Estimating disutilities in spinal muscular atrophy (SMA) using a stated preference survey: A UK general public study

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Background and objectives

- Spinal muscular atrophy (SMA) is a rare, inherited neuromuscular disease characterized by degeneration of lower motor neurons in the brain stem and spinal cord. The condition results in progressive muscle weakness, paralysis and premature death in severe cases.[1]
- New treatments have been developed for SMA in recent years.[2,3]
- Health technology assessments require data on societal preferences for treatment benefits to weight health outcomes such as quality of life (QoL) in cost-effectiveness analysis (CEA).[4]
- Stated preference (SP) research can be used to estimate societal preferences for treatment benefits by examining trade-offs people are willing to make to obtain different types and levels of treatment benefit in a discrete-choice experiment (DCE).
  - Disutilities for health outcomes and treatment burden can in turn be estimated from SP results using strength of preference for length of life as a benchmark.
- The objective of this study was to estimate disutilities for health outcomes and treatment burden in SMA using DCE survey data.

Methods

Attribute development and DCE design

- A targeted literature review and interviews with 3 SMA clinical experts were used to inform attribute selection, attribute descriptions and attribute levels for a DCE. The selected attributes are presented in Table 1.

Table 1: Overview of selected attributes and attribute levels

Attributes	Level 1	Level 2	Level 3	Level 4
Life expectancy	Not reduced	Reduced by 4 years	Reduced by 8 years	Reduced by 12 years
Motor function	Can sit, stand and walk independent for >10 metres	Can sit, stand and walk with assistance	Can sit but cannot stand	Cannot sit
Respiratory function *Mechanical support*	Not needed	Needed for <16 hours of the day	Needed for >16 hours of the day	-
Treatment administration	Oral liquid taken once daily at home	Injection in spine in hospital every 4 months	-	-
Treatment reactions *Fever, headache, vomiting and/or body pain*	No reactions	For 12 hours every 4 months	For 1–2 days every 4 months	For 3–4 days every 4 months
Ophthalmologic monitoring	Not required	Before and during treatment if symptoms	Before and during treatment, twice yearly for 2 years	-
Contraception	Not required	Must use contraception	-	-

- The attributes and levels were combined into 32 choice sets using an orthogonal fractional factorial array and a shifting procedure.

Survey content

- The survey included:
  - screener questionnaire and informed consent *(for eligible participants only)*;
  - background questions to collect sample data;
  - a lay introduction to SMA symptoms and summary of how it affects individuals, without naming the condition, followed by lay descriptions of each attribute and attribute levels;
  - DCE choice questions.

Ethical review

- This study was reviewed and received exempt status determination by the Western Institutional Review Board, prior to participant recruitment (date: 6th June 2019).

Sample and participant recruitment

- The sample consisted of members of the UK general population aged ≥18 years.
- Quotas for age, gender and region were set using UK census data to ensure sample representativeness.

Analysis

- Data of sample characteristics were analysed using descriptive statistics.
- DCE choice data were analysed using a random parameter logit model.
- Marginal rates of substitution were estimated between length of life and other attributes in order to estimate disutilities, weighted against average life expectancy.
- All estimated models used Level 1 of all attributes as the reference category.

Results: Sample characteristics

- A total of 506 participants from the UK general public were included in the final sample. Summary sample characteristics are shown in Table 2.

Table 2: Summary sample characteristics

Age	M=49 years (SD=17; range 18–82)
Gender	51% female, 49% male
Education	44% with degree, 24% left school at 18 years, 21% left school at 16 years, 11% other
Employment status	52% in employment, 24% retired, 7% homemaker, 3% education, 13% other
Ethnicity	92% White, 5% Asian, 2% Mixed, 1% Black
UK region	Regional distribution approximating UK census data

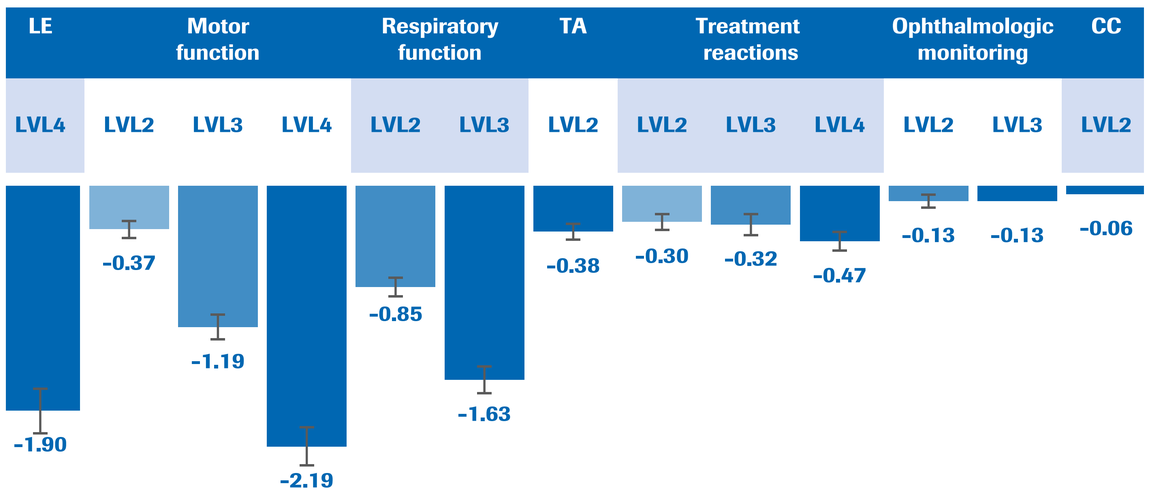
M, mean; SD, standard deviation.

Results: Treatment preferences and disutilities

General population preferences for treatment attributes

- Model results in Figure 1 indicate that participants were most willing to trade between attributes in order to avoid worse motor function, followed by reduced life expectancy and worse respiratory function (all P<0.001; *see Table 1 for attribute level labels*).
- Participants also made choices to avoid intrathecal injections (P<0.001), treatment reactions (P<0.001), ophthalmologic monitoring (P<0.001), and contraception (P<0.05).

Figure 1: Estimated coefficients for treatment attributes (preference weights)



CC, contraception; LE, life expectancy; LVL, level; TA, treatment administration. Level 1 is always used as the reference category.

Disutility estimates

- Disutility estimates are presented in Table 3; disutilities were largest for:
  - **motor function** – not being able to sit versus being able to walk independently;
  - **respiratory function** – mechanical support >16 hours of the day versus no support required.
- Disutilities for **intrathecal administration**, **treatment reactions**, **ophthalmologic monitoring** and **contraception** were smaller.

Table 3: Estimated disutilities for differences between DCE attribute levels

	MRS	Disutility	95% CI	
			L. bound	U. bound
Motor function				
Can sit, stand and walk with assistance	2.30	−0.068	−0.083	−0.053
Can sit but cannot stand	7.51	−0.222	−0.242	−0.201
Cannot sit	13.83	−0.408	−0.440	−0.377
Respiratory function				
Mechanical support for <16 hours of the day	5.37	−0.159	−0.174	−0.143
Mechanical support for >16 hours of the day	10.31	−0.304	−0.328	−0.281
Treatment administration				
Injection into spine in hospital every 4 months	2.40	−0.071	−0.085	−0.057
Treatment reactions				
Reactions for 12 hours every 4 months	1.92	−0.057	−0.071	−0.042
Reactions for 1–2 days every 4 months	2.04	−0.060	−0.078	−0.042
Reactions for 3–4 days every 4 months	2.94	−0.087	−0.103	−0.071
Ophthalmologic monitoring				
Before and during treatment if symptoms present	0.80	−0.024	−0.036	−0.012
Before and during treatment 2x a year for 2 years	0.79	−0.023	−0.037	−0.009
Contraception				
Must agree to use effective contraception	0.40	−0.012	−0.021	−0.002

L, lower; MRS, marginal rates of substitution; U, upper. Level 1 is always used as the reference category.

Conclusions

- This study demonstrates the value that the UK general population places on health outcomes and treatment benefits in a rare disease with characteristics of SMA.
- Disutilities for use in CEA were estimated using DCE survey data. This method for estimating disutilities is particularly suited to rare disease indications where estimation of disutilities via standard preference-based measures may not be feasible.
- Model results indicate participants chose to avoid intrathecal injections, treatment reactions, opthalmological monitoring, and contraception.

References

1. D'Amico, A, et al. *Orphanet J Rare Dis* 2011; 6:71;
2. EMA. SPINRAZA® prescribing information: https://www.ema.europa.eu/en/documents/product-information/spinraza-epar-product-information_en.pdf (Accessed April 2020);
3. FDA. ZOLGENSMA® prescribing information: https://www.fda.gov/media/126109/download (Accessed April 2020);
4. National Institute for Health and Clinical Excellence (NICE). Guide to the methods of technology appraisal. 2013. NICE. London.

Acknowledgments

The study was funded by F. Hoffmann-La Roche AG, Basel, Switzerland. Writing and editorial assistance was provided by MediTech Media, UK, in accordance with Good Publication Practice (GPP3) guidelines (http://www.ismpp.org/gpp3).

Abbreviations

CEA, cost-effectiveness analysis; DCE, discrete-choice experiment; LVL, level; M, mean; MRS, marginal rates of substitution; SD, standard deviation; SMA, spinal muscular atrophy; SP, stated preference; QoL, quality of life.

Presented at Virtual International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 2020, 18–20 May 2020.