Do caregivers and patients value the avoidance of lumbar punctures in spinal muscular atrophy (SMA)? A stated preference survey

Siu Hing Lo,[1] Noman Paracha,[2] Ksenija Gorni,[2] Andrew J. Lloyd[1]

1. Acaster Lloyd Consulting Ltd, London, UK;
2. F. Hoffmann – La Roche Ltd, Basel, Switzerland.

Background and objectives

- Spinal muscular atrophy (SMA) is a rare, severe, progressive, inherited neuromuscular disease resulting in loss of muscle function, paralysis and premature death.[1]
- Disease-modifying treatments have recently emerged, including treatment delivered via lumbar puncture.[2]
- This study was designed to understand the value that caregivers and patients place on novel treatments for SMA. Stated preference (SP) research using a discrete-choice experiment (DCE) was conducted to explore the relative value of treatment efficacy, treatment convenience and other treatment characteristics to patients and caregivers.
- The main study objective was to evaluate UK adult patient and caregiver treatment preferences in Type 2 (age of symptom onset between 7 and 18 months) and non-ambulatory Type 3 (age of symptom onset between 18 months and 17 years) SMA.
- A secondary objective was to measure caregiver health-realted quality of life (HRQoL).

Methods

Attribute development and DCE design

- A targeted literature review and interviews with three 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
Motor function*	Worse by one level after 12 months	Stable after 12 months	Better by one level after 12 months
Respiratory function* *Mechanical support*	Worse by one level after 12 months	Stable after 12 months	Better by one level after 12 months
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 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 *For adult patients only*	Not required	Must use contraception	–

*Increasing levels of motor and respiratory function are presented in Table 2.

- Attributes and levels were combined into 16 choice sets using an orthogonal fractional factorial array and a shifting procedure.

Sample and participant recruitment

- 84 adult patients and 83 caregivers of a child with Type 2 SMA and non-ambulatory (defined as unable to walk independently for >10 steps) Type 3 SMA were recruited through UK-based patient associations and included in the final samples.

Survey content

- The survey included:
  — screener questionnaire and informed consent *(for eligible participants only)*;
  — patient background questions *(patients: self reported; caregivers: proxy reported)*;
  — introduction to DCE task described as a choice between two hypothetical treatments, followed by lay descriptions of each attribute and attribute levels;
  — DCE choice questions;
  — caregiver HRQoL using EQ-5D-5L *(caregivers only)*.

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).

Analysis

- Patient baseline demographics were analysed using descriptive statistics.
- DCE choice data were analysed using a conditional logit model with clustering by respondent to allow for within-subject correlation.
- EQ-5D-5L utility scores were calculated using EQ-5D-5L Crosswalk Index values and analysed descriptively.[3]
- Disutilities were estimated using linear regression models with robust standard errors, adjusted for motor function and respiratory function, and demographic covariates.

Results: Patient background characteristics

- Summary patient clinical and demographic characteristics are shown in Table 2.

### Table 2: Patient clinical and demographic characteristics

		Adult patient survey (N=84)	Child caregiver survey (N=83)
Age, mean (SD)	Years	33.9 (11.5)	8.4 (3.4)
Gender, n (%)	Male	23 (27%)	75 (90%)
Reported SMA type, n (%)	Type 2	61 (73%)	76 (92%)
	Type 3	23 (27%)	7 (8%)
Motor function levels, n (%)	Cannot sit	5 (6%)	0 (0%)
	Can sit with some support	36 (43%)	3 (4%)
	Can sit independently few seconds	16 (19%)	0 (0%)
	Can sit independently longer than a few seconds	18 (21%)	67 (81%)
	Can stand with assistance	6 (7%)	13 (16%)
	Can walk with assistance	3 (4%)	0 (0%)
	Can walk a few steps independently	0 (0%)	0 (0%)
Respiratory function levels, n (%) *Mechanical support, n (%)*	>16hours per day	1 (1%)	0 (0%)
	<16hours per day	22 (26%)	43 (52%)
	No mechanical support	61 (73%)	40 (48%)
SMA treatment	SPINRAZA® (nusinersen)	1 (1%)	54 (65%)
	Surgery	17 (20%)	2 (2%)

Results: Treatment preferences and disutilities

Adult patient preferences for SMA treatment attributes

- Adult patients placed most value on stabilizing (or avoiding worsening) respiratory function (P<0.001) and motor function (P<0.001) – (Figure 1).
- Patients also made choices to have oral treatment over intrathecal injections (P<0.001).
- Treatment reactions, ophthalmologic monitoring and contraception did not significantly affect patient treatment choices (all P>0.05).

### Figure 1: Estimated adult patient preference weights for treatment attributes
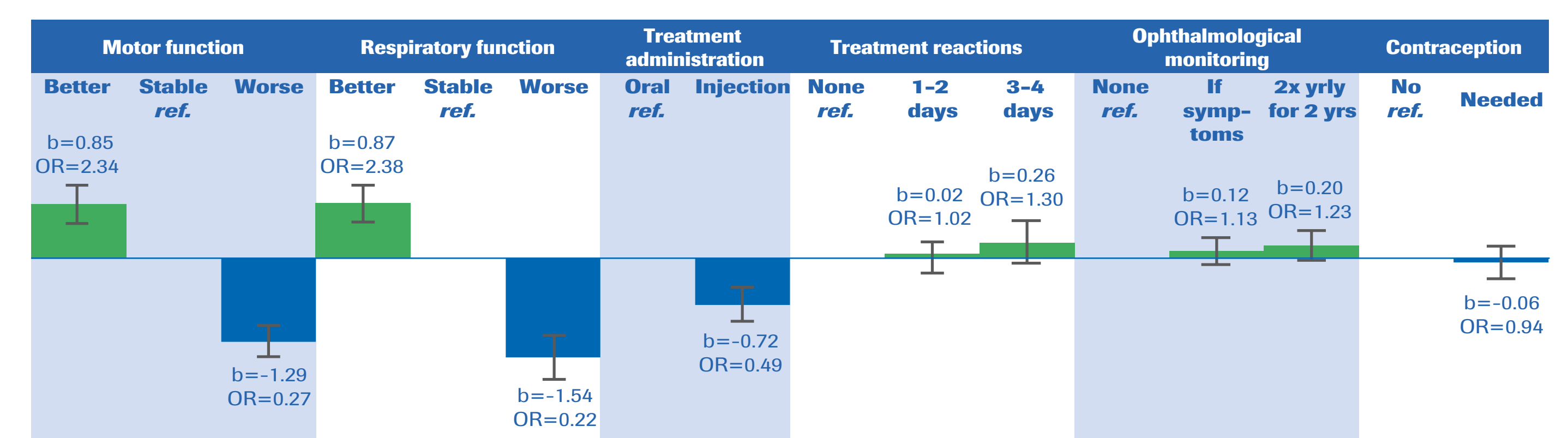
OR, odds ratio; b, beta coefficient.

Caregiver preferences for treatment attributes

- Caregivers most valued improved motor function (P<0.001), followed by improved respiratory function (P<0.001) – (Figure 2).
- Caregivers also made choices to have oral treatment over intrathecal injections (P<0.001) and to avoid the worst level (3-4 days) of treatment reactions (P<0.001).
- Shorter (1-2 days) treatment reactions and ophthalmologic monitoring did not significantly impact caregiver treatment choices (all P>0.05).

Figure 2: Estimated caregiver preference weights for treatment attributes
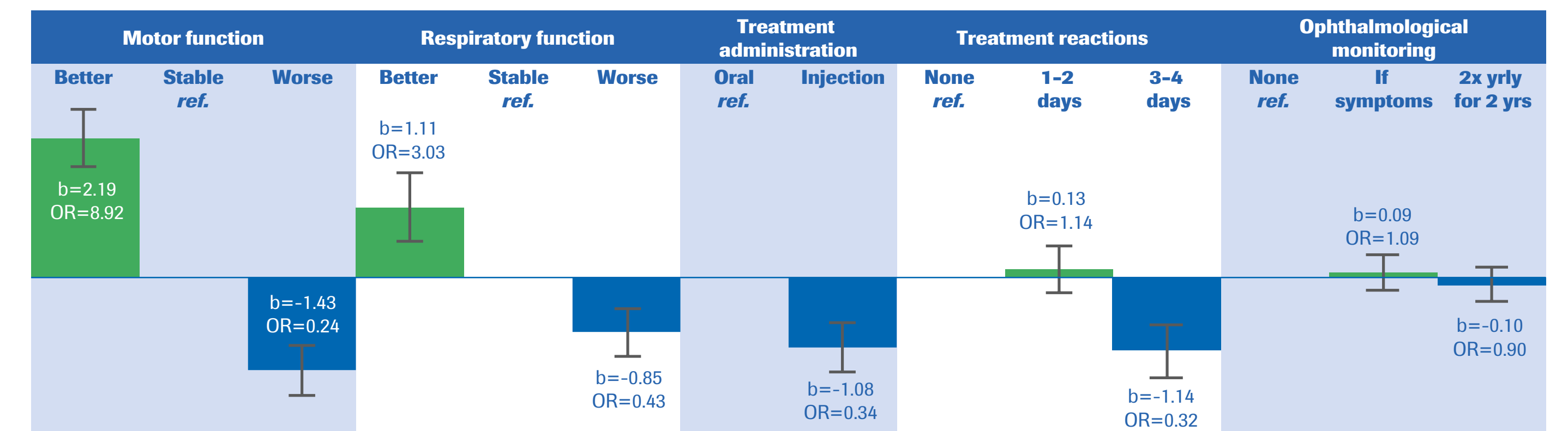
OR, odds ratio; b, beta coefficient.

Caregiver HRQoL and estimated disutilities

- The average caregiver EQ-5D-5L utility score was 0.940 (standard deviation [SD]=0.091).
- Small disutilities were associated with providing care for pediatric patients with worse motor function (P>0.05) and respiratory function (P<0.05) – (Table 3).

Table 3: Descriptive statistics of caregiver utilities and estimated disutilities by patient motor function and respiratory function

	Caregiver HRQoL	N	Mean	SD	Linear regression		Linear regression with covariates	
					Coeff.	Robust SE	Coeff.	Robust SE
Child's function								
Motor function	Can sit with some support	3	0.862	0.127	−0.075	0.054	−0.036	0.066
	Can sit independently longer	67	0.939	0.092	−0.003	0.023	0.010	0.023
	Can stand with assistance	13	0.964	0.074	Ref.	–	Ref.	–
Respiratory function	Mechanical support for <16 hours	43	0.915	0.099	−0.051*	0.020	−0.040*	0.021
	No mechanical support	40	0.968	0.075	Ref.	–	Ref.	–
Age		–	–	–	–	–	−0.005*	0.003
Gender		–	–	–	–	–	−0.077***	0.018

* P<0.05, *** P<0.001. Coeff, coefficient; SE, standard error; Ref., references.

Conclusions

- Patient choices were more strongly driven by stabilizing (or avoiding worsening) respiratory and motor functions than a preference to improve these functions.
- In contrast, caregivers made more trade-offs to improve motor and respiratory functions.
- The results suggest that an oral treatment was valued over intrathecal injections by both adult patients and caregivers in this study.

References

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2. EMA. SPINRAZA® prescribing information: https://www.ema.europa.eu/en/documents/product-information/spinraza-epar-product-information_en.pdf (Accessed April 2020);
3. van Hout B, et al. *Value in Health*. 2012; 15:707–715.

Acknowledgments

Abbreviations

b, beta coefficient; DCE, discrete-choice experiment; HRQoL, health-related quality of life; OR, odds ratio;SD, standard deviation; SMA, spinal muscular atrophy; SP, stated preference.