

Building a Research Roadmap for ASXL-related disorders: Determining family research priorities



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Background

The ASXL Rare Research Endowment (ARRE) Foundation is a family-led patient advocacy organization with the mission to improve the quality of life for individuals living with ultra-rare neurodevelopmental disorders caused by pathogenic variants in one of the ASXL genes: **Bohring-Opitz Syndrome (ASXL1)**, **Shashi-Pena Syndrome (ASXL2)**, and **Bainbridge-Ropers Syndrome (ASXL3)**.

Common clinical features of ASXL syndromes include developmental delay and intellectual disability, absent speech, seizures, hypotonia, feeding difficulties, severe constipation, and self-injury. It is thought that approximately 500 individuals are diagnosed with ASXL-related disorders world-wide and that many more remain undiagnosed.

Families living with ASXL-related disorders live in a sea of unknowns as there is currently limited research interest and no published standard of care.

Why did we do this?
To define the research that will have the biggest impact on the individuals and families who are affected by ASXL syndromes every day.

TAKE SURVEY

Methodology

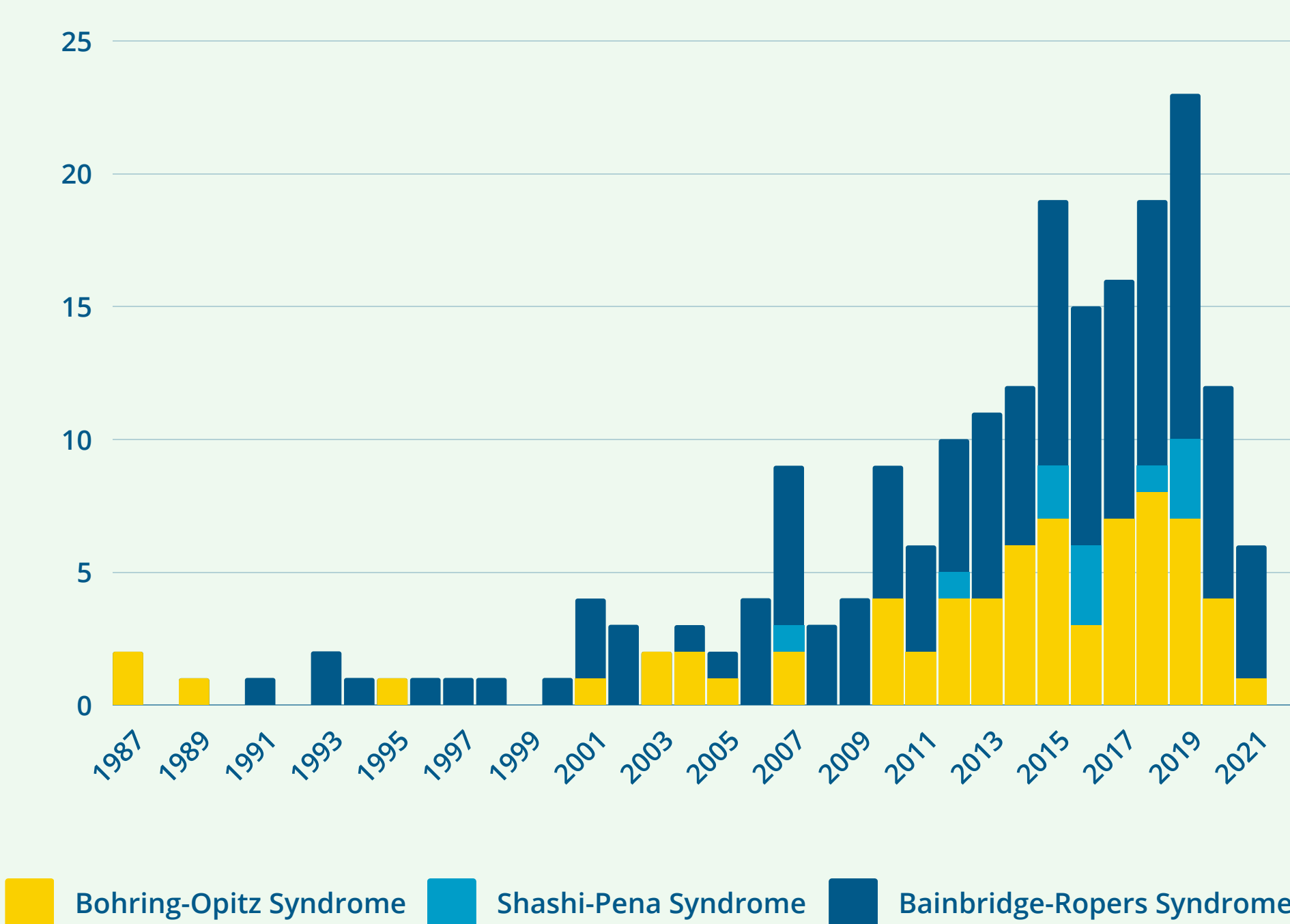
Prior to developing the survey, the ARRE Foundation conducted 3 virtual focus group meetings with families to understand what questions and informational needs families had to inform the development of the survey. Additionally, audits of each syndrome's online family support group were conducted to assess the breadth and frequency of concerns.

The final survey design included basic demographic questions as well as three research priority questions (below). Qualitative responses were coded by staff and grouped into common categories for analysis. The survey was distributed and promoted via ARRE Foundation's email list and social media accounts as well as within each syndrome's online support group.

Results

ARRE Foundation received 205 complete survey responses from caregivers in 28 countries ($N_{ASXL1}=69$, $N_{ASXL2}=11$, and $N_{ASXL3}=124$). The average age of affected individuals included was 9 years ($SD=6.9$) and ranged from 1-35 years (Figure 1). 77% of affected individuals were approximately 12 years or younger (born in 2010 or later).

Patients by birth year



Research priority questions

- If we knew more about _____, life would be better.
- Which symptom or challenge is the most important to you that we try to alleviate or improve?
- How should the ARRE Foundation balance the following:



What did we learn?

1

"Future-related" questions are a top priority.

"If we knew more about _____, life would be better."

ASXL1/Bohring-Opitz (N=69)	Frequency	ASXL2/Shashi-Pena (N=11)	Frequency	ASXL3/Bainbridge-Ropers (N=124)	Frequency
Future-related	13	Future-related	5	Syndrome itself	22
Syndrome itself	10			Future-related	21
Behavior	6			Communication	18
GI-related	5			GI-related	14
Pain	5			Behavior	11

"Future-related" questions included wanting to know more about the syndrome itself, wanting to know what's coming next in their loved one's life, and what their loved one is capable of achieving.

2

There is commonality across syndromes about important symptoms, but variation by syndrome and patient age.

Most important symptom (by syndrome)

ASXL1/Bohring-Opitz (N=69)	Frequency	ASXL2/Shashi-Pena (N=11)	Frequency	ASXL3/Bainbridge-Ropers (N=124)	Frequency
GI-related	21	Hypotonia	4	Communication	55
Communication	11	Behavior	3	Behavior	39
Respiratory issues	11	Intellectual disability	3	GI-related	27
Mobility	9	Seizures	2	Intellectual disability	13
Intellectual disability	7			Sleep	13

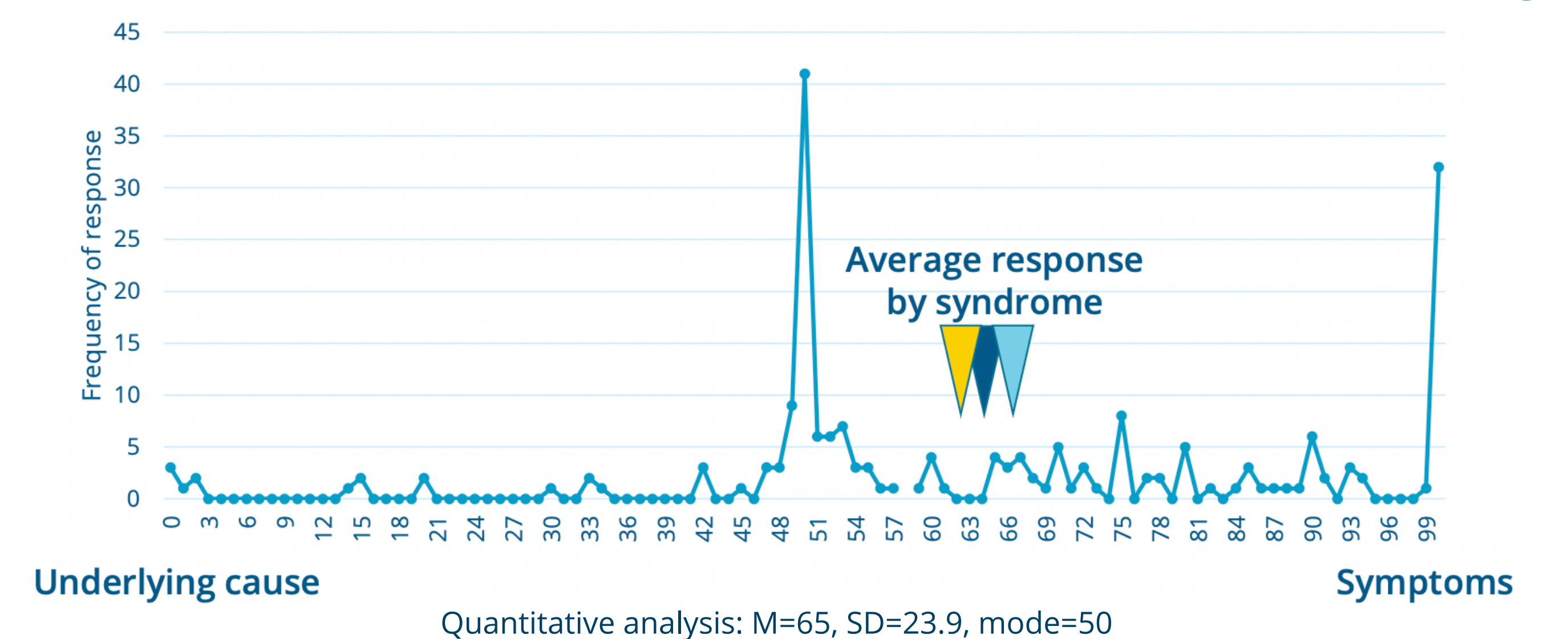
Most important symptom (by age group)

Infant/toddler (2021-2022) (N=9)	Frequency	Preschool (2018-2020) (N=54)	Frequency	Child (2010-2017) (N=98)	Frequency	Teen (2004-2009) (N=25)	Frequency	Adult (2003 and earlier) (N=21)	Frequency
Developmental delay	2	Communication	21	Communication	36	Behavior	8	Behavior	8
		GI-related	20	Behavior	27	Communication	6	Communication	4
		Hypotonia	7	GI-related	17	GI-related	6	GI-related	4
		Intellectual disability	7	Mobility	12	Intellectual disability	4	Mobility	2
		Behavior	5	Sleep	11	Mobility	4		

3

There is agreement across syndromes to support research that leans more toward symptom management.

How should the ARRE Foundation balance research addressing...



Conclusion

Results from this family survey indicated that the areas of greatest priority for families across syndromes were related to the management of GI-related symptoms, communication, behavior, and intellectual disability. Additionally, families hope to see the ARRE Foundation invest in research focused both on the underlying cause as well as symptom management.

Future work will include the development of a research strategic plan that is centered on the needs of families as defined through this survey.



arrefoundation.org/research-roadmap