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# Health State Utilities in Duchenne Muscular Dystrophy (DMD): A Longitudinal Study using the EQ5D and Health Utilities Index (HUI)


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## Introduction

- DMD progression is characterized by loss of ambulation and upper limb function, respiratory insufficiency, cardiomyopathy, and early mortality[1]
- DMD profoundly impacts health-related quality of life (HRQoL);[2-5] this impact is reflected in available utility values for DMD-specific health states[5]
- However, existing utility data in DMD are limited"
  - As the majority of utility data are derived from cross-sectional studies,[6] how utility changes over time in DMD is unclear
  - The impact of key functional transitions, such as loss of ambulation or hand function, on utility has not been explored

## Objectives

- To report changes in health utility values over 12 months, according to patients' baseline health state; and estimate change in utility among those experiencing key functional transitions in DMD

## Methods

- ***Study design:*** Longitudinal online survey[6]
- ***Data collection***: Individuals with physician-confirmed DMD in the US or their caregivers (both recruited through PPMD) completed the EQ-5D and HUI instruments online at baseline and 12 months[6,7,8]
- Participants completed a clinical questionnaire[6] to classify their health state (categorized as early ambulatory, late ambulatory, early non-ambulatory, and late-non-ambulatory)
- ***Analysis****:* As a high degree of agreement has been reported on utility between patient-caregiver dyads in DMD,[7] responses from patients and caregivers were combined
- Demographic characteristics and details of health status were summarized
- Mean (standard deviation [SD]) changes in EQ-5D, HUI-2, and HUI-3 utility values were estimated, and stratified according to baseline health state (Figure 1)
  - These changes were considered in the context of documented minimal clinically important differences (0.03 [HUI], and 0.07 [EQ-5D])[8]
- Scatterplots were used to visualize baseline and month 12 utility, and changes in utility, per instrument and health state
- The frequency of key functional transitions (declines in lower or upper limb function, development of cardiomyopathy, or need for daytime ventilation) was tabulated
- Linear mixed regression models were used to estimate changes in utility over 12 months among those experiencing key transitions

## Results

- From 236 initial survey participants (173 caregivers and 63 patients), 155 (65.7%; 122 caregivers and 33 patients) completed the 12-month survey
- Mean (SD) patient age was 15.4 (6.7) years, 52.3% were in an ambulatory state at baseline and 47.7% were in an ambulatory state at follow-up. Sample sizes according to baseline health states are presented in Figure 1
- Baseline patient characteristics did not vary substantially between those completing, and not completing, month 12 follow-up (data not shown)
- Over 12 months, mean (SD) change in observed utility was (Figure 2):
  - -0.01 (0.16) on the EQ-5D; and ranged from an increase of 0.03 (0.28) among those who were late ambulatory, to a decrease of 0.03 (0.13) among those who were early ambulatory
  - -0.03 (0.12) on the HUI-2; and ranged from no change (0.00 [0.22]) among those who were late ambulatory, to a decrease of 0.05 (0.12) among those who were early ambulatory
  - -0.04 (0.17) on the HUI-3; and ranged from no change (0.00 [0.10]) among those who were late non-ambulatory, to a decrease of 0.08 (0.18) among those who were early ambulatory
  - Changes in utility at the individual level over 12 months are presented as scatterplots (Figure 3)
- Seventeen (11.0%) patients experienced declines in lower limb function and clinically important losses in modeled mean utility were noted (-0.09 [0.03; EQ-5D], -0.16 [0.03; HUI-2] and -0.19 (0.05; HUI-3])
- Sixteen (10.3%) patients developed cardiomyopathy; while the modeled change in utility on the EQ-5D was small (-0.001 [0.05]), significant losses in utility were noted on the HUI-2 (-0.08 [0.03]) and HUI-3 (-0.12 [0.05])
- Loss of upper limb function (n=5) and progression to daytime ventilation (n=3) were infrequently observed

***Figure 1*** *Health states observed among the cohort**

| | Upper limb function | Respiratory support | Cardiomyopathy | n |
|---|---|---|---|---|
| Early ambulatory | Preserved UL | No daytime vent | Without sympt CM | 45 |
| | Mildly impaired UL | No daytime vent | Without sympt CM | 5 |
| | Mildly impaired UL | No daytime vent | With sympt CM | 1 |
| Late Ambulatory† | Preserved UL | No daytime vent | Without sympt CM | 19 |
| | Preserved UL | No daytime vent | With sympt CM | 1 |
| | Mildly impaired UL | No daytime vent | Without sympt CM | 3 |
| Early non-ambulatory | Preserved UL | No daytime vent | Without sympt CM | 11 |
| | Mildly impaired UL | No daytime vent | Without sympt CM | 29 |
| | Mildly impaired UL | No daytime vent | With sympt CM | 1 |
| | Mildly impaired UL | Night & Day vent | Without sympt CM | 1 |
| Late non-ambulatory | Mod impaired UL | No daytime vent | Without sympt CM | 20 |
| | Mod impaired UL | No daytime vent | With sympt CM | 5 |
| | Mod impaired UL | Night & Day vent | Without sympt CM | 3 |
| | Mod impaired UL | Night & Day vent | With sympt CM | 2 |
| | Loss of function | No daytime vent | Without sympt CM | 2 |
| | Loss of function | No daytime vent | With sympt CM | 1 |
| | Loss of function | Night & Day vent | Without sympt CM | 6 |

*classified according to level of lower and upper limb function, presence of respiratory support, and cardiomyopathy, †transitional ambulatory
Abbreviations: UL upper limb; ventvventilation; sympt CM=symptomatic cardiomyopathy

***Figure 2*** *Mean (SD) utility change over 12 months, by health state and instrument*

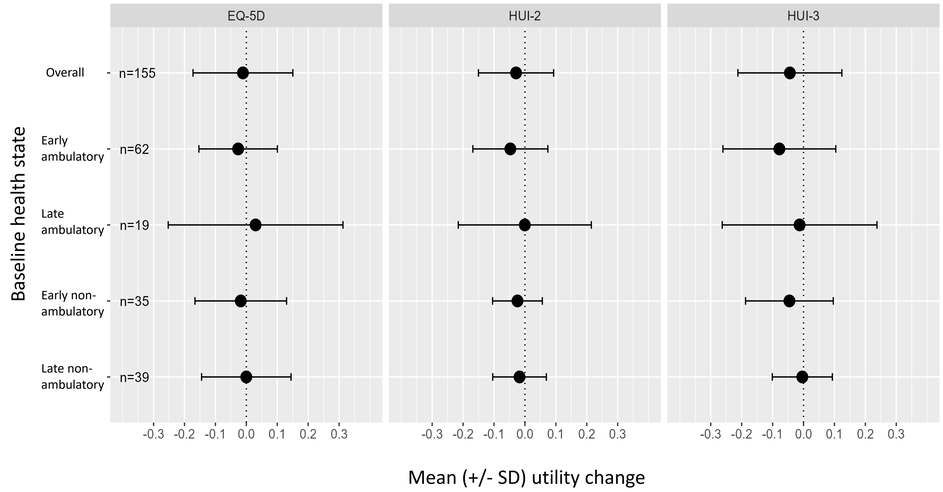
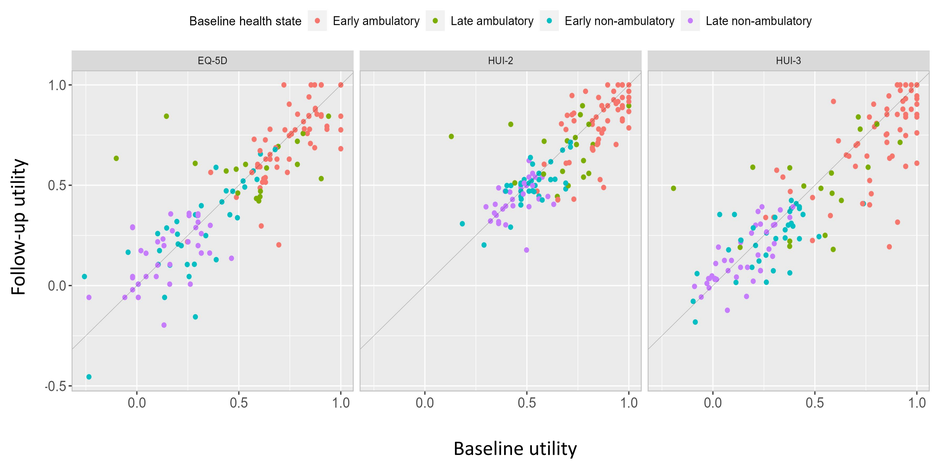



***Figure 3*** *Scatterplots of baseline vs. follow-up utility, by instrument and health state*





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## Key Findings and Conclusions

- **While on average there was little change in mean utility over 12 months, key functional transitions were associated with clinically important changes in utility in this large sample with DMD**
- **These findings contribute to understanding how functional changes are related to changes in utility in DMD**

## Discussion

- This longitudinal assessment demonstrated that, although individual scores varied, on average there was minimal change in utility over one year
  - However, those experiencing key functional transitions, and those who were in the early ambulatory state at baseline, experienced large and clinically important declines in utility[8,9]
- Not everyone experienced utility declines over time, even in slowly progressive diseases like DMD.
  - Potential explanation for improvements in utility could include the fluctuating patterns of symptoms that would impact utility on a given day;[10] the effects of accommodation;[11,12] and due to improvements in factors like emotional status (even without improvements in, for example, limb function)[12]
- Strengths include the longitudinal follow-up and relatively large sample size for a rare condition such as DMD. Nonetheless, the number experiencing key transitions was small
- While not all participants who completed the baseline survey returned for follow-up, no substantial differences in baseline characteristics were noted between those who did, and did not, complete the follow-up survey
- Finally, there are many factors that could impact utility within a given health state that are difficult to capture – for example, modifications to the built environment, individual characteristics or access to financial resources – which may also contribute to within health state variability.

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