Utility values for health states associated with Duchenne muscular dystrophy (DMD): A systematic review

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BACKGROUND

- DMD is a rare, severe progressive X-linked myopathy caused by mutations in the gene for dystrophin.[1,2]

- Patients experience muscle wasting, loss of ambulation in their early teens, cardiomyopathy, need for ventilation, and premature death by the second or third decade.[3,4]

- While a number of studies on utility values for DMD have recently been published, estimates have not been summarized across studies.

- Accurate measures of patient health state utilities are required to evaluate the cost-effectiveness of DMD therapies.
    - Utility values reflect the strength of individuals' preferences for health states, on a scale from 1 (full health) to 0 (dead).[5]
    - Numerous methods exist to elicit utility values, including direct (e.g. time trade-off, standard gamble or visual analogue scale (VAS)), and indirect (e.g. generic preference-based health-related quality-of-life [HRQoL] measures such as the EQ-5D or HUI) methods. [6-8]

- As DMD progression begins in early childhood, the disease affects the HRQoL of both DMD patients and their families.

- The objective of this study was to synthesize published evidence for the utility value of DMD health states from the perspectives of patients (or proxy respondents), and for the health states experienced by caregivers of DMD patients.

METHODS

- A systematic review was performed using MEDLINE and Embase, guided by study PICOS criteria (**Figure 1**), according to PRISMA guidelines. [9]
- Study screening and data extraction were performed in duplicate from publications reporting utility values for DMD patients or caregivers.
- Data were extracted on study and patient characteristics, health states considered, approach to measuring utility (including the HUI-3 and EQ-5D) and reported utility values.
- Mean utility values, and the number of individuals contributing to each estimate, were summarized according to health state: overall, and by clinically important subgroup (e.g. by ambulatory status or need for ventilation).
- Mean utility values were stratified by respondent type, country, and instrument.
- Quality appraisal of included studies was performed using the method by Papaionannou et al (2013; *data not shown*).[10]

Figure 1. PECOS criteria[9]
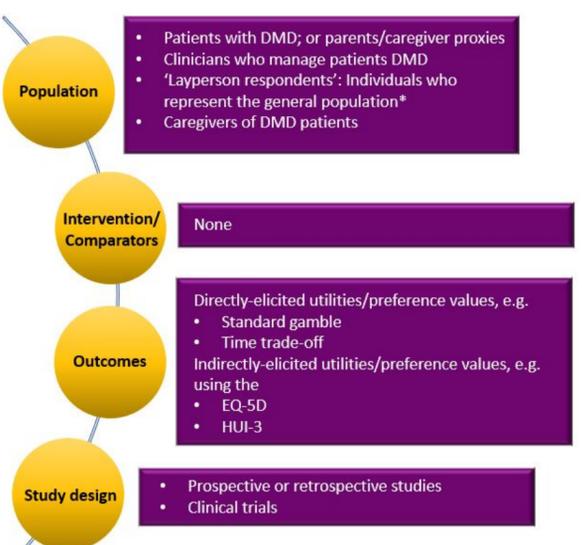
DMD: Duchenne muscular dystrophy; EQ-5D: Euro-QoL 5-dimension survey; SF-6D: Short-form 6-D; HUI-3: Health Utilities Index Mark 3
*Layperson respondents were considered should vignette-based exercises be identified as sources of utility estimates
Note: Case reports or case series, animal studies, and articles not in English were excluded.
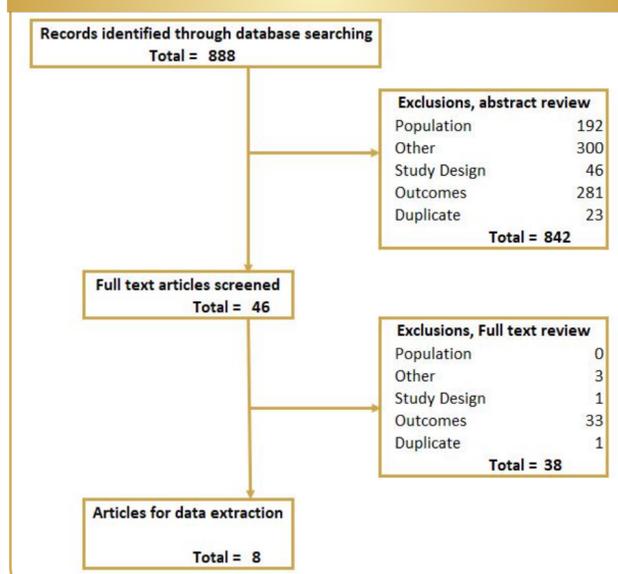
FUNDING & DISCLOSURES

RESULTS

- From 888 abstracts, 8 publications describing 5 eligible studies were identified (**Figure 2**).[11-18]
    - No longitudinal studies were identified. Selected respondent and study characteristics are presented in **Table 1**.
- DMD utility estimates were identified for a limited number of health states from indirect preference-based measures only. These were presented stratified by ambulatory status, need for ventilation, and age (**Figure 3**).
    - Patient/proxy utility values ranged from 0.75 (HUI-3) for those with early ambulatory DMD to 0.05 (HUI-3) for those on day-and-night ventilation.
    - Published caregiver utility values ranged from 0.87 (for caregivers of adult patients with DMD; EQ-5D-3L) to 0.71 (for caregivers of predominantly childhood DMD patients; EQ-5D-3L).
- Patient utilities tended to be lower with more severe DMD health states. Caregiver utilities showed less variability.
- Variability in utilities was also observed based on the choice of measure, respondent type (**Figure 3**), study selection criteria, and country (*data not shown*).
- No utilities for other DMD-related health states (for example scoliosis, upper limb function or developmental disability) were identified.

Table 1. Study and patient characteristics

| Citation	Objective	Countries	Data source	Respondents	Mean (range or *SD*) age (y)	Utility measure
Cavazza et al., 2016[11]	HRQoL and economic burden of DMD in Europe	Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, UK	Parent Project MD	Community-dwelling males with DMD	14.7 (11.3-23.9)[b]	EQ-5D utility and VAS
				Caregivers of community-dwelling DMD patients	44.3 (25.0-49.6)[b]	EQ-5D utility and VAS
Landfeldt et al., 2014*[12]	Economic burden of DMD	Germany, Italy, UK, US	TREAT-NMD	Males with DMD aged ≥5 years	14 (8-17)	HUI-3
				Caregivers of males with DMD aged ≥5 years	44 (39-50)	EQ-5D utility
Landfeldt et al., 2016*[13]	Health-related quality-of-life impact of DMD	Germany, Italy, UK, US	TREAT-NMD	Males with DMD aged ≥5 years	14 (8-17)	HUI-3
				Males with DMD on ventilatory support	NR	HUI-3
Landfeldt et al., 2016*[14]	Burden among caregivers of patients with DMD	Germany, Italy, UK, US	TREAT-NMD	Caregivers of males with DMD aged ≥5 years	44 (39-50)	EQ-5D utility and VAS
Landfeldt et al., 2018[15]	Psychometric properties of PedsQL NMM	UK, US	TREAT-NMD	DMD patients who could complete the PedsQL NMM	16 (*7*)	HUI-3
Magnetta et al., 2018*[16]	Cost-effectiveness model for treatment for advanced HF in DMD		NA	Hypothetical cohort of patients with DMD and advanced HF	NA	EQ-5D utility
Pangalila et al., 2012[17]	Burden among caregivers of adult patients with DMD	Netherlands	NA	Patients with DMD aged ≥20 years	27 (*6.1*)	EQ-5D utility
				Caregivers of patients with DMD aged ≥20 years	57 (*6.8*)	EQ-5D utility
Landfeldt et al., 2015*[18]	Psychometric properties of the DMDSAT	UK	TREAT-NMD	Males with DMD aged ≥5 years	14 (5-43)	HUI-3
				Caregivers of males with DMD aged ≥5 years	NR	EQ-5D

*Four publications from the same related sample/overall study; Landfeldt 2015 focused on the UK subset only
[a]Utilities were based on a previous EQ-5D data collection exercise; [b]Mean age = 14.7 years; and the range reflects the mean age of each country-specific sample contributing to the overall estimate
DMD: Duchenne muscular dystrophy; HF: heart failure; UK: United Kingdom; US: United States; SD: standard deviation; HUI: Health Utility Index; EQ-5D: EuroQoL 5 dimensions; VAS: Visual analogue scale; MD: Muscular dystrophy; NMD: Neuromuscular dystrophy.

Figure 2. PRISMA diagram[9]

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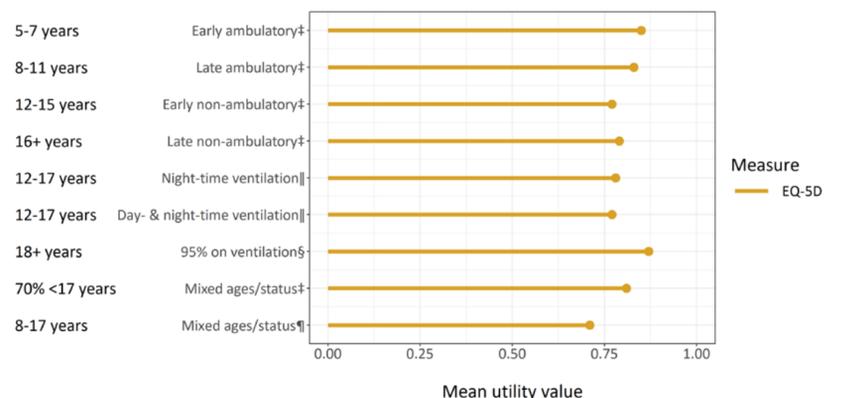18. Landfeldt, E.M. et al. *Neuromuscular Disorders.* 2015; 25(12):937-944

Figure 3. a) DMD health state utility values, and b) DMD caregiver utility values; by patient age and ambulatory/respiratory status

a) Patient/proxy utility values
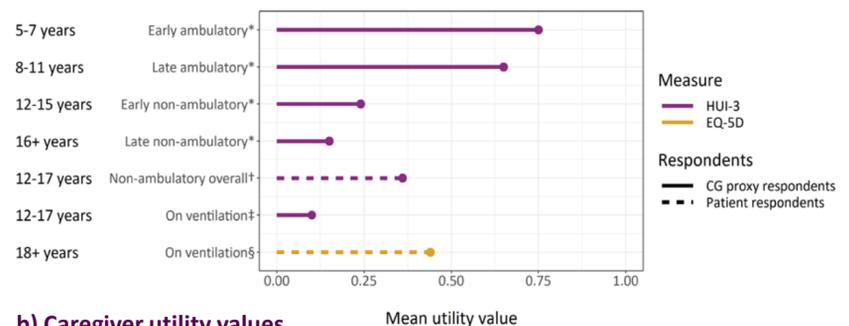
b) Caregiver utility values

Abbreviations: CG = caregiver; EQ-5D = Euro-QoL 5-dimension survey; HUI-3 = Health Utilities Index-3
*Landfeldt et al., 2014; † Landfeldt et al., 2018; ‡ Landfeldt et al., 2016, ventilation type unspecified; § Pangalila et al., 2012. 96% of patients were on at least some type of ventilation, and 47% had a tracheostomy; || Landfeldt et al., 2015; ¶ Cavazza et al., 2016
NR = not reported; CG = caregiver; HUI-3 = Health Utilities Index – Mark 3; EQ-5D = EurolQoL 5-dimensions survey

CONCLUSIONS

- Published health state utility values document the detrimental impact of DMD on HRQoL and patient health status, particularly as the disease progresses
- Relatively few published studies were identified
    - All estimates were derived from preference-based measures
    - Health states with utility estimates were largely limited to those described by ambulatory status and need for ventilation
- Future initiatives to describe patient utilities for a wider range of DMD milestones are warranted, particularly for non-ambulatory patients