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The EQ-5D and Health Utilities Index (HUI) for Assessing Health-Related Quality-of-Life (HRQoL) Impact in Duchenne Muscular Dystrophy (DMD)

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Objective

To **compare the descriptive systems** of the EQ-5D and HUI measures for assessing HRQoL in DMD; and **evaluate the perceived meaning and relevance** of the dimensions of their descriptive systems to individuals living with DMD

DISCUSSION AND CONCLUSIONS

- Understanding the relevance and interpretation of items on preference-based measures is important for interpreting the utility values generated by these instruments
  - The results of this study help inform our understanding of the perceived relevance of the health state classifications represented by the HUI and EQ-5D instruments to those living with DMD
- Study findings highlight that, while both the EQ-5D and HUI assess DMD-relevant dimensions, how the dimensions are described is not always sufficient to fully characterize the DMD experience
  - For example, while participants generally preferred how the HUI more broadly characterized ambulation, neither instrument fully captures the ability to mobilize with a wheelchair or other walking aids
- Nonetheless, participants generally felt that HUI response options allowed an easier classification of current health status, and that with DMD disease progression, the HUI permits a more nuanced categorization for individuals with more varied health statuses
- There are few studies comparing the appropriateness and relevance of utility instruments
  - A study by Crossnohere et al, concluded that the EQ-5D had some value, but other instruments may be more sensitive to DMD-specific impacts[13]
  - While comparative evidence from other therapeutic areas is also scarce, it would have limited relevance as the appropriateness of the instrument needs to be considered in the context of the condition specifically
- While this study was strengthened by the large sample representing patients of varied clinical statuses, the sample comprises individuals willing to participate in both a research survey and interview, and thus the generalizability may be limited
- The results of this study can help inform an understanding of the extent to which individuals living with DMD associate with the health states they are categorized into by the HUI and EQ-5D instruments. Additionally, these patient-derived data can help inform instrument selection in HRQoL studies using generic instruments

BACKGROUND

- **The progression of Duchenne muscular dystrophy (DMD)**, a rare neuromuscular disease characterized by loss of ambulation and early mortality,[1–3] has profound effects on the health-related quality-of-life (HRQoL) of patients and their caregivers[1–5]
- The Health Utilities Index (HUI) and EQ-5D are preference-based instruments commonly used to assess patient health status in terms of HRQoL impact and to estimate utility values[6,7]
- Prior research has demonstrated variability in utility values in DMD, both within health states but also between instruments[8]
  - Heterogeneity in the DMD clinical course and timing of disease milestones are known to contribute to variability in health state utility
  - However, variability may also be driven by differences in each instrument's descriptive system, both in terms of health dimensions covered as well as in the way that HRQoL impact is described
- An additional factor that may contribute to variability is how individuals interpret the items within the HUI and EQ-5D instruments
  - Cognitive debriefing is a method regularly used to establish the acceptability and relevance of patient-reported outcome instruments[9,10]
  - These methods may be valuable for understanding the content validity of questions on ambulation for non-ambulatory individuals with DMD, for example

METHODS

- **Cognitive debriefing** interviews were conducted with English-speaking individuals with DMD, or caregivers reporting on their behalf, who live in the US and participated in a previous study[8]
- Participants provided information on demographics and clinical status before completing the EQ-5D and HUI preference-based measures as part of an online survey[6,11]
  - The HUI classifies health status according to two complementary systems
    - **HUI2:** Sensation, mobility, emotion, cognition, self-care, pain, and fertility (optional)
    - **HUI3:** Vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain
  - The **EQ-5D (5L)** measures health status based on dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
- Participants then completed a 30-minute Zoom-based interview conducted by trained interviewers using a semi-structured guide. Within that interview the following topics were explored:
  - The **relevance** of the dimensions and items included within each instrument
  - The **meaning, interpretation, and comprehensiveness** of item questions and response options
  - For similar dimensions covered within both instruments, a comparison of the perceived appropriateness as it applies to DMD
    - For example, emotion/mental health impact on the HUI is assessed by Q7 (degree of happiness) and Q14 (frequency of feeling fretful, angry, irritable, anxious, or depressed) vs degree of anxiety or depression on the EQ-5D
  - Whether any important aspects of HRQoL impact in DMD were missing from the instruments
- Interview responses were analyzed using summative content analysis to identify key concepts mentioned and the percentage of participants reporting those[12]
- Responses were summarized according to item and instrument; feedback regarding the appropriateness of the instruments for capturing patient experiences in DMD was illustrated using direct quotes
- Ethical approval was provided by WIRB-Copernicus Group (WCM), and all participants provided informed consent

RESULTS

- **Forty-seven** participants (33 caregivers and 14 patients) were interviewed
- Mean patient age was 16.6 years and 65% were non-ambulatory (**Table 1**)
- Mean (SD) EQ-5D utility was 0.40 (0.32), HUI2 utility was 0.61 (0.21), and HUI3 utility was 0.39 (0.31)

Relevance of instrument dimensions to DMD

- **All participants regarded the dimensions covered within the EQ-5D and HUI as relevant to DMD in general**, even if no longer relevant to their current disease state (eg, questions about ambulatory status to an individual who can no longer walk)
  - However, participants thought the **dimensions represented are not sufficiently broad** to cover all important aspects of their respective latent constructs relevant to DMD

"To have to answer 'unable to walk at all' doesn't fully encapsulate what he is able to do since he goes out by himself, with his dog, and with his friends in his power wheelchair" – P091

- Participants had **difficulty with response options** that assumed an **impact occurred at a constant level** over time; for example, on the EQ-5D, "I have slight pain or discomfort" vs "I have moderate pain or discomfort"

"This could change daily—some days he has no pain, other days it's moderate/severe. So, answering for today is easy, but answering in general would be difficult. I think wording it to be more specific would be helpful, for example, does it fluctuate, does it happen daily, etc" – P143

- Participants thought **patient coping strategies** and **access to external resources that could moderate HRQoL impact** were important points not presently considered in the surveys, as well as **social impact**

Table 1: Demographic and Clinical Characteristics

	Overall (n=47)
Patient age, mean (SD) years	16.6 (8.1)
Caregiver age, mean (SD) years	46.7 (7.8)
Ambulatory status, n (%)	
Ambulatory	12 (25.0)
Transitional	5 (10.4)
Non-ambulatory	30 (63.8)
Ventilation status, n (%)	
No ventilation	29 (60.4)
Nighttime ventilation/BiPAP	12 (25.0)
Night and daytime ventilation	6 (12.8)
Cardiomyopathy, n (%)	
No cardiomyopathy	24 (51.1)
Asymptomatic cardiomyopathy	20 (41.7)
Symptomatic cardiomyopathy	3 (6.2)
Upper limb function, n (%)	
Preserved upper limb function	19 (40.4)
Mildly impaired	15 (31.9)
Moderately impaired	7 (14.9)
Loss of upper limb function	6 (12.8)

BiPAP=bilevel positive airway pressure.

Perceptions of the EQ-5D and HUI

On the EQ-5D:

- Simple or **vague descriptions** of impact that lack nuance can **create challenges** for patients and caregivers to understand where the patient falls with respect to function

"…age and expectation are important, as there are nuances. So, when they are older and in a chair, they can still do small things within a big task; so, if you are too broad you might miss this" – P074A

- Terms **slight, moderate, and severe were considered subjective**, and participants found those difficult to use for classification without a more nuanced explanation of likely impacts of these varying levels of problems on patients' lives

"I think the statements (for 'self care') were very broad, more examples would be helpful. I am not sure what slight, moderate, or severe is in relation to dressing himself—maybe if it was rated as no problems at all, some problems, or requiring help" – P143

On the HUI:

- Most participants found **classifying health status easier on the HUI** vs the EQ-5D because response options were more granular. For example, the question on ambulation offers "able to walk around the neighborhood with difficulty; but did not require walking equipment or the help of another person"
- Response options for **HUI ambulation** appeared **equally relevant to individuals who are ambulatory, or who use walking devices or wheelchairs,** compared with the EQ-5D that only describes mobility for those who are independently ambulant
- Participants generally **preferred the timeframe of the HUI**, "in the last week" vs the EQ-5D timeframe of "today," as reporting on function on any given day could inaccurately represent the patient's general wellbeing

"I do like the timeframe of last week, because 'today' could be really good or really bad. On the day he fell, he would have a very different pain experience than normal days" – P085

For similar dimensions included in both instruments

- Participants generally **preferred** how dimensions were described in the **HUI compared with the EQ5D**

Mobility/ambulation

- Most participants **(91%)** preferred how the **HUI more broadly conceptualized mobility** (considering the use of mobility aids) and provided more explicit descriptions that allowed participants to more easily identify where their levels of function fell

"I like the context of the HUI 'walking around neighborhood' as you get a more consistent answer, as what I think is moderate [on the EQ-5D], someone else may think of as slight" – P085

Basic activities/self-care

- Most participants **(63%)** preferred the **more descriptive HUI response options**; although participants struggled with response options for both instruments in cases where response options combined multiple activities on which individual performance can differ (e.g., self-care)

"I think lumping together eating, bathing, and dressing is difficult, as my son can do a lot of aspects of things for himself, you don't have to do everything for him… I find it weird to lump them together… the answer could vary, as he can eat alone but he can't get into the shower" – P074

Pain/discomfort

- **All** participants preferred the questions and response options of the **HUI**, as the specifications around pain relief and impact on activities **made their pain/discomfort easier to classify**

"I like [HUI Q15] as it seems there is a clear threshold of maybe where I would consider giving Tylenol rather than seeking a doctor. I like this context around nonprescription drugs. I also like [reference to their] normal activities—for DMD boys, activities are already moderated… so it is important to think of what activities are normal for them [and not necessarily normal for others of their age]" – P085

Emotional/mental health

- Most participants (93%) found that HUI Q14 that asked about the frequency of feeling fretful, angry, irritable, anxious, or depressed is more relevant than questions on the extent of happiness (HUI Q7) or anxiety/depression (EQ-5D) where it was assumed these emotional impacts were constant over the assessment period

"I think HUI Q14 is most helpful… I like the word irritable, occasional, and generally as these best describe DMD—that it fluctuates, and they are not always extremely experiencing any emotion" – P083

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