

Estimating Health State Utilities in LGMD 2E/R4, 2D/R3, and 2C/R5: Analysis of EQ-5D Baseline Data From the JOURNEY Natural History Study

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Background

- Limb-girdle muscular dystrophies (LGMDs) are a group of rare, heterogeneous, autosomal neuromuscular disorders causing progressive weakness and wasting of the shoulder and pelvic girdle musculature^{1–3}
 - Sarcoglycanopathies are ultra-rare subtypes that account for ~15% of LGMD cases in the US⁴ and are caused by defects in the genes encoding 1 of the 4 cell membrane glycoproteins contributing to the sarcoglycan complex (*SGCB*, *SGCA*, *SGCG*, and *SGCD*)^{2,3}
- Insufficient information is currently available on the impact of LGMD disease progression on health-related quality of life (HRQoL), which limits modeling of the potential benefits of a treatment
- JOURNEY (NCT04475926) is a natural history study investigating the clinical phenotype, disease course, and HRQoL of patients with LGMD, including the natural variability among ambulatory and nonambulatory populations

Objectives

- To analyze baseline EuroQol 5-Dimension (EQ-5D) data and EQ Visual Analog Scale (EQ-VAS) from sarcoglycanopathy subtypes LGMD 2E/R4, 2D/R3, and 2C/R5 patients enrolled in JOURNEY
- To stratify health state utilities and EQ-VAS scores by ambulatory status, LGMD subtype, age group, and reporter type (self or proxy)

Methods

EuroQoL 5-Dimension Health Questionnaire

- Caregivers completed the EQ-5D 5-Level (EQ-5D-5L) Proxy Version 1 for patients aged 4–7 years
- Patients aged 8–17 years completed the EQ-5D Youth (EQ-5D-Y)
- Patients aged ≥18 years completed the EQ-5D-5L
- Since normative US population data were not available for EQ-5D-Y, normative German population data were used to calculate utilities
- The EQ-VAS records the patient’s self-rated health on a vertical VAS
- Statistical significance of trends was explored by analysis of variance (ANOVA)

Results

Baseline Characteristics

- Data were available for 9 parent proxy reports and 97 patient self-reports
- Baseline characteristics were similar for the EQ-5D-Y and EQ-5D-5L among patients by LGMD subtype and ambulatory status (**Table 1**)

EQ-5D Scores

- Mean (SD) utilities declined with increasing age in ambulatory (4–7 years, 0.84 [0.16]; 8–17 years, 0.75 [0.22]; ≥18 years, 0.56 [0.22]) and nonambulatory (8–17 years,0.47 [0.35]; ≥18 years,0.15 [0.27]) patients (**Table 2, Figure 1**)
- An ANOVA test of linear trends found that this pattern was significant ($F_{2,88} = 10.35$, $P<0.0001$)
- Mean utilities were higher in ambulatory vs nonambulatory patients (8–17 years, 0.75 vs 0.47; ≥18 years, 0.56 vs 0.15)

EQ-VAS Scores

- Mean (SD) VAS scores in ambulatory patients declined in older age groups: 4–7 years, 85.22 (15.77); 8–17 years, 79.03 (17.65); ≥18 years, 70.56 (16.42) (**Table 3, Figure 2**)
- Mean VAS scores were higher in ambulatory vs nonambulatory patients: (8–17 years, 79.03 vs 63.41; ≥18 years, 70.56 vs 64.52)

Table 1 Baseline Characteristics by LGMD Subtype and Ambulatory Status					
	2C/R5 (n=39)	2D/R3 (n=38)	2E/R4 (n=29)	Ambulatory (n=55)	Nonambulatory (n=51)
4–7 y cohort, n	2	4	3	9	–
Age mean (SD)	6.5 (0.71)	5.8 (1.50)	6.0 (1.00)	6.0 (1.12)	–
Sex, female, n (%)	2 (100.0)	2 (50.0)	2 (50.0)	4 (44.4)	–
8–17 y cohort, n	24	16	12	30	22
Age mean (SD)	13.2 (2.57)	12.4 (2.92)	12.1 (2.50)	11.7 (2.40)	14.3 (2.47)
Sex, female, N (%)	14 (58.3)	8 (50.0)	8 (50.0)	17 (56.7)	15 (65.2)
≥18 y cohort, n	13	18	14	16	29
Age mean (SD)	29.1 (7.31)	36.7 (13.99)	34.4 (9.88)	35.0 (13.21)	33.1 (10.41)
Sex, female, N (%)	9 (69.2)	13 (72.2)	13 (72.2)	9 (56.2)	21 (72.4)

LGMD=limb-girdle muscular dystrophy; y=years.

Table 2 EQ-5D Utilities by LGMD Subtype and Ambulatory Status

	2C/R5 (n=39)	2D/R3 (n=38)	2E/R4 (n=29)	Ambulatory (n=55)	Nonambulatory (n=51)
4–7 y cohort, n	2	4	3	9	–
Mean (SD)	0.94 (0.08)	0.76 (0.16)	0.86 (0.19)	0.84 (0.16)	–
Median (Q1, Q3)	0.94 (0.91, 0.97)	0.71 (0.67, 0.80)	0.94 (0.79, 0.97)	0.88 (0.69, 1.00)	–
8–17 y cohort, n	24	16	12	30	22
Mean (SD)	0.61 (0.29)	0.65 (0.34)	0.66 (0.34)	0.75 (0.22)	0.47 (0.35)
Median (Q1, Q3)	0.64 (0.52, 0.79)	0.65 (0.40, 0.89)	0.74 (0.58, 0.87)	0.80 (0.64, 0.87)	0.53 (0.40, 0.65)
≥18 y cohort, n	13	18	14	16	29
Mean (SD)	0.15 (0.21)	0.32 (0.42)	0.39 (0.20)	0.56 (0.22)	0.15 (0.27)
Median (Q1, Q3)	0.10 (0.01, 0.26)	0.47 (0.06, 0.62)	0.38 (0.31, 0.46)	0.58 (0.46, 0.72)	0.16 (0.01, 0.32)

EQ-5D=EuroQol 5-Dimension; LGMD=limb-girdle muscular dystrophy; y=years.

Table 3 EQ-VAS by LGMD Subtype and Ambulatory Status

	2C/R5 (n=39)	2D/R3 (n=38)	2E/R4 (n=29)	Ambulatory (n=55)	Nonambulatory (n=51)
4–7 y cohort, n	2	4	3	9	–
Mean (SD)	89.50 (0.71)	88.75 (19.31)	77.67 (17.50)	85.22 (15.77)	–
Median (Q1, Q3)	89.50 (89.25, 89.75)	97.50 (86.25, 100.00)	78.00 (69.00, 86.50)	90.00 (78.00, 95.00)	–
8–17 y cohort, n	24	16	12	30	22
Mean (SD)	70.46 (23.14)	76.06 (15.35)	71.50 (28.55)	79.03 (17.65)	63.41 (24.88)
Median (Q1, Q3)	75.00 (58.25, 86.25)	80.00 (68.75, 83.75)	82.50 (55.25, 92.00)	81.50 (73.50, 90.00)	60.00 (50.00, 80.00)
≥18 y cohort, n	13	18	14	16	29
Mean (SD)	59.31 (22.24)	66.78 (20.06)	73.36 (22.68)	70.56 (16.42)	64.52 (24.18)
Median (Q1, Q3)	60.00 (51.00, 70.00)	68.00 (56.25, 79.00)	80.50 (63.50, 88.00)	70.00 (64.50, 81.25)	66.00 (51.00, 82.00)

EQ-VAS=EuroQol Visual Analog Scale; LGMD=limb-girdle muscular dystrophy; y=year.

Figure 1 EQ-5D Utility Scores by Age and Ambulatory Status

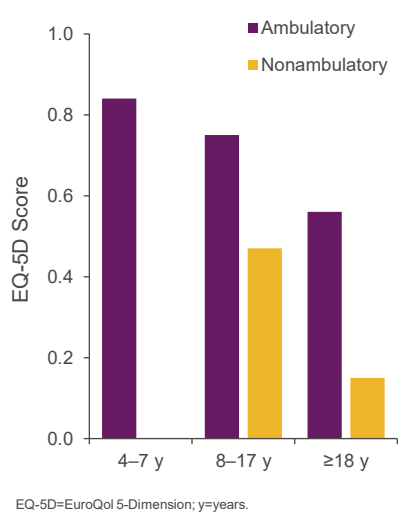
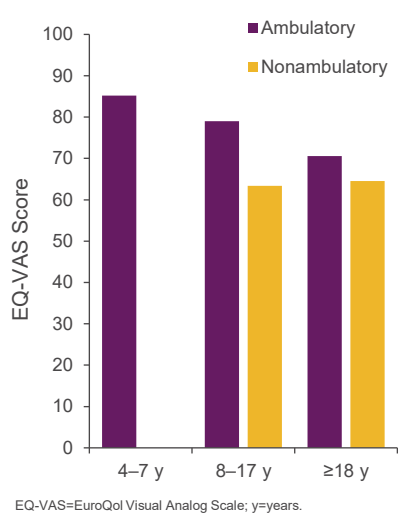


Figure 2 EQ-VAS Scores by Age and Ambulatory Status



Key Finding

EQ-5D utilities and VAS scores offer distinct views on a health status, reflecting societal and personal perspectives. The divergence between these scores grows with age and declining ambulatory function, with a sharper decline in EQ-5D utilities.



Conclusions

EQ-5D health state utilities and VAS scores were lower for nonambulatory patients compared with ambulatory patients.

EQ-5D utility and VAS scores appeared to decrease with increasing age.

As patients age, both EQ-5D utility and VAS scores decline, with a more pronounced decline in utility scores. This may indicate that patients perceive their health status as less burdensome than societal assessments suggest.

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