Understanding neurologist perspectives on the clinical meaningfulness of 'any point differences' on the Hammersmith Functional Motor Scale–Expanded in SMA

Poster P183

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INTRODUCTION

- Spinal muscular atrophy (SMA) is a severe neuromuscular disease characterized by the irreversible loss of spinal motor neurons and progressive skeletal muscle atrophy, leading to weakness and motor function decline[1]
- Despite substantial advances in diagnosis and treatment of SMA, patients with SMA report gaining muscle strength and stabilizing or achieving new motor function as significant unmet needs[2,3]
- SMA treatment efficacy is traditionally measured by motor function assessments, including the Hammersmith Functional Motor Scale–Expanded (HFMSE)[4]; however, treatment impact on clinically meaningful change remains difficult to ascertain and usually requires additional insights from patients with SMA or their caregivers
- Identifying which motor function changes are clinically meaningful to patients with SMA, their caregivers, and providers will improve our understanding of the importance of specific motor function changes and their real-world impact on patients' daily lives

OBJECTIVES

- Examine perspectives on clinically meaningful outcomes among providers (neurologists and physical therapists)
- Identify and understand which motor function changes on the HFMSE are considered clinically meaningful to providers (neurologists and physical therapists)
- Inform future research on SMA to incorporate additional clinically meaningful endpoints
- Here, we focus on understanding neurologists' perspectives on the clinical meaningfulness of functional changes measured by the HFMSE

METHODS

- 60-minute, web-based, in-depth qualitative interviews were conducted with providers (neurologists and physical therapists) experienced with treating SMA and using the HFMSE; this analysis focuses on interviews with neurologists
- Neurologists meeting the inclusion criteria were eligible for study enrollment (**Table 1**)

Table 1. Inclusion criteria

Key inclusion criteria	Neurologists or pediatric neurologists with a Medical Doctor (MD) or Doctor of Osteopathy (DO) degree currently practicing in the United States
	Provides care/services to patients with SMA
	Reports being familiar or very familiar with HFMSE
	Administers or uses results from the HFMSE assessment to evaluate their patients with SMA ≥5 times per year
	Practicing neurology for ≥5 years

HFMSE, Hammersmith Functional Motor Scale–Expanded; SMA, spinal muscular atrophy.

- A semistructured discussion guide was informed by a focused targeted literature review (**Figure 1**)
- The discussion guide included open-ended questions to elicit and examine perspectives and experiences on:
  - How clinical meaningfulness is interpreted
  - What constitutes meaningful change at the individual item level on the HFMSE
  - How meaningful change in specific motor function abilities may impact the patient's ability to perform activities of daily living (ADLs), quality of life (QoL), independence, and psychosocial health
- Interview transcripts were analyzed using the constant comparative method, an iterative approach to aggregate and synthesize qualitative data

Figure 1. Study approach overview

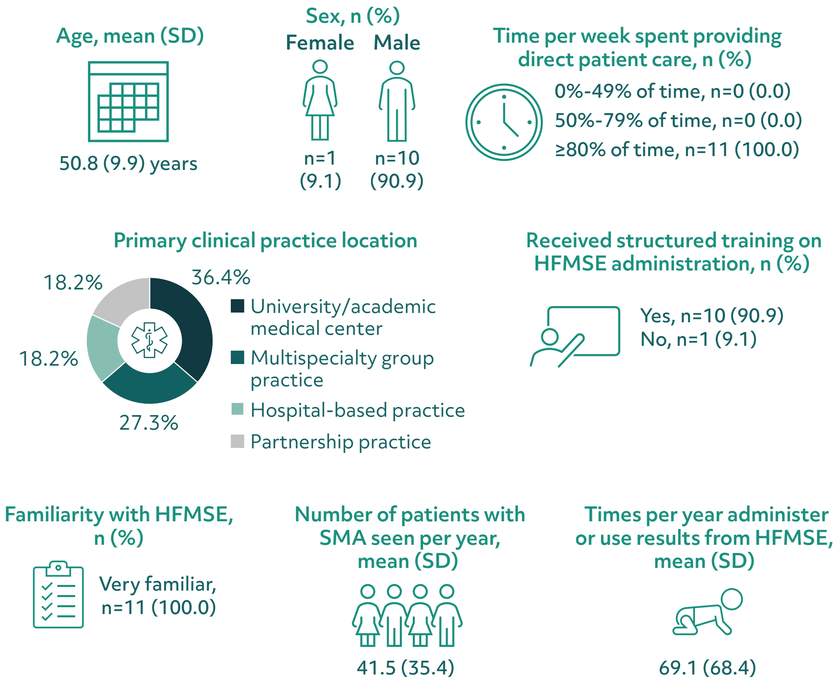
Focused targeted literature review (fTLR)	Develop qualitative study materials	Data collection and analysis
• Performed using PubMed and Google Scholar databases • Informed the development of study documents (eg, interview discussion guide) • Conducted to understand clinical meaningfulness in SMA and of select outcome measures	• Developed study documents – Study protocol – Interview discussion guides	• Conducted semistructured, in-depth interviews with providers (neurologists and physical therapists) • Data collected during the interviews were coded and synthesized • Study findings were contextualized using information from the fTLR

fTLR, focused targeted literature review; SMA, spinal muscular atrophy.

RESULTS

- Eleven of the 20 eligible providers interviewed were neurologists (**Figure 2**)
  - Neurologists' responses per HFMSE task grouping are listed in **Table 2**
  - For outcomes from physical therapist interviews, please see poster 110, also by Nelson and colleagues

Figure 2. Neurologist demographics and characteristics



HFMSE, Hammersmith Functional Motor Scale–Expanded; SD, standard deviation; SMA, spinal muscular atrophy.

Table 2. Number of neurologist responses for each HFMSE task grouping

HFMSE item number	Task	Neurologists (n=11)
1	1 Plinth/chair sitting	4
2	2 Long sitting, legs straight	5
3, 4	3 One hand to head in sitting 4 Two hands to head in sitting	6
5-9	5 Supine to side-lying 6, 7 Rolls prone to supine over R/L 8, 9 Rolls supine to prone over R/L	5
10, 14	10 Sitting to lying 14 Lying to sitting	5
11	11 Props on forearms	4
13	13 Props on extended arms	5
12, 17	12 Lifts head from prone 17 Lifts head from supine	7
15, 16	15 Four-point kneeling 16 Crawling	6
18-20	18 Supported standing 19 Unsupported standing 20 Stepping	9
21-27	21, 22 Hip flexion in supine (R/L) 23, 24 High kneeling to half kneel (R/L) 25, 26 High kneeling to stand leading with R/L leg 27 Stand to sit	6
28, 29	28 Squat 29 Jump 12"	2
30-33	30 Ascends stairs with rail 31 Descends stairs with rail 32 Ascends stairs without rail 33 Descends stairs without rail	3

HFMSE, Hammersmith Functional Motor Scale–Expanded; L, left; R, right.

- Neurologists' perspectives regarding HFMSE score changes were centered on patient experiences
  - A change that significantly impacts a patient's functioning, independence, and QoL, particularly their ability to perform ADLs and other essential life tasks, is clinically meaningful (**Figure 3**)
  - Objective score changes may not always reflect true clinical relevance or what matters most to patients in terms of ADLs and QoL
  - Generally, any point differences or stability across functional tasks within the HFMSE can represent meaningful indicators of functional and psychological impacts that influence a patient's independence and QoL (**Figure 4**)

Figure 3. Neurologist perspectives on clinical meaningfulness

"It's a very **patient-centered** concept, I think. It's **all about a patient's goal**, essentially. To me, a clinical meaningful change is, with time, is this **patient better able to perform things from a day-to-day** basis, whether it's ADLs or things like that."
Neurologist with >20 years in practice

"...we have a **direct conversation with the patient and caregiver** and say, 'How has that change made an impact on your day-to-day life?' If the answer comes out as [...] 'we **have seen a dramatic decline in our quality of life**' then yes, that is a **very meaningful change** and vice versa, improvement in quality of life."
Neurologist with >20 years in practice

"Honestly speaking, **I rely more upon what patients were able to do and what the expectations are**. [...] Scores to me means nothing, honestly speaking. All the scores [...] could be good looking scores or bad looking scores, but if [a] **patient is happier with a score**, which you can improve, **that's what means a lot to them and to me also**."
Neurologist with >20 years in practice

"I think, understandably so, if you feel pretty independent throughout the day, at baseline, you're going to have a **higher sense of quality of life or of independence, of confidence**. One can surmise there's a **direct correlation with their mental health**, how they're doing **based on the ability to be independent** throughout the day."
Neurologist with 5-10 years in practice

Neurologist quotes have been edited for readability.
ADL, activities of daily living.

Figure 4. Neurologist perspectives on clinically meaningful changes reflected in HFMSE tasks

HFMSE task 10 (sitting to lying): 1→2
Well, it's not just 1 point, it makes a **tremendous change in their quality of life and their motor functioning** and their ability to perform the motor work.
Neurologist with 11-15 years in practice

HFMSE task 1 (chair sitting): 0→1
I think it'll be huge in this case because [...] not only are they having a physical benefit from this, but a **massive psychological benefit**, too, as well. Oftentimes, in these cases, **they can feel very motivated** [...] In turn, based on their physical improvement, [the patients] also **find themselves being happier**, too.
Neurologist with 5-10 years in practice

HFMSE tasks 23, 24 (high kneeling to half kneel): 1→2
A **1 to a 2 is—that's the dream**, again, because you can **get up by yourself**, and reach that alarm clock [...] and sit upright to—well, at least you can begin the process of sitting upright to eat breakfast in bed.
Neurologist with >20 years in practice

HFMSE tasks 18, 19 (standing): 1→2
Standing alone, you can probably take a shower that way by yourself, dress by yourself. **That's big**.
Neurologist with >20 years in practice

HFMSE task 20 (stepping): Stability
I think that stability gives them—I think **it protects them and makes them more used to their daily life** and by having them more used to their daily life, they can get used to just doing—**living, and not necessarily just focused on their disease**.
Neurologist with 11-15 years in practice

HFMSE task 12 (lifts head from prone): 0→2
[...] If you're now able to better detect things around you, that, in turn, **improves your spatial awareness and improves your coordination, improves your balance**. These have **real tangible positive implications** from a neurodevelopment perspective.
Neurologist with 5-10 years in practice

HFMSE task 2 (long sitting): 2→1
These are patients that are going to need to be fed. They need meals given to them. They need help going to the bathroom, all that. The **level of dependence rises drastically, and that's disheartening**.
Neurologist with >20 years in practice

HFMSE task 13 (props on extended arms): 1→0
I would say that would **literally make them unable to do things at all**, which in my opinion can not only impact their ability to proceed to the next level of motor function, **not be able to play, but also the fear that it might make the movements less and the respiratory secretions may increase**.
Neurologist with >20 years in practice

HFMSE task 28 (squatting): 2→1
It's a **safety risk**, too. Because if you **can't squat, you can't break a fall**. That leads to **orthopedic injuries**.
Neurologist with >20 years in practice

Neurologist quotes have been edited for readability.
HFMSE, Hammersmith Functional Motor Scale–Expanded.

CONCLUSIONS

- Based on neurologists' responses, clinically meaningful change is best understood through a patient-centered perspective, where improvements or declines in daily functioning and independence are evaluated in the context of individual goals and lived experiences
- Neurologists generally agreed that any point differences or stability in HFMSE scores, regardless of functional task, can reflect significant impacts on patients' independence and QoL, underscoring the importance of measuring and charting small changes
- Stability was generally regarded as important to patients' QoL and independence, as functional declines have meaningful negative impacts

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LN is a consultant for AveXis, Biogen Inc., F. Hoffmann-La Roche, Novartis, and Scholar Rock, Inc. **NL** is an employee of Precision AQ. **MCM** is an employee of Precision AQ and owns equity interest in Precision AQ's parent company, Precision Medicine Group. **TB**, **CC**, and **MG** are employees of and stockholders in Scholar Rock, Inc.

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