

Correlation analysis between Health Utilities Index (HUI) and the North Start Ambulatory Assessment (NSAA) scores in Duchenne muscular Dystrophy

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BACKGROUND

- DMD is a rare, progressive 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
- There are numerous measures to quantify disease progression in DMD, including the NSAA, a 14-point functional assessment scale that documents performance on activities such as walking, running, and stair climbing.
- The relentless, progressive functional loss in DMD dramatically affects health-related quality-of-life (HRQoL).
- 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 cost-effectiveness evaluations of new therapies.
 - However, data on utility scores in DMD are limited, and the relationship between function and utility is unclear.

OBJECTIVE

- To estimate the association between function, measured by NSAA score, and health state utility, measured by HUI3 and HUI2 score, among patients 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 NSAA, timed rising from floor (RFF) and 10-meter walk/run (10MWR) tests were assessed at baseline and every 12 weeks by trained assessors.
- 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).
- Analyses
 - Baseline characteristics of the sample were summarized.
 - Mean baseline and change over time scores were computed and the correlation between HUI2 and HUI3 utility, and NSAA, at baseline and 48 weeks was calculated using Spearman's coefficient.⁶
 - These relationships were also explored visually.
 - The analyses were also conducted for each HUI attribute individually with NSAA score.

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).
- Mean (SD) baseline HUI3 utility was 0.82 (0.19) and HUI2 utility was 0.87 (0.13).
- Mean change over 48 weeks (Figure 1) was -0.06 (0.19; HUI3, n=57), -0.05 (0.14; HUI2, n=54), and -2.9 (4.7; NSAA, n=58).

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

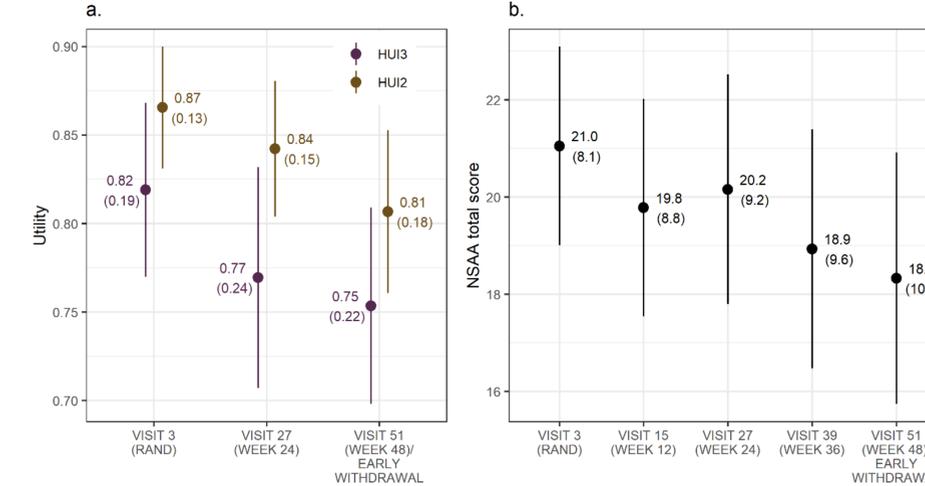
	Mean (SD)
Age, years	8.0 (2.4)
NSAA total score	21.0 (8.1)
6MWD (m)	348 (92)
Timed 10m walk test (s)*	7.5 (3.6)
Timed RFF (s)*	13.4 (15.9)
Unable to RFF, even with use of a chair, n (%)	6 (10)
Unable to RFF independently, n (%)	19 (31)

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

- Weak positive correlations were observed between baseline NSAA score and utility (HUI3: r=0.17; HUI2: r=0.29), and over 48 weeks (HUI3: r=0.15, HUI2: r=0.16; Figure 2)
- Moderate positive correlations were observed between NSAA score and the HUI3 ambulation (r=0.41), HUI2 mobility (n=0.41), and HUI2 self-care (r=0.42) scores; NSAA scores were weakly correlated with HUI3 pain (r=-0.20; Figure 3).

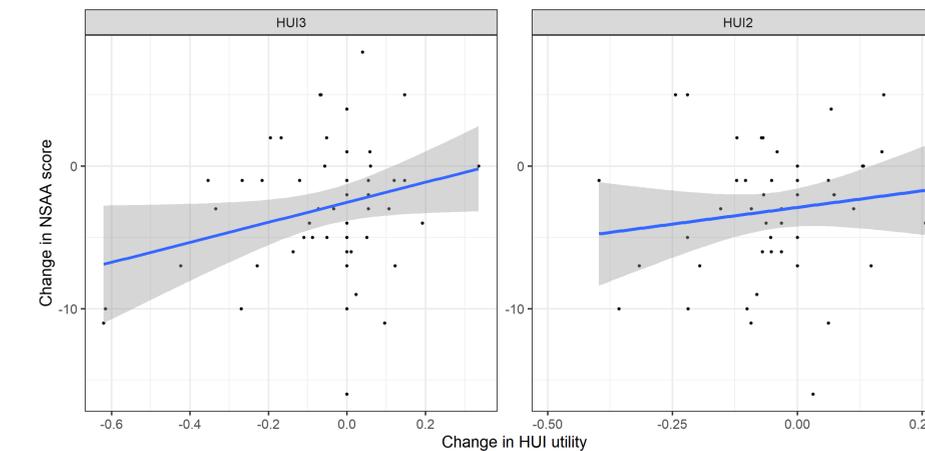
RESULTS, CONT.

Figure 1. Mean (SD) (a) utility and (b) NSAA total score by visit. Whiskers represent 95% confidence intervals.



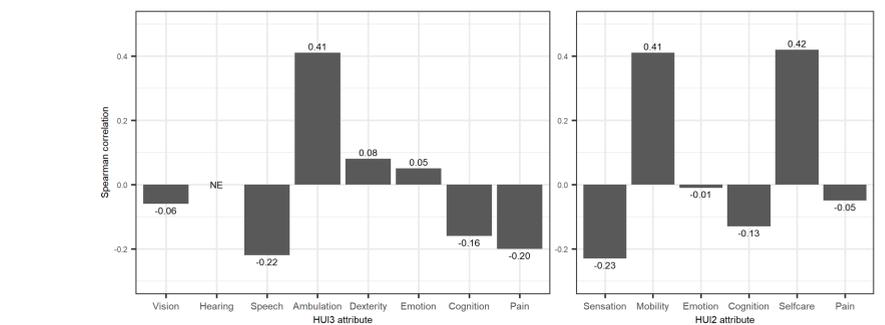
- Visual inspection of scatterplots revealed potentially inconsistent combinations of scores which would have impacted the correlation between the two measures:
 - Patients with high HUI scores and low levels of function, and
 - Patients with large variability in utility at the same levels of NSAA function.
- For example, 4 patients with relatively stable NSAA had large changes in utility due to deteriorations in emotion (1 patient dropped 2 levels), pain (3 patients dropped 1 level), cognition (1 patient dropped 2 levels and another, 3 levels), vision (1 patient dropped 3 levels), and speech (1 patient dropped 1 level).

Figure 2. Scatterplots of change (week 48 - baseline) in NSAA score vs change in HUI utility with a best-fit line



RESULTS, CONT.

Figure 3. Correlation of NSAA scores with particular HUI attribute scores across all visits



DISCUSSION

- Among this sample of ambulatory boys with DMD, NSAA is not strongly correlated with overall HUI utility.
 - Visual inspection of the relationships between NSAA and HUI scores demonstrates the presence of outliers; individuals with low levels of function but with high utility, and individuals with good physical functioning but low utility.
- It is important to note that there were stronger correlations with individual domains including ambulation, mobility, and ability for self-care.
- Limitations include the small sample size and limited follow up over which to assess change in utility and functional status.

CONCLUSIONS

While NSAA score is correlated with the ambulatory components of the HUI, additional important drivers of utility exist. Functional status alone cannot explain HUI utility estimates in ambulatory DMD patients. In clinical trials, it is therefore important to consider both measures as they evaluate different and meaningful concepts.

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