

Mapping the Top Concerns of Caregivers of Individuals With Rett Syndrome With Items on the Rett Syndrome Behaviour Questionnaire to Identify Clinically Meaningful Outcomes

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BACKGROUND

- Rett syndrome (RTT) is a severe genetic neurodevelopmental disorder characterized by multiple neurological and behavioral impairments¹
 - The prevalence of RTT is about 1 in 10,000–15,000 live female births²
 - Regression in RTT begins around 6–18 months of age³ and is characterized by loss of purposeful hand use and verbal communication as well as limited nonverbal skills, impaired motor skills, seizures, and behavioral and gastrointestinal issues¹
 - RTT has significant impact on family and caregiver quality of life⁴
 - Currently, there are no pharmacological treatment options for RTT
- The Rett Syndrome Behaviour Questionnaire (RSBQ) is a 45-item, caregiver-completed scale that assesses observable behaviors of individuals with RTT⁵

OBJECTIVE

- To associate items from the RSBQ to RTT-related health concerns that caregivers identified as problematic and most in need of treatment, which will be helpful when interpreting the meaningfulness of data from clinical trials

METHODS

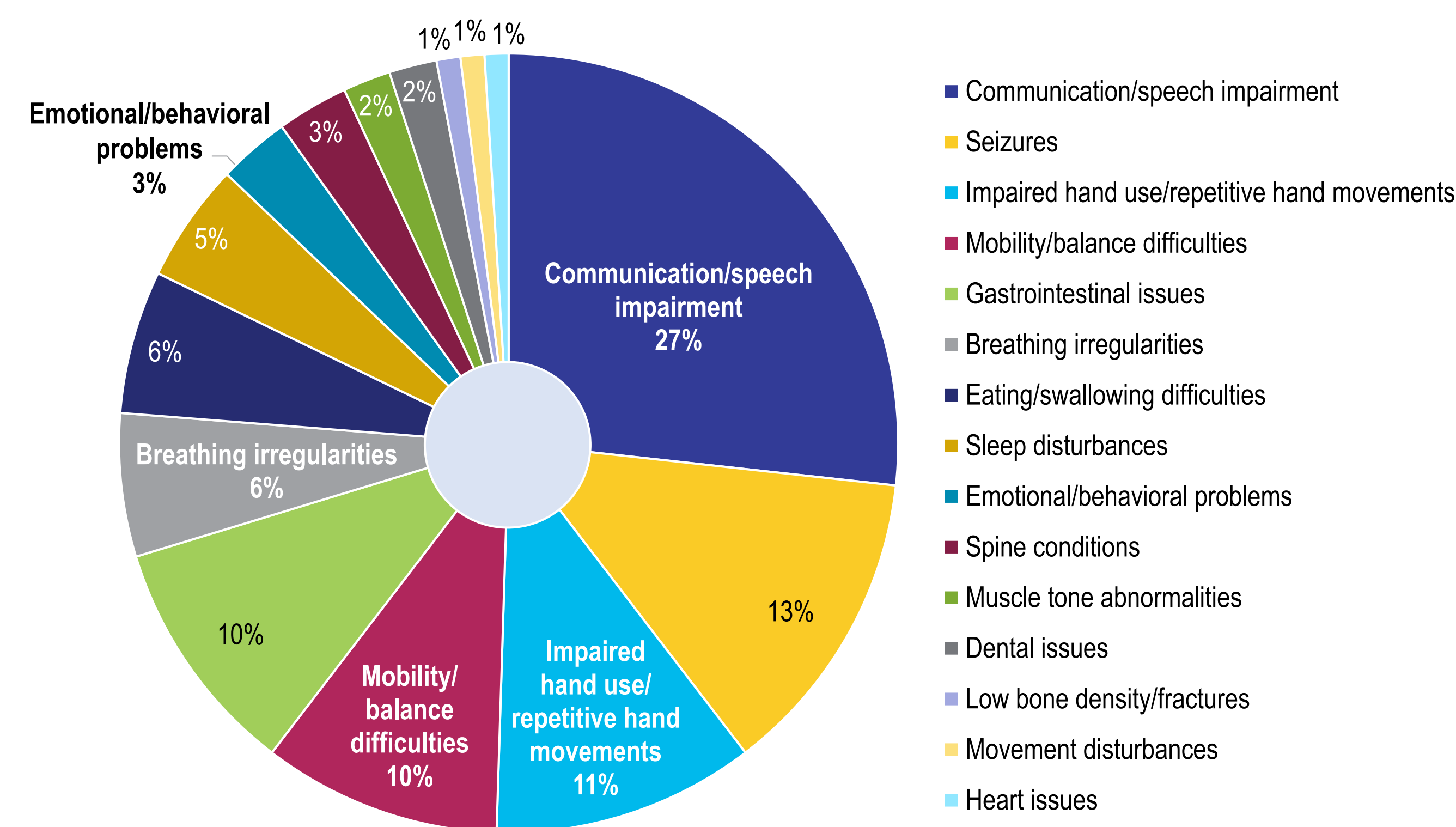
- The virtual Rett Syndrome Externally Led Patient-Focused Drug Development Meeting (PFDD) was held on March 11, 2022⁶
 - This PFDD provided an opportunity for key stakeholders, including the U.S. Food & Drug Administration, to gain feedback on RTT symptoms, daily impact, and perspectives on treatment directly from individuals with RTT and their families and caregivers and patient advocates
- During the PFDD, caregivers responded to questions via a real-time online survey, including “Select the top 3 most troublesome RTT-related health concerns that you have or have had” and “Which aspects of RTT would you rank today as most important for a possible new therapeutic to improve?”
- Although the questions during the PFDD included a range of answer choices, for the purpose of this analysis, only observable behavioral and emotional symptoms have been included, as aligned with the RSBQ
- Following the PFDD, a group of clinicians (a clinical psychologist, a pediatric neurologist, and a psychiatrist), all conducting research in intellectual/developmental disabilities, mapped the items on the RSBQ to the key observable symptoms/areas of need identified by the caregivers

RESULTS

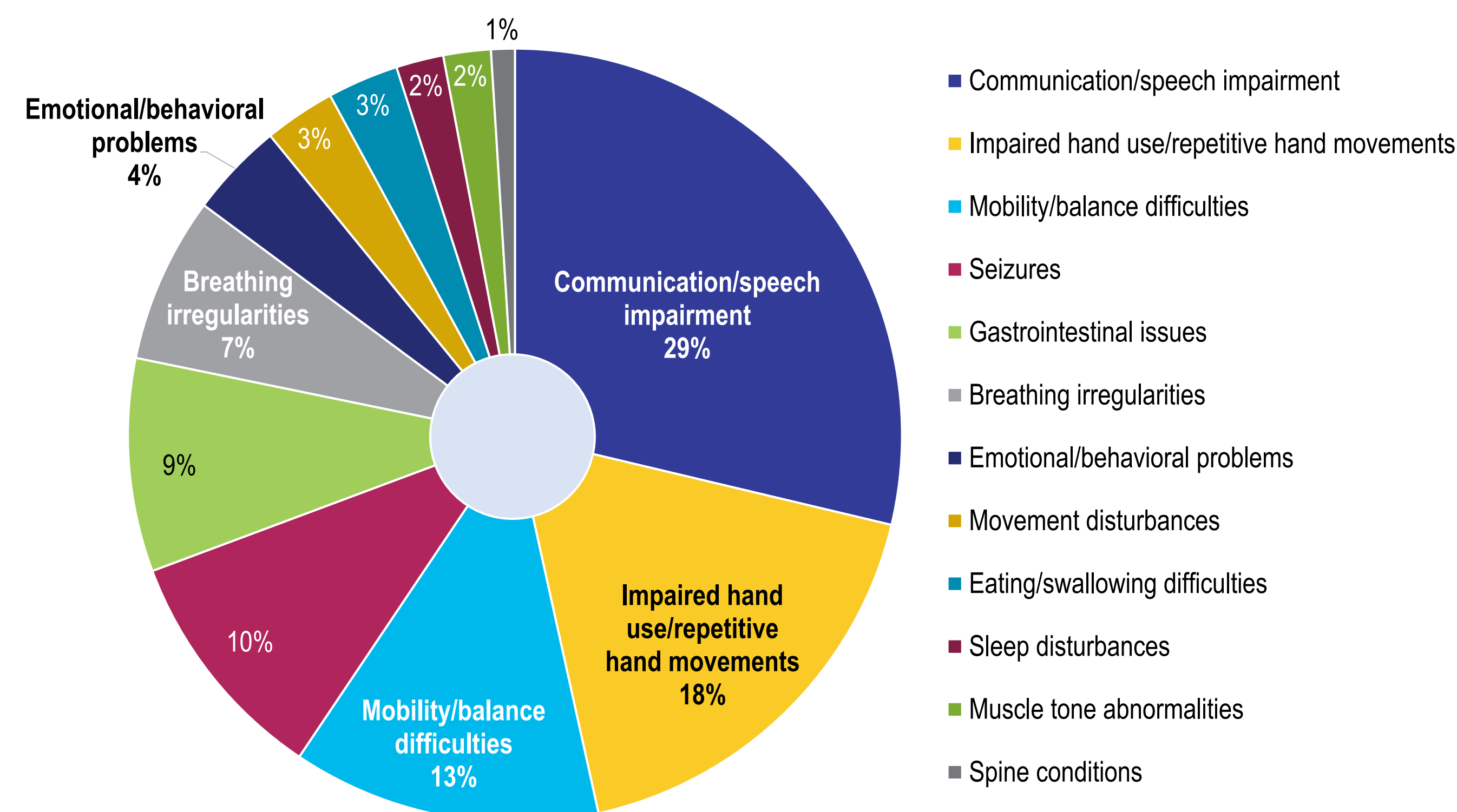
- The top 5 observable behavioral and emotional symptoms identified by caregivers as top RTT-related health concerns and areas in need of treatment were: communication/speech impairment; impaired hand use/repetitive hand movements; mobility/balance difficulties; breathing irregularities; and emotional/behavioral problems (Figure 1)
 - An analysis of the RTT Natural History Study, a long-term, longitudinal, observational study of >1000 individuals with RTT,^{7,8} also found symptoms that align well with those identified as top concerns of caregivers, including lack of effective communication, lack of hand use, abnormal walking/balance issues, and repetitive hand movements⁹

Figure 1. Caregiver responses to the PFDD online questions^a

Select the top 3 most troublesome RTT-related health concerns that you have or have had



Which aspects of RTT would you rank today as most important for a possible new therapeutic to improve? Select the top 3



^aAnswers are shown as percentages of the total responses. Bold text labeling within the graphs indicates responses for observable behavioral and emotional symptoms that were mapped to RSBQ questions. PFDD, Rett Syndrome Externally Led Patient-Focused Drug Development Meeting; RSBQ, Rett Syndrome Behaviour Questionnaire; RTT, Rett syndrome

- Of the 45 items from the RSBQ, 31 mapped to the top 5 observable behavioral and emotional symptom domains identified by caregivers during the PFDD as areas in need of treatments (Figure 2)
 - Other top concerns of caregivers, such as seizures and gastrointestinal issues, are not assessed by the RSBQ

Figure 2. The top 5 observable behavioral and emotional symptoms identified by caregivers of individuals with RTT (bold) mapped to items of the RSBQ

<p>Communication/speech impairment</p> <ul style="list-style-type: none"> Uses eye gaze to convey feelings, needs, and wishes 	<p>Breathing irregularities</p> <ul style="list-style-type: none"> There are times when the breath is held There are times when breathing is deep and fast Air or saliva is expelled from the mouth with force Swallows air Abdomen fills with air and sometimes feels hard
<p>Impaired hand use/repetitive hand movements</p> <ul style="list-style-type: none"> Does not use hands for purposeful grasping Hand movements are uniform and monotonous Restricted repertoire of hand movements Has difficulty in breaking/stopping hand stereotypies Makes repetitive movements involving fingers around the tongue Tendency to bring hands together in front of the chin or chest Has wounds on hands as a result of repetitive hand movements Makes repetitive hand movements with hands apart Amount of time looking at objects is longer than the time spent holding or manipulating them 	<p>Emotional/behavioral problems</p> <ul style="list-style-type: none"> Spells of screaming for no apparent reason during the day Abrupt changes in mood Times when appears miserable for no apparent reason Screams hysterically for long periods of time and cannot be consoled There are times when irritable for no apparent reason Spells of inconsolable crying for no apparent reason during the day Spells of apparent anxiety/fear in unfamiliar situations Seems frightened when there are sudden changes in own body position Spells of apparent panic Spells of screaming for no apparent reason during the night Spells of laughter for no apparent reason during the night Spells of inconsolable crying for no apparent reason during the night Spells of laughter for no apparent reason during the day Rocks self when hands are prevented from moving
<p>Mobility/balance</p> <ul style="list-style-type: none"> Although can stand independently, tends to lean on objects or people Walks with stiff legs 	

RSBQ, Rett Syndrome Behaviour Questionnaire; RTT, Rett Syndrome

CONCLUSIONS

- The RSBQ assesses core, global aspects of RTT identified by caregivers as being the most troublesome and most in need of novel therapeutics
- As such, the RSBQ can be used to assess important, relevant observable symptoms of RTT and can be used in clinical trials as a clinically meaningful outcome measure

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DISCLOSURES

DD and JMY are employees of and stakeholders in Acadia Pharmaceuticals Inc. PV is an employee of Yale University Child Study Center and Cogstate Ltd.

