Poster #8

Understanding adult patient perspectives on the clinical meaningfulness of "any point differences" on the Hammersmith Functional Motor Scale–Expanded in SMA

Alicia Henriquez,[1] Stacy Dixon,[2] Tina Duong,[3] Natalie Land,[4] Amal Jamaleddine,[4] Thomas Brown,[5] Christabella Cherubino,[5] Mouhamed Gueye,[5] Ashley Stanley-Copeland,[6] Leslie Nelson[7]

[1]Seattle Children's Hospital and University of Washington, Seattle, WA, USA; [2]University of Colorado School of Medicine, Aurora, CO, USA; [3]Stanford University, Palo Alto, CA, USA; [4]Precision AQ, New York, NY, USA; [5]Scholar Rock, Inc., Cambridge, MA, USA; [6]University of Texas at Austin, Dell Medical School, Austin, TX, USA; [7]University of Texas Southwestern Medical Center, Dallas, TX, USA

INTRODUCTION

- Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by gradual and irreversible degeneration of spinal motor neurons, progressive muscle atrophy and weakness, and motor function decline[1]
- Traditional evaluation of treatment efficacy relies on in-clinic motor function assessments such as the Hammersmith Functional Motor Scale–Expanded (HFMSE)[2]; however, motor function scores alone cannot fully convey the meaningfulness of changes without context provided by patients or their caregivers
- To better understand the clinical meaningfulness of functional changes within the HFMSE, we conducted 60-minute semistructured interviews with adult patients with SMA

OBJECTIVES

- Examine perspectives on clinically meaningful outcomes among adult patients with SMA
- Identify and understand which motor function changes on the HFMSE are clinically meaningful to adult patients with SMA
- Understand adult patients' perspectives on the clinical meaningfulness of functional changes measured by the HFMSE
- Inform future research on SMA to incorporate additional endpoints of interest to adult patients with SMA

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.

- 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

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

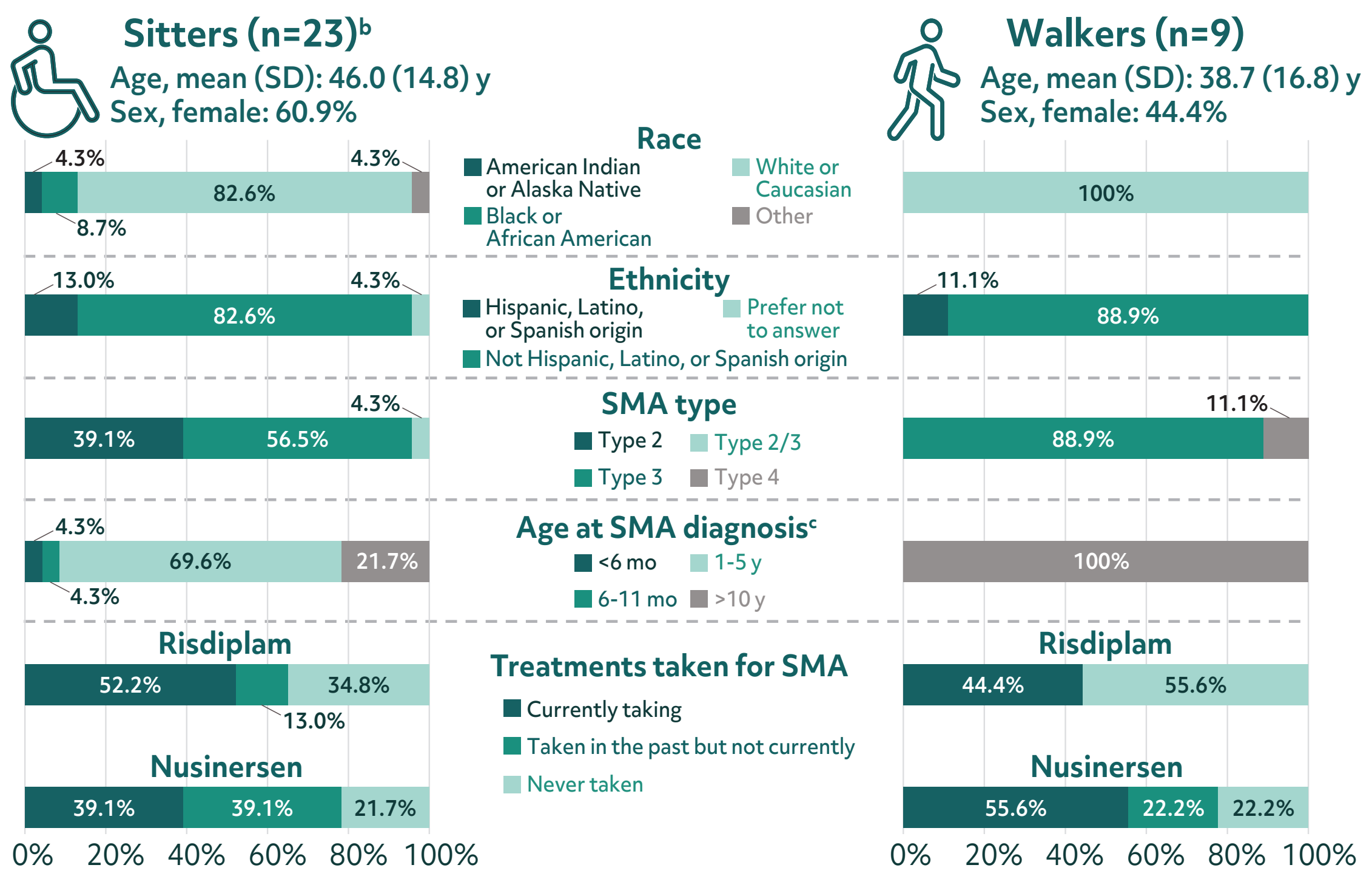
Data collection and analysis
- Conducted semistructured, in-depth interviews with patients
- Data collected during the interviews were coded and synthesized
- Study findings were contextualized using information from the fTLR

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

RESULTS

- Overall, 32 adult patients participated; mean (range) age was 44 (18-72) years, and 56.3% were female (**Figure 2**; **Table S1**)
- 72% and 28% of patients self-identified as sitters and walkers, respectively
  - 14/23 (61%) sitters reported having previously been able to walk without any help/support but could not walk without help/support at the time of the study
- 94% were receiving SMA treatments at the time of the study
  - 50% risdiplam
  - 44% nusinersen
  - 3% no longer receiving SMA treatment
  - 3% never received SMA treatment
- 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]14/23 (61%) of sitters reported having previously been able to walk without help/support but could not walk without any help/support at the time of the study. [c]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
2	2 Long sitting, legs straight	23	3
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
13	13 Props on extended arms	13	7
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 Ascend stairs without rail 33 Descends stairs without rail	0	9

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

- Patients often described "clinically meaningful change" as a change that impacts physical or emotional health, QoL, independence, or daily functioning, with even small or gradual changes able to make a meaningful difference (**Figure 3**)
- In general, any potential point improvements or stabilization within any HFMSE-related task would be meaningful as it could indicate functional or emotional gains
- Adult patients prioritized tasks that were relevant to their daily lives and critical to maintaining their current functional abilities, independence, ADLs, and QoL
  - Sitters prioritized sitting unsupported, bringing hands to the head, rolling, and transitioning between sitting and lying (**Figure 4**, **Figure S1**)
  - Walkers prioritized maintaining walking-related mobility, including standing, stepping, standing to sitting, and climbing stairs (**Figure 4**, **Figure S2**)
  - HFMSE changes were deemed less relevant or meaningful for tasks that were unfamiliar to patients due to their functional ability (eg, rolling onto or from the stomach for a patient who does not typically utilize that position)
- Across tasks, worsening was associated with impacts on daily functioning and emotional, psychosocial, caregiver, and financial well-being (**Figure 5**)
- Please also see the Virtual Poster: "Assessing the impact of 'any point differences' or 'stability' in the Hammersmith Functional Motor Scale–Expanded on activities of daily living in adult patients with SMA" presented by our group

Figure 3. Adult patient perspectives on the term "clinically meaningful change"

"The **changes that are significant in my life may be small** enough that they don't show up. They're not represented as clinically meaningful change, but they still have an impact in my life. **It can be beneficial for me, but it may not be big enough that insurance companies would say, 'Yes, let's continue this treatment,' things like that.**"
Sitter, aged 30 years

"'Meaningful' to me would be [to] just be able to continue to do the everyday activities that I do... Things that would be considered clinically meaningful for me now will be just being **able to do things as much as possible independently,** being able to go to my job, be independent, get home, be able to—if my wife and son are gone, to be able to do all the things I usually do on my own."
Walker, aged 49 years

"…my perspective of clinically meaningful change might be different than a medical professional's… when I first started [treatment], one thing I noticed that no test measures is **recovery time from fatigue**. Let's say I pull an all-nighter grading student speeches. I might be so fatigued it might take me a week or 2 before [treatment] to get back to my normal. After [treatment], it felt like it only took me 2 or 3 days. To me, **that'd be clinically meaningful change that's not something that's measured by any kind of a test.**"
Sitter, aged 47 years

"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

Example quotes have been edited for readability.

Figure 4. Adult patient perspectives on HFMSE task score changes

Sitters

Stability

HFMSE task 2 (long sitting) score: Stability
I want to be able to…contribute and **do the things that I'm used to doing…I want to be able to be a part of all the things that my peers, my family, my partner, my 'whoever' is doing.** I want to be able to participate in activities with my nieces and nephews, and I think that **having stability and having good health allows me to do those things.**
Aged 45 years

Improvement

HFMSE task 10 (sitting to lying) score: 0→1
It would give me **more mobility, which would impact my life and quality of life in a positive way**…It would…give me **more ability, more independence.**
Aged 48 years

HFMSE task 17 (lifts head from supine) score: 1→2
I could put on my BiPAP independently, which would be huge. I'd love to…be able to shift in bed…like when my hair gets caught underneath my back, I could just lift my head and move my hair. That would be amazing… **that would have a big impact on my day-to-day life.**
Aged 30 years

HFMSE task 1 (chair sitting) score: 1→2
If I could sit without having to use my hands… **that would mean I'd had enough strength to extend my arm and maybe drink…Maybe I would be able to brush my teeth…**Probably would **help me with my eating.** I could probably put the TV on or turn on an appliance.
Aged 60 years

Worsening

HFMSE task 1 (chair sitting) score: 2→0
Honestly, I think **it would be very scary to not have any sense of control over my body.** I think part of my spinal muscular atrophy, one of the challenges for me, has been that I've had to give up a sense of control over all of the years. Meaning, who I was, what I wanted to do, what I planned, all those sorts of things, and **so that piece makes it challenging to think about.**
Aged 45 years

Walkers

Stability

HFMSE task 20 (stepping) score: Stability
It's pretty important to be able to—because, obviously, you walk everywhere. You could move. You could get a wheelchair. It's just hard to maneuver. My life, right now, I couldn't be in a wheelchair. **I would have to make huge changes to the way I live and what I do.**
Aged 18 years

Improvement

HFMSE task 16 (crawling) score: 1→2
I know, when I have kids, it'll make it **easier to be able to be on the floor with them and play with them** and stuff. Just **another way that I can move.**
Aged 18 years

HFMSE tasks 25, 26 (kneeling to standing) score: 1→2
It would make things a lot easier. It would mean being able to basically move around freely. For example, exercising would be a lot easier…I would be able to transfer from different places to a standing position or a sitting position, even sit on the ground. **That would really help me move around basically and gain a lot of independence.**
Aged 25 years

HFMSE task 27 (stand to sit) score: 1→2
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

Worsening

HFMSE task 5 (rolls supine to side-lying) score: 1→0
I would lose all independence…my wife [would] have to force me to or help me do what I need to do to be able to get onto my sides…**it would be a big, big change.**
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.
BiPAP, bilevel positive airway pressure; HFMSE, Hammersmith Functional Motor Scale–Expanded.

Figure 5. Perceived impacts of changes on HFMSE tasks

	Perceived impact on:							
Change in HFMSE task score(s)	QoL	Independence	Mobility	ADLs	Planning	Caregiver burden	Financial burden	Safety
Increase	IMPROVED	IMPROVED	IMPROVED	IMPROVED	IMPROVED	IMPROVED	IMPROVED	IMPROVED
Decrease	WORSENED	WORSENED	WORSENED	WORSENED	WORSENED	WORSENED	WORSENED	WORSENED

ADLs, activities of daily living; HFMSE, Hammersmith Functional Motor Scale–Expanded; QoL, quality of life.

CONCLUSIONS

- Based on responses from adult patients with SMA, clinically meaningful change can be generally represented by any point differences or stability in HFMSE score, especially if one's independence and QoL are enhanced
- Across HFMSE tasks, there was a general consensus by adult patients that changes of any magnitude or stabilization could alter planning burden and affect physical and emotional health, emphasizing the importance of documenting small changes that may nevertheless be meaningful to individual patients

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.

Acknowledgments

This study is funded by Scholar Rock, Inc. We thank Melissa Culhane Maravic, PhD, MPH, and Claire Cagle, MPH, of Precision AQ for their important contributions to this project. Medical writing and editorial support were provided by James Banigan, PhD, and Dena McWain of Apollo Medical Communications, part of Helios Global Group, and funded by Scholar Rock, Inc. Project management support was provided by Taryn Bosquez-Berger, PhD, CMPP, of Scholar Rock, Inc.

Disclosures

AH has served on advisory boards and/or as a consultant for Biogen, Catalyst, J&J, Sarepta, and Scholar Rock, Inc. **SD** has served on advisory boards for Alexion, argenx, Biogen, CSL Behring, Genetech, Immunovant, and Sarepta. **TD** has served on advisory boards and/or as a consultant for Biogen, Cure SMA, Duchenne UK, Dyne, Genentech, Roche, Scholar Rock, Inc., and Trinds. **NL** and **AJ** are employees of Precision AQ. **TB**, **CC**, and **MG** are employees and stockholders of Scholar Rock, Inc. **AS-C** has served on an advisory board for and/or received consulting fees from Catalyst, Novartis, and Scholar Rock, Inc. **LN** has served as a consultant for Avexis, Biogen, F. Hoffman-La Roche, Novartis, and Scholar Rock, Inc.

To download a copy of this poster, **scan QR code**.

Presented at the 8th TREAT-NMD® International Conference | 10-12 February 2026 | Lisbon, Portugal

Email: medicalinformation@scholarrock.com

Understanding adult patient perspectives on the clinical meaningfulness of “any point differences” on the Hammersmith Functional Motor Scale–Expanded in SMA

Alicia Henriquez,[1] Stacy Dixon,[2] Tina Duong,[3] Natalie Land,[4] Amal Jamaleddine,[4] Thomas Brown,[5] Christabella Cherubino,[5] Mouhamed Gueye,[5] Ashley Stanley-Copeland,[6] Leslie Nelson[7]

[1]Seattle Children’s Hospital and University of Washington, Seattle, WA, USA; [2]University of Colorado School of Medicine, Aurora, CO, USA; [3]Stanford University, Palo Alto, CA, USA; [4]Precision AQ, New York, NY, USA; [5]Scholar Rock, Inc., Cambridge, MA, USA; [6]University of Texas at Austin, Dell Medical School, Austin, TX, USA; [7]University of Texas Southwestern Medical Center, Dallas, TX, USA

SUPPLEMENTARY MATERIAL

Table S1. Adult patient demographics and baseline characteristics[a]

Characteristic	Full sample (N=32)
Motor function status, n (%)	
Sitter	23 (71.9)[b]
Walker	9 (28.1)
Age, years	
Mean (SD)	44.0 (15.5)
Range	18-72
Sex, n (%)	
Female	18 (56.3)
Male	14 (43.8)
Race, n (%)	
American Indian or Alaska Native	1 (3.1)
Black or African American	2 (6.3)
White or Caucasian	28 (87.5)
Other	1 (3.1)
Ethnicity, n (%)	
Hispanic, Latino, or Spanish origin	4 (12.5)
Not Hispanic, Latino, or Spanish origin	27 (84.4)
Prefer not to answer	1 (3.1)
SMA type, n (%)	
Type 2	9 (28.1)
Type 3	21 (65.6)
Type 4	1 (3.1)
Other: Type 2/3	1 (3.1)
Age at SMA diagnosis, n (%)	
<6 months	1 (3.1)
6 to 11 months	1 (3.1)
1 to 5 years	16 (50.0)
6 to 10 years	0 (0.0)
>10 years	14 (43.8)
Treatments taken for SMA, n (%)	
Risdiplam	
Currently taking	16 (50.0)
Taken in the past but not currently	3 (9.4)
Never taken	13 (40.6)
Nusinersen	
Currently taking	14 (43.8)
Taken in the past but not currently	11 (34.4)
Never taken	7 (21.9)

[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]14/23 (61%) of sitters reported having previously been able to walk without help/support but could not walk without any help/support at the time of the study.

SD, standard deviation; SMA, spinal muscular atrophy.

Figure S1. Additional adult patient perspectives on HFMSE task score changes: Sitters

HFMSE tasks 21, 22 (hip flexion in supine) score: 0→2
“**I would be able to do a lot more exercise and help me get mobile** a little bit more...That would be a big plus.”
Aged 49 years

HFMSE task 14 (lying to sitting) score: 0→2
“That would mean that even if I was maybe traveling in different situations, different beds, different heights, different layouts, **I could probably still do that and be safe and independent, and that would be wonderful.**”
Aged 30 years

HFMSE task 5 (supine to side-lying) score: 0→1
“It would impact my **day-to-day quality of life in a tremendous way**…any increase at all is helpful to us in a major way. Because **that’s more things we get to do by ourselves and less things we have to ask other people for help for.**”
Aged 48 years

HFMSE tasks 3, 4 (hands to head) score: 0→1
“It would allow me to **put in an earphone** that I would use to either **listen to something or to communicate out**…anything that **would definitely be meaningful for me** because, right now, that is one of the tasks that I have to do on a day-to-day basis **both for work and just for my personal use.**”
Aged 38 years

HFMSE task 2 (long sitting) score: 0→2
“**You're talking about rolling my disease back 20 years**…If I had that kind of strength back and flexibility back, I'd be working again.”
Aged 72 years

HFMSE task 5 (supine to side-lying) score: 0→2
“It wouldn't only impact my quality of life, but **it would impact my wife's quality of life as well**…She has to wake up every time I need her to turn me over, so she never gets a full night of sleep…It's changing not only my quality but the people who have to be around me as well.”
Aged 48 years

HFMSE, Hammersmith Functional Motor Scale–Expanded.

Figure S2. Additional adult patient perspectives on HFMSE task score changes: Walkers

HFMSE task 27 (standing to sitting on the floor) score: 0→2
“**That changes everything.** Something like that, having that ability…**gives you any number of different things that you do on your daily activities,** that makes things easier for you.”
Aged 49 years

HFMSE tasks 18, 19 (standing) score: Stability
“**It allows me to do a lot of things** that I don’t have to have support or have any kind of assistance with. **It allows me to be a lot more independent.**”
Aged 49 years

HFMSE task 27 (stand to sit) score: Stability
“**I don't want to regress on that** part of it just because I think **I need that motor skill of being able to get down lower and on the floor to get things and to work on things.** I think, for me, I’m a person that likes to be active and likes to do things.”
Aged 64 years

HFMSE task 19 (stand unsupported) score: 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.**”
Aged 25 years

HFMSE task 31 (descend stairs) score: 2→0
“That’d be huge, because I wouldn’t be able to live in the house that I live in and just—**it’d change my whole family…it wouldn’t just affect me.**”
Aged 18 years

HFMSE tasks 30-33 (stairs) score: 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.**”
Aged 25 years

HFMSE, Hammersmith Functional Motor Scale–Expanded.

Email: medicalinformation@scholarrock.com