Meaningfulness of ‘any point change’ or ‘stabilization’ in the HFMSE on the psychosocial well-being of adult patients with spinal muscular atrophy

Poster #181 M

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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]
- SMA treatment efficacy is traditionally measured by motor function assessments such as the Hammersmith Functional Motor Scale–Expanded (HFMSE)[2]; however, calculated score changes alone may not fully reflect the real-world impact of changes and often require input from patients with SMA or their caregivers
- To better understand how changes in HFMSE scores are perceived in terms of real-world impact, we conducted 60-minute semistructured interviews with adult patients with SMA

OBJECTIVES

- Examine perspectives on clinically meaningful outcomes among adult patients with SMA
- Gain perspectives from adult patients with SMA on how changes in specific HFMSE task scores would impact their psychosocial well-being

METHODS

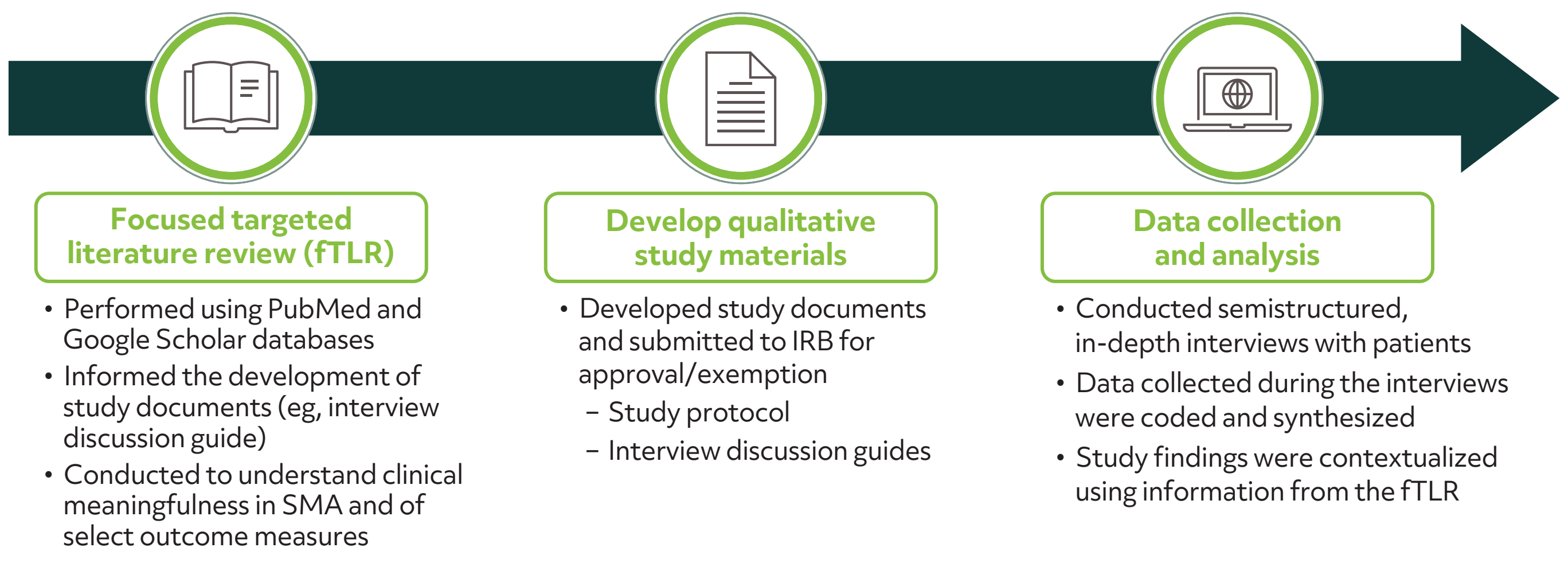
- 60-minute, web-based, in-depth qualitative interviews were conducted with adult patients with SMA
- Patients meeting the inclusion criteria were eligible for study enrollment (**Table 1**)
- A semistructured discussion guide was informed by a focused targeted literature review (**Figure 1**)

Table 1. Inclusion criteria

Key inclusion criteria	Self-reported SMA diagnosis
	Current self-reported 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)
	Age of majority in state of residence[a]
	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]≥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.

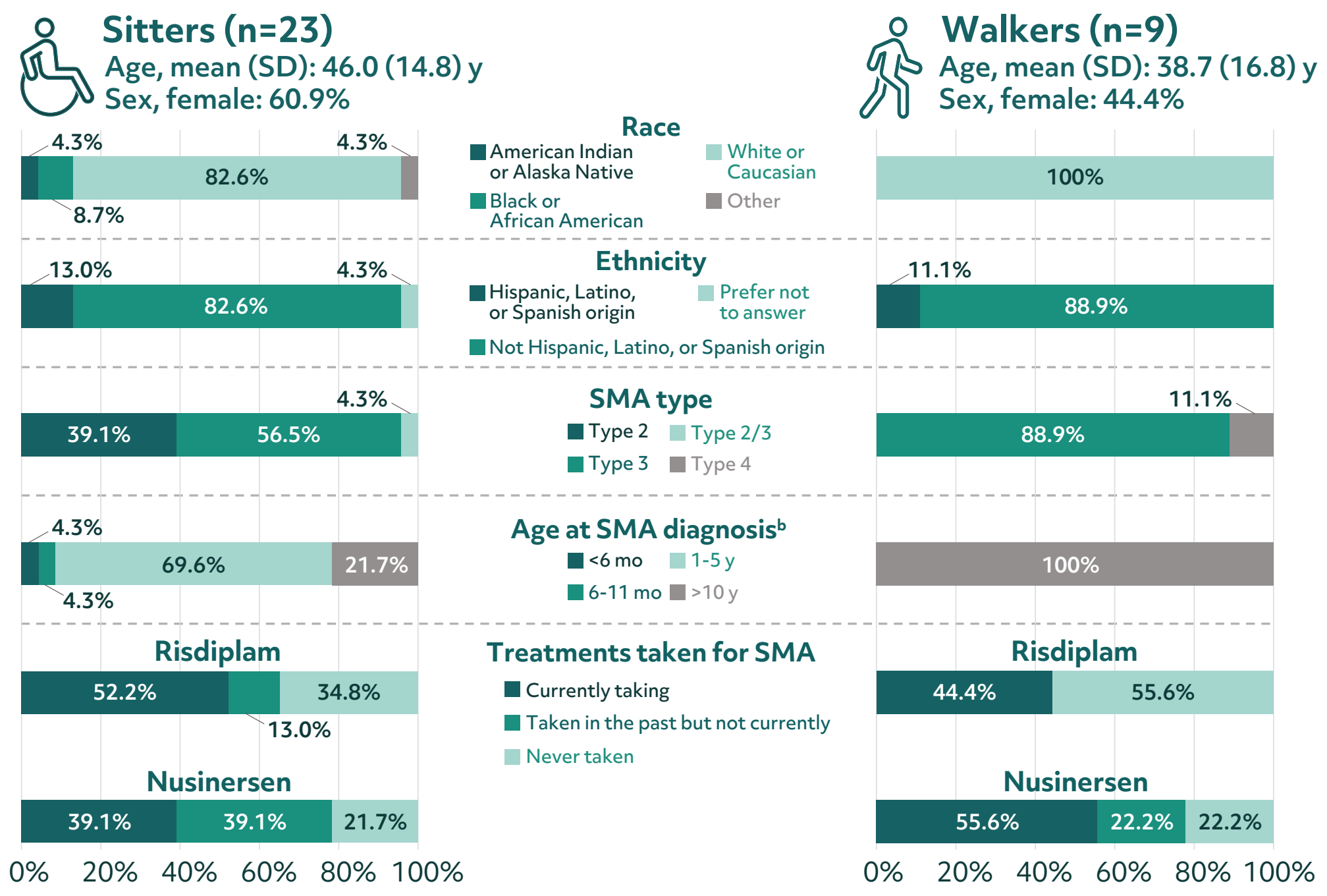
- The discussion guide included open-ended questions to elicit and examine perspectives and experiences on:
  - How clinical meaningfulness is interpreted
  - What constitutes meaningful change at the individual item level on the HFMSE
  - How meaningful change in specific motor function abilities may impact the patient’s ability to perform activities of daily living (ADLs), as well as their psychosocial well-being, independence, and quality of life (QoL)
- Interview transcripts were analyzed using the constant comparative method, an iterative approach to aggregate and synthesize qualitative data

RESULTS

Patients

- Overall, 32 adult patients participated; mean (range) age was 44.0 (18-72) years, and 56.3% were female (**Figure 2**; **Table S1**)
- 71.9% and 28.1% of patients self-identified as sitters and walkers, respectively
  - Of the 23 self-identified sitters, 14 (60.9%) reported having previously been able to walk without any help/support but could not walk without help/support at the time of the study
- Of the study patients, 50.0% were currently receiving risdiplam and 43.8% were currently receiving nusinersen at the time of the study
- Patients’ responses generally focused on HFMSE tasks they were familiar with; some patients found it challenging to envision unfamiliar changes (**Table 2**)

Figure 2. Adult 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 the patients. [b]None of the patients were diagnosed with SMA at age 6-10 y.
mo, months; SD, standard deviation; SMA, spinal muscular atrophy; y, years.

Table 2. Number of patients who provided commentary on each HFMSE task grouping

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

To support the synthesis of item-level findings, HFMSE items were grouped according to previously used functional categories in addition to data-driven insights and Scholar Rock guidance.
[a]For walkers, n=1 was asked about tasks 1 and 2 together and n=2 were asked only about task 2, thus responses were summarized together. [b]For walkers, n=1 was asked about task 11 and n=7 were asked only about task 13, thus responses were summarized together.
HFMSE, Hammersmith Functional Motor Scale–Expanded; R/L, right/left.

Clinical meaningfulness

- Adult patients 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**)
  - **Patients noted that functional tests do not always capture what is meaningful to them**, such as changes in levels of fatigue, being able to unbutton a shirt, or the effort it takes to get out of a chair
- Patients generally noted that any point changes or stability in motor functions measured by HFMSE tasks can be seen as clinically meaningful and potentially linked to impacts on psychosocial well-being (**Figure 4**):
  - Mental and emotional health
  - Socialization
  - Independence
  - ADLs
  - QoL

Figure 3. Adult patient 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*

> “Clinically meaningful change to me would be in the measures and the different tests that they use, whether or not you have progressed or improved or declined a little bit in those measures…**With the ADLs it’s a matter of how you respond. A lot of that is more subjective than objective.** Because they don't have a score assigned to it, but they [ask], ‘Can you still do this?’ ‘Are you able to do that?’ It's really your opinion. I think **it's a matter of assessing your activities of daily living in conjunction with the Hammersmith and in conjunction with how you're feeling emotionally and mentally and physically**.”
>
> *Sitter, aged 62 years*

> “I guess ‘meaningful’ for me would be… **just be able to continue to do the everyday activities that I do**. Over time, since when I've been diagnosed till now, obviously, those are much different things. Things that would be considered clinically meaningful for me now will be just **being able to do things as much as possible independently**.”
>
> *Walker, aged 49 years*

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

Figure 4. Adult patient perspectives on HFMSE task score changes

	HFMSE task(s)	Psychosocial impact	Patient quotes
SITTERS	Chair sitting (Task 1)	Emotional well-being, security/safety	**Impact of stability** **It means that I'm not scared** about all the little moments when I am transferred to a seated position. Will I be able to maintain it today? Is this an iffy thing? **It's a strong, stable thing that I know I can depend on, and I don't feel nervous** about that. It also helps me, I'd say, plan and forecast out for my future. *Aged 30 years*
	Long sitting (Task 2)	Socialization	**Impact of improvement (1→2)** If I could long sit comfortably and independently, if I had the function to do that, then I would consider getting on the floor more and being with [nieces and nephews] and being in their space and **being able to interact and play more** with my nieces and nephews…It feels really effortful for me right now, so that **would be a really happy thing to be able to do**. *Aged 30 years*
	Hands to head (Tasks 3, 4)	Emotional well-being, self-image, and independence	**Impact of stability** I think, for me, **it's how I'm able to continue to function based off of who I identify myself to be today**. Again, that's not to say that that won’t change because it might have to, but **it's just something that I want to hold onto as long as I can**. *Aged 45 years*
	Supine to prone (Task 8, 9)	Socialization, independence, safety/security	**Impact of improvement (1→2)** Now that would change everything…because you know, when I'm on my back, I'm scared. **That's a scary feeling to not be able to move and to be stuck**. It **affects you mentally**, too. I think that **will boost my mentality up knowing that I can do it and not worrying** about what's going to happen or have to get somebody to do it for me…**It will make a big difference**. *Aged 49 years*
	Sitting to lying (Tasks 10)	Confidence, independence	**Impact of worsening (1→0)** I feel like **I'm constantly planning my life** and my day around who's around, what's happening, who’s gonna be here to help me. All of that…**becomes tiresome** because I feel like I have a plan A, and a plan B, and a plan C in case any of the other plans fall through. **That, on a daily, can really trigger, create, anxiety for me**. *Aged 45 years*
	Props on extended arms (Task 13)	Emotional well-being, security/safety	**Impact of worsening (2→1)** …**It [would] be scary** that you can't do it, and I think **mentally and physically it’ll be harder for yourself and probably those around you**. *Aged 49 years*
WALKERS	Lifts head from prone (Task 12)	Emotional well-being, security/safety	**Impact of worsening (1→0)** I feel I would lose comfort in being able to sleep without somebody nearby, without somebody else in the house. **That’s kind of scary if you need to move and you can’t**. *Aged 35 years*
	Crawling (Task 16)	Socialization	**Impact of improvement (1→2)** I know, **when I have kids, it’ll make it easier to be able to be on the floor with them and to be able to play with them** and stuff. Just another way that I can move. *Aged 18 years*
	Lifts head from supine (Tasks 17)	Emotional well-being, independence	**Impact of stability** **I wouldn't want to lose that ability** to be able to raise my head or being able to turn and look at things. As you lose that skillset, I think **it affects other things like being able to see people** or see items or being able to make changes with your body as things happen. *Aged 64 years*
		Independence	**Impact of stability** **It comes down to freedoms**; I'm pretty independent, stubborn, the more I can do things on my own without having to have assistance **will keep my mind working better, keep my attitude much better**. *Aged 62 years*
	Stepping (Task 20)	Independence, emotional well-being	**Impact of worsening (2→1)** I think the **quality of life would go way down**. If that's all I could walk, I probably couldn't continue to work at the job that I have. At home, **it would take a lot of the joy out of what I like doing away from me**. *Aged 64 years*
	Stand to sit (Task 27)	Independence, socialization	**Impact of improvement (1→2)** [It would provide] just **so much more freedom** that I don't have now…If I think about getting on the floor it's because I've fallen, not that **I can sit down and play with the dogs, play with grandkids and not have to worry about hurting myself would be a huge, huge benefit**. *Aged 62 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

- Patient reflections generally suggest that any point change (ie, improvement or decline) or stabilization in motor function would be meaningful and can be linked to impacts on psychosocial well-being
- Collecting patient perspectives remains critical to gaining a holistic understanding of real-world treatment impacts, including those on psychosocial well-being

References

1. Mercuri E, et al. *Nat Rev Dis Primers*. 2022;8(1):52.
2. Ramsey D, et al. *PLoS One*. 2017;12(2):e0172346.
3. Coratti G, et al. *Eur J Neurol*. 2024;31(8):e16309.

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