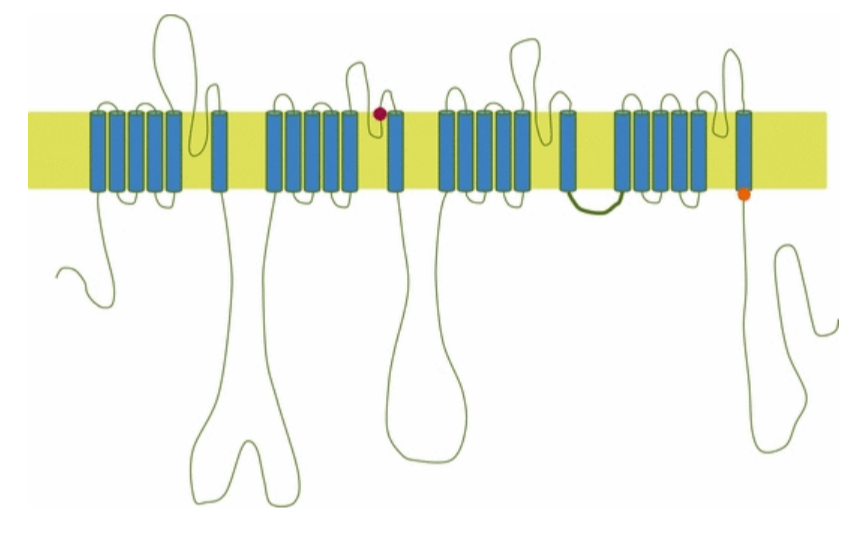


Background

- SCN8A-related epilepsy is a rare form of pediatric epileptic encephalopathy associated with pathogenic variants in the SCN8A gene encoding the voltage-gated sodium channel alpha subunit Na_v1.6, with devastating neurodevelopmental consequences.^{1,2}
- The phenotypic spectrum is broad, involving seizures, movement disorders, intellectual disability, and feeding challenges including swallowing difficulty and lack of head control.¹
- A recent caregiver survey found nearly 50% feeding tube use in patients with SCN8A-related epilepsy.²
- Importantly, enteral feeding is highly variable in this population, ranging from temporary to permanent.
- Feeding challenges extend to patients who do not require enteral feeds, and difficulties relate to a combination of medical, motor, behavioral, and sensory factors.
- These challenges have important implications for medication intake and are associated with appreciable negative impact on patients and their caregivers.
- Given the heterogeneity in feeding needs in this population, we aimed to explore medication formulation considerations and priorities for patients with SCN8A-related epilepsy via a caregiver survey.



No. 1.6 mutations associated with SCN8A-related epilepsy (Oliva, Berkovic & Petrou 2012 Epilepsia)

Methods

- An explorative qualitative research design was utilized, comprising a feeding and medication formulation survey conducted by The Cute Syndrome Foundation in collaboration with Praxis and other partners in an SCN8A-caregiver population.
- Participants were recruited from an online (Facebook) support group of 355 families.
- The survey was conducted electronically from May-July 2021 and consisted of 20 questions capturing participant feeding and medication delivery methods, needs, challenges and formulation preferences.
- Findings are summarized for all participants, regardless of feeding method, and further within oral and enteral feeders separately.

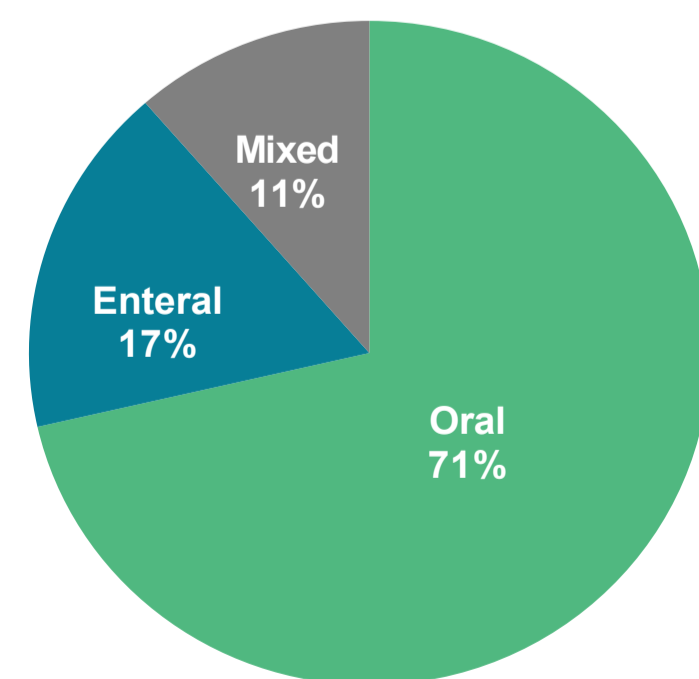


Participant Feeding Patterns

Participant Feeding Patterns

- A total of 35 survey responses were received from caregivers of participants with SCN8A-related epilepsy.
- These included responses from caregivers representing (Fig. 1):
 - 25 oral feeders
 - 6 exclusive enteral feeders
 - 4 mixed oral and enteral feeders

Figure 1. Participant feeding patterns



Participant Age & Formulation Preferences

Participant Age

- Participants ranged in age from 13 months to 23 years
- The majority of responses were from caregivers of children aged 2-5 years and 6-10 years (Table 1).

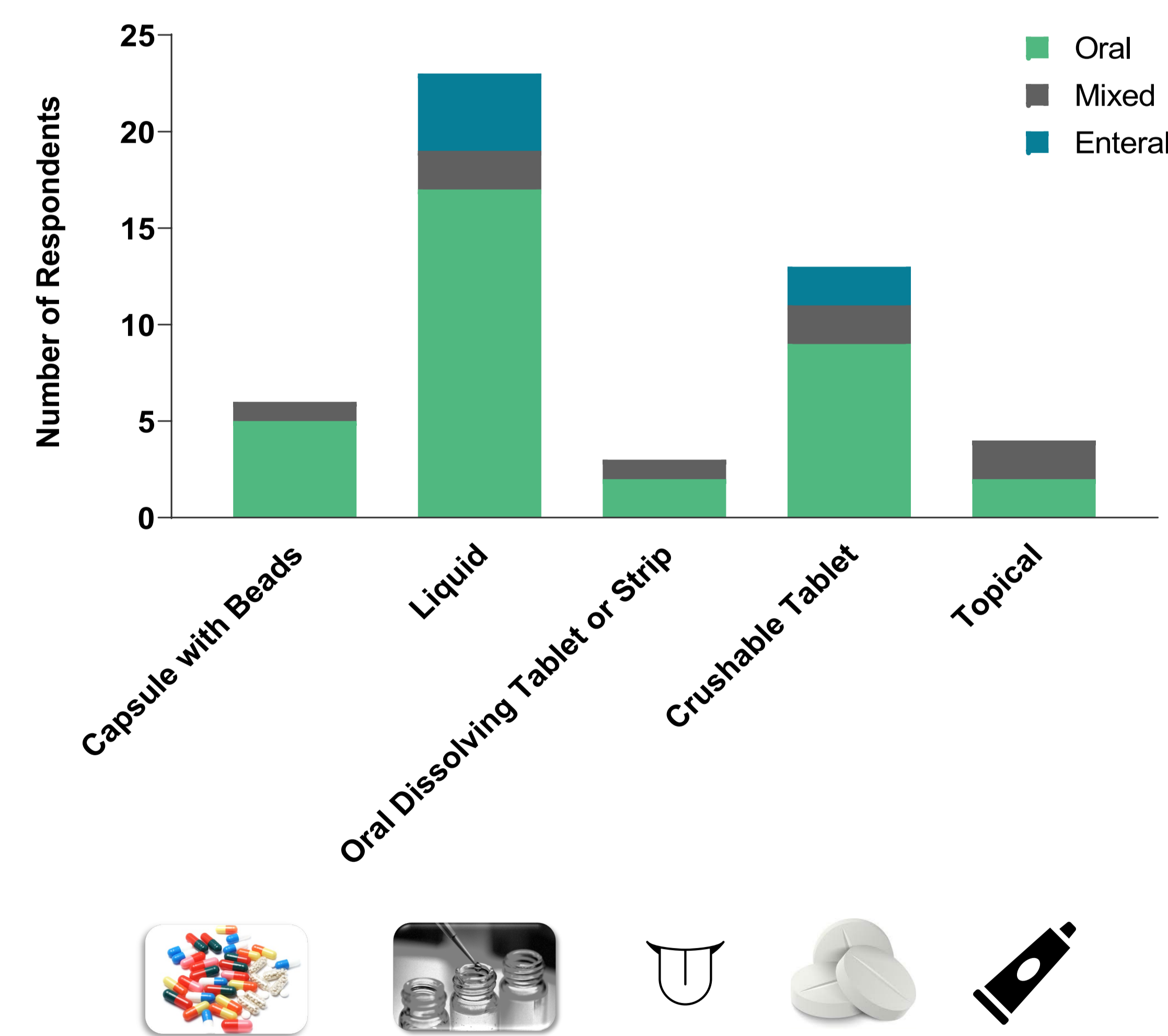
Table 1. Participant age breakdown

Participant age	Frequency
< 2 years	4 (11.4%)
2 – 5 years	10 (28.6%)
6 – 10 years	15 (42.9%)
≥ 11 years	6 (17.1%)

Formulation Preferences

- Across all participants, the most convenient medication formulation was liquid (Fig. 2)
 - 23 (66%) respondents, regardless of feeding pattern
 - 17 oral, 2 mixed, 4 enteral
- The second most convenient formulation was crushable tablet (Fig. 2)
 - 13 (37%) respondents (9 oral, 2 mixed, 2 enteral).
- Survey feedback indicated that non-crushable tablets are problematic for both oral feeders (who may be unable to swallow pills) and tube feeders (due to inability to fully suspend tablet).

Figure 2. Medication formulation preferences

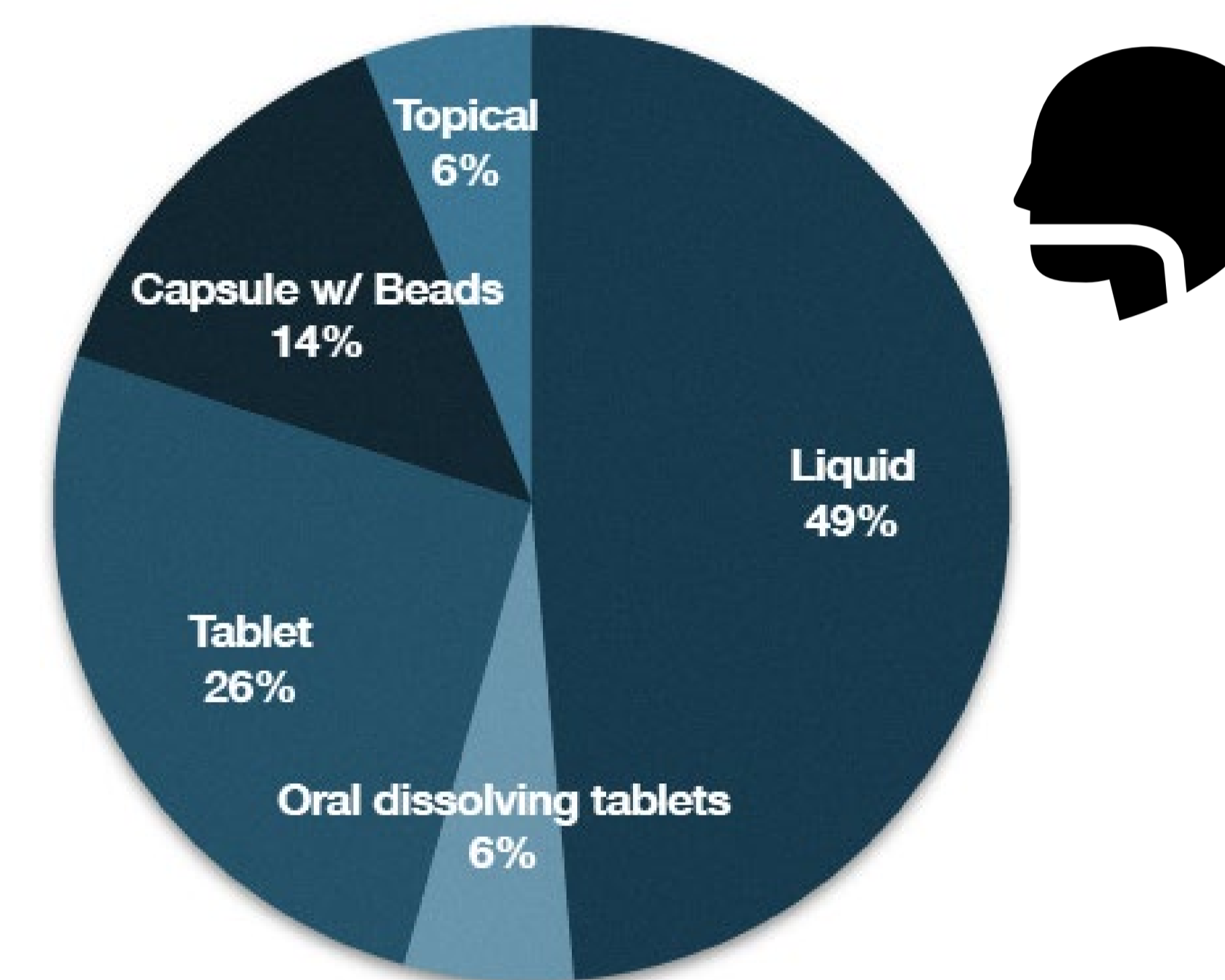


Formulation Preferences by Feeding Type

Learnings Specific to Oral Feeders

- Within oral feeders, liquid formulation was preferred by 49% of respondents, followed by crushable tablet formulation (26%) (Fig. 3)

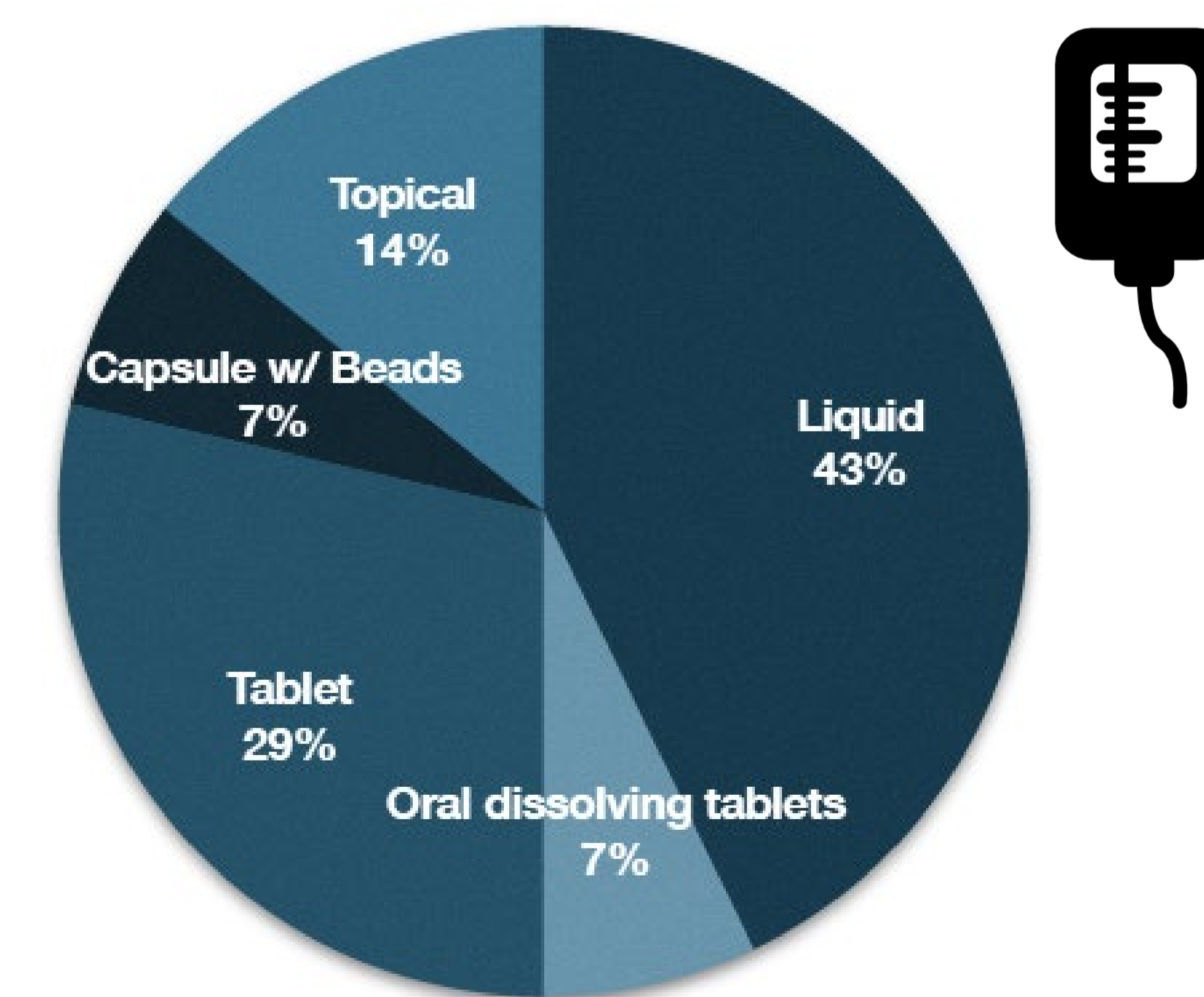
Figure 3. Medication formulation preferences in oral feeders



Learnings Specific to Enteral (Tube) Feeders

- Similarly, within tube feeders, liquid formulation was deemed more convenient (43%), followed by crushable tablet formulation (29%) (Fig. 3).

Figure 4. Medication formulation preferences in enteral (tube) feeders



Patient & Caregiver Perspectives

Summary of preferences

- Liquid formulations preferred, followed closely by crushable tablets
- Preference for liquid formulations that are keto-friendly
- Flavorless or near-flavorless formulations for oral eaters, allowing caregivers to flavor and/or use carriers most effective for their child
- Consideration of tube-clogging as a particular concern for tube feeders (particularly with capsules and coated tablets)
- Clearly stated limitations to administration (eg, mixing with other medications before ingestion)
- Clearly stated instructions where flexibility is allowable (eg, mixing with carrier foods)
- Convenient packaging for liquid formulations that makes transportation easy (including syringe caps and a carrying case)
- Easy-to-divide tablets, if necessary
- Limited number of capsules, for ease of opening

Conclusions

- This survey provides important patient-guided perspectives for consideration in drug development efforts in SCN8A, specifically as they relate to medication formulation preferences among patients and their caregivers.
- Regardless of patient feeding method, liquid formulation was preferred, followed by crushable tablet.
- Our findings further emphasize the heterogenous nature of this population, and highlight the need for investigations into liquid formulations, enteral tube-compatible formulations, as well as formulations allowing as much flexibility in administration as is feasible, safe, and effective to reduce the disease impact on patients and caregivers, while facilitating medication intake.
- Findings from this study are anticipated to inform clinical trial design and patient-guided drug development efforts in SCN8A-related epilepsy.

References

1. Wagnon et al. 2015 *Annals Clin Transl Neurol*
2. Grayson et al. 2020 *AAN Annual Meeting*
3. Oliva, Berkovic & Petrou 2012 *Epilepsia*

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