

# Leveraging insights about the Rett syndrome patient experience to inform development of clinical trials

## INTRODUCTION

Over the years, caregivers become Rett syndrome experts. It is important that their needs, perspectives, experiences, and priorities are captured and incorporated in gene therapy research and development. Working with caregivers early in the research process can help improve study design, support recruitment, enhance the impact of findings, improve health knowledge, and build meaningful relationships with communities for ongoing collaboration.<sup>1</sup>

Regulatory authorities—including the US Food and Drug Administration, European Medicines Agency, Health Canada, and Medicines and Healthcare products Regulatory Agency—encourage the inclusion of the caregiver and patient viewpoints in the product development and regulatory process.<sup>2-4</sup>

## PARTICIPANTS/METHODS

Caregivers of females with Rett syndrome were recruited from the US, Canada, UK, and Israel with the assistance of patient advocacy groups to share insights in an online survey.\*

N=318 across participating countries:

- United States: N=82
- Canada: N=45
- United Kingdom: N=115
- Israel: N=76

Survey addressed challenging symptoms, meaningful clinical outcomes of potential treatments, and thoughts on gene therapy for caregivers of loved ones **aged 2-38 years**.

Deeper qualitative insights were captured through online questionnaire, discussion forum, and live video focus group.

- N=20 US caregivers of females with Rett syndrome aged **2-41 years**

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## CONTACT

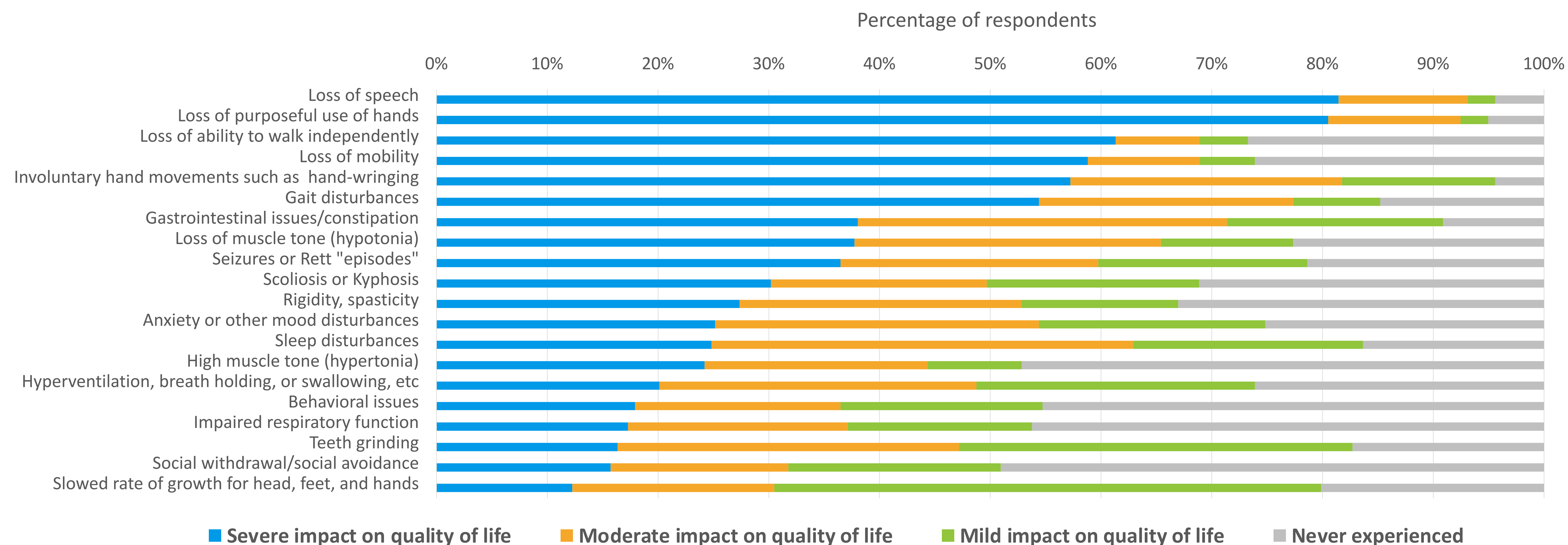
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## CAREGIVER INSIGHTS

### CAREGIVER-REPORTED IMPACT OF SYMPTOMS ON QUALITY OF LIFE



- Difficulties communicating needs and preferences resulting mainly from loss of speech and loss of purposeful hand use were identified as the greatest challenges
- Loss of purposeful hand movements, involuntary hand movements (eg, hand-wringing), and limited mobility impeded activities of daily living and independence; limited mobility also made falls and injury a safety concern
- Management of constipation and gastrointestinal pain were viewed as challenging, with a negative impact of their loved one's quality of life

*"She requires help with every day-to-day essential things – she needs to be hand-fed, can't select items on a communication device, can't hold a cup or even a toy."*

– Rett caregiver (Canada, child aged 0-6)

*"It must be so frustrating for her to not be able to do the simplest of things; move a piece of hair out of her eyes, scratch an itch somewhere. Someone has to be 100% attentive to her 100% of the time."*

– Rett caregiver (US, child aged 13-17)

*"The communication problem is the worst because there is no way to understand what she wants, especially when she is crying or nervous, and this increases her frustration and ours as well."*

– Rett caregiver (Israel, child aged 7-12)

*"Being unable to communicate is the hardest. When my daughter is in pain, I have no way of knowing what the cause is, and I am blindly trying to remedy it – I feel helpless."*

– Rett caregiver (UK, child aged 7-12)

*"We are aging along with her, and getting from point A to point B is more difficult; it also limits where we can take her, and what we can do."*

– Rett caregiver (US, child aged 18-26)

*"This is very frustrating for my child, and it is very hard on us as she needs assistance when trying to walk – it is very hard on our bodies as well."*

– Rett caregiver (Canada, child aged 13-17)

### CAREGIVER-REPORTED DESIRED IMPROVEMENTS FROM GENE THERAPY

#### Communication

The most important improvement evaluated by caregivers is the patient's **ability to express their needs and opinions**—it is invaluable

#### Hand Use

**Performing daily activities of living, such as eating and grooming**, are most impactful to both patients and caregivers; becomes more challenging as patients age

#### Mobility

**Ability to stand and take steps** becomes more concerning as patients age and become more difficult to carry and manage for caregivers

#### GI Issues

**Dependence on medication and the ability to reduce overall pain and anxiety** were the largest concerns; bowel issues were less concerning for respondents

#### Overall Anxiety

As age and patients become more agitated, the crying and screaming fits become more challenging for caregivers and families to manage

#### Breathing

Breath-holding and hyperventilation are highly concerning for caregivers—a key source of anxiety

### ATTITUDES TOWARD GENE THERAPY AND CLINICAL TRIALS

- Nearly all caregivers indicated they would be **willing to consider participation** in a gene therapy clinical trial
- Caregivers hopes for gene therapy varied based on their loved one's age
  - Seeking to stem the tide of regression, those with **girls less than 7 years** sought to **treat the genetic root cause**
  - Those with a daughter **age 7+** sought **symptom reduction and halting or slowing disease progression** in order to preserve or potentially improve their loved one's quality of life
  - **Caregivers of late teens and adults were wary of a treatment that only prolonged life span** since this group tends to worry a great deal about who will care for their daughters when they are no longer able to do so

### CAREGIVER INPUT INTO STUDY DESIGN

In developing the clinical trial protocols for 2 planned studies in females with Rett syndrome, endpoints were selected to reflect major concerns cited by caregivers:

- **Communication:** Observer-Reported Communication Ability (ORCA)
- **Hand use:** Rett Syndrome Hand Function Scale (RSHFS)
- **Mobility, Breathing, and Anxiety:** Revised Motor Behavior Assessment (R-MBA); Functional Mobility Scale in Rett Syndrome, Rett Syndrome Behavior Questionnaire
- **GI issues:** Gastrointestinal Health Questionnaire for Rett Syndrome

Additional caregiver-centric assessments include:

- Parental Global Impressions-Improvement
- Caregiver Top 3 Concerns Visual Analog Scale
- Rett Syndrome Caregiver Burden Inventory.

## CONCLUSION

Overall, caregivers reported that incremental improvements in speech, hand use, and mobility would improve the ability to communicate and perform daily tasks of living. Is it important to consider caregivers' insights when designing clinical trials, who are experts in caring for people living with Rett syndrome.