


SIMONS SEARCHLIGHT

MED13L

August 5-7, 2022

Dr. Wendy Chung

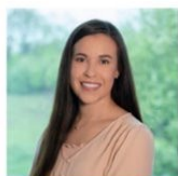
A close-up photograph of two hands clasped together in a supportive grip. The hand on the left is larger and has a reddish-brown sleeve, while the hand on the right is smaller and has a green sleeve. The background is a soft, out-of-focus yellowish-green. The text is centered at the bottom of the image.

Simons Searchlight is an international research program with the goal of accelerating science and improving lives for people with rare genetic neurodevelopmental disorders.

Simons Searchlight Team



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Tempus



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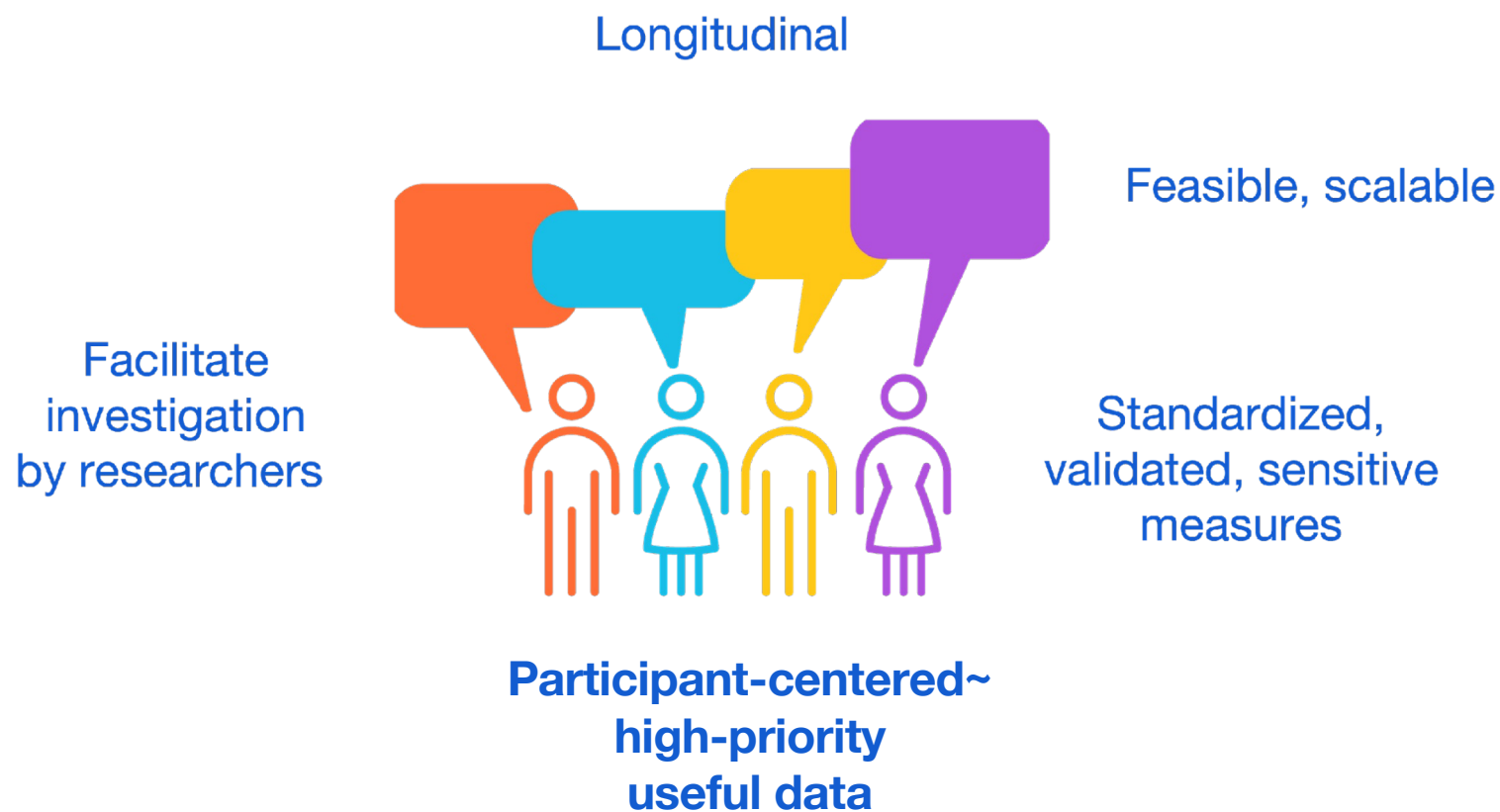
Lauren Walsh
Geisinger



Curtis Weaver
Geisinger

SIMONS
SEARCHLIGHT

Priorities for Searchlight Data Collection



What are the **goals** of Simons Searchlight?

Our mission is to shed light on these conditions by collecting high quality natural history data and building strong partnerships between researchers, industry and families.



Collect detailed **medical and behavioral histories** along with blood **samples**



Synthesize the information you provide and **share results back to families**



Freely share data and samples with qualified researchers



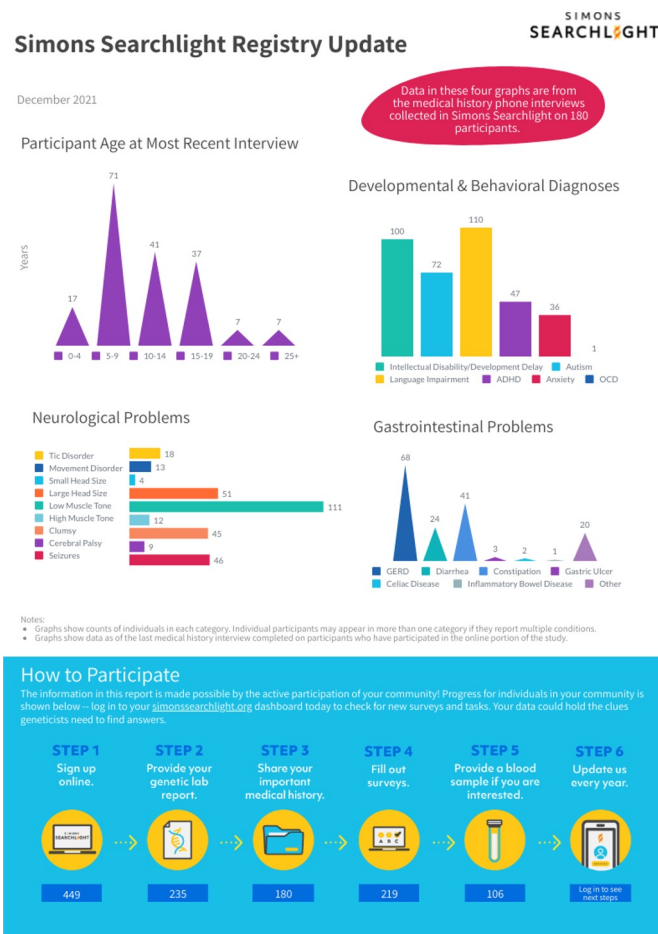
Connect participants and researchers from around the world



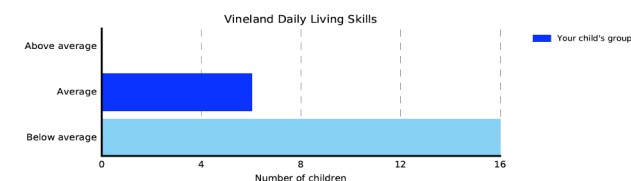
Promote better understanding of these genetic changes

Information for Families

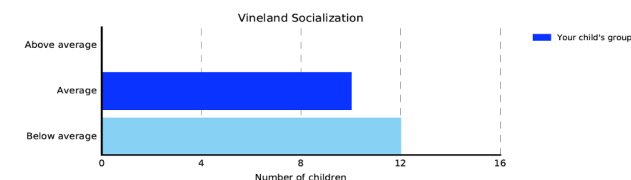
- Personalized reports: SCQ, SRS, CBCL and Vineland located on your dashboard
- Summary snapshots on your gene page
- Presentations at conferences and meetings



The Vineland Daily Living Skills scale is a survey of everyday self-care, household skills and responsibilities. For younger children this might include dressing or potty-training, and for older children this might include helping to clean the house or using money.



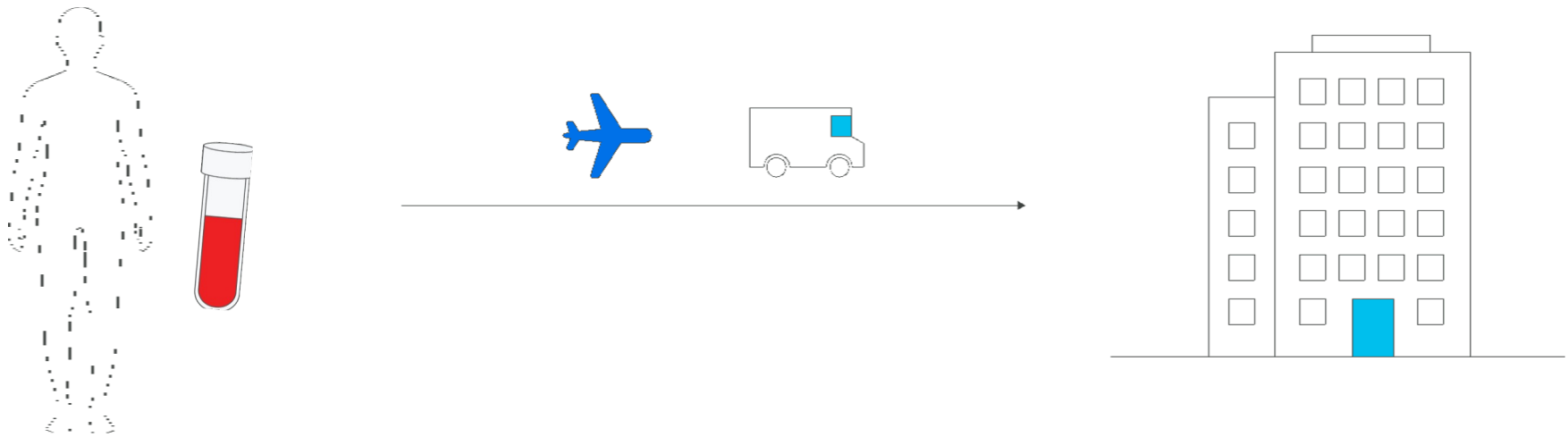
The Vineland Socialization scale is a survey of social skills. For younger children this might include playing with others, and in older children this might include following social "rules".



Thank you for contributing to the Simons VIP study!

Please remember these results are based on your responses to an online computerized research survey. They are not monitored or evaluated by a professional, and they do not represent a clinical evaluation or clinical feedback. No questionnaire is 100 percent accurate. If you ever have any questions or concerns, please talk to your doctor.

Simons Searchlight participants can donate a blood sample



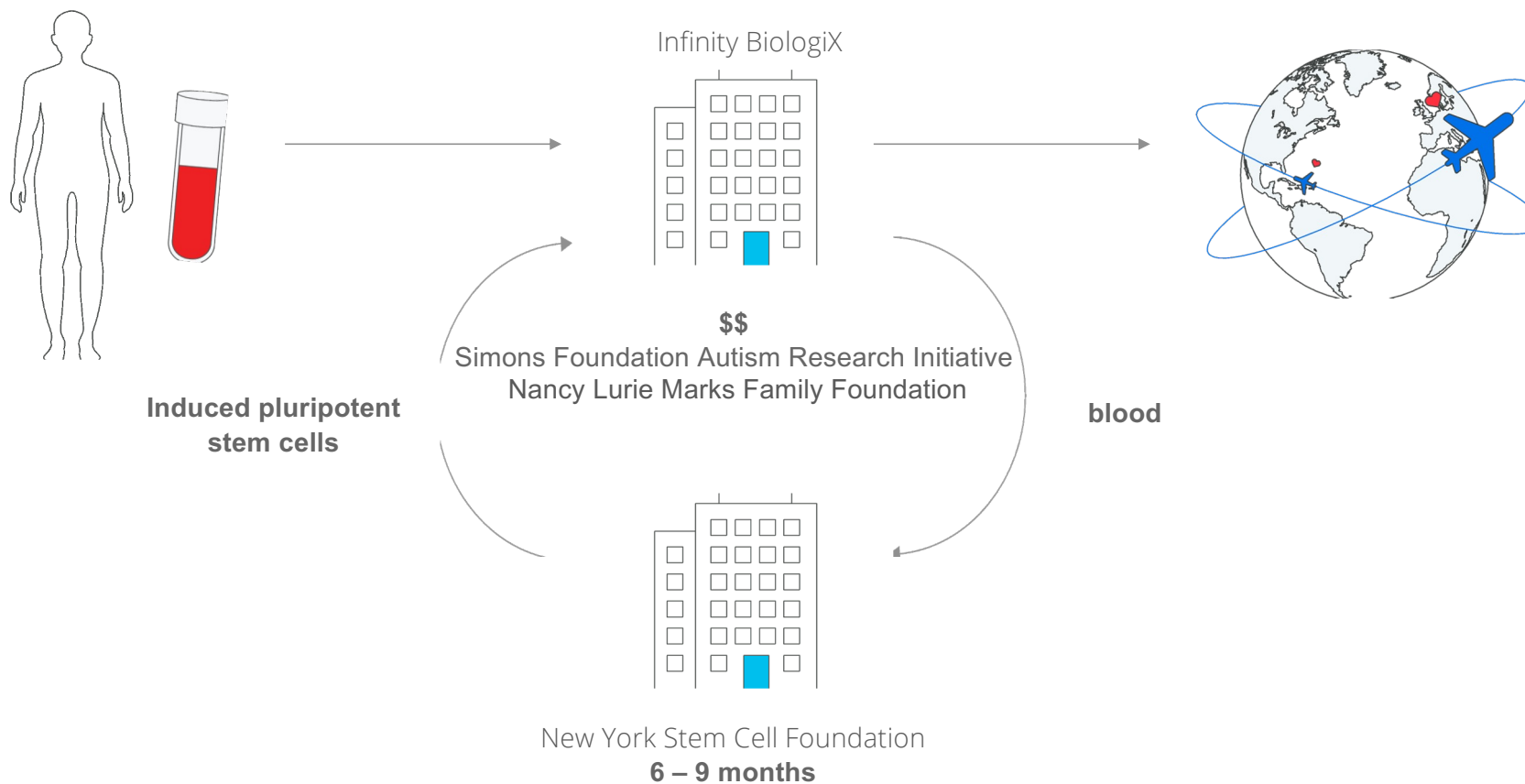
Blood collection steps

Step 1: A blood sample kit is mailed to you free of charge

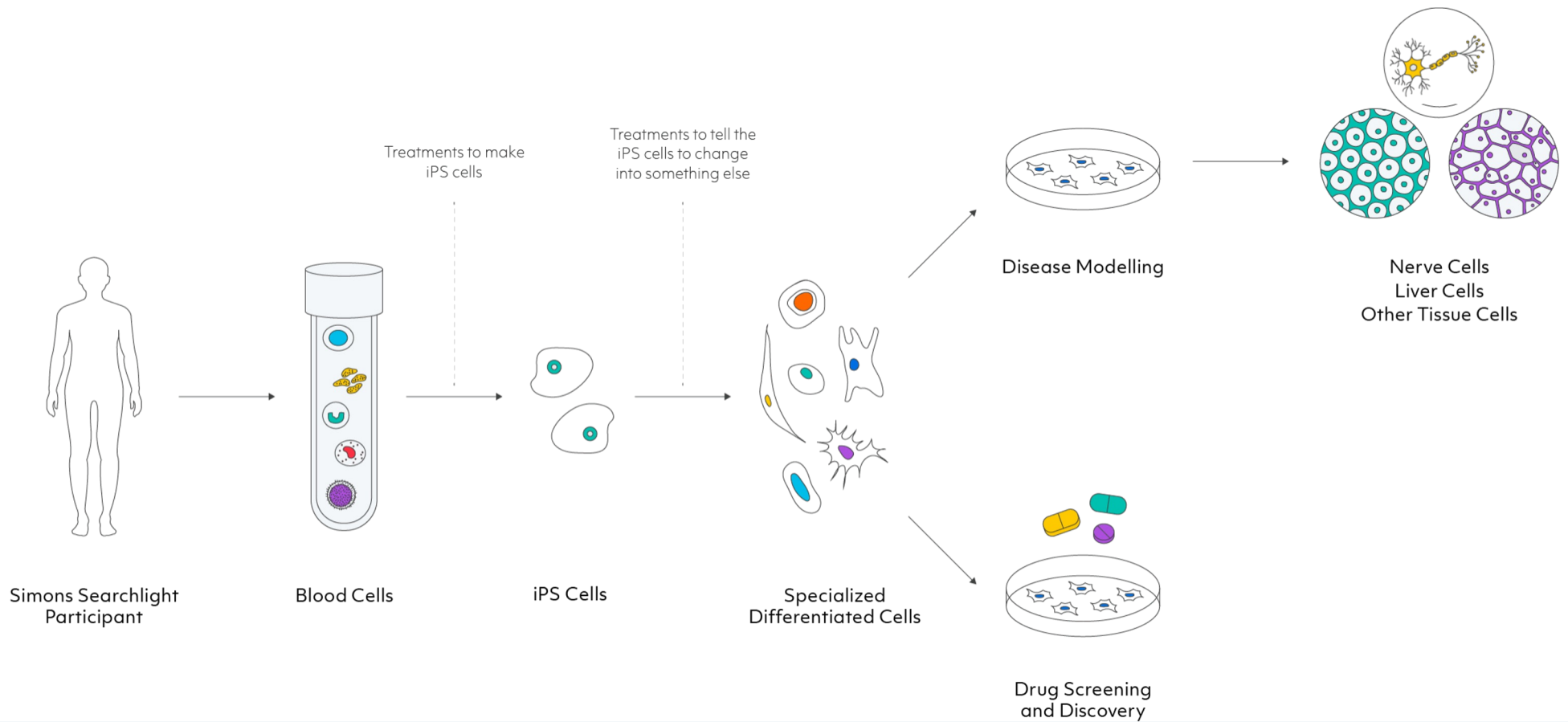
Step 2: Make an appointment at a local Quest Labs to have the blood drawn

Step 3: The lab mails the kit back to Simons Searchlight

How will the sample be used in research and why is this important?



What are induced pluripotent stem cells (iPSCs)?



Quality of Life Survey

Quality of Life Inventory - Disability

(18 individuals with MED13L)

Health & Well-being

Is in good health

83%

Sleeps well

72%

Has energy for daily activities

94%

Is alert and aware

100%

Activities & the Outdoors

Enjoys moving their body

83%

Enjoys feeling steady during activities

72%

Enjoys physical activities

83%

Enjoys outings

56%

Enjoys time outdoors

72%

Feelings & Emotions

In a good mood

89%

Smiles

94%

Expresses happiness using body language

78%

Laughs or giggles

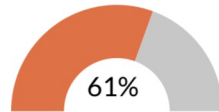
89%

Quality of Life Inventory - Disability

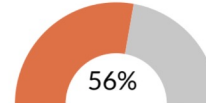
(18 individuals with MED13L)

Family & Friends

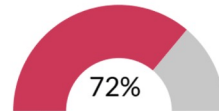
Happy when they are understood



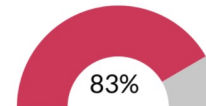
Enjoys socializing at mealtimes



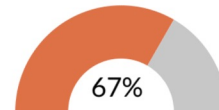
Feels relaxed while making eye contact



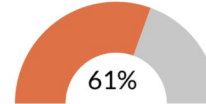
Enjoys interacting with others



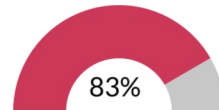
Initiates greetings with others



Excited by upcoming activities

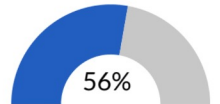


Happy to be included

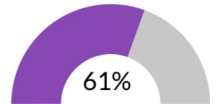


Daily Life

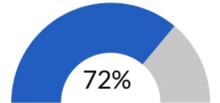
Expresses their needs



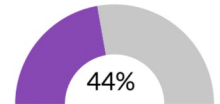
Makes own choices for activities



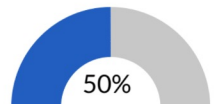
Likes using technology



Helps with routines



Enjoys making things



The MED13L Registry in Simons Searchlight

Progress of Individuals with MED13L



We are a long-term study, gathering new information from you every year.

MED13L Biospecimens

12 individuals contributed to the available biospecimens

Available Sample	MED13L Carriers
Induced pluripotent stem cells (iPSCs)	-
Lymphoblastoid cell lines	2
Whole blood DNA	5
Saliva DNA	2

* 6 iPSCs coming soon

MED13L iPS Cells

	p. nomen	# of Carriers	Available
1	p.Gln 1537 *	1	Upcoming
2	p. Asp 697 Glufs*19	1	Upcoming
3	p.Trp 88 *	1	Upcoming
4	p.Trp 1359 *	1	Upcoming
5	p.Arg 1900 *	1	Upcoming
6	p.Pro 866 Leu	1	Upcoming

- Researchers worldwide can request (non- and for-profit), nominal fee \$120/sample
- Request through SFARI Base
- Researchers can submit requests now

Variants Observed in MED13L 57 individuals

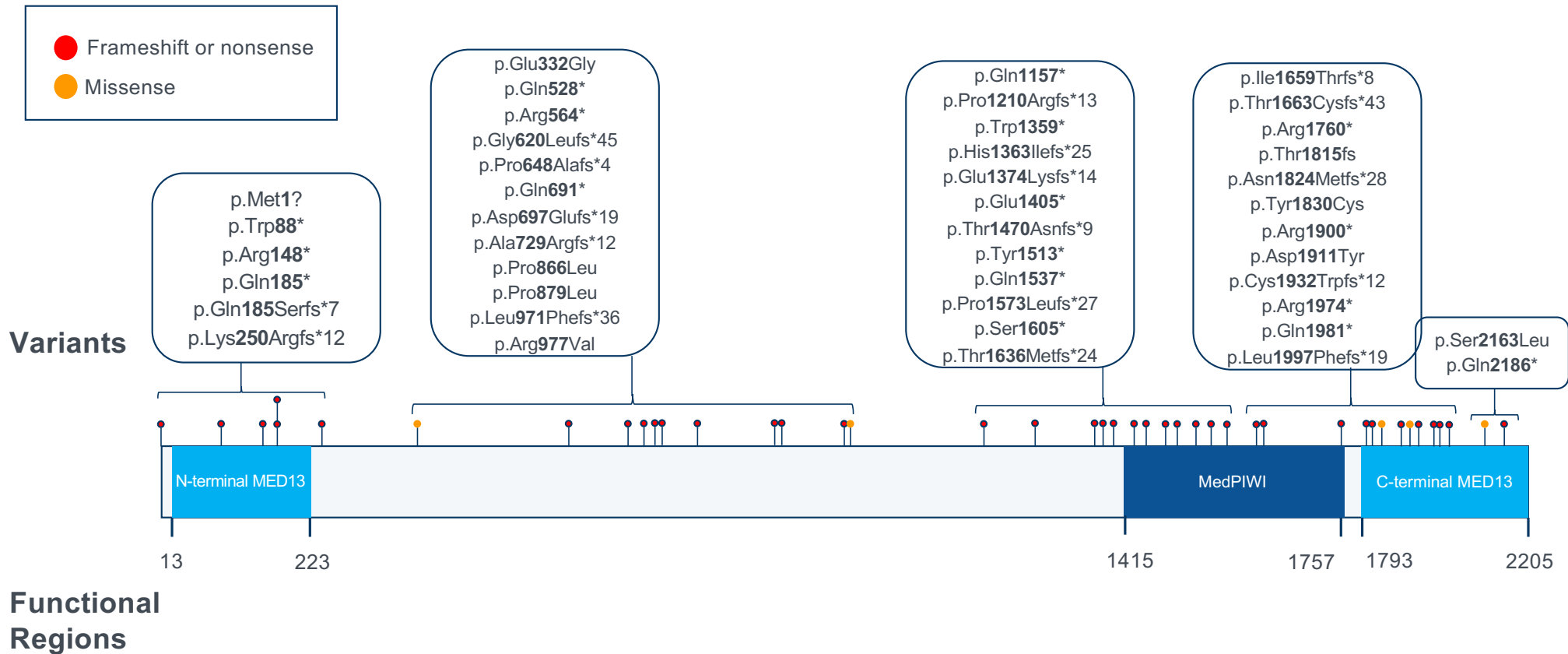
Variant Category	Number	Breakpoints	Variant Classification
CNV breakpoints	2*	Chr12:116673140-116676995	Pathogenic
		Chr12:116472293-116558850	Pathogenic
		Chr12:116528514-116605811	Likely Pathogenic
		Chr12:116427981-116560895	Pathogenic
		Chr12:116475997-116622480	Likely Pathogenic
		Chr12:114895862-115110038	Pathogenic
		Chr12:116500909-116569088	Pathogenic
Variant Category	Number	c. nomen	Variant Classification
Splice site or intronic		2790+1G>A	Pathogenic
	2*	5588+1 G>A	Likely Pathogenic
		6226-1G>C	Pathogenic
Variant Category	Number	p. nomen	Variant Classification
Missense		p.Glu332Gly	Likely Pathogenic
	2	p.Pro866Leu	Pathogenic
		p.Pro879Leu	Likely Pathogenic
		p.Arg977Val	Likely Pathogenic
		p.Asp1911Tyr	Likely Pathogenic
		p.Ser2163Leu	Likely Pathogenic

Variant Category	Number	p. nomen	Variant Classification
Frameshift or nonsense		p.Met1?	Pathogenic
		p.Trp88*	Pathogenic
	2	p.Arg148*	Pathogenic
		p.Gln185*	Likely Pathogenic
		p.Gln185Serfs*7	Pathogenic
		p.Lys250Argfs*12	Pathogenic
		p.Gln528*	Pathogenic
	2*	p.Arg564*	Pathogenic
		p.Gly620Leufs*45	Pathogenic
		p.Pro648Alafs*4	Pathogenic
		p.Gln691*	Pathogenic
		p.Asp697Glufs*19	Pathogenic
		p.Ala729Argfs*12	Pathogenic
		p.Leu971Phfs*36	Pathogenic
		p.Gln1157*	Pathogenic
		p.Trp1359*	Pathogenic
		p.His1363Ilefs*25	Likely Pathogenic
		p.Glu1374Lysfs*14	Pathogenic
		p.Glu1405*	Pathogenic
		p.Thr1470Asnfs*9	Pathogenic
		p.Tyr1513*	Pathogenic
		p.Gln1537*	Pathogenic

Variants Observed in MED13L 57 individuals (continued)

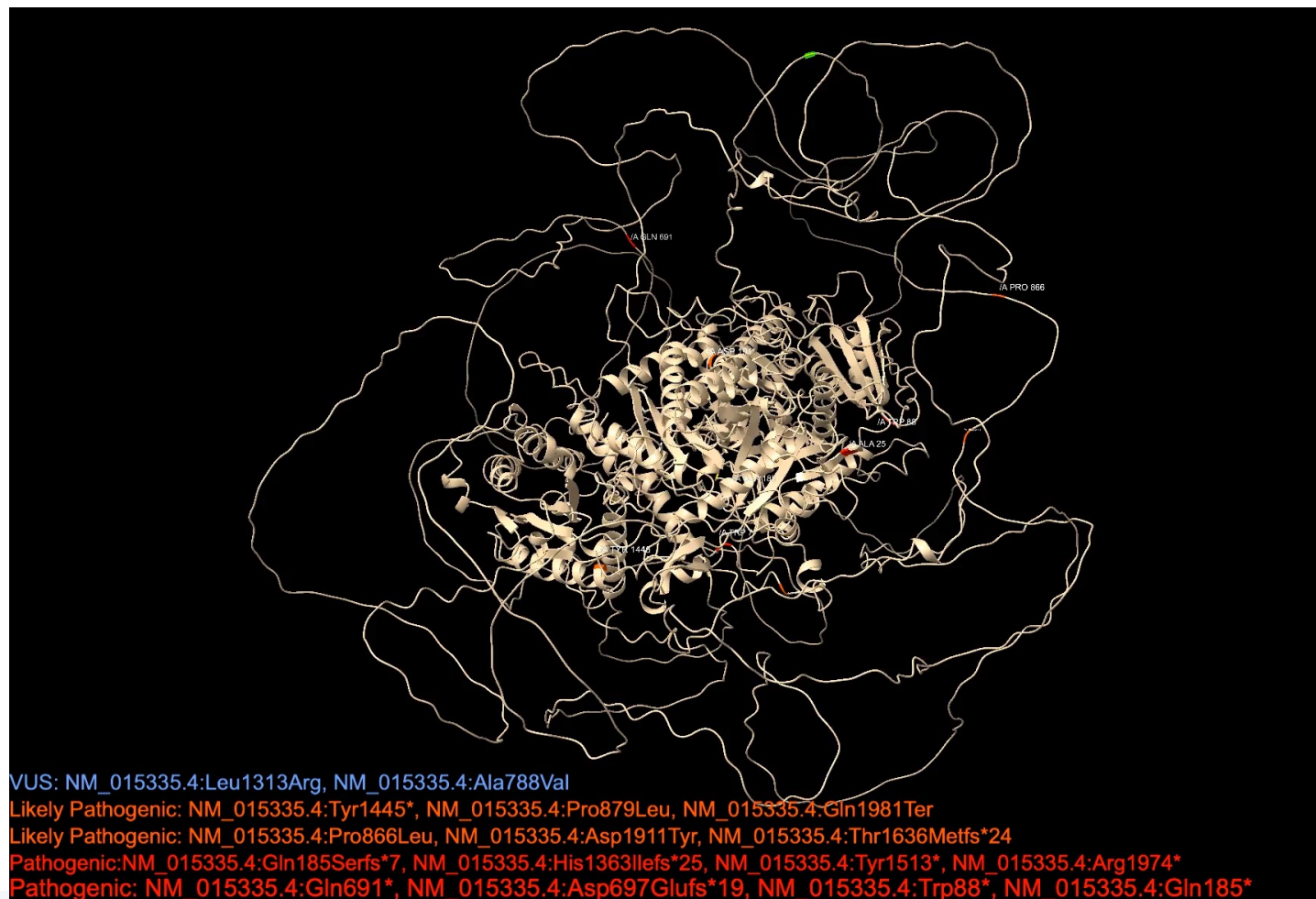
Variant Category	Number	p.nomen	Variant Classification
Frameshift or nonsense		p.Pro1573Leufs*27	Pathogenic
		p.Ser1605*	Pathogenic
		p.Thr1636Metfs*24	Likely Pathogenic
		p.Ile1659Thrfs*8	Pathogenic
		p.Thr1663Cysfs*43	Pathogenic
		p.Arg1760*	Pathogenic
		p.Thr1815fs	Pathogenic
		p.Asn1824Metfs*28	Pathogenic
		p.Arg1900*	Pathogenic
		p.Cys1932Trpfs*12	Pathogenic
		p.Arg1974*	Pathogenic
		p.Gln1981*	Likely Pathogenic
		p.Leu1997Phefs*19	Pathogenic
		p.Gln2186*	Likely Pathogenic

Variants Observed in MED13L



6 VUS, not shown

Protein structure of MED13L

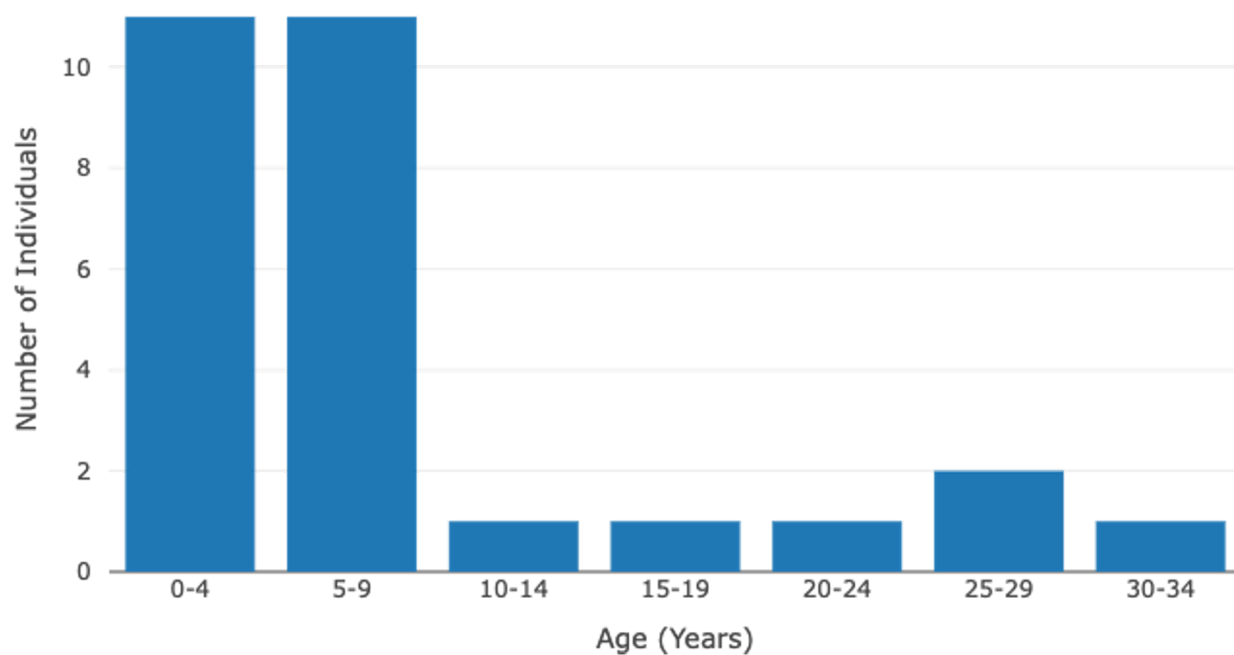


Simons Searchlight MED13L Medical History Data



28 participants with pathogenic or likely pathogenic variants

Age at Most Recent Medical History Interview (28 individuals)



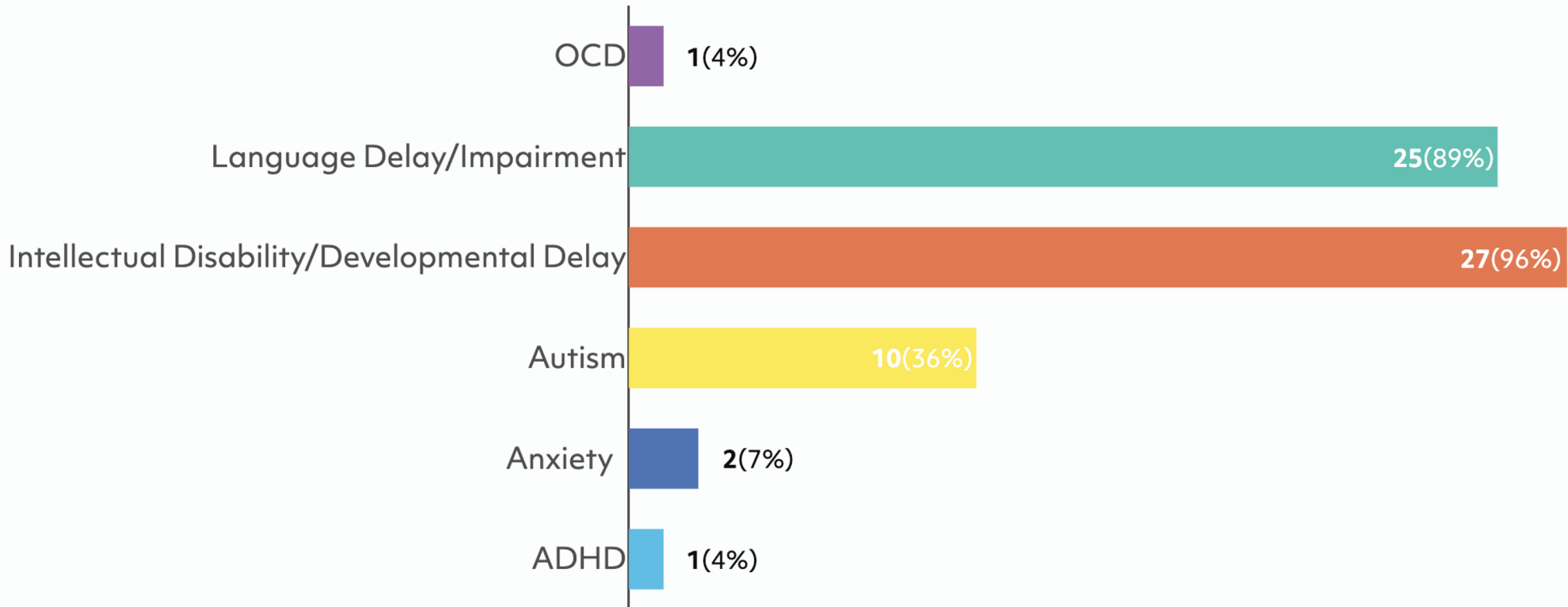
Age Range
2yr(s) - 30yr(s)

24
Participants under 18

Average Age
8 yr(s)

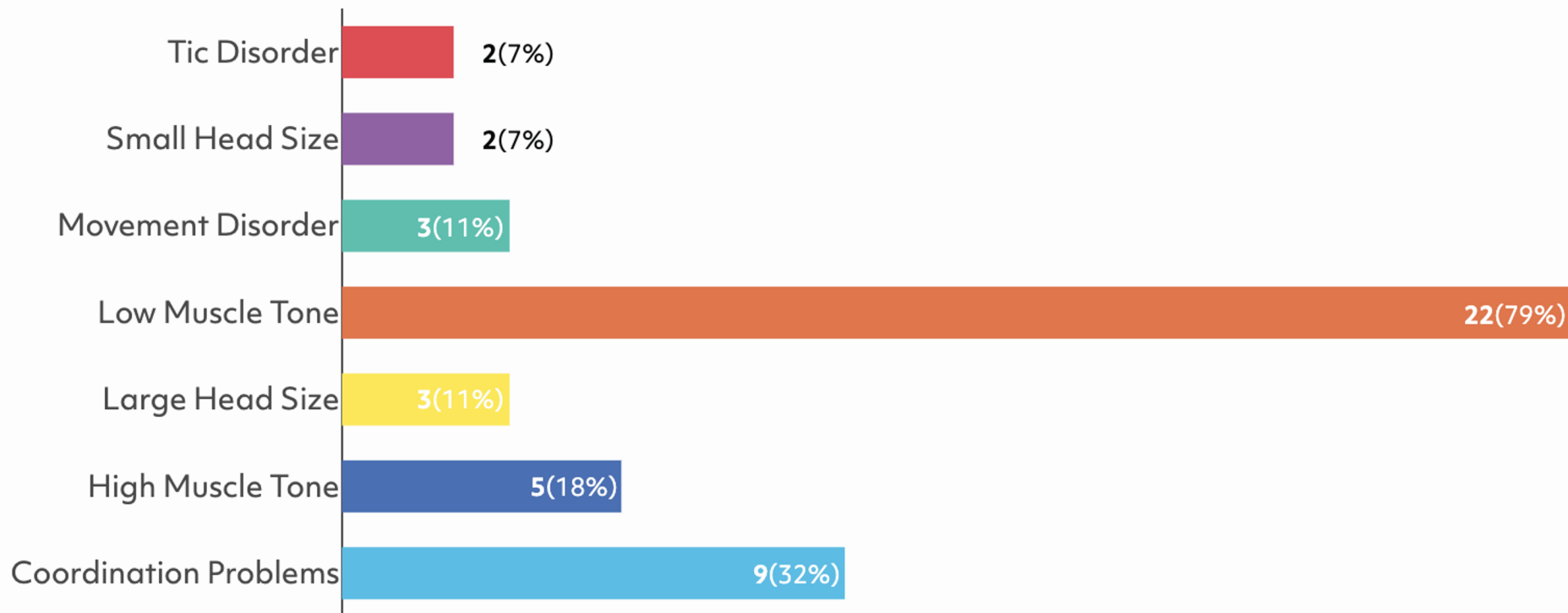
Developmental and Behavioral Conditions

(28 individuals)

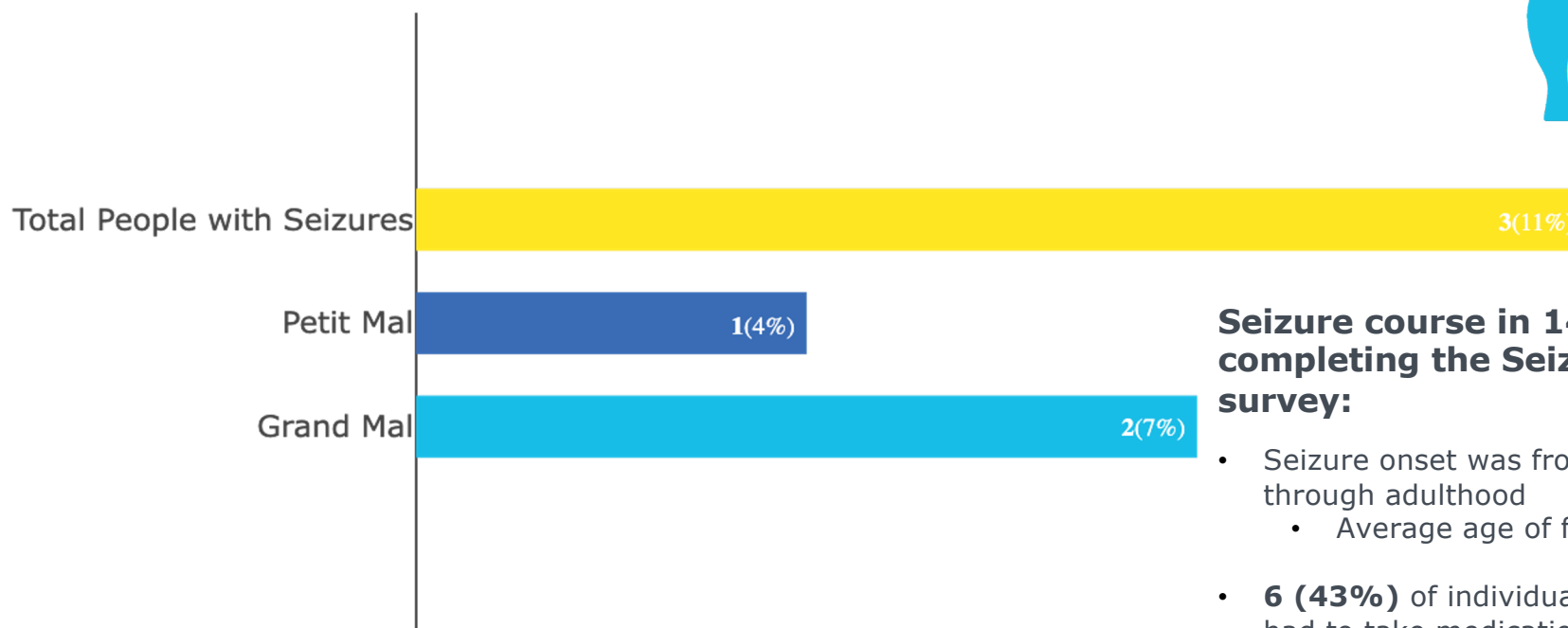


Neurological Problems

(28 individuals)



Seizure Disorders (28 individuals)

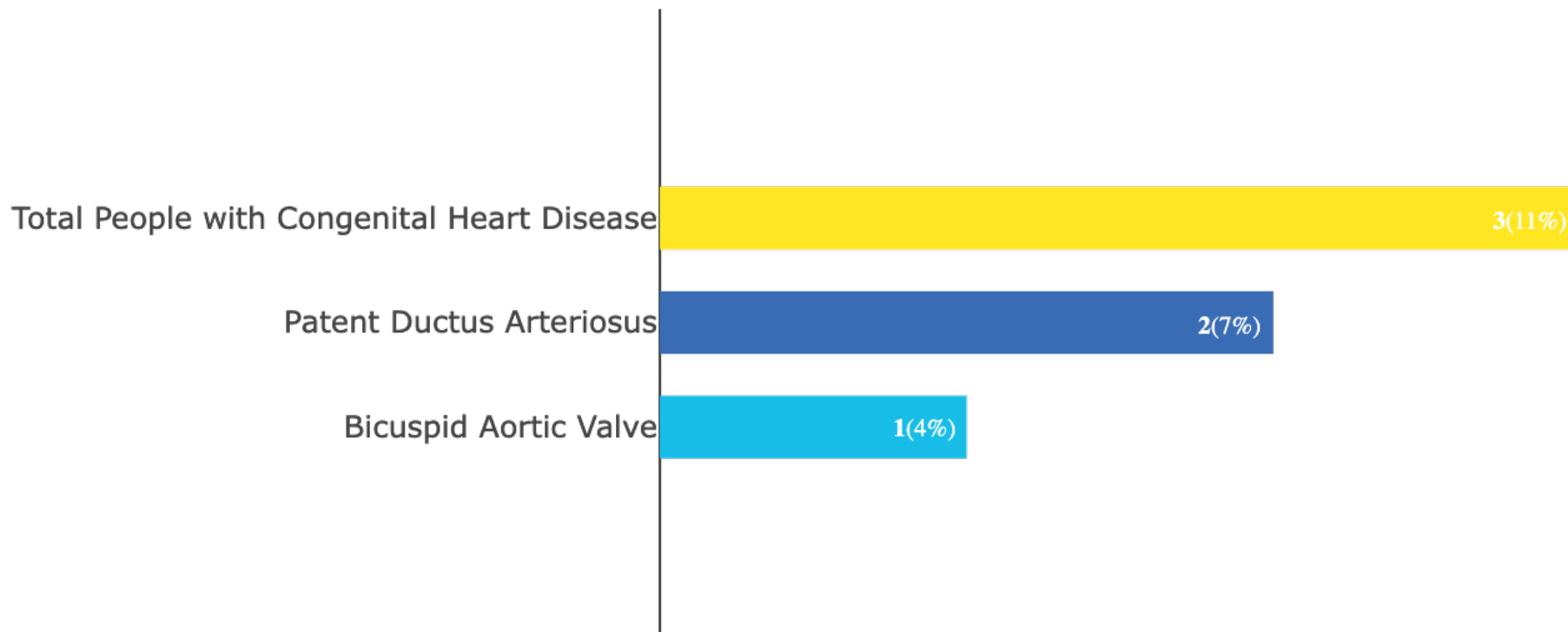


Seizure course in 14 individuals completing the Seizure History survey:

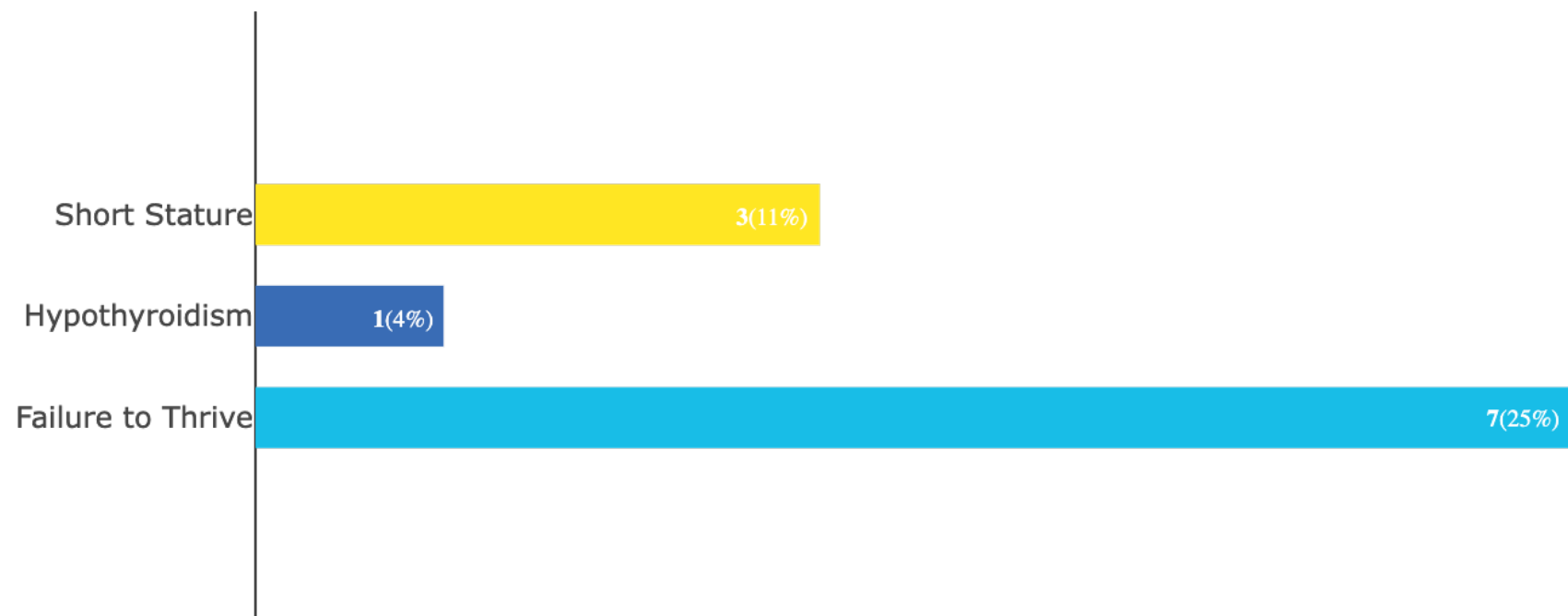
- Seizure onset was from 5 months of age through adulthood
 - Average age of first seizure is 7 years
- **6 (43%)** of individuals with seizures have had to take medication for their seizures
 - **5 (36%)** continue to take preventative medication for their seizures (1 resolved)
- **4 (29%)** of caregivers reported that their child's seizures are under control
 - Average age at seizure control was 6 years

Heart

(28 individuals)

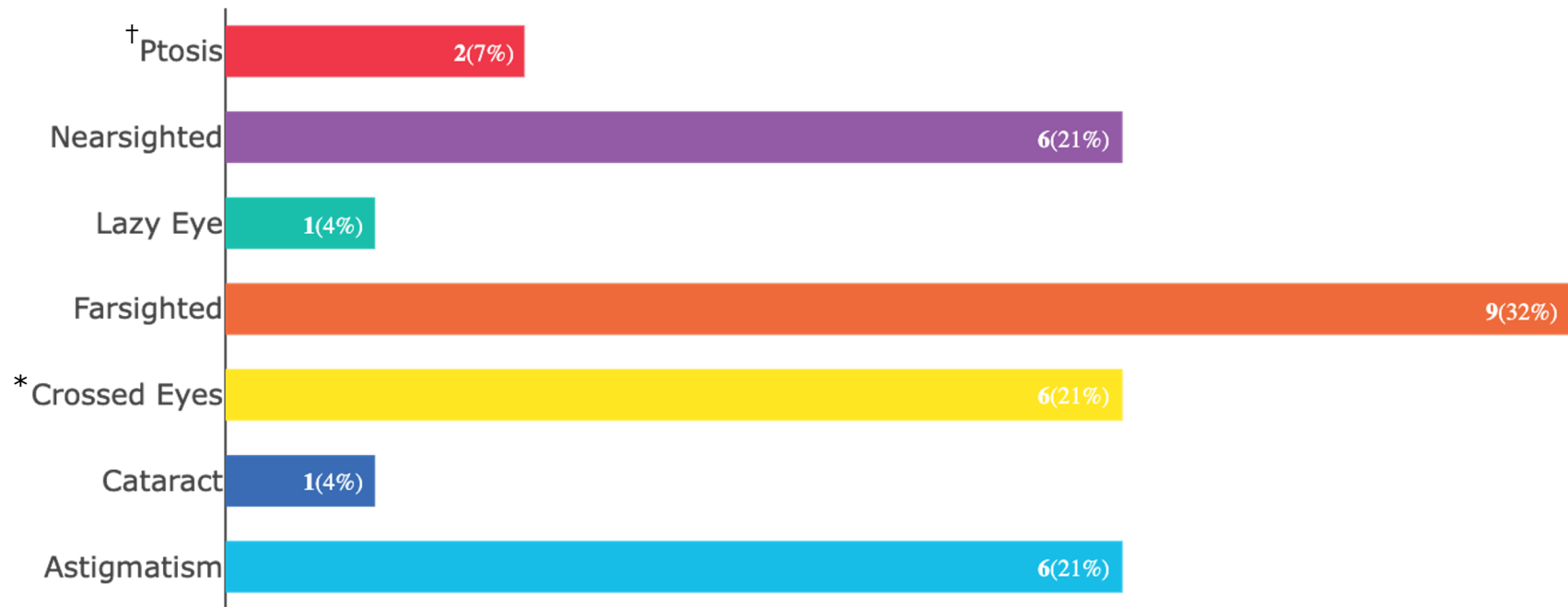


Endocrinologic (28 individuals)



Vision Problems

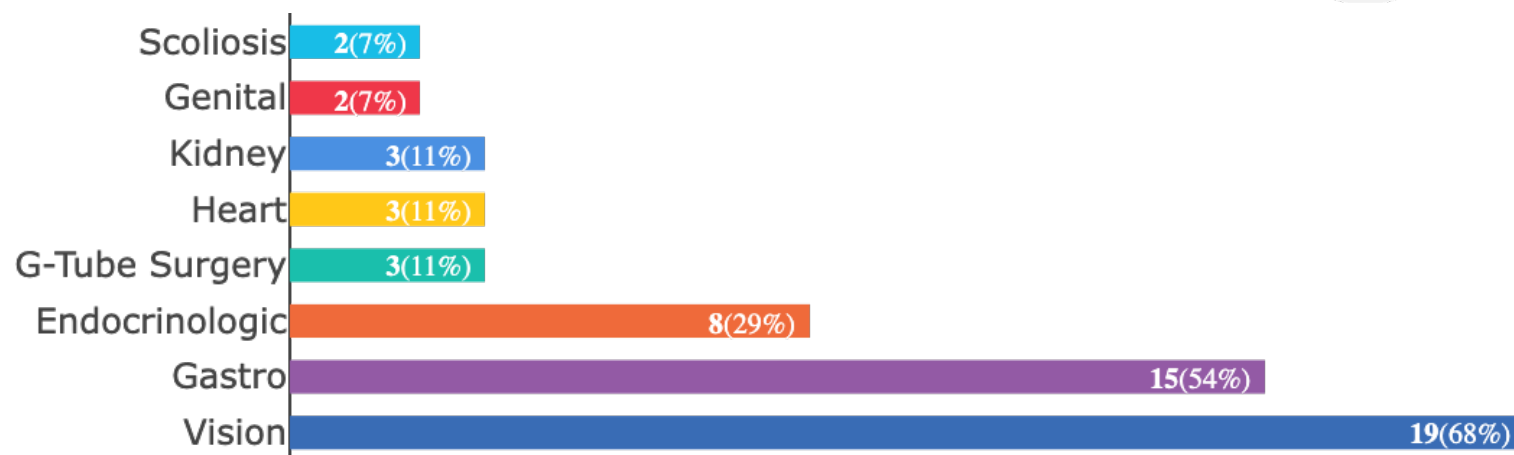
(28 individuals)



* 3 resolved through surgery
† 1 resolved through surgery

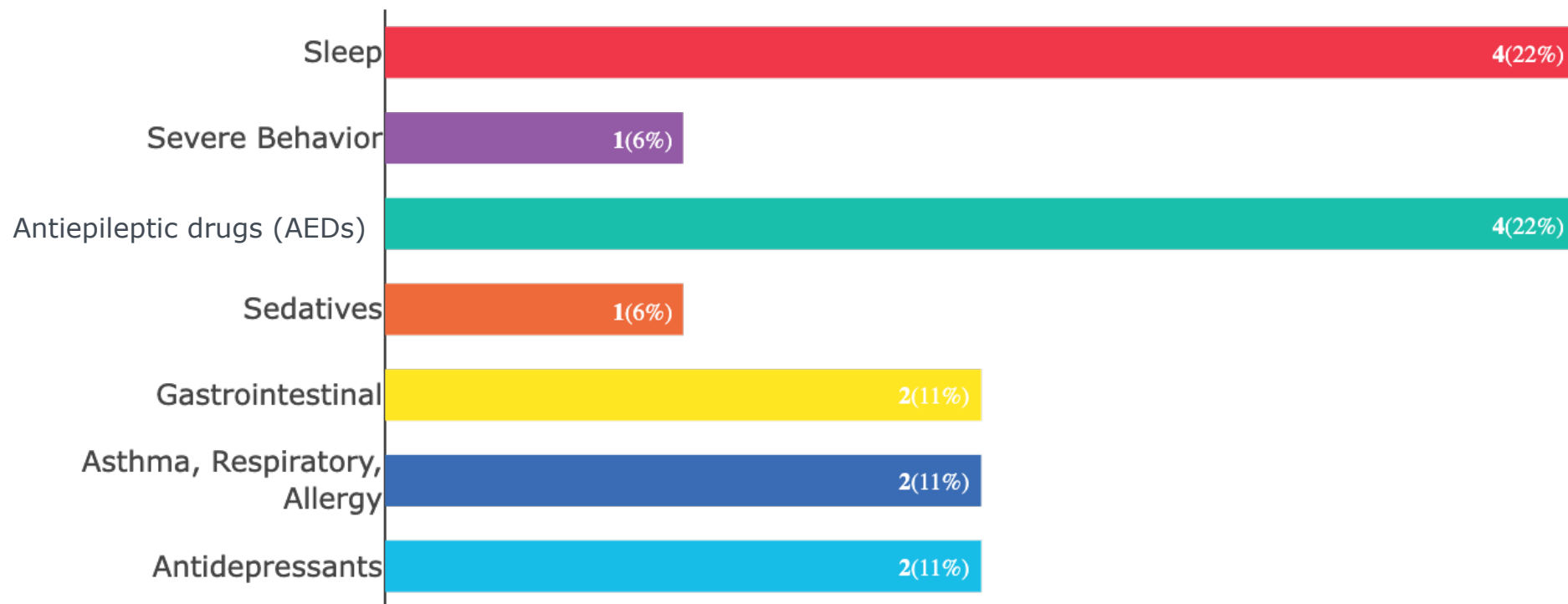
Additional Medical Issues

(28 individuals)



Medication Use

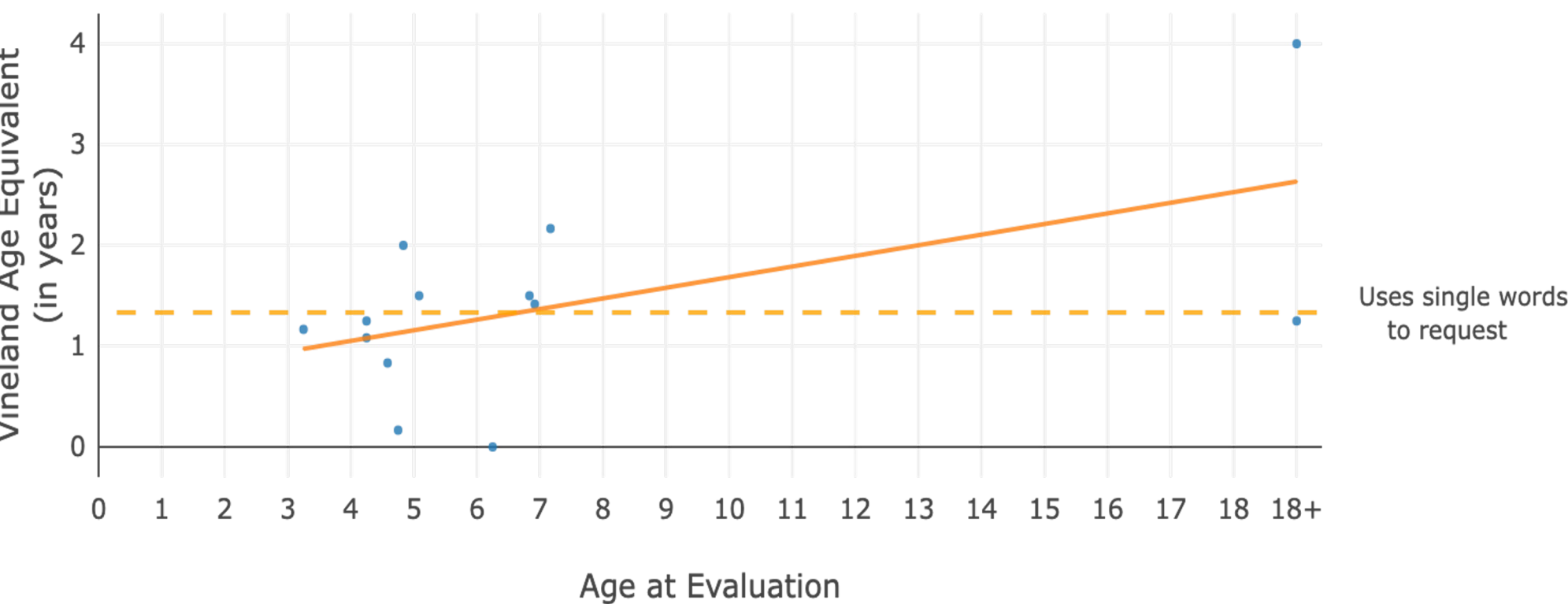
(18 individuals)



Vineland Adaptive Behavior Scales Developmental Growth Charts (Vineland-3)

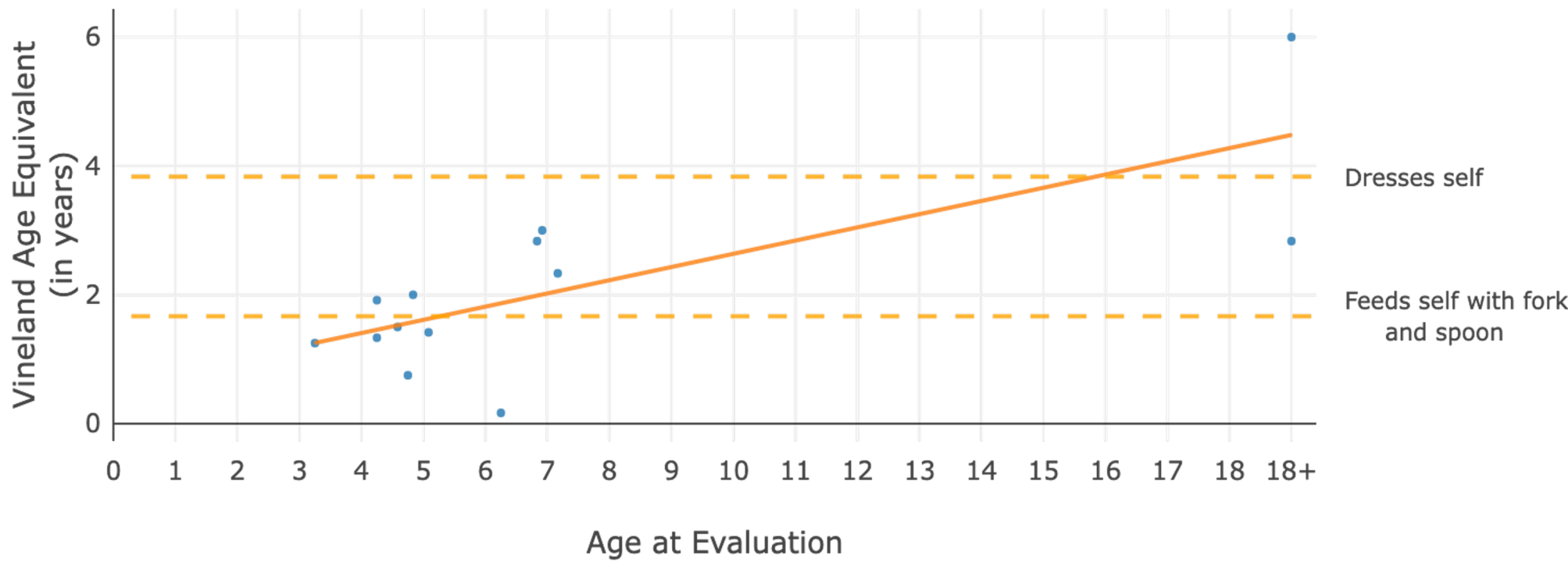
Expressive Language Development

(13 individuals)

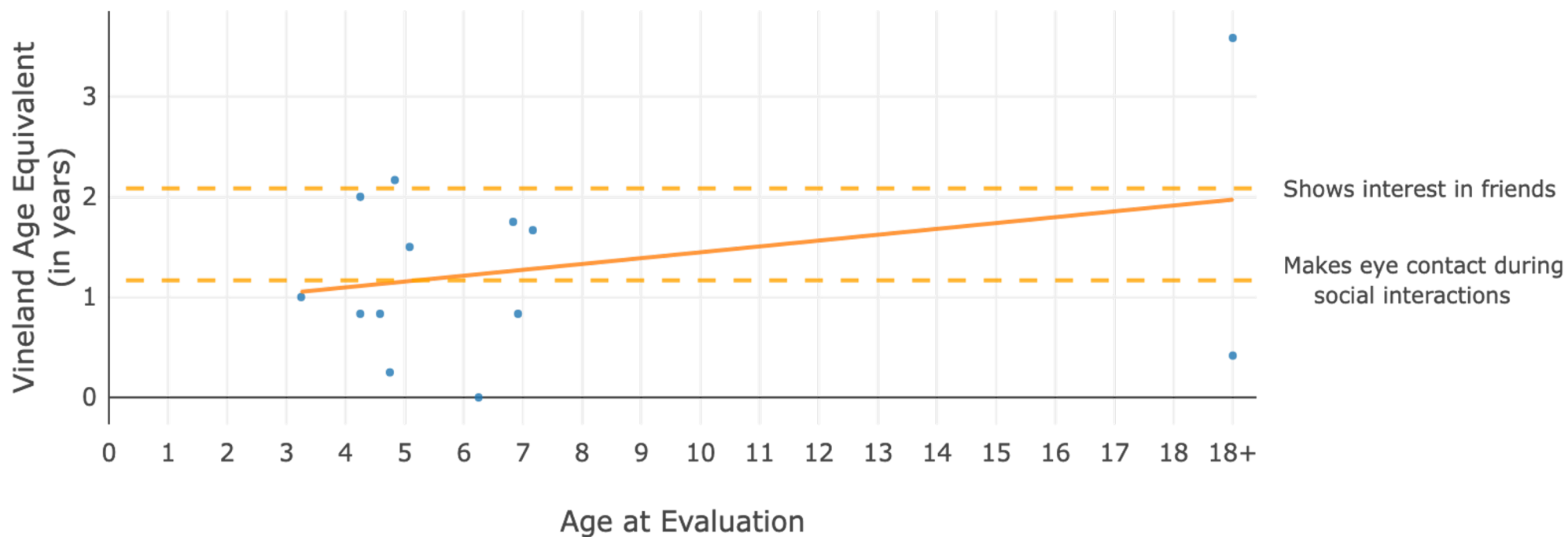


Personal Care Skills

(13 individuals)

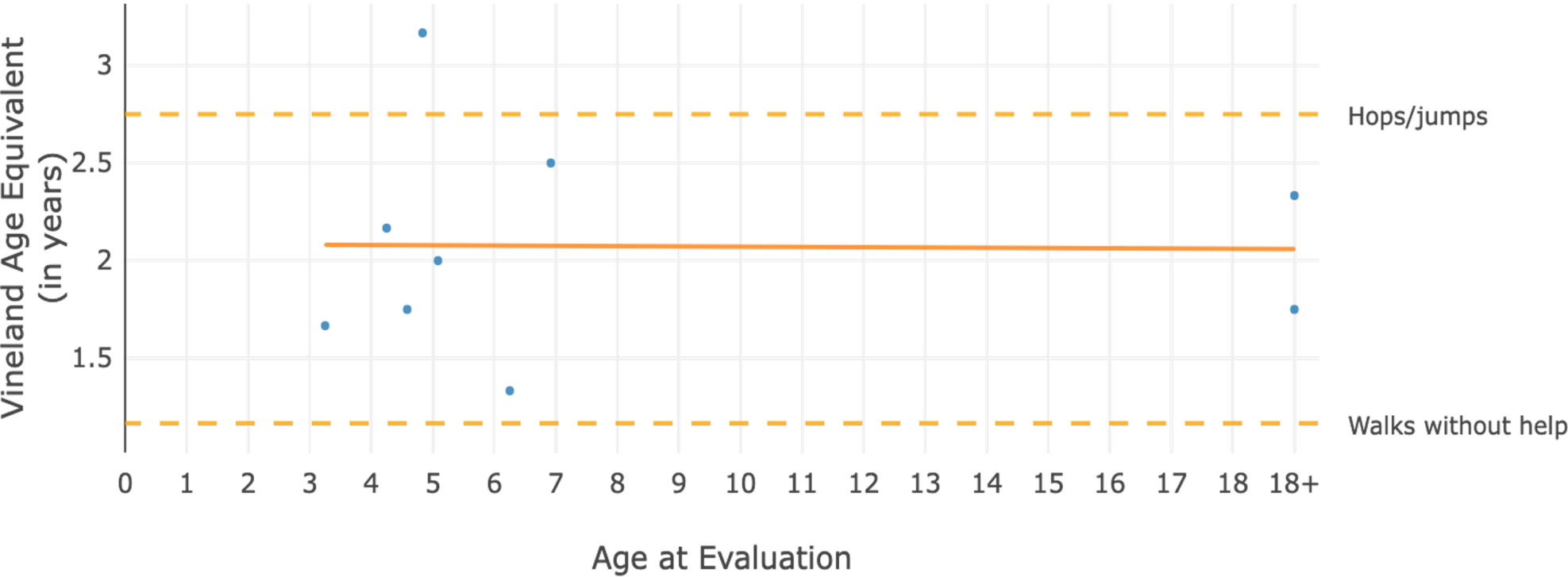


Social Development (13 individuals)



Gross Motor Development

(9 individuals)

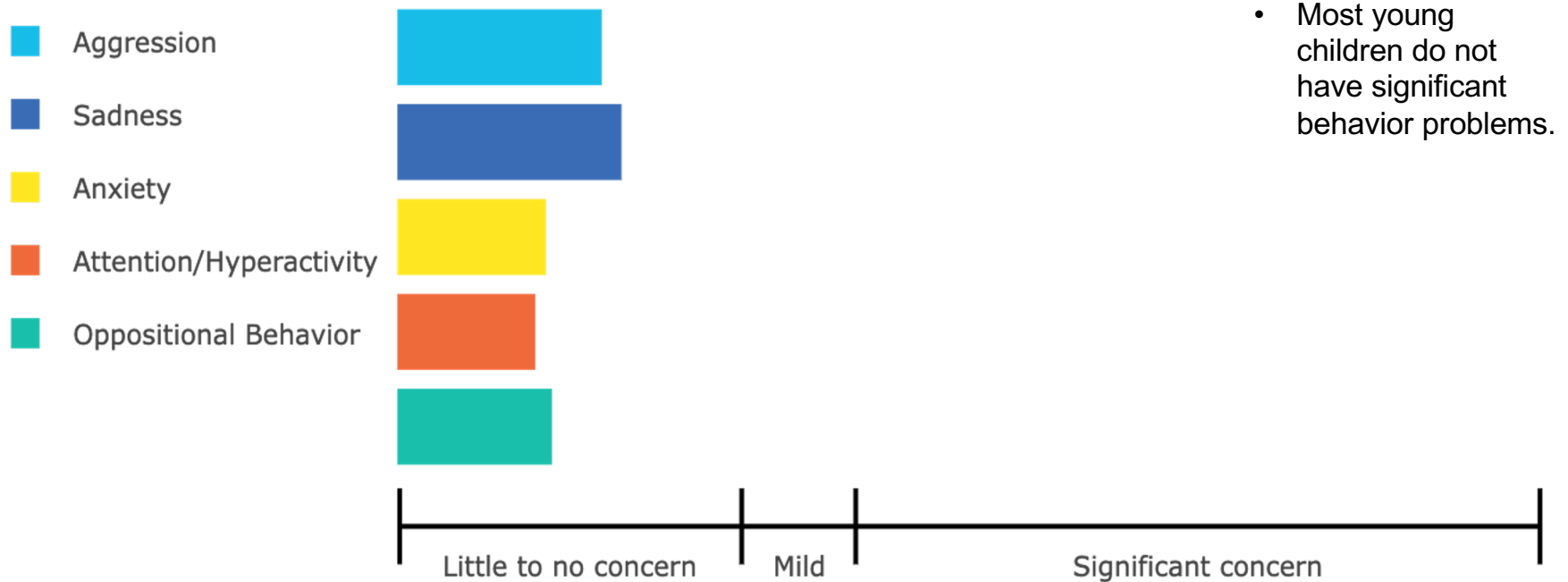


Child Behavior Checklist (CBCL)

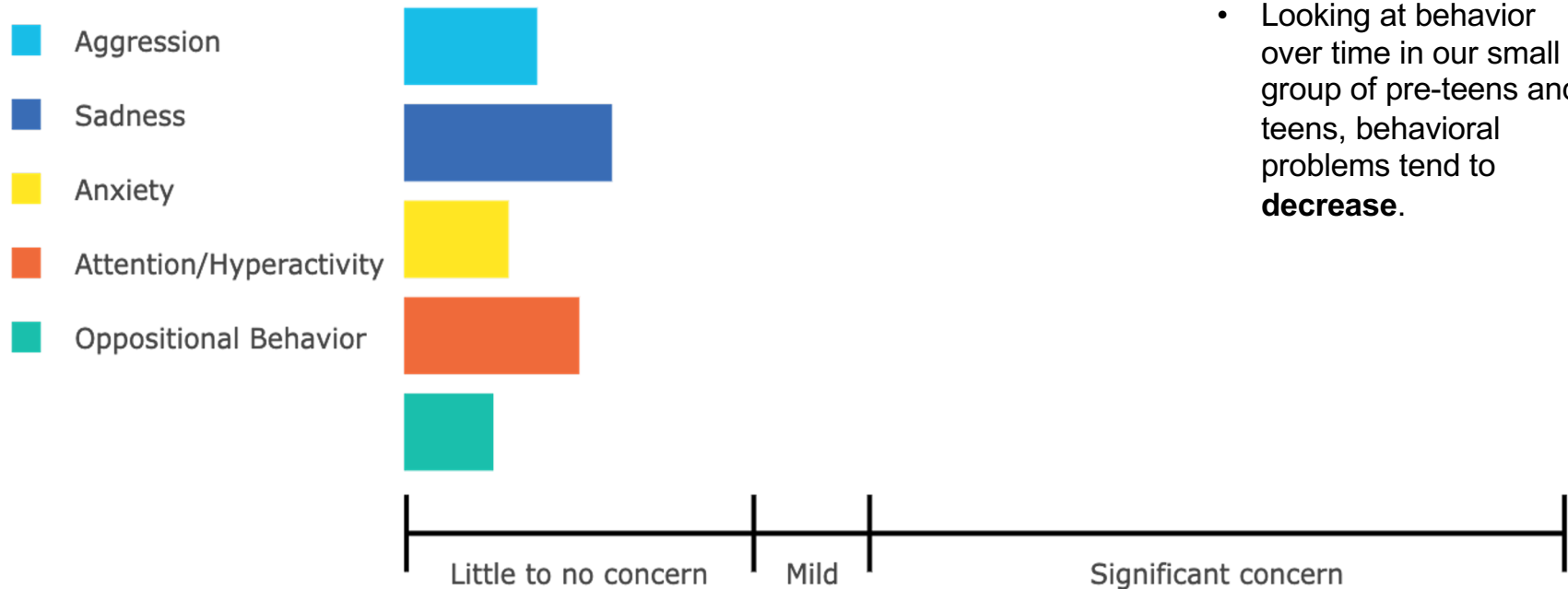
Child Behavior Checklist

Behavioral and Emotional Concerns

Ages 1.5-5 Years (22 individuals)



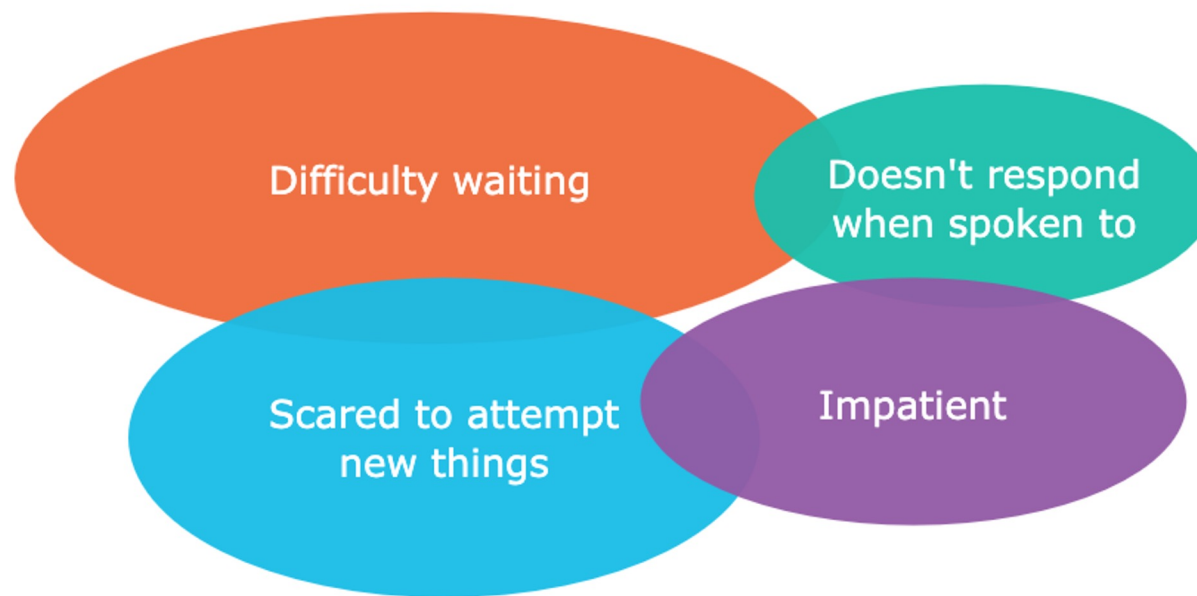
Child Behavior Checklist Behavioral and Emotional Concerns Ages 6-18 Years (17 individuals)



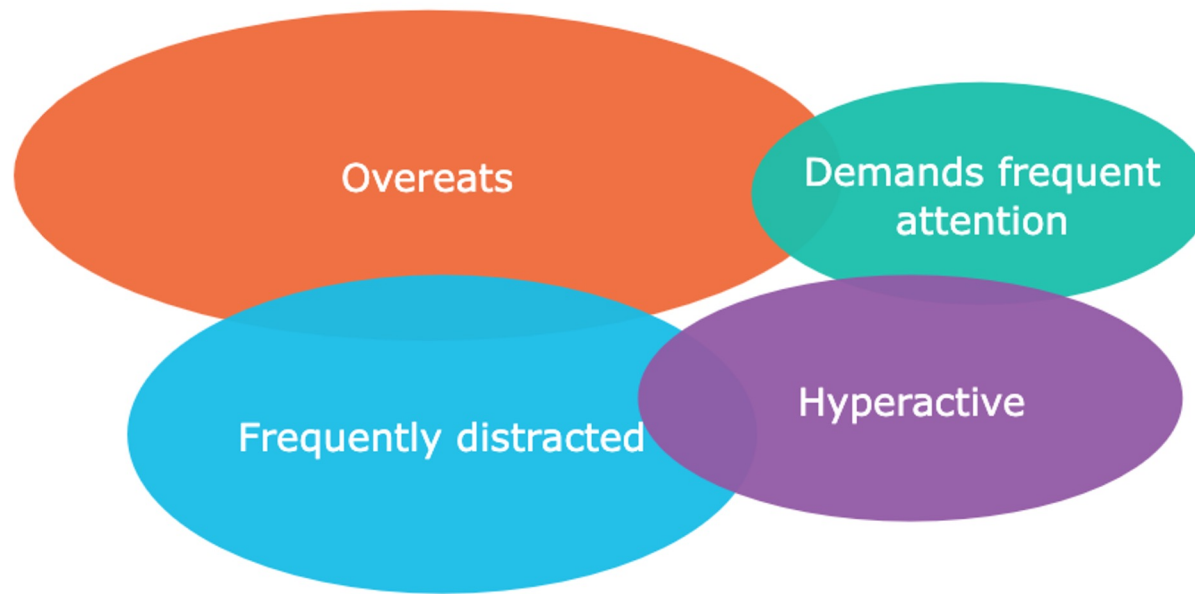
Child Behavior Checklist

Top Behavioral and Emotional Concerns

Ages 1.5-5 Years (22 individuals)



Child Behavior Checklist
Top Behavioral and Emotional Concerns
Ages 6-18 Years (17 individuals)



Summary: MED13L Medical and Behavioral Phenotypes



Common issues

- Intellectual disability and developmental delay
- Language delay
- Hypotonia (low muscle tone)

Other issues

- Autism
- Coordination problems
- Hypertonia (high muscle tone)
- Seizures
- Growth issues
- Eye/vision issues
- Anxious
- Impatience
- Overeating
- Attention/hyperactivity

Thank you