Estimating utility values for health states in metachromatic leukodystrophy (MLD)

PCR176

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BACKGROUND

- MLD is a rare inherited lysosomal storage disease caused by a deficiency in arylsulfatase A or sphingolipid activator protein B, leading to sulfatide accumulation in the central and peripheral nervous systems.[1,2]
- Late-infantile MLD (LI-MLD) is the most common and rapidly progressing subtype of MLD, found in 50–60% of patients.[1,3]
- Economic evaluations are key to demonstrating the value of emerging MLD therapies.

METHODS

- Health-state patient and caregiver vignettes were developed based on a targeted literature review and qualitative interviews with caregivers and clinicians with experience in LI-MLD.
  - Each vignette represented health-related quality of life (HRQoL) at a level of the Gross Motor Function Classification in MLD (GMFC-MLD) scale, Expressive Language Function Classification in MLD (ELFC-MLD) scale and other MLD symptoms, in addition to varied levels of feeding-tube and/or breathing support (**Table 1**).
- **Sixteen patient vignettes** were developed and valued by samples of adults in the general population (UK), clinicians with experience in LI-MLD (UK/USA) and caregivers of people with progressive pediatric neuromuscular diseases (UK/USA).
  - 'Core' patient vignettes based on GMFC-MLD levels were defined (**Table 1**).
- **Four caregiver vignettes** were developed and valued by samples of adults in the general population (UK) and caregivers of people with progressive pediatric neuromuscular diseases (UK/USA).

Table 1. Overview of patient vignettes.

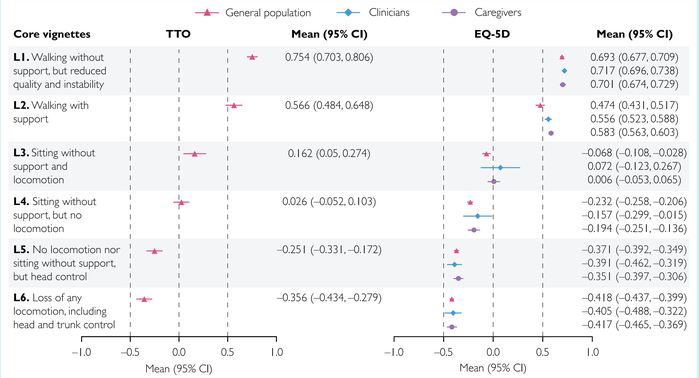
Patient vignette number	GMFC-MLD	ELFC-MLD	Feeding support	Breathing support
P1	L1	E0	No tube	No support
P2	**L1**	**E1**	**No tube**	**No support**
P3	**L2**	**E1**	**No tube**	**No support**
P4	L3	E0	Partial tube	Support at night
P5	L3	E1	Partial tube	Support at night
P6	L3	E1	No tube	No support
P7	**L3**	**E2–3**	**Partial tube**	**Support at night**
P8	L4	E1	Partial tube	Support at night
P9	**L4**	**E2–3**	**Partial tube**	**Support at night**
P10	L4	E2–3	No tube	Support at night
P11	L4	E2–3	Partial tube	No support
P12	L5	E2–3	Partial tube	Support at night
P13	**L5**	**E4**	**Partial tube**	**Support at night**
P14	L5	E4	Tube-dependent	Support at night
P15	L5	E4	Tube-dependent	Constant support
P16	**L6**	**E4**	**Partial tube**	**Constant support**

Bold health states represent core states of a 'typical' patient at each GMFC-MLD level.
E, ELFC-MLD level; ELFC-MLD, Expressive Language Function Classification in MLD; GMFC-MLD, Gross Motor Function Classification in MLD; L, GMFC-MLD level; MLD, metachromatic leukodystrophy; P, patient.

OBJECTIVE

- Using a vignette-based approach, we estimated health-state utilities/disutilities for patients with LI-MLD and their caregivers to inform cost–utility evaluations of MLD treatments.

Figure 1. TTO and EQ-5D scores for 'core' patient health states based on GMFC-MLD levels across all populations.

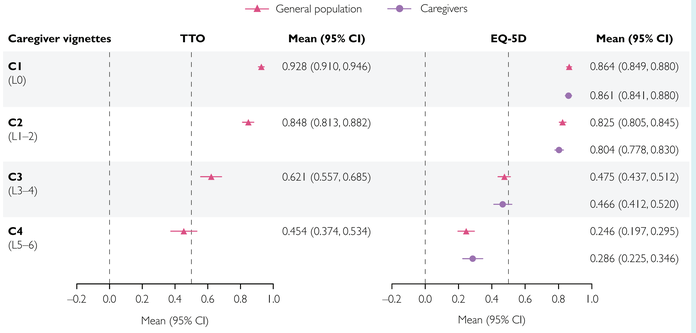


CI, confidence interval; GMFC-MLD, Gross Motor Function Classification in MLD; L, GMFC-MLD level; MLD, metachromatic leukodystrophy; TTO, time trade-off.

Figure 2. Expressive language impairment health-state disutilities valued by all populations.

CI, confidence interval; E, ELFC-MLD level; ELFC-MLD, Expressive Language Function Classification in MLD; GMFC-MLD, Gross Motor Function Classification in MLD; L, GMFC-MLD level; MLD, metachromatic leukodystrophy; TTO, time trade-off.

Figure 3. Caregiver health-state utilities valued by the general population and caregivers.



Caregiver health states were defined based on GMFC-MLD (e.g. C1 utilities reflect caregivers of children with GMFC-MLD L0).
CI, confidence interval; GMFC-MLD, Gross Motor Function Classification in MLD; L, GMFC-MLD level; MLD, metachromatic leukodystrophy; TTO, time trade-off.

- **Valuations were relatively similar across all populations, consistently showing a large monotonic effect of gross motor function deterioration on valuations of health states for patients with LI-MLD.**
- **The observed differences in levels of communication problems, feeding-tube dependency and mechanical breathing were modest.**
- **Our findings highlight the significant impact of LI-MLD and the benefit that could be achieved with treatments that delay or prevent disease progression.**

- Time trade-off (TTO) and lead-time TTO valuations were used in the general population, and an EQ-5D valuation (EQ-5D-5L) was used across the general population, clinicians and caregivers.
  - For TTO, participants were asked to choose whether they preferred to live in a health state for 10 years followed by death or to live in [10–X] years of full health, where X ranged from 0 to 10 years, until the point of indifference was identified.
  - Lead-time TTO was used if a health state was considered worse than dead.
    - Participants were asked whether they would prefer to live for 10 years in full health followed by 10 years in a health state, or to live for X years of full health (X < 10) to determine how much worse than dead they considered the health state to be.
- For the EQ-5D valuation, participants were asked to provide a proxy assessment of the HRQoL of each of the defined health-state vignettes.
- Resulting positive utility values ranged from 0 (dead) to 1 (full health); values less than 0 indicated a state considered to be worse than dead.
- Disutilities for communication problems and feeding-tube/breathing support dependency were calculated based on the difference between utility values for health states with different levels of the aspect of interest but otherwise identical states.

RESULTS

- Overall, health-state valuations were conducted by 198 individuals from the general population, nine clinicians and 40 caregivers.
- Valuations of the six 'core' states (GMFC-MLD levels 1–6) were similar across the three populations, indicating a large effect of gross motor function deterioration and 'typical' associated deterioration in other functions and symptoms (**Figure 1**).
  - The steepest decline in health utility was consistently observed between GMFC-MLD levels 2 and 3, and the smallest decline was between levels 5 and 6.
- The ability to communicate showed relatively modest disutilities in the general population valuation (**Figure 2**), with a similar trend in clinicians and caregivers.
  - Moving from complete sentences to 1–2 words yielded larger TTO disutilities than moving from normal to reduced-quality sentences.
  - Moving from normal to reduced-quality sentences had a larger TTO disutility at GMFC-MLD level 1 than at level 3.
- TTO and EQ-5D utilities showed small effects of feeding-tube support dependency (no tube vs partial tube vs tube-dependent) and mechanical breathing (no support vs partial support [at night] vs constant support) on the general population valuation (data not shown).
- TTO and EQ-5D caregiver utilities showed a substantial impact of caring for patients with LI-MLD across general population and caregiver valuations, with the steepest decline between C2 and C3 (transition from walking with support to inability to walk) (**Figure 3**).

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DISCLOSURES

Siu Hing Lo is an employee of Acaster Lloyd Consulting. **Shun-Chiao Chang** is an employee of Takeda Development Center Americas, Inc. and a stockholder of Takeda Pharmaceutical Company Limited. **Sarah Acaster** is an employee and a stockholder of Acaster Lloyd Consulting.

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