Quality of Life, Unmet Needs, and Treatment Experience of People Living with MPS II and Their Caregivers: A Community Survey

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Introduction

- MPS II (Hunter syndrome) is a rare, progressive lysosomal disease; all affected individuals have somatic disease manifestations, and about two-thirds of patients born each year also experience central nervous system manifestations[1]
  - MPS II affects approximately one per 100 000–170 000 live births[2,3]
- Although the medical aspects of MPS II are well documented, less is known about the lived experiences of those affected and their caregivers
  - To address this gap, our survey aimed to capture real-world perspectives on daily challenges, priorities, and unmet needs, with a goal of informing care, supporting services, and advocating for research which reflects the voices of people living with MPS II and their caregivers

Conclusions

- Our survey focused on the impact of MPS II on affected individuals and their caregivers
  - Responses reveal significant unmet needs relating to both cognition and somatic disease across the MPS II community
- Insights from our survey highlight the opportunity to inform care and to support families living with MPS II by optimizing disease management
- Emerging treatments should aim to mitigate cognitive disruption and concerns of progressive physical limitations, as experienced by individuals living with MPS II

Methods

Survey design

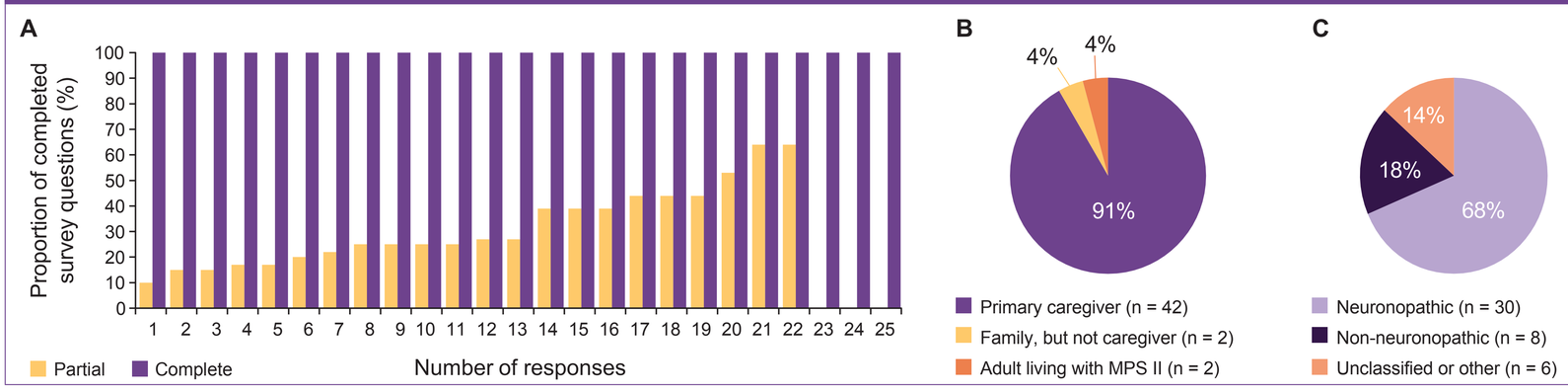
- This 27-question, online, sponsor-unblinded survey of US families was created and conducted by Denali Therapeutics and Project Alive
- Families and respondents were identified through the contacts of Project Alive, a US-based patient advocacy group dedicated to providing education and resources to the MPS II community and supporting MPS II research
- The survey gathered real-world perspectives on the daily challenges and unmet needs of people living with or caring for someone with MPS II, experiences with current treatment and care, and priorities for emerging treatments (scan QR code for full survey questions in **Table S1**)

Results

Survey demographics

- Out of 60 individuals who opened the survey between December 2024 and January 2025, 25 complete and 22 partial responses were collected (**Figure 1A**)
- Most respondents were primary caregivers (91%; 42/46) (**Figure 1B**)
  - Mean (range) current age of affected individuals was 12.5 (1–68) years, and the mean (range) age at diagnosis was 3.3 (0–25) years
- Most affected individuals were reported as having nMPS II (68%; 30/44) (**Figure 1C**)

Figure 1. Survey responses (**A**) and demographics including respondent type (n = 46) (**B**) and phenotype of affected individuals (n = 44) (**C**)

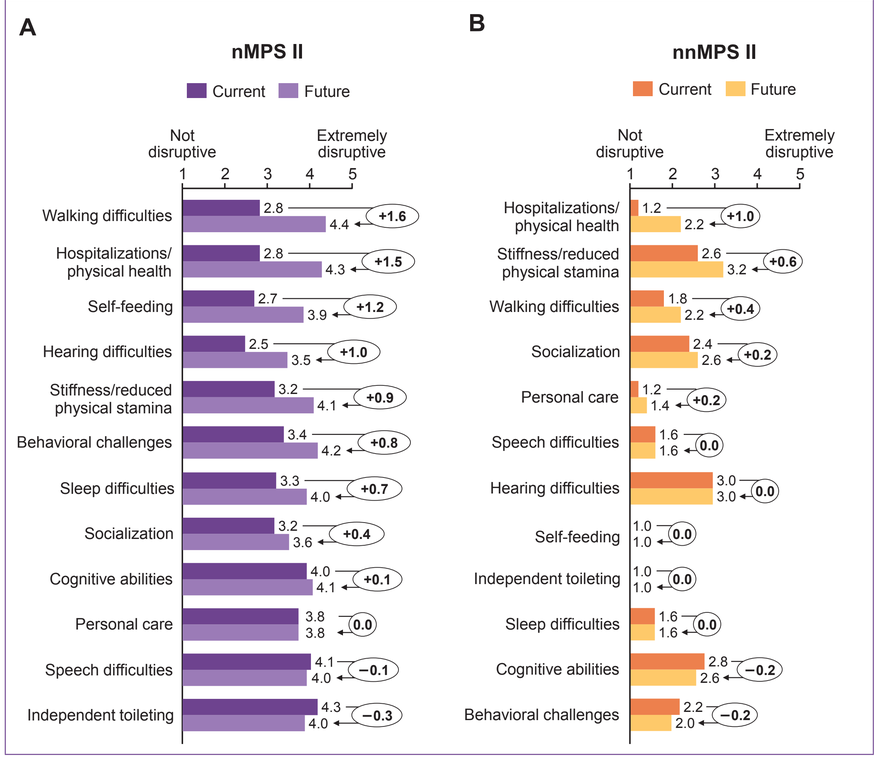


Impact on QoL

Although the impact on QoL was higher in individuals with nMPS II than in those with nnMPS II, substantial unmet need remains in both affected groups

- On a 5-point scale (with 5 being extremely disruptive), families living with nMPS II (n = 23) reported many current burdensome symptoms affecting QoL, with the most disruptive relating to independent toileting (4.3/5), speech difficulties (4.1/5), and cognitive abilities (4.0/5) (**Figure 2A**)
  - Open-text responses revealed that pain and seizures were also extremely disruptive (5.0/5) for one respondent each
- For families living with nnMPS II (n = 5), the current most burdensome symptoms related to hearing difficulties (3.0/5), cognitive abilities (2.8/5), and stiffness/reduced physical stamina (2.6/5) (**Figure 2B**)
- Families living with nMPS II (n = 21) had much greater concerns for the future than those living with nnMPS II (n = 5), especially surrounding progressive physical limitations (**Figure 2**)

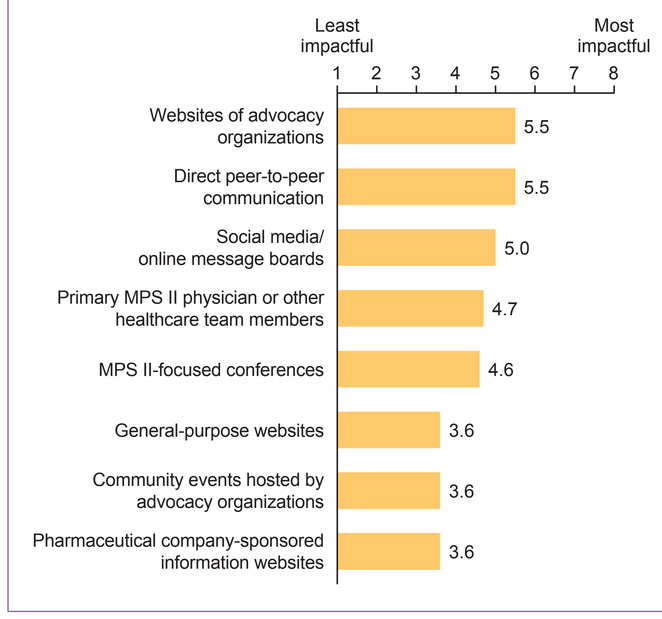
Figure 2. Current impact and worries regarding future impact of MPS II symptoms on QoL among individuals with nMPS II (current, n = 23; future, n = 21) (**A**) and nnMPS II (current and future, n = 5) (**B**)



Resources and education needs

- When looking for information on living with MPS II, respondents (n = 31) found websites of advocacy organizations and direct peer-to-peer communication the most impactful resources (both 5.5/8, with 8 being most impactful) (**Figure 3**)
  - 44% of families (14/32) desire further information on living with MPS II, particularly surrounding clinical trials, lifestyle, and symptoms

Figure 3. Key sources of information on living with MPS II (n = 31)

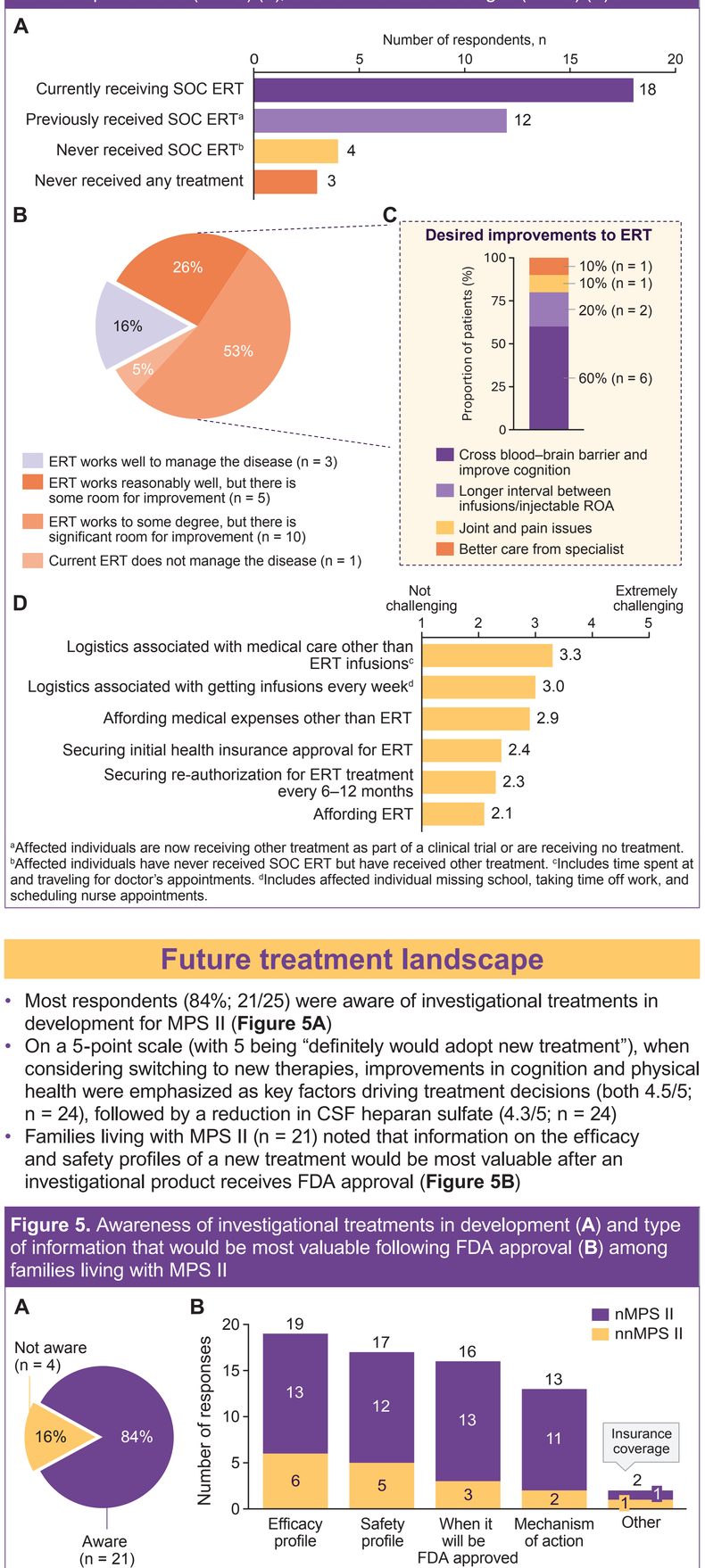


Challenges with SOC ERT

- The majority of affected individuals (81%; 30/37) were receiving or had previously received SOC ERT (**Figure 4A**)
- When considering perceived effectiveness, 84% of families (16/19) reported that SOC ERT did not manage the disease or acknowledged room for improvement (**Figure 4B**)
  - The ability to cross the blood–brain barrier and improve cognition was the most desired improvement to currently available SOC ERT (n = 6/10; **Figure 4C**)
- On a 5-point scale (with 5 being the most challenging), the most challenging non-medical aspects of SOC ERT (aspects of treatment not directly linked to efficacy or safety) were logistics with medical care (3.3/5; n = 16) and with weekly infusions (3.0/5; n = 16; **Figure 4D**)

Challenges with SOC ERT (cont.)

Figure 4. Current and previous use (n = 37) (**A**), perceived effectiveness (n = 19) (**B**), desired improvements (n = 10) (**C**), and non-medical challenges (n = 16) (**D**) of ERT



[a]Affected individuals are now receiving other treatment as part of a clinical trial or are receiving no treatment. [b]Affected individuals have never received SOC ERT but have received other treatment. [c]Includes time spent at and traveling for doctor's appointments. [d]Includes affected individual missing school, taking time off work, and scheduling nurse appointments.

Future treatment landscape

- Most respondents (84%; 21/25) were aware of investigational treatments in development for MPS II (**Figure 5A**)
- On a 5-point scale (with 5 being "definitely would adopt new treatment"), when considering switching to new therapies, improvements in cognition and physical health were emphasized as key factors driving treatment decisions (both 4.5/5; n = 24), followed by a reduction in CSF heparan sulfate (4.3/5; n = 24)
- Families living with MPS II (n = 21) noted that information on the efficacy and safety profiles of a new treatment would be most valuable after an investigational product receives FDA approval (**Figure 5B**)

Figure 5. Awareness of investigational treatments in development (**A**) and type of information that would be most valuable following FDA approval (**B**) among families living with MPS II

ABBREVIATIONS

CSF, cerebrospinal fluid; ERT, enzyme replacement therapy; MPS II, mucopolysaccharidosis type II; nMPS II, neuronopathic mucopolysaccharidosis type II; nnMPS II, non-neuronopathic mucopolysaccharidosis type II; QoL, quality of life; ROA, route of administration; SOC, standard of care.

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3. Muenzer J *et al. Orphanet J Rare Dis* 2017;12:82.

ACKNOWLEDGMENTS

We give a special thank you to the families and individuals of the MPS II community who generously contributed through their participation in the survey. We also thank the Denali Therapeutics and Project Alive teams for their collaboration in the conduct of the survey and data collection.

DISCLOSURES

This poster was sponsored by Denali Therapeutics Inc. Medical writing support was provided by Jack Penhaligan PhD of PharmaGenesis Cambridge, Cambridge, UK, and was funded by Denali Therapeutics Inc. The original survey was coded and fielded by LifeSci Consulting LLC, New York, NY, USA. **KM** is an employee of Project Alive, which receives grants and event sponsorships from Denali Therapeutics Inc., JCR Pharmaceuticals, RegenxBio, and Takeda Pharmaceuticals. **AA** and **SG** are employees and stockholders of Denali Therapeutics Inc., which has filed patent applications related to the subject matter.

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Presented at WORLD*Symposium*™, February 2–6, 2026, San Diego, CA, USA

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Table S1. MPS II (Hunter syndrome[a]) Community Survey

Question		Response options
1	Which one best describes you?	Adult living with MPS II
		Primary caregiver for someone living with MPS II
		Family member of someone living with MPS II but not primary caregiver (e.g. sibling)
2	What is your current age/age of the person living with MPS II under your care?	0–99 years
3	What age were you/they at diagnosis?	0–99 years
4	How would you best describe the type of MPS II?	Neuronopathic
		Non-neuronopathic
		Not been classified into neuronopathic or non-neuronopathic
		Other (please explain): [*open text response*]
5	How much do the following symptoms of living with MPS II affect your quality of life/the quality of life of your family currently? 1) Walking difficulties 2) Speech difficulties 3) Hearing difficulties 4) Self-feeding 5) Independent toileting 6) Personal care (getting dressed, brushing teeth) 7) Sleep difficulties 8) Cognitive abilities (brain fog, difficulty concentrating) 9) Stiffness/reduced physical stamina 10) Behavioral challenges (withdrawal, aggression) 11) Socialization (school, work) 12) Hospitalizations/physical health (cardiac, respiratory) 13) Other: [*open text response*]	1. Not disruptive
		2. Minimally disruptive
		3. Moderately disruptive
		4. Very disruptive
		5. Extremely disruptive

6	How much do you worry about these above symptoms of MPS II getting worse in the future?	1. Not worried 2. Minimally worried 3. Moderately worried 4. Very worried 5. Extremely worried
7a	(Currently receiving) What treatment or care plan are you/the person under your care currently on (if any)?	Standard of care ERT Hematopoietic stem cell transplant (HSCT) Clinical trial for novel ERT Clinical trial for gene therapy Clinical trial – other No treatment
7b	(Previously received) What treatment or care plan were you/the person under your care on (if any)?	Standard of care ERT Hematopoietic stem cell transplant (HSCT) Clinical trial for novel ERT Clinical trial for gene therapy Clinical trial – other No treatment
8	When thinking about switching to a new treatment plan (both previously and looking forward to the future), which of the following influences your decision? 1) Main physician responsible for treating my/my child's MPS II 2) Other members of healthcare team (other than primary physician) – Specify [*open text response*] 3) Peers in my network (other people living with MPS II/caregivers) 4) Information we read online from pharmaceutical manufacturers 5) Information we read online from advocacy organizations such as Project Alive, National MPS society etc. 6) Other: [*open text response*]	1. Least impactful 2. Minimally impactful 3. Moderately impactful 4. Very impactful 5. Most impactful
9	When thinking about collaborating with your/the person under your care's physician/care team to determine the best treatment course for your/their MPS II, which of the following best describes your approach?	We have an MPS II specialist at a local hospital, and we see them for treatment decisions and disease monitoring We see an MPS II specialist but we travel to do so We see a local physician (non-MPS II specialist)/care team for MPS II treatment

	Please respond with respect to your/their main MPS II treater (not specialists treating specific MPS II manifestations like cardiologist, gastroenterologist etc.).	We primarily see a local physician/care team but we also travel to consult with an MPS II specialist on a regular basis (even if infrequently)
		Other: [*open text response*]
10	Where do you typically look for information about living with MPS II? 1) Websites of advocacy organizations such as Project Alive, National MPS Society 2) General purpose websites (MedLine, hospital websites) 3) Pharmaceutical company-sponsored informational websites (e.g. HunterPatients.com) 4) MPS II-focused conferences 5) Community events hosted by advocacy organizations 6) Direct peer-to-peer communication (I ask other people living with MPS II/other caregivers) 7) Social media/Online message boards 8) I ask my primary MPS II physician or other members of my healthcare team	1. Least impactful
		2.
		3.
		4.
		5.
		6.
		7.
		8. Most impactful
11	Is there any type of information about living with MPS II that you wish was available but have so far not been able to find to a satisfactory degree?	No – everything I would want to know, I have been able to find
		Yes – Explain [*open text response*]
12	As an adult, how has your primary MPS II-treating physician and MPS II care team changed over time?	Has not changed since I was a child
		Has changed – transition from pediatric to adult care team was seamless
		Has changed – transition from pediatric to adult care team was troublesome and/or stressful
		Not applicable – I was diagnosed as an adult
13a	Has neurocognitive testing been performed beyond the initial stage as part of receiving a diagnosis, as part of a clinical study?	Yes
		No
13b	Has neurocognitive testing been performed beyond the initial stage as part of receiving a diagnosis, as part of regular care (outside clinical studies)?	Yes, conducted every [*open text response*] years to monitor disease progression
		Yes, conducted every [*open text response*] years as a school requirement
		No – we decided together with our clinical care team that it is not needed
		No – although the doctor encouraged us to get it, we opted against it
14		Bayley Scales of Infant and Toddler Development (BSID)

	What neurocognitive test was typically performed during regular care (outside clinical studies)?	Kaufman Assessment Battery for Children (KABC)
		Differential Ability Scales (DAS)
		Vineland Adaptive Behavior Scales (VABS)
		Other test: [*open text response*]
		I don't know what test was performed
15	Were the following tests done for you/the person under your care? 1) Urinary GAGs 2) CSF heparan sulfate 3) Serum NfL 4) I2S enzyme activity	Done at diagnosis
		Done at diagnosis AND on an ongoing basis (monitoring)
		Never done
		Unsure
16	Do you find tests for urinary GAGs helpful in monitoring your disease/the disease of the person under your care?	Yes – I believe this is a good way to monitor how the disease is progressing and impact of treatment efficacy, at least outside the brain
		Somewhat – I know they may be a good indicator of the state of the disease, but the numbers are not very useful
		No – I don't think these numbers are useful
		I don't know
		Does not apply to me – the doctor does not routinely test for urinary GAGs
17	Where do/did you/the person under your care receive ERT?	At home
		At the center/hospital where our key MPS II-treating physician is located
		At a local infusion site/local hospital nearby
		Other: [*open text response*]
18	Why do you/the person under your care not receive ERT infusions at home?	Recently started ERT – planning to transition to home infusion in the future
		Prefer to keep home separate from treatment location
		Feel more comfortable with extra supervision at a healthcare center
		Other: [*open text response*]
19	Which best describes your current experience of ERT treatment as it exists today?	ERT works well to manage the disease
		ERT works reasonably well but there's some room for improvement
		ERT works to some degree but there's significant room for improvement
		Current ERT does not manage the disease
20	What improvements would you want to see in ERT treatment?	[*open text response*]
21	How challenging are each of the following non-medical aspects of ERT treatment for you/your family?	1. Not challenging

	1) Securing initial health insurance approval for ERT 2) Securing re-authorization for ERT treatment every 6–12 months 3) Affording the ERT 4) Affording medical expenses other than the ERT 5) Logistics associated with getting infusions every week (e.g. child missing school, taking time off work, scheduling nurse etc.) 6) Logistics associated with medical care other than ERT infusions (e.g. taking time and traveling for doctors' appointments) 7) Other: [*open text response*]	2. Minimally challenging 3. Moderately challenging 4. Very challenging 5. Extremely challenging
22	What was the primary reason you/the person under your care decided to discontinue ERT?	Treatment was not effective Weekly infusions were a burden Did not tolerate the treatment well Other reason: [*open text response*]
23	What was the reason you decided to not receive treatment for yourself/the person under your care?	I did not believe it would be effective Symptoms are mild enough to make weekly infusions not worth it Could not get it approved by my health insurance Other reason: [*open text response*]
24	In thinking about new investigational treatments that may be FDA approved in the future, which best matches your current approach for yourself/the person under your care after discussing with your/the person under your care's doctor and care team?	Plan to switch to the first new FDA-approved treatment that is available, assuming it will address these needs: [*open text response*] Plan to switch to a new FDA-approved treatment, but will wait to see which new treatment seems to be working better (even if I may have to wait a few more months to switch) Will consider switching, pending advice from my physician and my network Current treatment works well enough, I see no reason to switch
25	On a scale of 1–5, how likely would each of the following types of improvements be in driving you to switch to a new FDA-approved treatment? 1) Walking 2) Communication 3) Hearing 4) Cognition 5) Physical health (heart function, liver/spleen size etc.) 6) Urinary GAGs 7) CSF heparan sulfate	1. Definitely not adopt 2. Unlikely to adopt 3. May adopt 4. Likely to adopt 5. Definitely would adopt
26	Are you aware of any investigational treatments in development for MPS II?	I am not aware of any investigational treatments I am aware of investigational treatments

		As you are aware of investigational treatment, please select and explain: [*treatment name*] I have heard of this treatment, but don't know much/anything about it I have heard some good things of this treatment I am enthusiastic to try this treatment as soon as there is an opportunity I have some concerns about this treatment
27	Once an investigational product receives FDA approval, what information is most important to you about the new treatment?	Mechanism of action (how it works) Efficacy profile (how it's been shown to improve the disease) Safety profile (what side effects one can expect) When it will be FDA approved and available to us Other: [*open text response*]

[a]MPS II was referred to as Hunter syndrome in the original survey.

CSF, cerebrospinal fluid; ERT, enzyme replacement therapy; GAG, glycosaminoglycan; I2S, iduronate-2-sulfatase; MPS II, mucopolysaccharidosis type II; NfL, neurofilament light chain

Disclosures

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