



Angelman Syndrome (AS) Hope in Action Survey Results

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Caregiver Voices are Integral to Patient-Focused Drug Development in AS

- FAST and ASF collaborated on a caregiver-reported patient experience survey in 2024 to assess the **most impactful Angelman syndrome (AS) symptoms, understand treatment priorities, and explore willingness to enroll the person with AS in a clinical trial.**
- The “Hope in Action” Survey represents a **large and meaningful caregiver sample** for a rare disease population.
- Caregivers provided information about patients’ experiences with AS because **people with AS cannot reliably and validly self-report.**
- The survey data enhance community understanding of **what matters to caregivers, providing specific examples of meaningful changes to individuals and their caregivers.**

ASF and FAST Hope in Action Survey: Methods

- Global online survey (English only)
- Developed by senior patient experience researchers, AS experts, advocates, and caregivers.
- Survey development followed FDA Guidances on Patient Focused Drug Development.
- Informed by existing AS literature.
- Caregivers were recruited by ASF and FAST.

The survey included 3 sections:

1. **Most impactful AS symptoms** (ranking of symptom domains followed by symptom rating)
2. **Treatment priorities** (symptom ranking, with “smallest meaningful change” defined through open responses)
3. **Willingness to participate and clinical trial opinions** (rating scales).

ASF and FAST Hope in Action Survey: Demographics

Caregiver Respondents
N=342

Reporting about
people with AS



95% parent of
individual with AS



81% female



Mean age 46.0 yrs



75% with Bachelor's
degree or higher

Caregiver Race	n (%)
White	277 (81.0%)
Asian	27 (7.9%)
Black/African American	9 (2.6%)
Other/Unknown	11 (3.2%)



53% male



64% deletion
16% mutation
13% UPD/ICD



Mean age 11.3 yrs
(1-51)

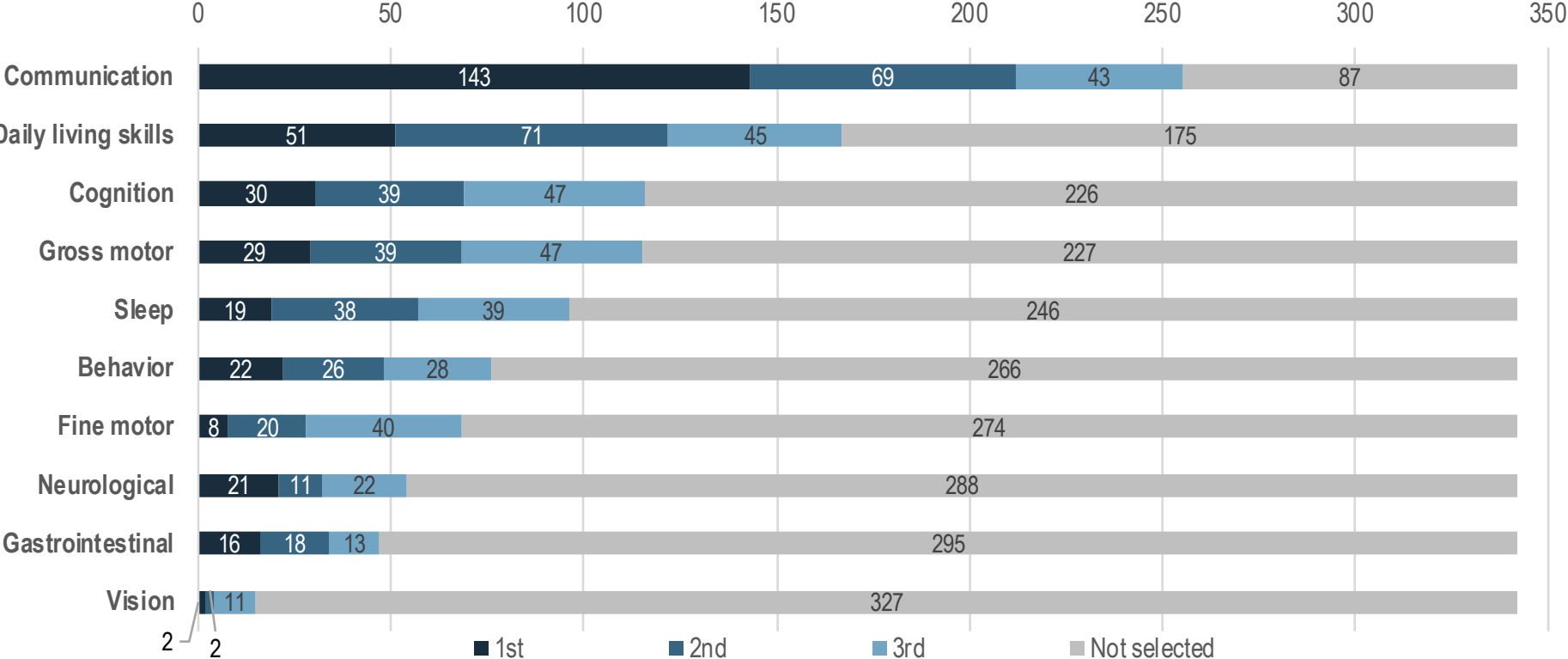
Person with AS Race	n (%)
White	280 (86.2%)
Asian	29 (8.9%)
Black/African American	13 (4.0%)
Other/Unknown	18 (5.5%)

What did our survey show about how symptoms impact daily life for people with AS?

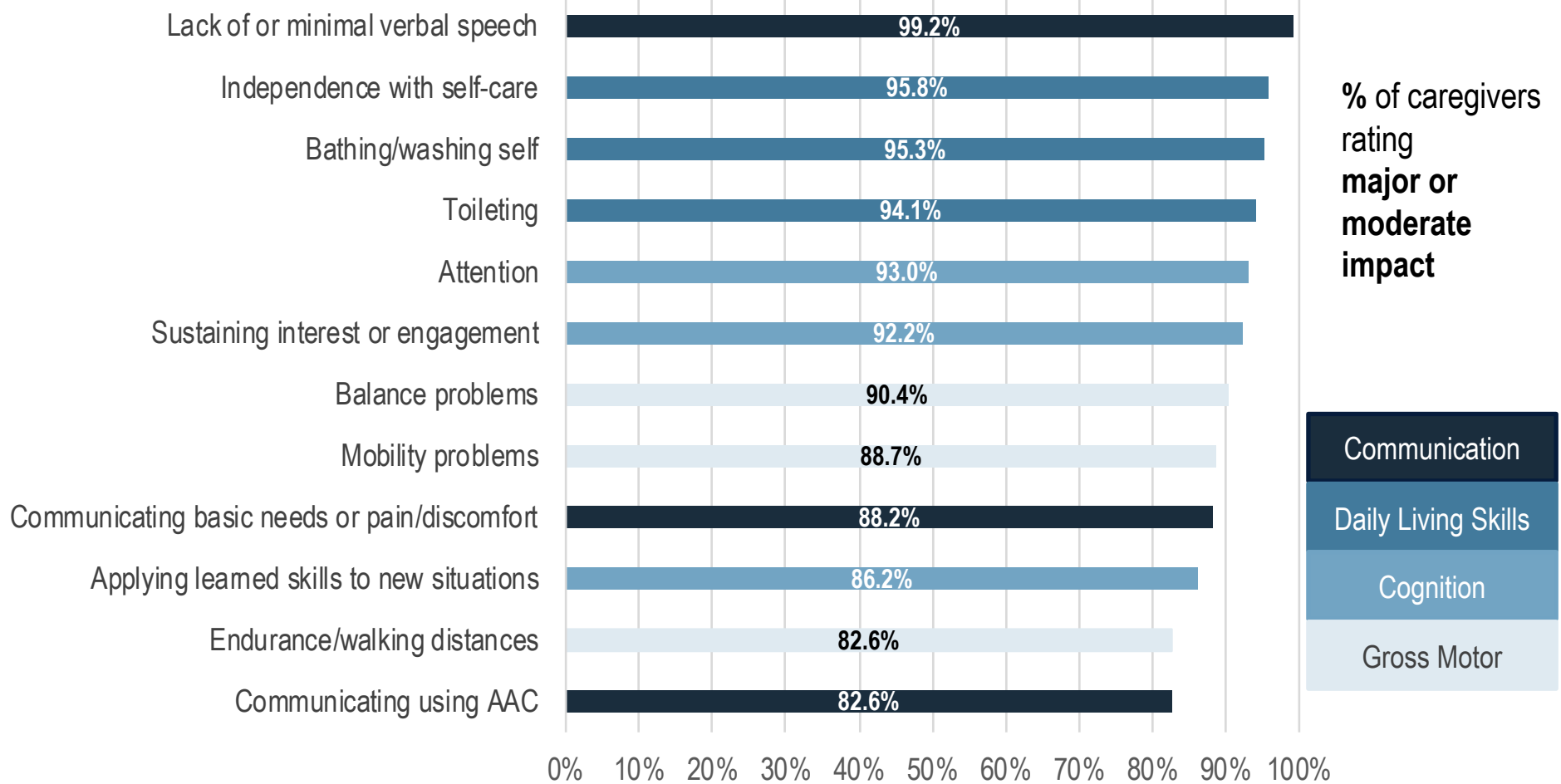


Caregivers **selected the most impactful symptom areas (domains) and reported on the most impactful symptoms**

Top 3 Symptom Domains Having the Most Impact on Individuals with AS, According to their Caregivers (N=342)



Symptoms Having the Highest Impact

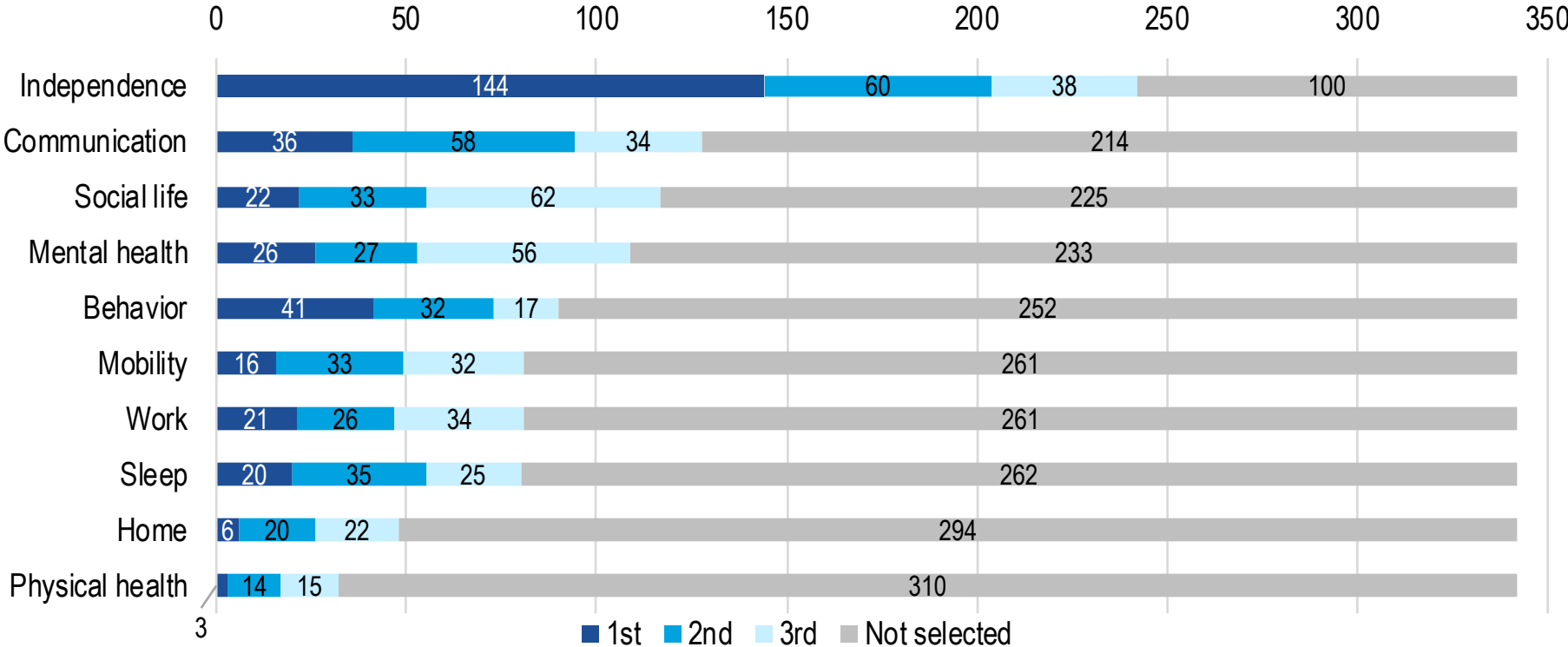


What did our survey show about caregiver impact



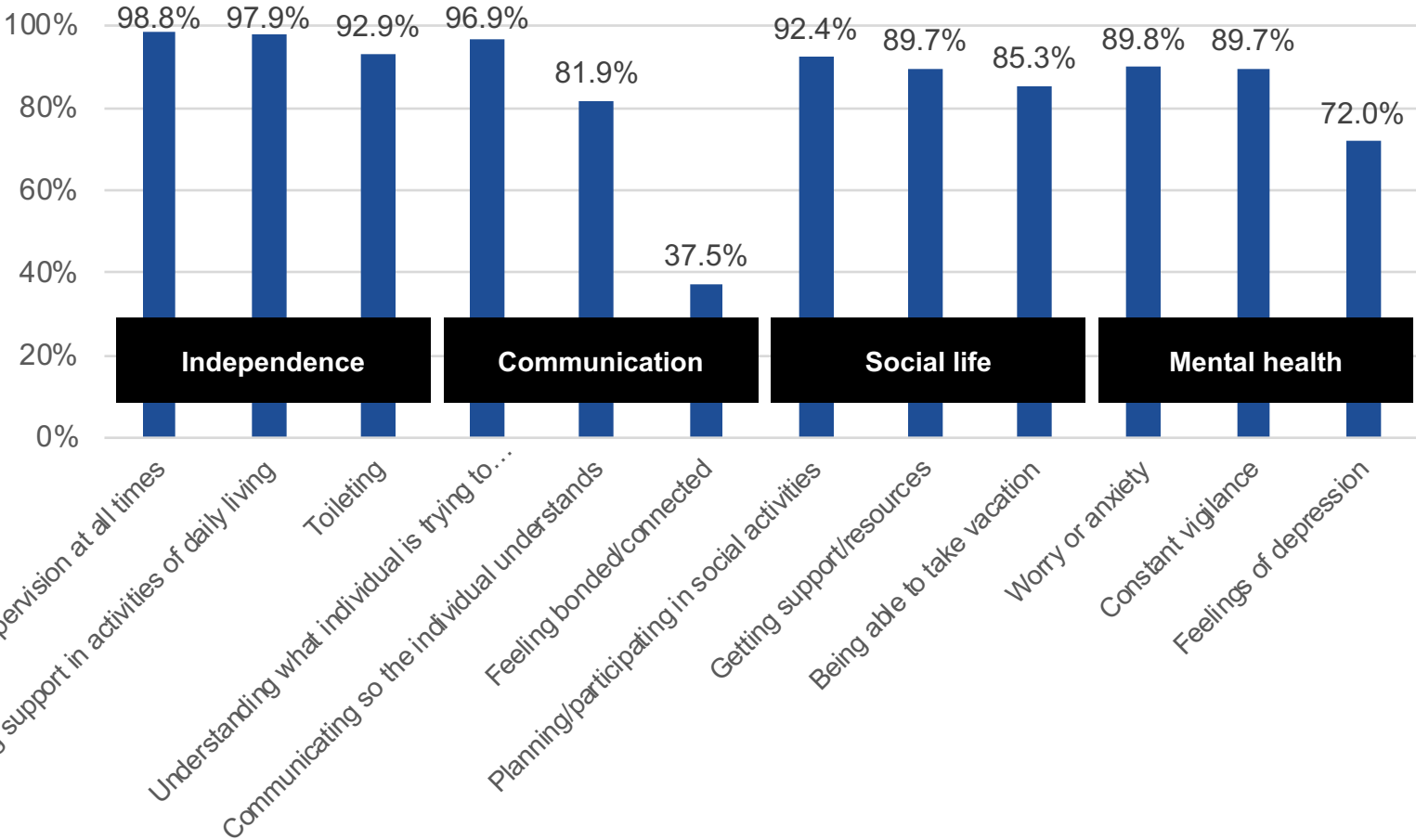
When asked what groups of symptoms had the most impact on the caregivers for persons with AS, this is how caregivers ranked the groups. They ranked “top 3”.

Symptoms ranked as having the most impact on Caregivers (They ranked “top 3”)



Symptoms rated as having high impact on the caregiver

% of caregivers rating major or moderate impact



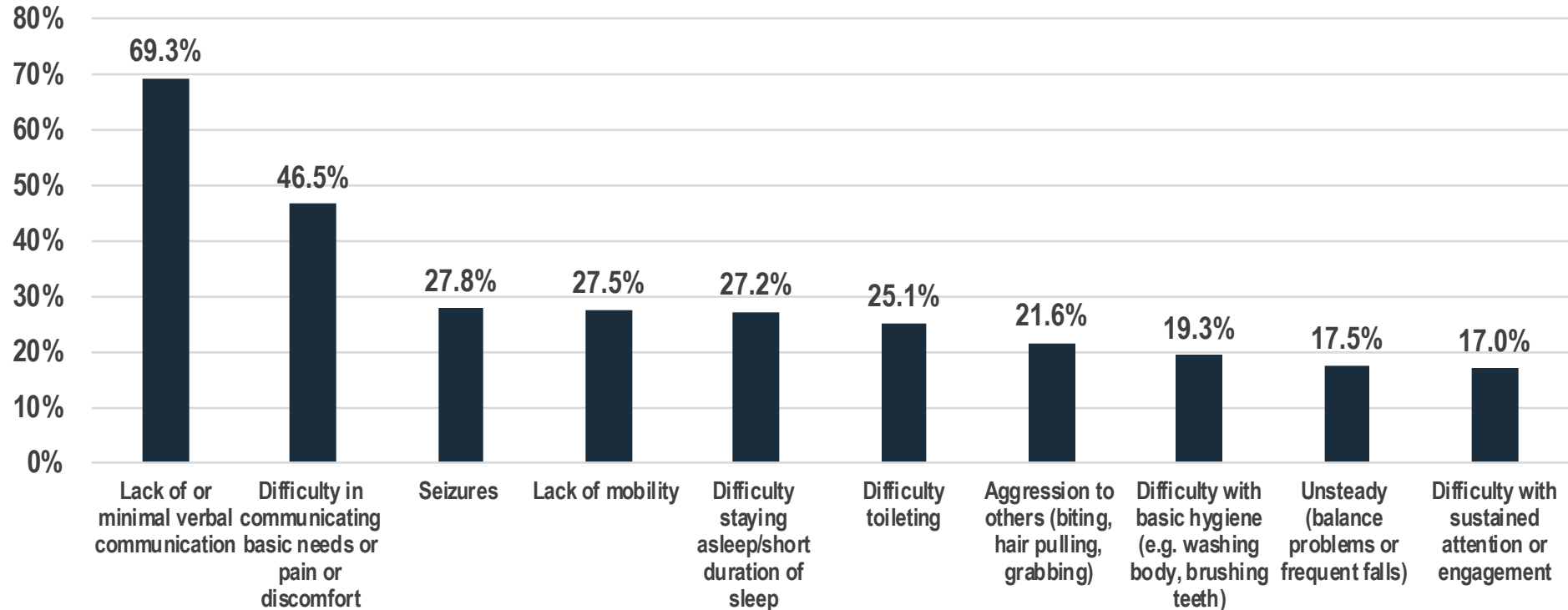
What did our survey show about treatment priorities?



Caregivers chose **symptoms that are treatment priorities.**

Top 5 Treatment Priorities* According to the Caregiver

*Ranked from 40 symptom choices



What did our
survey show
about
treatment
priorities?



Caregivers described the “**smallest meaningful change**” in symptoms

Communication



1 Communicate "yes" or "no"

"I would give my life for him to be able to answer 'yes' or 'no' questions because he is cognitively able to understand what he is being asked." – Caregiver of 24-year-old with deletion

1

2 Speak a few words (range 3 to 50)

"Single words would be amazing! If she said "eat", "drink", "potty", that would be huge!" – Caregiver of 23-year-old with deletion

2

3 Communicate basic needs in any way

"She would be able to tell me when she's sick, where she hurts and what she needs. It's a guessing game every time... It's scary, what if I guess wrong?" – Caregiver of 33-year-old with deletion

3

4 Use adaptive equipment effectively

"My child could communicate her needs using an AAC... and maybe say a few words." – Caregiver of 2-year-old with deletion

4

Seizures



1 Decreased seizure frequency, duration, or severity

Improvement or elimination of seizures would improve her independence, her cognition, her communication, her emotional regulation, her mobility, and her general health." – Caregiver of 18-year-old with UBE3A mutation

1

2 Prevent febrile seizures

"Not to have to check his temperature constantly." – Caregiver of 3-year-old with deletion

2

3 Reduce or eliminate need for medications

"Consistent seizure control with only one drug." – Caregiver of 42-year-old with deletion

3

4 Eliminate breakthrough seizures

"Her seizures affect everything. Getting these better controlled would be a game changer." – Caregiver of 4-year-old with UPD

4

Mobility & Balance

1

Walk across a room without support

"If she stopped falling over, I think her walking would improve immensely. Seems like balance would trickle down into a lot of things. Everything stems from balance." – Caregiver of 3-year-old with deletion

1

2

Navigate with a walker or gait trainer

"Willingness and strength to use gait trainer would create lessen stress on my body and help with all daily activities." – Caregiver of 6-year-old with deletion

2

3

Improve balance to reduce chance of injury

"If he could maintain his balance, it would reduce injuries." – Caregiver 9-year-old with UPD

3

4

Stand independently for a brief time (1 minute)

"If he could even just stand and support his own weight that would help in almost every way." – Caregiver of 9-year-old with deletion

4

5

Decrease need for caregiver to carry the person with AS

"He needs helps to move around. Most of the time we need to carry him. He is getting heavy." – Caregiver of 3-year-old with deletion

5

Sleep

1

More consistent and longer sleep

"Sleeping through the night would help him develop better physically, cognitively and mentally." – Caregiver of 2-year-old with deletion

1

2

Improved performance due to better sleep

"I imagine better sleep for him would result in a ripple effect for learning, communication, attention and more." – Caregiver of 9-year-old with deletion

2

Hygiene

1 Independence in simple tasks (washing and drying self)

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-
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"Mastering personal hygiene skills would be life changing." – Caregiver of 39-year-old with unknown subtype

2 Reduced resistance to hygiene tasks

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-
-

"It is such a struggle to bathe her and brush her teeth and dress her. She has to be in the mood to want to help. I am often exhausted at the end of the bath and bedtime routine. I would love for her to help...without putting up a fight." – Caregiver of 6-year-old with UBE3A mutation

3 Complete hygiene tasks with only partial assistance

"If he could manage some of his hygiene needs or just need a little assistance instead of full assist, would mean the difference in us handling this situation as we age." – Caregiver of 24-year-old with deletion

Toileting

1 Remove toileting-related barriers to access and independence

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-
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"Also, if she was potty trained, we would be able to go many places without worrying about bringing all the pull ups and wipes and all that goes with that and save a ton of money if we didn't have to use pull ups anymore." – Caregiver of 7-year-old with deletion

2 Remove diaper or pull-up related stress

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-
-

"This is an exhaustive battleground. Wets the bed every night and won't wear pull-ups. It limits him as to what he can do and who with. Would give him so much more independence and increase self-control/confidence." – Caregiver of 19-year-old with UPD

3 Ability to take off own clothes to toilet

"A small improvement in toileting skills would allow my daughter to participate in recreational and educational activities that are otherwise restricted because of being not potty trained." – Caregiver of 6-year-old with unknown subtype

Attention

1 Ability to focus on an activity for longer periods of time

"He is curious and smart but cannot stay on task. I would welcome anything that gives him a chance to demonstrate learning." – Caregiver of 11-year-old with deletion

2 Ability to engage with therapists and educators

"Remaining engaged for longer than 10 seconds would improve her chance at being successful in therapies." - Caregiver of 2-year-old with deletion

3 Ability to play with toys in a meaningful way

"I would love to see her play with toys. At least a good attempt to play with toys in a meaningful fashion." – Caregiver of 34-year-old with deletion

4 Better focus for greater participation in family activities

"Engagement would allow us to do activities together as a family." – Caregiver of 21-year-old with deletion

Aggression

1 Improve self control

"Increased self-control in new situations or the ability to stay calm instead of lashing out." – Caregiver of 5-year-old with UPD

2 Reduce impulsivity

"If this could just decrease a bit, we could leave the house and participate in life more and not feel so isolated." – Caregiver of 24-year-old with deletion

3 Increase communication skills to prevent aggression

"Quality of life would improve drastically, as he/me/we would be able to go to countless places and participate in countless activities. There are many programs he'd be able to participate in." – Caregiver of 26-year-old with UBE3A mutation

4 Reduce behaviors: hair-pulling, biting, hitting, kicking

"This one breaks my heart. I don't want people to be afraid of my child." – Caregiver of 5-year-old with ICD

What did our survey reveal about willingness to enroll the individual with AS in a clinical trial?



Caregivers were presented with a hypothetical trial scenario **and asked about their willingness to participate**

Willingness to enroll in a trial

Description of hypothetical trial:

The objective of the trial is to see if a possible new treatment is **safe** and **provides meaningful improvement** in specific AS symptoms.



The trial will be conducted over **1 year**.

You would need to visit the study site **every 2 months** (for a total of 6 visits).

Each site visit would last **6-8 hours**.



Some participants will receive the study drug, and some will not (they would receive a placebo,

During the study, **you will not know if your person with AS is getting the study drug (in the active group) or if they are in the placebo group.**



After 1 year, if the data from the main trial looks promising, every participant will be invited into an extension study where all participants would get the study drug.



The drug will be given by lumbar puncture, which is similar to having a spinal tap. A small needle is inserted into the person's back and the treatment is given directly through the needle into the fluid around the spine.

The lumbar puncture requires sedation (anesthesia) every time.

Willingness to enroll in a hypothetical trial

Description of possible side effects and risks of the hypothetical trial:

Imagine the doctor told you that these are the possible side effects. While most people with AS do not have these side effects, they are not uncommon.

- Vomiting (throwing up)
- Fever
- Seizures may become more frequent
- Headache
- Pain at the site of the needle puncture
- Bleeding at the site of the needle puncture

These are uncommon (rare) but **more serious** possible risks:

- Infection that causes swelling around the brain and severe headache
- Swelling, bleeding, and pain at the spinal cord
- Leg weakness
- Spinal cord or nerve injury
- The chance for other unanticipated but serious risks

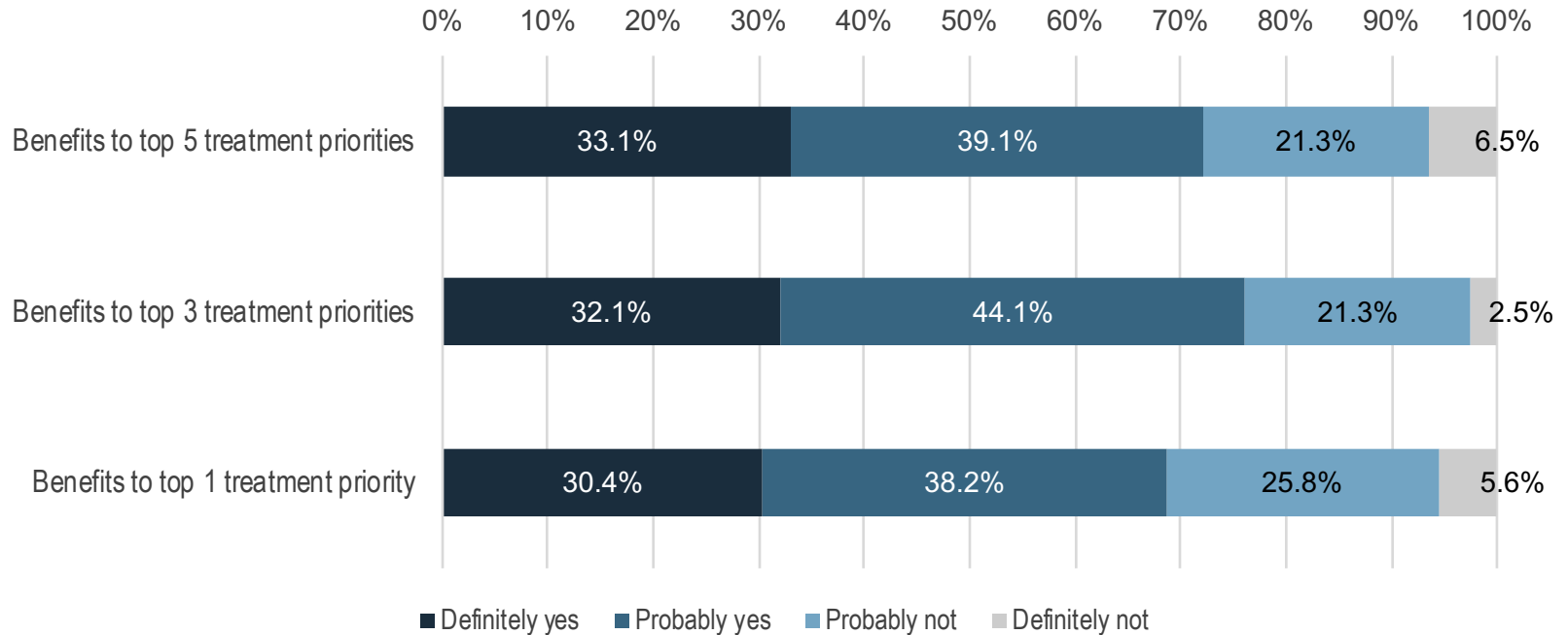
If the person with AS experienced one of these uncommon but more serious side effects, they would have to stay in the hospital until the doctor felt it was safe for them to go home and would need specific treatments to manage the side effects.

What did our survey reveal about willingness to enroll the individual with AS in a clinical trial?



Caregivers were then presented with potential benefits (1,3, or 5) that matched their priority choices and asked if they would enroll in such a trial...

Willingness to Participate in a Clinical Trial that Aims to Improve 5, 3, or 1 Priority Symptoms



- We did an analysis to try to identify things that make caregivers more willing to enroll in a clinical trial. We found that caregivers of younger people with AS and those with more research experience were more willing to enroll.

Predictor	Effect
Age of person with AS	▼ Lower age → ▲ more willingness to enroll
Prior research experience	▲ More research experience → ▲ more willingness to enroll
Deletion status	↔ No effect
Caregiver race/ethnicity	↔ No effect
Caregiver education	↔ No effect
USA status	↔ No effect



Summary and Implications

ASF and FAST Hope in Action Survey: Summary & Implications

- Areas of most significant negative impact on person with AS were **communication, daily living skills, and cognition.**
- Priority-to-treat symptoms were **communication, seizures, lack of mobility, and sleep.**
- Symptoms with high impact were reported **across domains.**

PFDD Implications: The domains identified as high impact and meaningful should be factored into endpoint selection and, in fact, they are being used in clinical trials.

ASF and FAST Hope in Action Survey: Summary & Implications

- Caregiver-reported treatment priorities spanned cognitive, neurological, behavioral and motor symptom sets, reinforcing the **multi-symptom nature of AS** with high unmet treatment needs.
- Caregivers describe the **importance of small changes** to AS symptoms that would have a meaningful impact.

PFDD Implications: There is a critical need for therapeutic developments that target meaningful improvements (**even if small**), particularly in **communication, daily living skills and cognition**.

ASF and FAST Hope in Action Survey: Summary & Implications

- Most caregivers indicated a **willingness to enroll** the person with AS in a trial.

PFDD Implications: Caregivers' willingness to participate in trials, **even if only one priority symptom is improved**, speaks to the unmet need in working toward independence for the person with AS.