Poster 18

Assessing the impact of "any point differences" or "stability" in the Hammersmith Functional Motor Scale–Expanded on the independence of patients with SMA

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INTRODUCTION

- Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by the irreversible loss of spinal motor neurons and progressive skeletal muscle atrophy, leading to weakness and motor function decline[1]
- Motor function assessments such as the Hammersmith Functional Motor Scale–Expanded (HFMSE) are validated, well-established tools for evaluating treatment efficacy in SMA[2]; however, calculated HFMSE total score changes may not fully capture the broader, clinically meaningful impacts of treatment on patients' daily lives[3]
- Insights from patients or their caregivers can contextualize HFMSE changes and enhance the interpretation of what is clinically meaningful
- Identifying motor function changes that are clinically meaningful to patients living with SMA and their caregivers will improve our understanding of their real-world impact on patients' daily lives

OBJECTIVES

- Examine perspectives on clinically meaningful outcomes among patients living with SMA and their caregivers
- Identify and understand which motor function changes on the HFMSE are clinically meaningful to patients living with SMA and their caregivers
- Gain perspectives from patients living with SMA and their caregivers on how changes in specific HFMSE task scores would impact their goals for independence

METHODS

- 60-minute, web-based, in-depth, qualitative interviews were conducted with patients living with SMA and their caregivers
- Patients meeting the inclusion criteria were eligible for study enrollment (**Table 1**)
- A semistructured discussion guide was informed by a focused targeted literature review (**Figure 1**)

Table 1. Inclusion criteria

Key inclusion criteria	Adult[a] patient with self-reported SMA diagnosis, or adult[a] primary informal (unpaid) caregiver for a pediatric patient (2-12 years old) with a reported SMA diagnosis, or dyad of adult[a] caregiver and adolescent patient (13-17 years old)
	Current self-reported (adult patients) or caregiver-reported (pediatric patients) motor function ability categorized as a sitter (can sit independently but cannot walk without help/support) or walker (can walk without using any help/support)
	English language proficient
	United States resident
	Had access to technology (eg, smartphone, computer) to participate in interview
	Completed informed consent to participate in the study and to audio recording of the interview discussion

[a]Age of majority in state of residence: ≥18 years of age, except if a Mississippi resident (≥21 years of age) or a resident of Alabama or Nebraska (≥19 years of age).
SMA, spinal muscular atrophy.

Figure 1. Study approach overview

Focused targeted literature review (fTLR)
- 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

Develop qualitative study materials
- Developed study documents and submitted to IRB for approval/exemption
  - Study protocol
  - Interview discussion guides

Data collection and analysis
- Conducted semistructured, in-depth interviews with patients
- Data collected during the interviews were coded and synthesized
- Study findings were contextualized using information from the fTLR

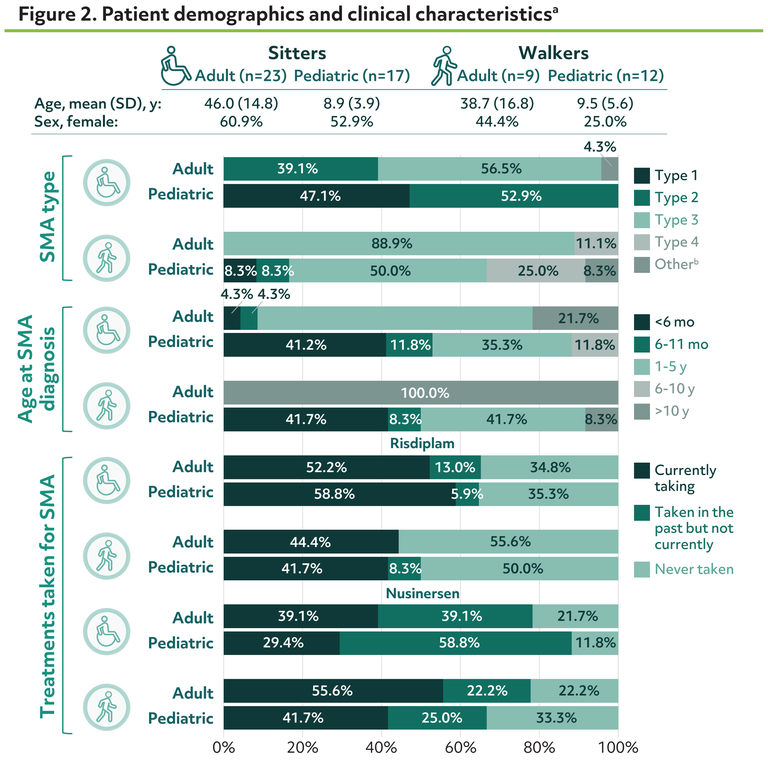
IRB, institutional review board; SMA, spinal muscular atrophy.

- 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), in addition to their psychosocial well-being, independence, and quality of life (QoL)
- Survey transcripts were analyzed using the constant comparative method, an iterative approach to aggregate qualitative data

RESULTS

- Overall, 32 adult patients and 29 caregivers/dyads participated (**Figure 2**; **Table S1**)
- 71.9% and 58.6% of adult and pediatric patients were sitters, respectively, whereas 28.1% and 41.4% were walkers
  - Of the 23 adult and 17 pediatric sitters, 14 (60.9%) and 1 (5.9%) reported having previously been able to walk without any help/support but could not walk without help/support at the time of the study
- At the time of the study, 50.0% of adult and 51.7% of pediatric patients were receiving risdiplam; 43.8% of adult and 34.5% of pediatric patients were receiving nusinersen
- Patient and caregiver responses generally focused on HFMSE tasks they were familiar with (**Table S2**); some patients found it challenging to envision unfamiliar changes

Figure 2. Patient demographics and clinical characteristics[a]



[a]All demographic information and clinical characteristics, including SMA type and current motor function ability (eg, sitter or walker), were self-reported by adult patients or caregivers of pediatric patients. [b]Includes Type 2/3, other, and don't know/not sure.
mo, months; SD, standard deviation; SMA, spinal muscular atrophy; y, years.

Results: Clinical Meaningfulness

- Patients and caregivers generally regarded clinical meaningfulness as changes or stabilization that affect their physical or emotional health, QoL, or ability to perform ADLs, with even small or gradual changes being potentially meaningful (**Figure 3**)
- Adult patients frequently noted that gaining or maintaining the ability to eat, practice self-care, dress, work, reposition, transfer, conduct household tasks, and being mobile or navigating their surroundings is fundamental to preserving and strengthening their overall sense of independence (**Figure 4**)
- Pediatric patients and their caregivers highlighted the importance of social interaction, play, and participation in school-related activities for augmenting patients' sense of freedom
- Importance of item-level HFMSE tasks was largely driven by current functional abilities (**Table 2**)
  - Across sitters, tasks that were most frequently associated with being critical to independence, ADLs, and QoL included sitting unsupported, bringing hands to the head, rolling, and transitioning between sitting and lying; crawling-related tasks were additionally important for pediatric patients
  - Walkers also valued these HFMSE items but put greater emphasis on walking-related (stepping and stairs) and transitioning-related tasks

Table 2. HFMSE task importance by patient age and functional ability

Sitters		Walkers	
Adult patients (n=23)	**Pediatric patients (n=17)**	**Adult patients (n=9)**	**Pediatric patients (n=12)**
• Sitting unsupported (Task 1) • Bringing hands to head (Tasks 3, 4) • Rolling (Tasks 5-9) • Transition sitting → lying (Tasks 10, 14)		• Stepping (Task 20) • Stairs (Tasks 30-33)	
	• Crawling-related tasks (Tasks 15, 16)	• Standing (Tasks 18, 19) • Transition standing → sitting (Task 27)	• Transition sitting → lying (Tasks 10, 14) • Head lifting (Tasks 12, 17) • Kneeling transitions (Tasks 23-26)

HFMSE, Hammersmith Functional Motor Scale–Expanded.

Figure 3. Patient and caregiver perspectives on the term "clinically meaningful change"

"I feel like **stability gives me purpose**, and it gives me meaning to living. **Not just existing, but doing things that are important to me, whether it be within my community or for myself** that continue to have value."
Sitter, aged 45 years

"In my own words, **it means changes that are visible to me** and my doctors and the people around me, my caregivers and me mostly, and **changes that affect the quality of life that I have and how I can do things**."
Walker, aged 25 years

"Something that we can identify that **actually would impact the quality of life for my child** and how he's able to function in the world or how he's able to function compared to what we perceive his abilities today."
Caregiver of sitter, aged 7 years

"I can see [gradual improvement or stability] being very relevant to our situation…over these last 6 years, her progress has slowed, as expected, but **she still continues very subtly to improve. It's slow and it's over time. Is it meaningful to us, yes**…If you were to measure her with a scale, it would probably score the same. **To me, that is an important factor**."
Caregiver of walker, aged 6 years

Example quotes have been edited for readability.

Figure 4. Patient and caregiver perspectives on HFMSE task score changes

	HFMSE task(s)	Anticipated impact on independence
Adult Sitters	Hands to head in sitting (Tasks 3, 4)	**Impact of stability** **It means independence for a lot longer, and independence in things that are personal and important to me.** I like to be able to put on my own makeup. I like to be able to brush my teeth whenever I want to, to not have to wait for someone else to do that. *Patient aged 30 years*
	Rolling supine to prone (Tasks 8, 9)	**Impact of improvement (1→2)** I think that will boost my mentality up knowing that I can do it and not […] have to get somebody to do it for me. **The point of me not having to ask people to do it for me or being independent** where I can't sleep the way I want to at night, **it will make a big difference**. *Patient aged 48 years*
	Chair sitting (Task 1)	**Impact of worsening (1→0)** I think that right now I feel that I'm able to tell my caregivers what I need, and I'm able to support some of my own needs based off of my current abilities, but to have **to put that completely in somebody else's hands, that feels really vulnerable.** *Patient aged 45 years*
Pediatric Sitters	Chair sitting (Task 1)	**Impact of stability** That one's one of the most important ones for us just because **it's his only real independence.** When he is sitting up by himself, not being held onto by anyone or anything, **he can 100 percent do what he wants to do, so that's a big independent thing for him. That's an important – really important one.** *Caregiver of patient aged 9 years*
	4-point kneeling (Task 15)	**Impact of improvement (1→2)** Dynamically, I do think that there is an understanding that that's the motion to being able to crawl, being able to pull up, being able to stand independently. That's a stair step **up much broader scale of independence and mobility, and so that's a desirable move. We want it.** *Caregiver of patient aged 7 years*
	Hands to head in sitting (Tasks 3, 4)	**Impact of worsening (2→1)** I think **it greatly reduces that propensity for independence**, especially in those categories, grooming and hygiene and dressing and things like that. *Caregiver of patient aged 7 years*
Adult Walkers	Stepping (Task 20)	**Impact of stability** **It just gives me a lot more freedom.** Here recently, my wife has had to go on disability so when she was working, I wanted to be able to do chores around the house, be able to vacuum, be able to mop the floor, to clean the bathrooms. **Still being able to do that just gives me the independence I need.** *Patient aged 62 years*
	Ascends stairs with rail (Task 30)	**Impact of improvement (1→2)** It would just make me feel a lot safer. It would mean having to go places without needing anyone to come with me. **That would mean getting more independent, which always improves your quality of life.** *Patient aged 25 years*
	Stand unsupported (Task 19)	**Impact of worsening (1→0)** **It would mean pretty much losing all independence**…It would mean having a full-time caregiver, not only someone from my family that helps… **which would complicate things a lot economically and just on a day-to-day life basis.** *Patient aged 25 years*
Pediatric Walkers	Squat (Task 28)	**Impact of stability** It's great that he can still do that. If he drops something on the floor, it allows him to get to that and get back up, seated, what not. **It gives him some freedom.** *Caregiver of patient aged 11 years*
	Descends stairs with rail (Task 31)	**Impact of improvement (0→1)** The **ability to do even 2 or 3 steps independently would be significant.** It would be a meaningful change. *Caregiver of patient aged 15 years*
	Lifts head from supine (Task 17)	**Impact of worsening (1→0)** **It would really change things**, because then I don't think that he would be able to do the sitting independently or walking. If he can't lift his head, I feel **we'd have a lot more intervention and a lot more additional support.** *Caregiver of patient aged 4 years*

Patients were read descriptions of abilities/tasks within HFMSE items, asked to self-assess their functional status according to HFMSE scoring[3] (2: performs without modification/adaptation/compensation; 1: performs with modification/adaptation/compensation; 0: unable to perform), and asked to comment on how they would be impacted by changes in their score. Example quotes have been edited for readability.
HFMSE, Hammersmith Functional Motor Scale–Expanded.

CONCLUSIONS

- Based on both patient and caregiver perspectives, any point gain or stabilization within any HFMSE-related task may be considered individually meaningful, as these outcomes generally align with patients' goals for independence
- Sitters and walkers prioritized distinct sets of tasks that were critical to maintaining their current functional abilities and enhancing their independence
- These findings underscore the importance of integrating patient perspectives when assessing treatment efficacy, enabling a more holistic understanding of what constitutes clinically meaningful change

REFERENCES

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DISCLOSURES

SD has served on advisory boards for Alexion, argenx, Biogen, CSL Behring, Genentech, Immunovant, Sarepta, and Scholar Rock. **AH** has served on advisory boards and/or as a consultant for Biogen, Catalyst, J&J, Sarepta, and Scholar Rock. **TD** has served on advisory boards and/or as a consultant for Biogen, Cure SMA, Duchenne UK, Dyne, Genentech, Roche, Scholar Rock, and TRiNDS. **NL** and **CCagle** are employees of Precision AQ. **TB** and **MG** are employees of and stockholders in Scholar Rock. **CCherubino** is a former employee of and may hold stock/stock options in Scholar Rock. **AS-C** has served on an advisory board and/or received consulting fees from Catalyst, Novartis, and Scholar Rock. **LN** is a consultant for AveXis, Biogen, F. Hoffmann-La Roche, Novartis, and Scholar Rock.

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SUPPLEMENTAL MATERIAL

Table S1. Patient demographics and baseline characteristics[a]

Characteristics	Adult patients (N=32)	Pediatric patients (N=29)
Motor function status, n (%)		
Sitter	23 (71.9)	17 (58.6)
Walker	9 (28.1)	12 (41.4)
Age, years		
Mean (SD)	44.0 (15.5)	9.2 (4.6)
Sex, n (%)		
Male	14 (43.8)	17 (58.6)
Female	18 (56.3)	12 (41.4)
Race, n (%)		
American Indian or Alaska Native	1 (3.1)	0
Asian	0	2 (6.9)
Black or African American	2 (6.3)	1 (3.4)
Native Hawaiian or other Pacific Islander	0	1 (3.4)
White or Caucasian	28 (87.5)	19 (65.5)
2 or more races	0	5 (17.2)
Other	1 (3.1)	0
Prefer not to answer	0	1 (3.4)
Ethnicity, n (%)		
Hispanic, Latino, or Spanish origin	4 (12.5)	4 (13.8)
Not Hispanic, Latino, or Spanish origin	27 (84.4)	24 (82.8)
Prefer not to answer	1 (3.1)	1 (3.4)
SMA type, n (%)		
Type 1	0	9 (31.0)
Type 2	9 (28.1)	10 (34.5)
Type 3	21 (65.6)	6 (20.7)
Type 4	1 (3.1)	0
Other: Type 2/3	1 (3.1)	0
Other	0	3 (10.3)
Don't know/not sure	0	1 (3.4)
Age at SMA diagnosis, n (%)		
<6 months	1 (3.1)	12 (41.4)
6 to 11 months	1 (3.1)	3 (10.3)
1 to 5 years	16 (50.0)	11 (37.9)
6 to 10 years	0	2 (6.9)
>10 years	14 (43.8)	1 (3.4)
Treatments taken for SMA		
Risdiplam	16 (50.0)	15 (51.7)
Currently taking	3 (9.4)	2 (6.9)
Taken in the past but not currently	13 (40.6)	12 (41.4)
Never taken		
Nusinersen		
Currently taking	14 (43.8)	10 (34.5)
Taken in the past but not currently	11 (34.4)	13 (44.8)
Never taken	7 (21.9)	6 (20.7)

[a]All demographic information and clinical characteristics, including SMA type and current motor function ability (eg, sitter or walker), were self-reported by adult patients or caregivers of pediatric patients.

SD, standard deviation; SMA, spinal muscular atrophy.

Table S2. Number of patient/caregiver responses for each HFMSE task grouping

		Adult patients		Pediatric patients	
HFMSE item number	Task	Sitters (n=23)	Walkers (n=9)	Sitters (n=17)	Walkers (n=12)
1	1 Plinth/chair sitting	23	1	16	5
2	2 Long sitting, legs straight	23	3	14	7
3, 4	3 One hand to head in sitting 4 Two hands to head in sitting	23	4	16	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	23	7	16	7
10, 14	10 Sitting to lying 14 Lying to sitting	21	3	15	4
11	11 Props on forearms	9	1	13	7
13	13 Props on extended arms	13	7	12	6
12, 17	12 Lifts head from prone 17 Lifts head from supine	18	9	15	12
15, 16	15 Four-point kneeling 16 Crawling	15	9	14	10
18-20	18 Supported standing 19 Unsupported standing 20 Stepping	7	8	6	7
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	19	9	12	12
28, 29	28 Squat 29 Jump 12"	2	9	2	12
30-33	30 Ascends stairs with rail 31 Descends stairs with rail 32 Ascends stairs without rail 33 Descends stairs without rail	0	9	2	12

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

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