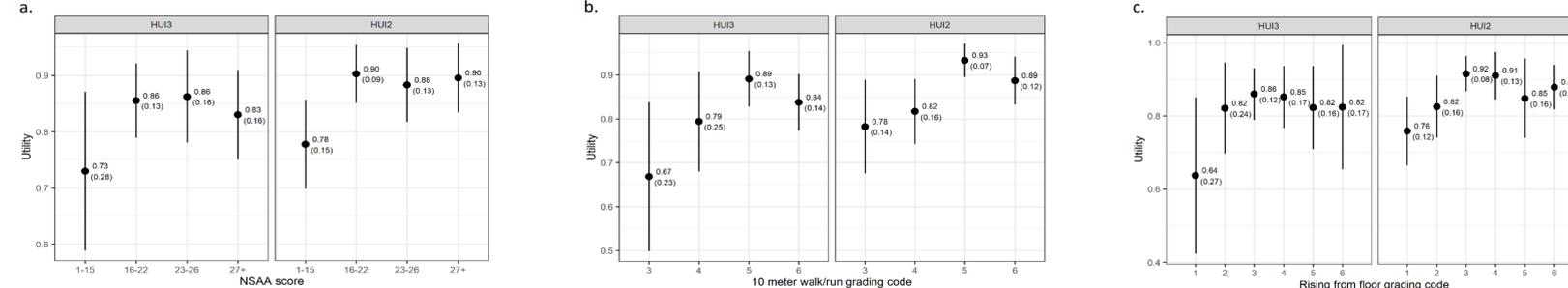
- At baseline the mean (range) age of the 61 ambulant boys was 8.0 (5-16) years and mean (SD) NSAA score was 21 (8) (Table 1).

Table 1. Characteristics for DMD population (n = 61)

	Mean (SD)
Age, years	8.0 (2.4)
NSAA total score	21.0 (8.1)
6MWD (m)	348 (92)
Timed 10m walk test (s)*	7.5 (3.6)
Timed RFF (s)*	13.4 (15.9)
Unable to RFF, even with use of a chair, n (%)	6 (10)
Unable to RFF independently, n (%)	19 (31)

6MWD = six-minute walk distance; NSAA = North Star Ambulatory Assessment; RFF = rise from floor; SD = standard deviation. The NSAA is a 17-item instrument with potential scores ranging from 0-34; lower scores indicate a higher degree of functional impairment. *n=55

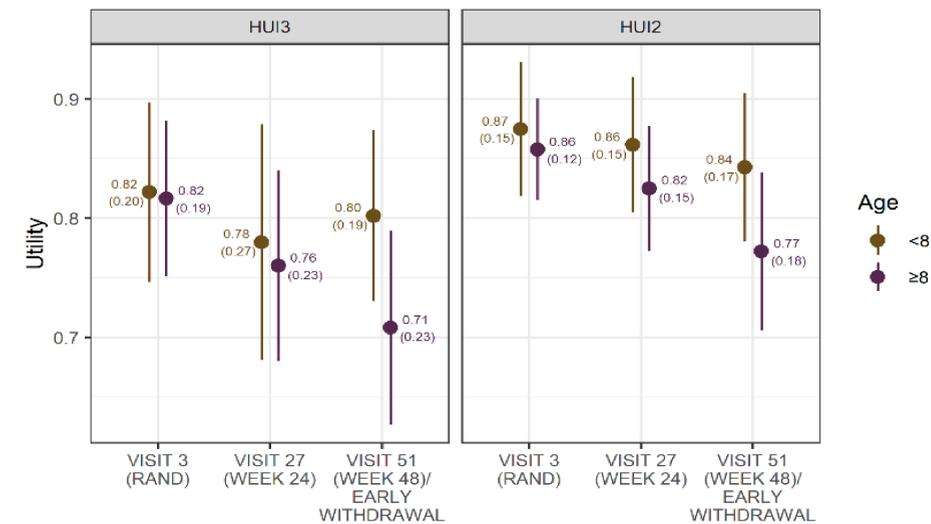
Figure 2. Mean (SD) HUI3 and HUI2 utility at baseline by (a) NSAA score, (b) 10MWR grading code, and (c) RFF grading code. Whiskers represent 95% confidence intervals.



*10MWR grading codes range from 1 (Unable to walk independently) to 6 (Runs and gets off both feet off the ground [with no double stance phase]); RFF grading codes range from 1 (Unable to stand from supine, even with use of a chair) to 6 (Stands up without rolling over or using hands); NSAA scores range from 0 to 34 and are calculated as a sum of 17 activity grades, each ranging from 0 (Unable to achieve independently) to 2 (Normal – no obvious modification of activity).

RESULTS, CONT.

Figure 1. Mean (SD) HUI3 and HUI2 utility by visit stratified by baseline age. Whiskers represent 95% confidence intervals.



- Mean (SD) baseline HUI3 utility was 0.82 (0.19) and HUI2 utility was 0.87 (0.13); values were similar between younger and older boys (Figure 1).
- At 48 weeks, mean (SD) HUI3 utility was 0.75 (0.22) and HUI2 utility was 0.81 (0.18); mean utility had dropped more among older vs. younger boys (Figure 1).
- Six boys (9.8%) lost ambulation over the 48-week period; the mean (SD) utility across patient-visits after LOA was 0.35 (0.15) for HUI3 and 0.52 (0.05) for HUI2, based on a mean decline in utility of 0.25 for HUI3 and 0.18 for HUI2.
 - Change in ambulation levels explained 88% of the drop in HUI3 utility after LOA, while change in emotional status explained 11%.
- Exploratory analyses were conducted to understand the impact of other patient characteristics on utility at baseline (Figure 2).

RESULTS, CONT.

- Mean (SD) utility values from the exploratory analyses were:
 - Lowest among those in the lowest quartile of NSAA score (HUI3: 0.73 (0.28), HUI2: 0.78 (0.15)) and similar among patients in the higher quartiles.
 - Generally higher among those with higher (better) 10MWR grading codes or RFF grading codes.

DISCUSSION

- Among this sample with DMD, utility scores were higher for both ambulant and non-ambulant boys, compared to published HUI3 and HUI2 estimates; there was considerable variability in utility scores.
 - Mean baseline utilities for ambulant boys were 0.82 (HUI3) and 0.87 (HUI2); and 0.35 (HUI3) and 0.52 (HUI2) after LOA;
 - Published estimates for ambulant boys range from 0.65-0.75; and for non-ambulant boys from 0.05 to 0.44.⁶
- Baseline utility values tended to be higher among those with higher scores on functional assessments.
 - The lack of a linear relationship between functional measures and utility suggests that additional drivers of utility exist beyond motor function.
- While the utility of younger boys remained relatively stable over time, older boys and those losing ambulation experienced important declines over follow-up.
- Limitations include the small sample size, particularly of those experiencing LOA, and limited follow up over which to assess change in utility.

CONCLUSIONS

Findings from this study help identify potential factors that may impact health state utility in DMD. In addition to motor function, other aspects of HRQoL that may also be important include dexterity, ability for self-care, and pain. These data also help add to the growing body of evidence, by better defining utility values for ambulant boys with DMD.

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