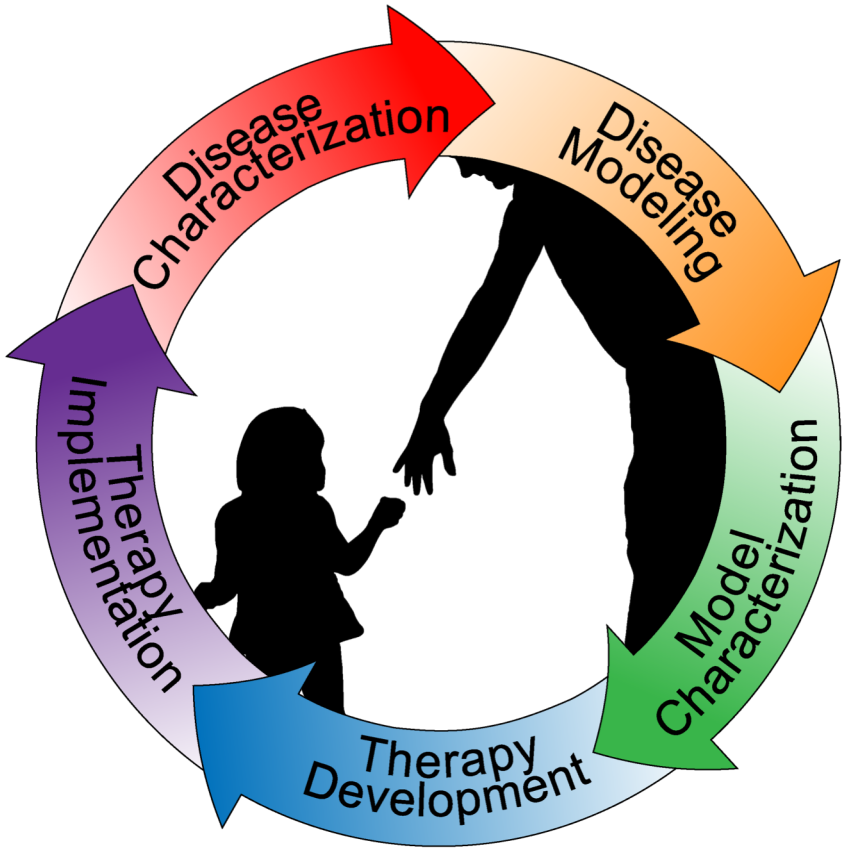
What we've learned from the KAND natural history study

July 9, 2021

Lia Boyle, PhD

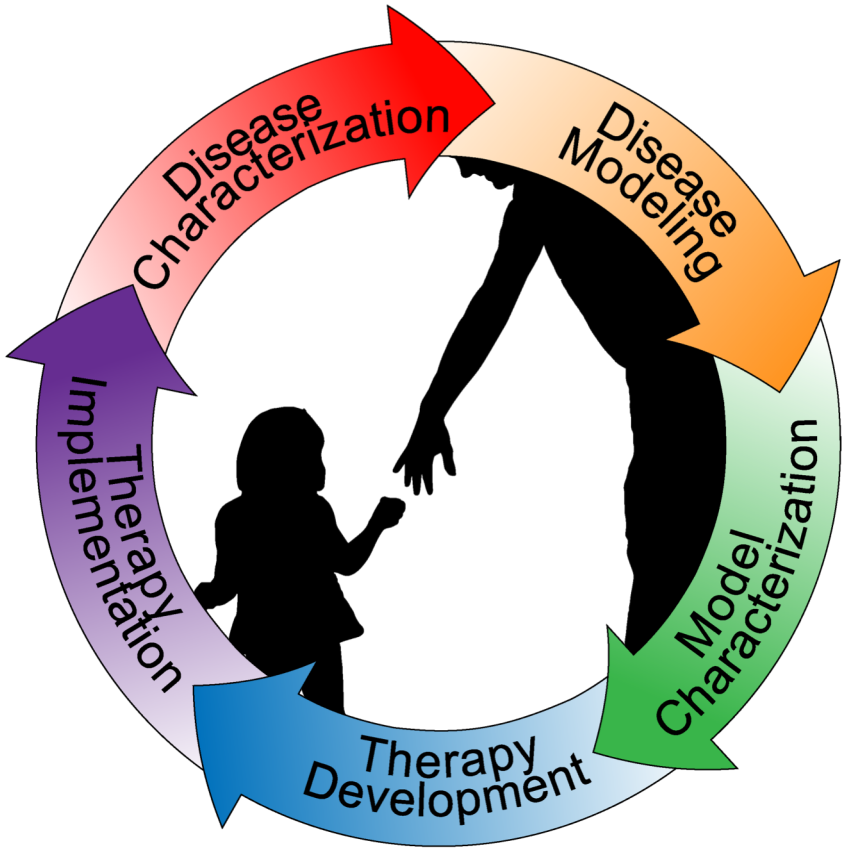
Chung lab, Columbia University

A Precision Medicine Approach to KAND



1. **Characterization**
2. **Modeling**
3. **Understanding the model**
4. **Developing therapies**
5. **Implementing therapies**

A Precision Medicine Approach to KAND



1. Characterization
2. Modeling
3. Understanding the model
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5. Implementing therapies

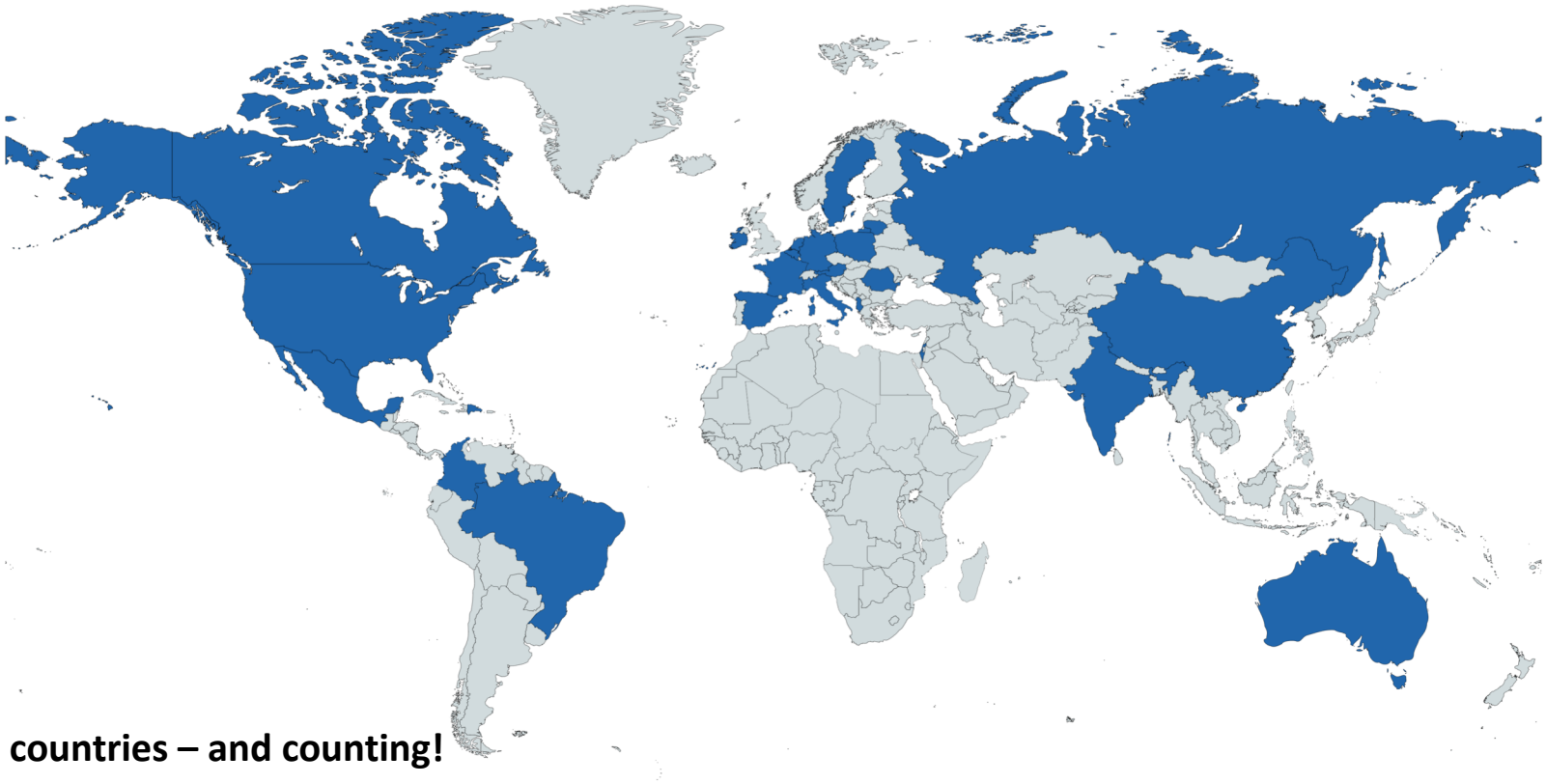
Outline

- Chung lab KAND history
- Natural history study: why is it important?
- Background on our study
- What's in a name? KAND vs SPG30 vs NESCAV
- Refresher on overall symptoms
- New symptom information from our follow up survey
- Focus on seizures
- How you can participate


April 2017


August 2019

KAND worldwide



25 different countries – and counting!

Why do we need a natural history study?

- Helps clinicians and scientists understand disease progression
- Important for identifying and developing best clinical practices
- Identifies factors that affect disease severity
- A critical step in clinical trial readiness

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Participating in the study makes sure
***your* voice is heard and *your* family is represented**

What's in a name: KAND vs NESCAV vs SPG30

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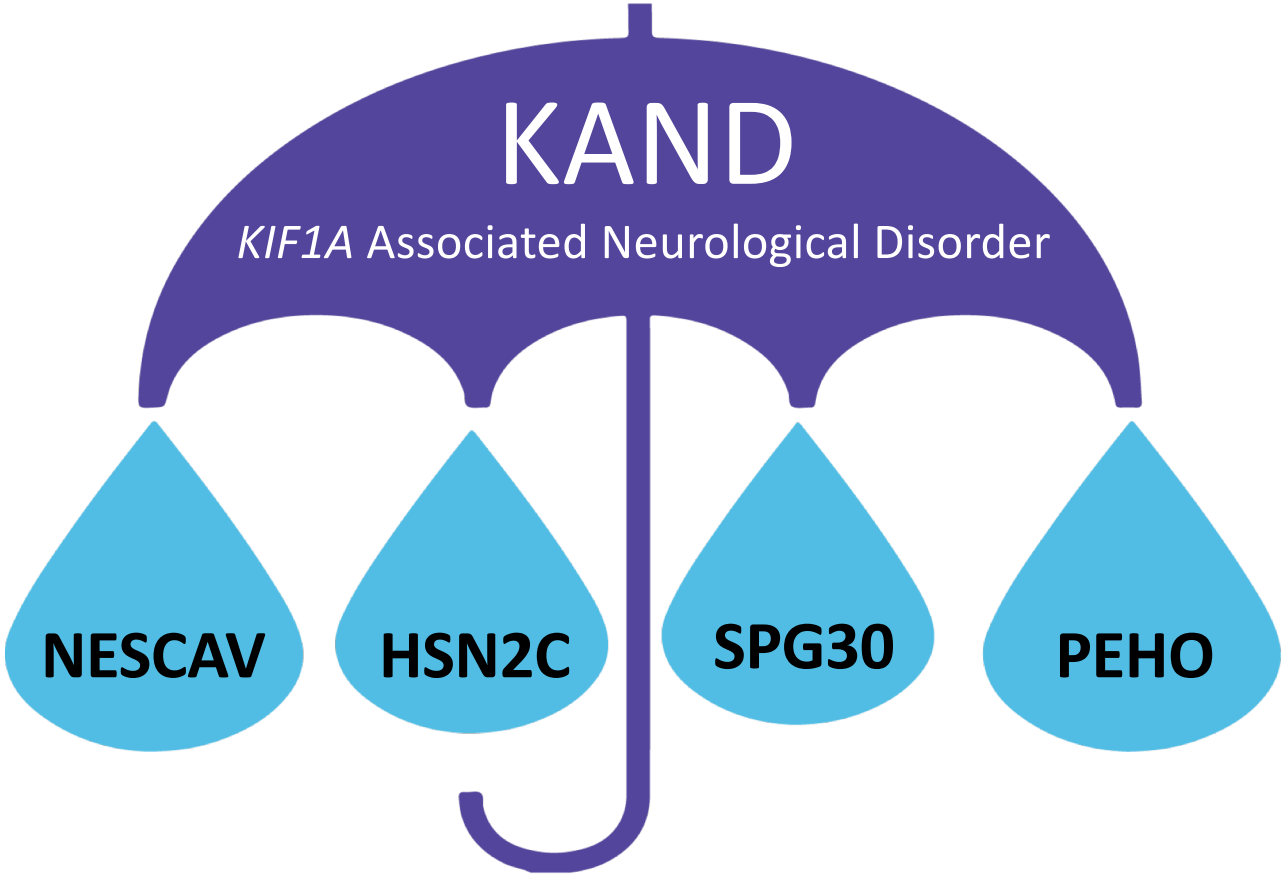


KAND affects the whole body

Cognition, Epilepsy & Behavior

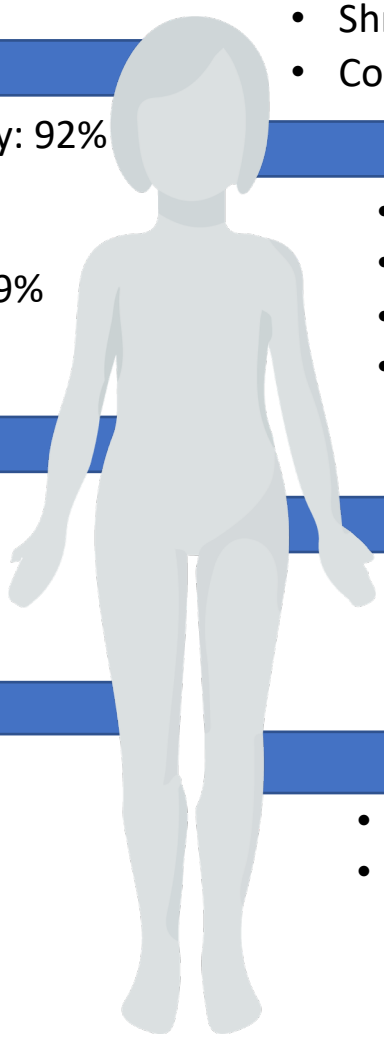
- Developmental delay/intellectual disability: 92%
- Epilepsy: 42%
- Autism: 24%
- Attention deficit/hyperactivity disorder: 19%
- Obsessive compulsive disorder: 5%

Stomach & Digestion

- Reflux: 40%
- Diarrhea: 17%
- Constipation: 39%

Neurological & Musculoskeletal

- Hypotonia: 84%
- Hypertonia/spasticity: 81%
- Peripheral neuropathy: 27%
- Scoliosis: 14%



Neuroimaging abnormalities

- Shrinking of the cerebellum: 35%
- Shrinking of the cortex: 6%
- Corpus callosum abnormalities: 11%

Vision & Eyesight

- Optic nerve atrophy: 50%
- Cortical visual impairment: 20%
- Strabismus: 26%
- Cataracts: 8%

Urinary & Reproductive

- Irregularity in genitalia: 13%
- Kidney problems: 3%

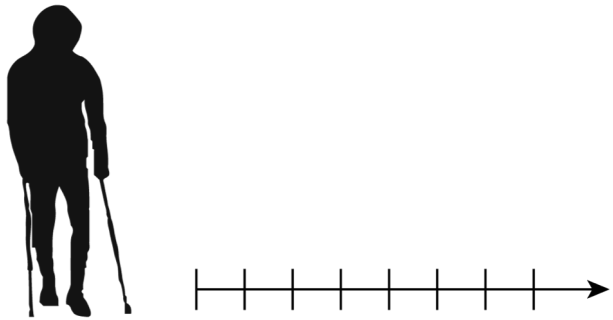
Growth

- Short stature: 13%
- Absence of growth hormone: 3%

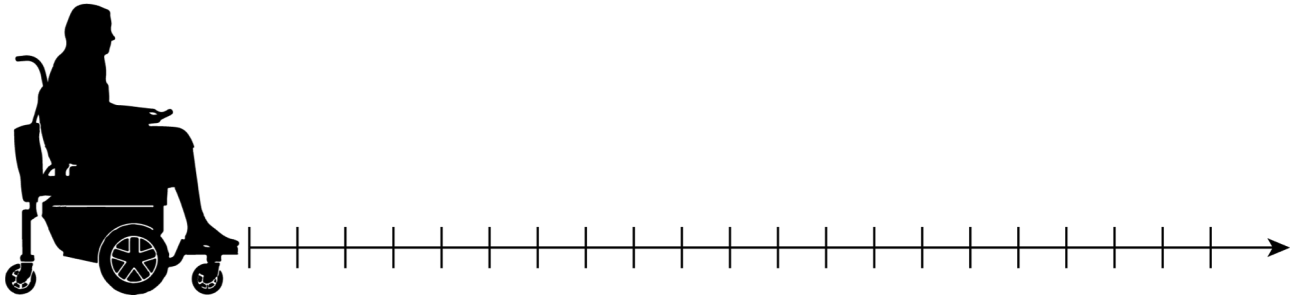
Data from Boyle et al., *HGG Advances*, 2021

How symptoms can appear: an example

7 year old boy



20 year old woman



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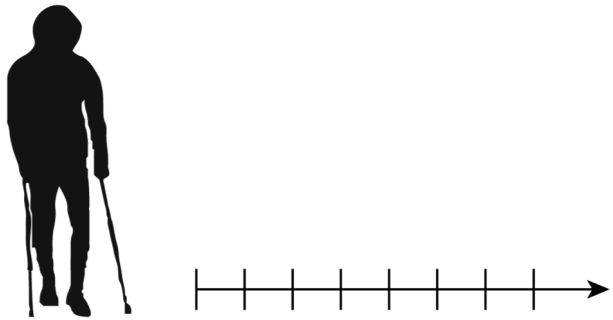

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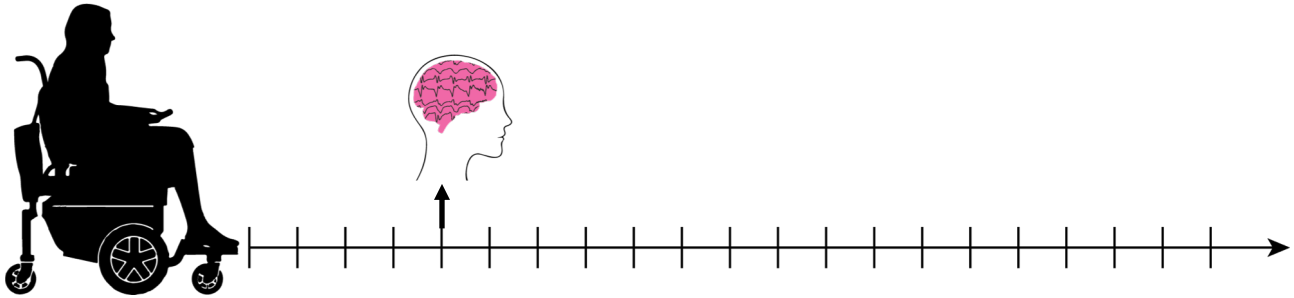
- First seizure at 4



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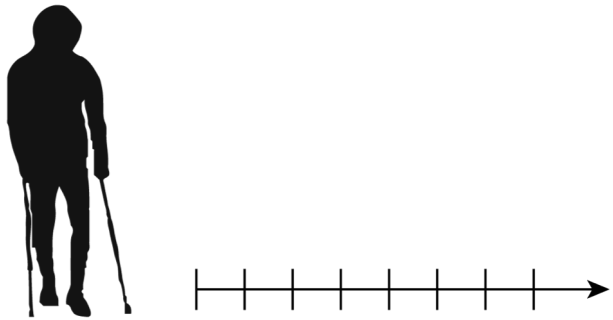

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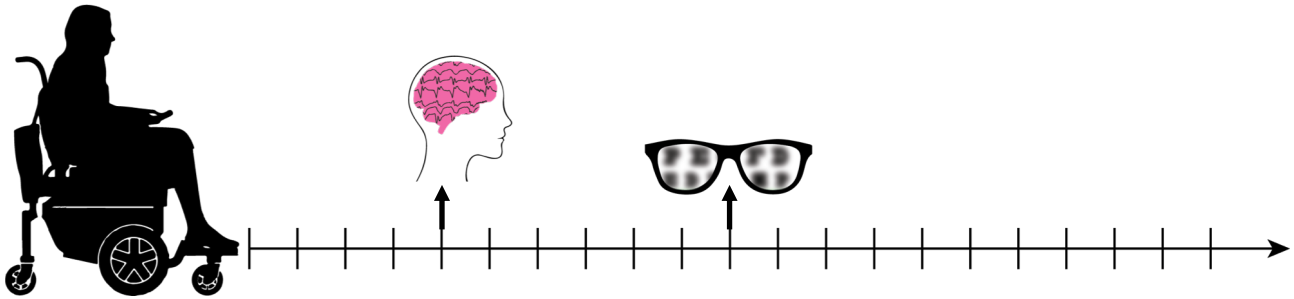

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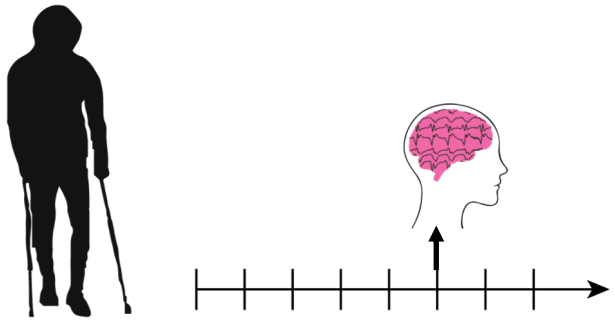

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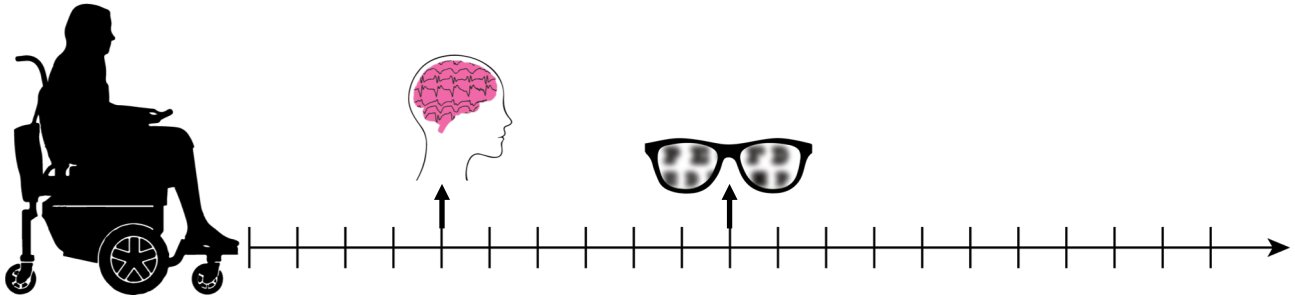

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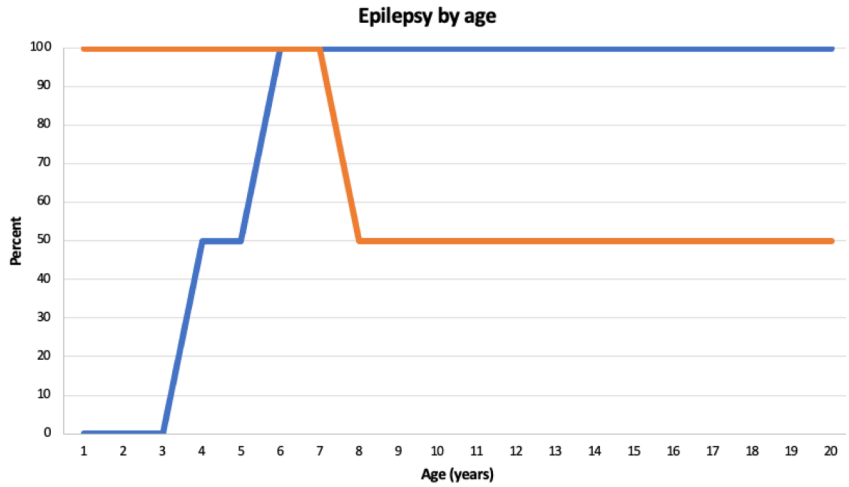

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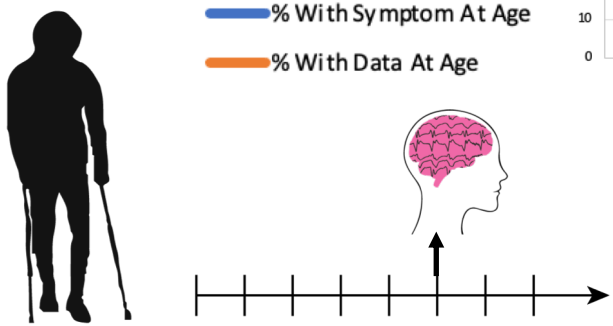

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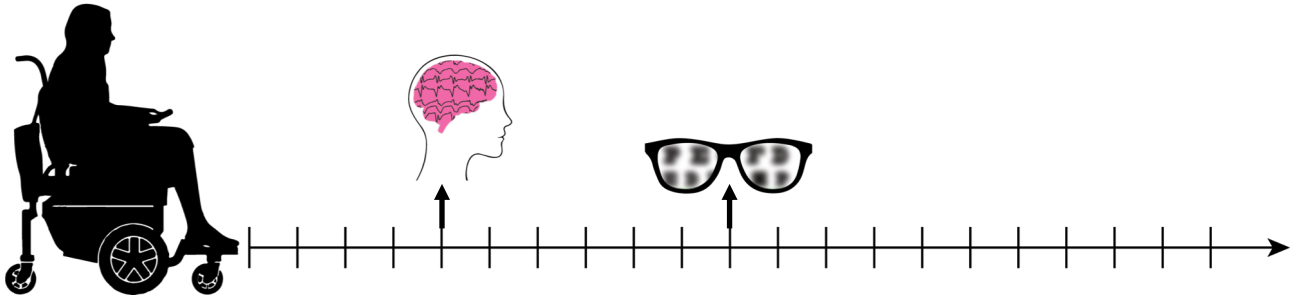

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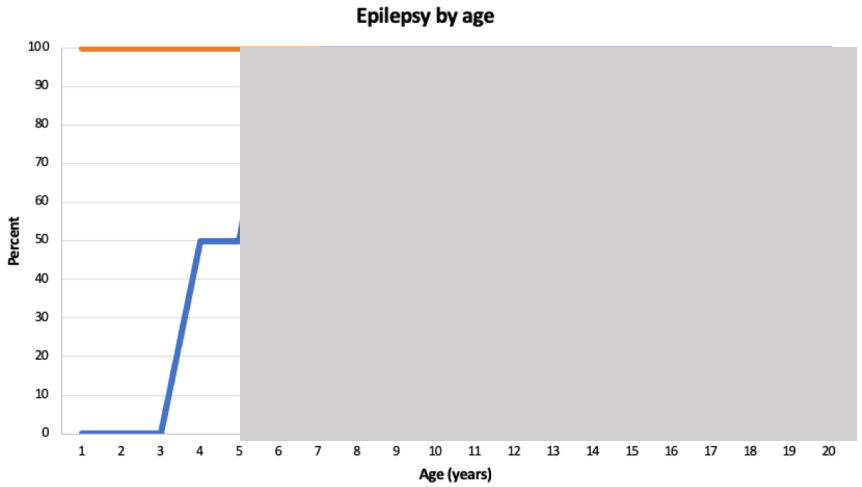

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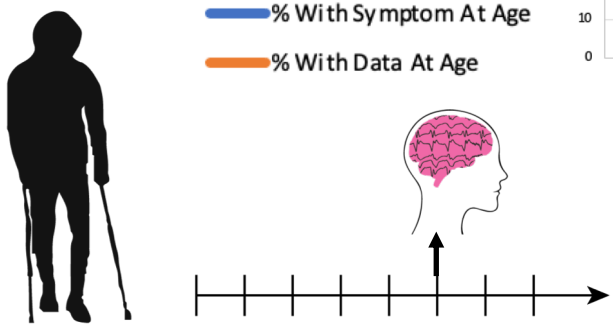

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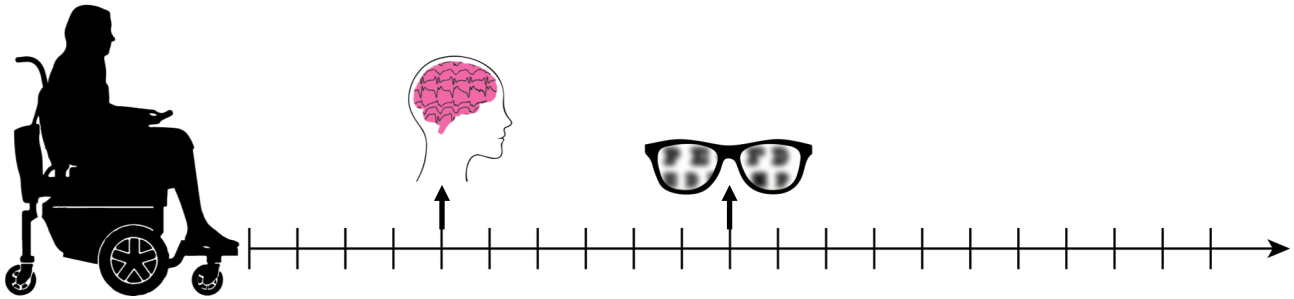

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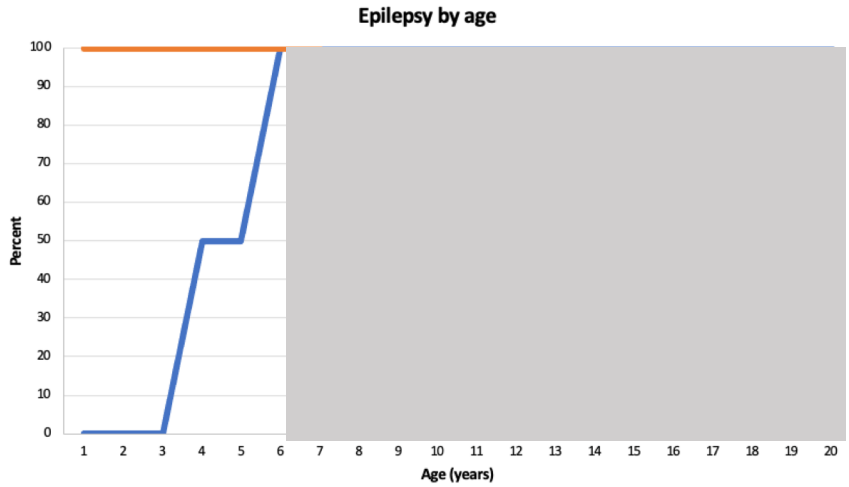

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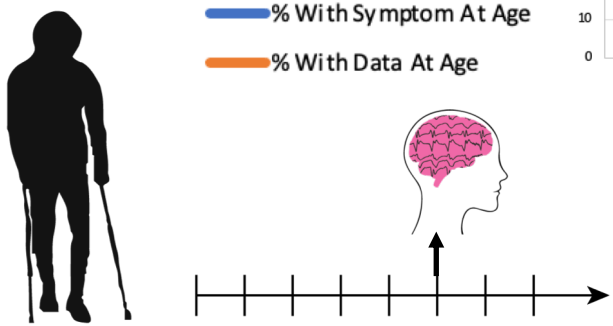

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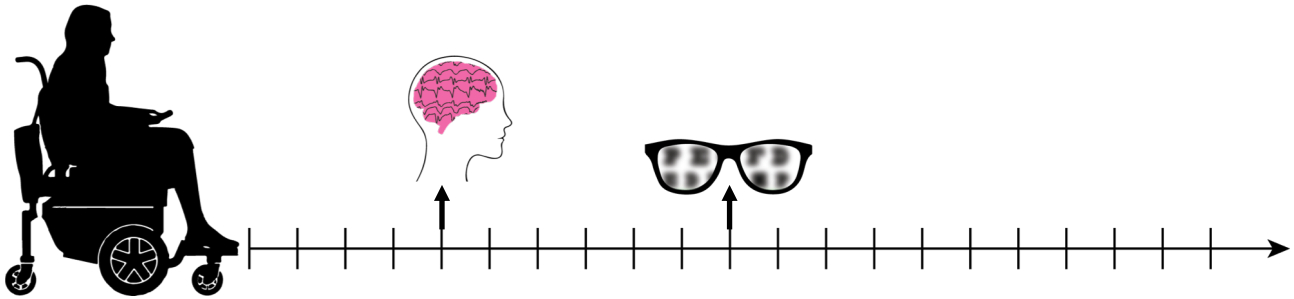

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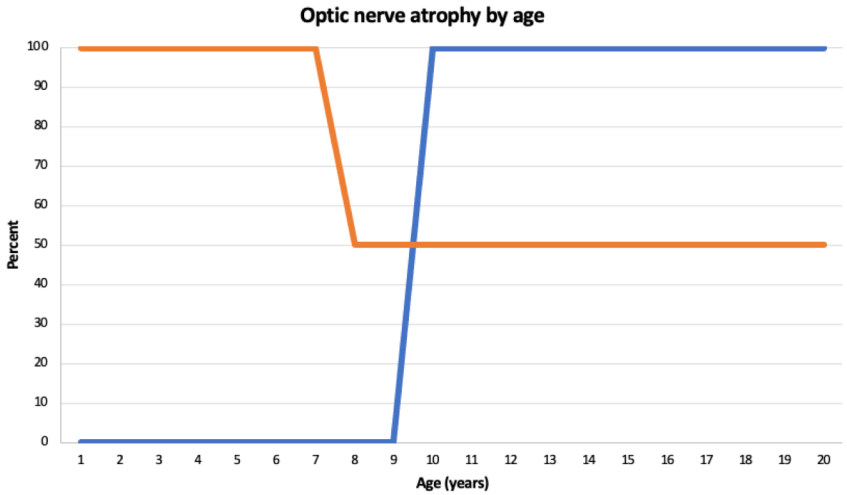

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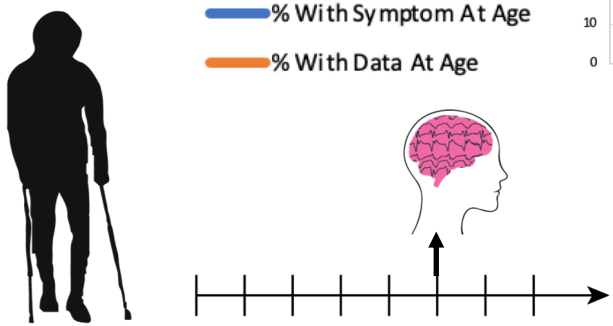

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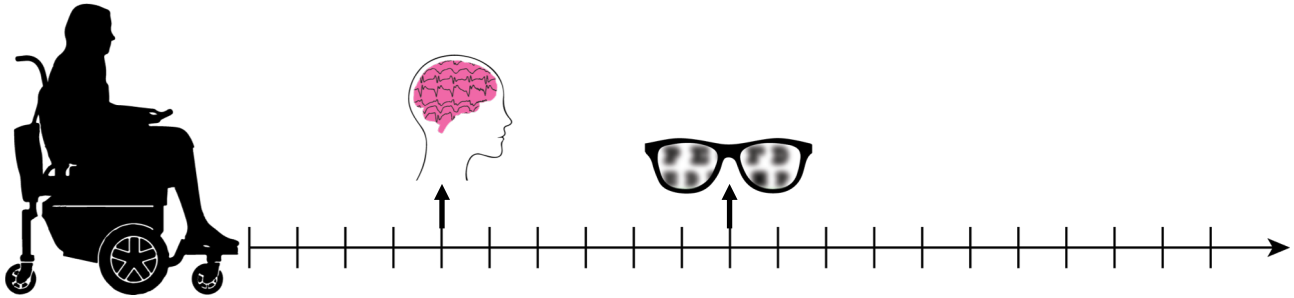

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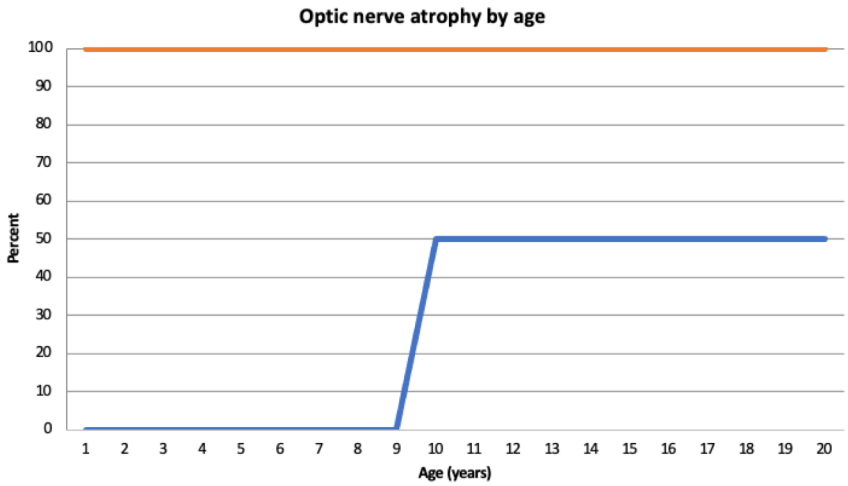

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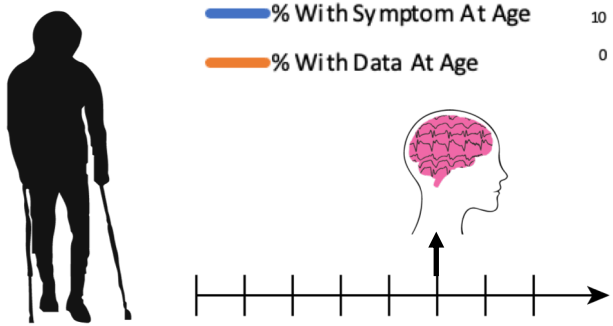

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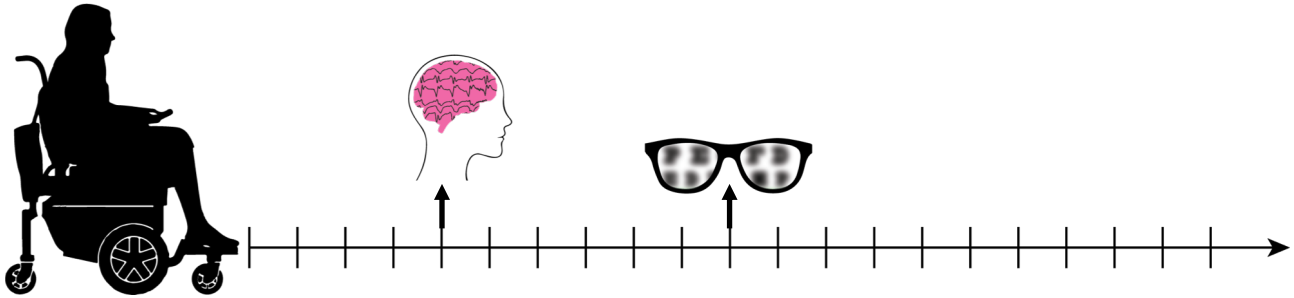
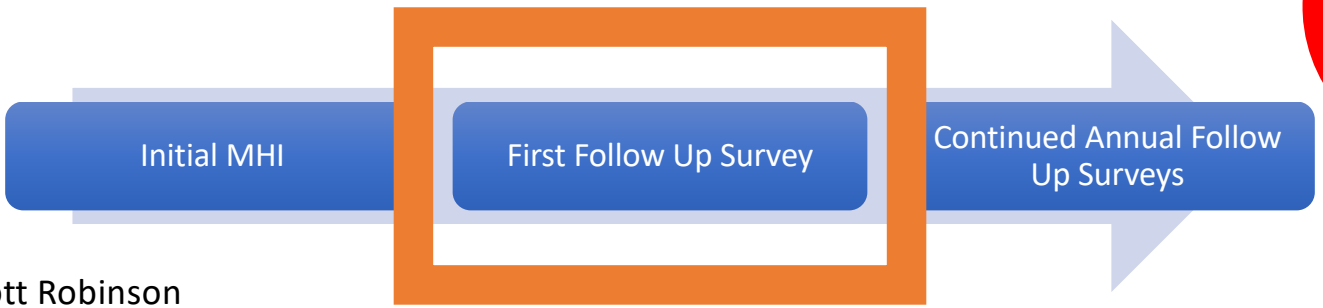
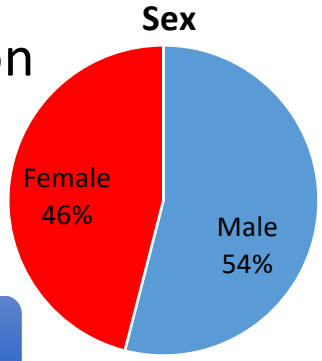


KAND natural history follow up survey

- Participants eligible if initial study interview completed ≥1 year ago
- Follow up surveys received for 74 participants
- Average age at initial interview: 9.5 years old
- Average age at follow up: 11.3 years years old
- Roughly equal males and females with similar age distribution
- 47 unique variants





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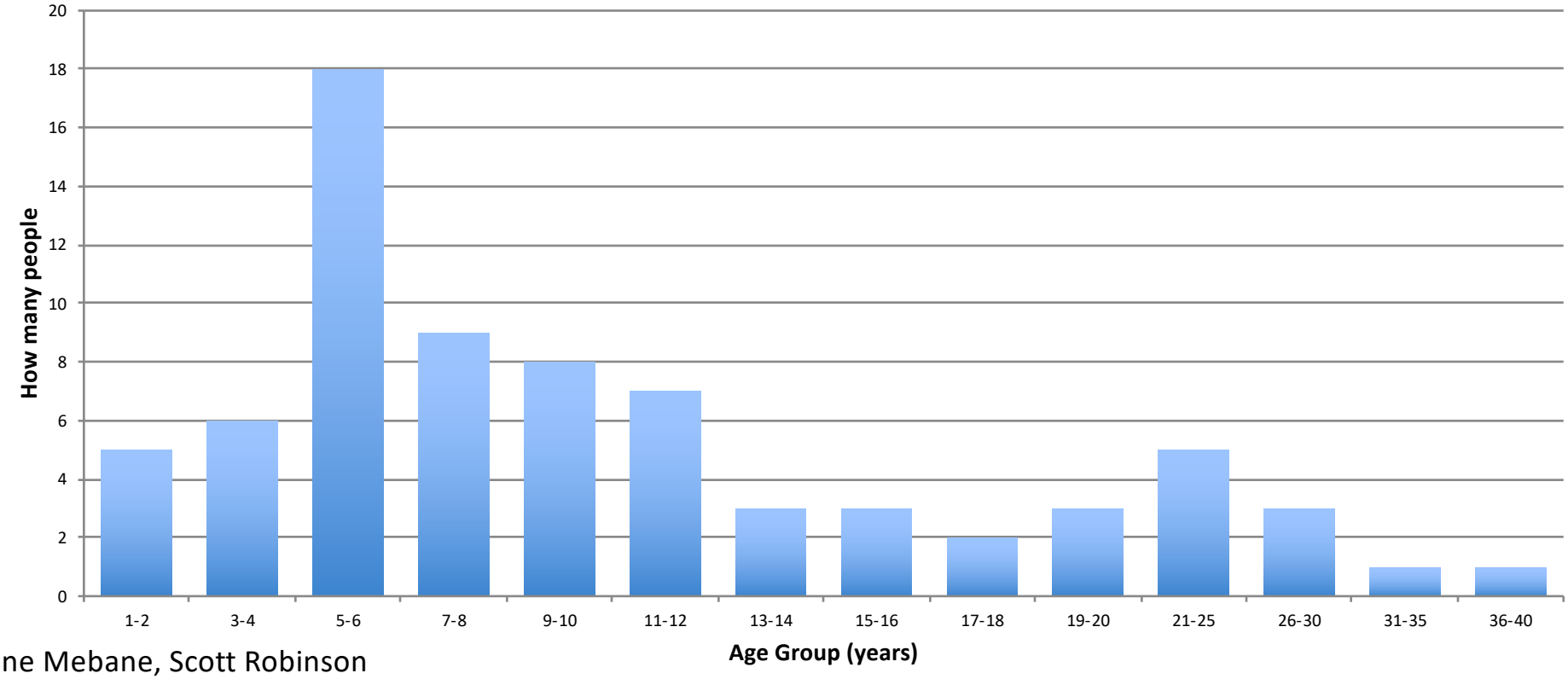
Age at follow up



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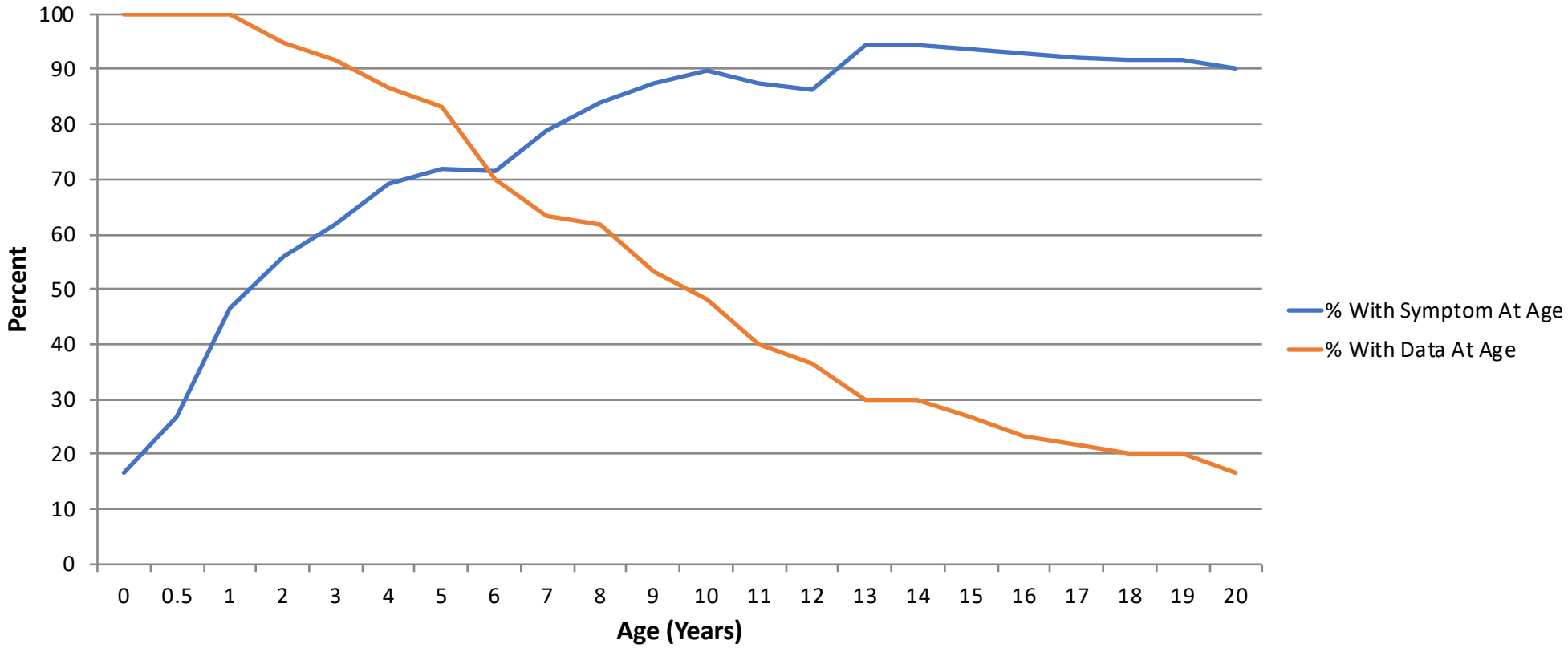
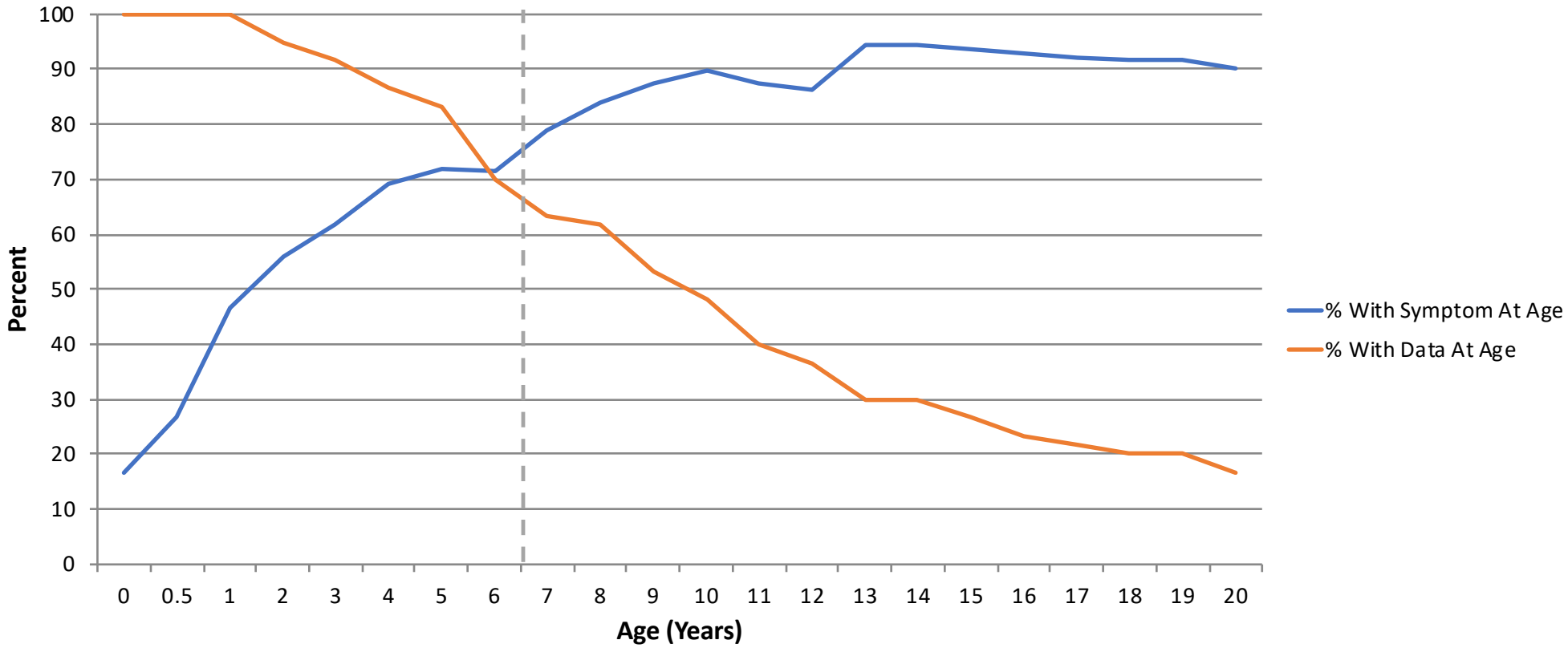
Hypertonia/spasticity by age



Caroline Mebane

n=60

Hypertonia/spasticity by age



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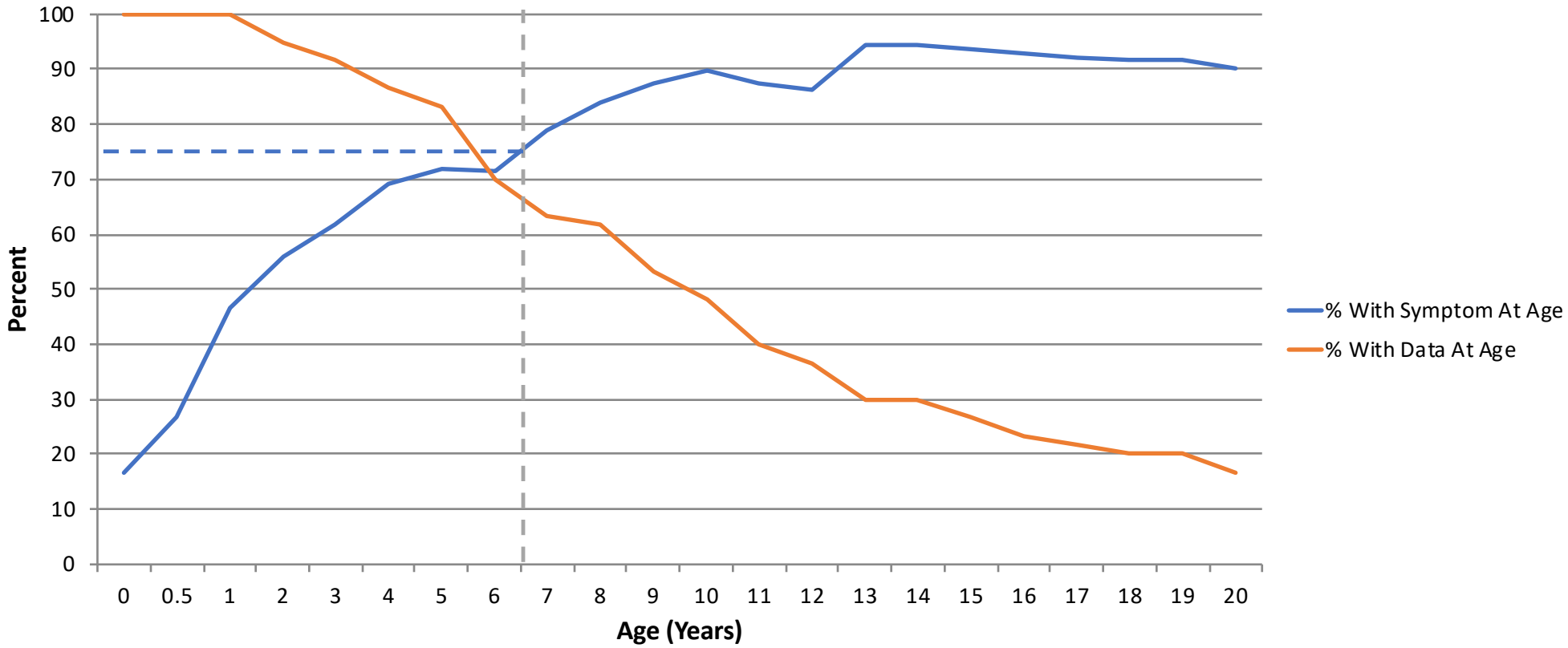

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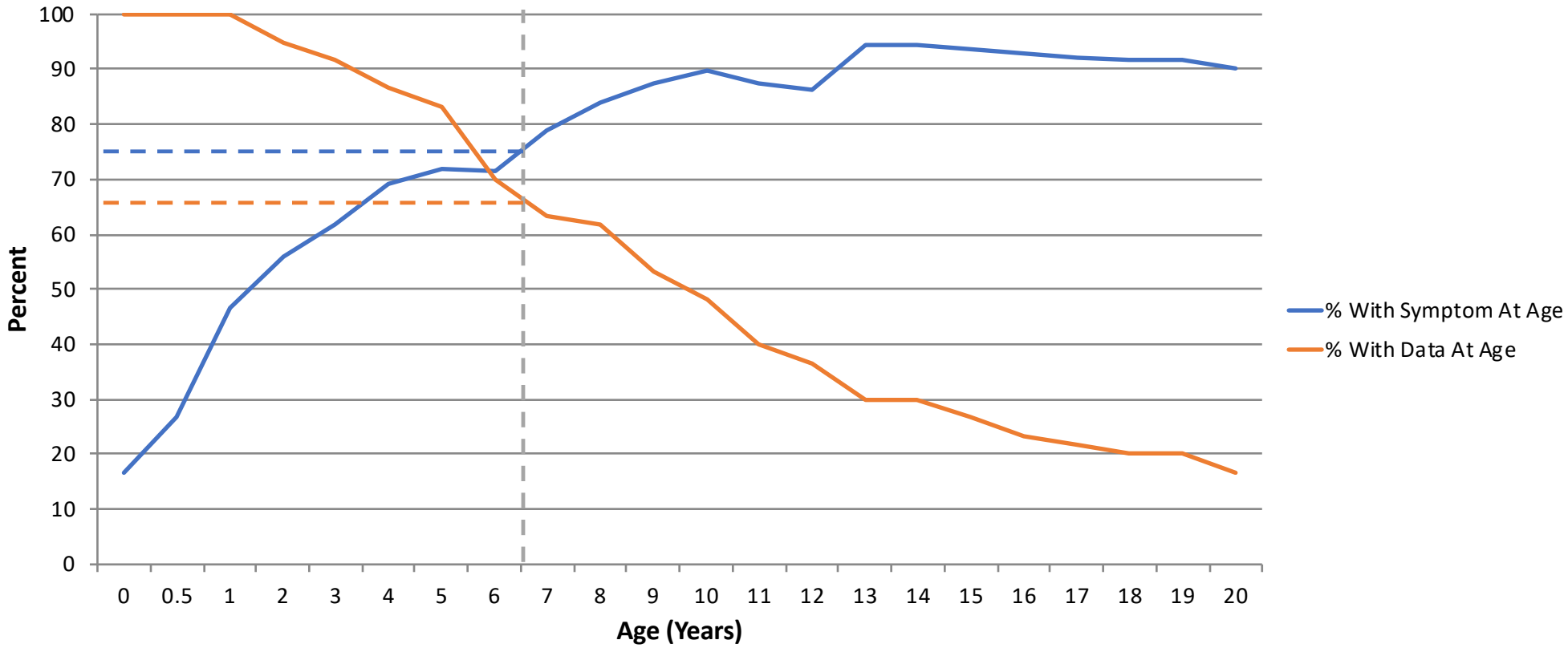

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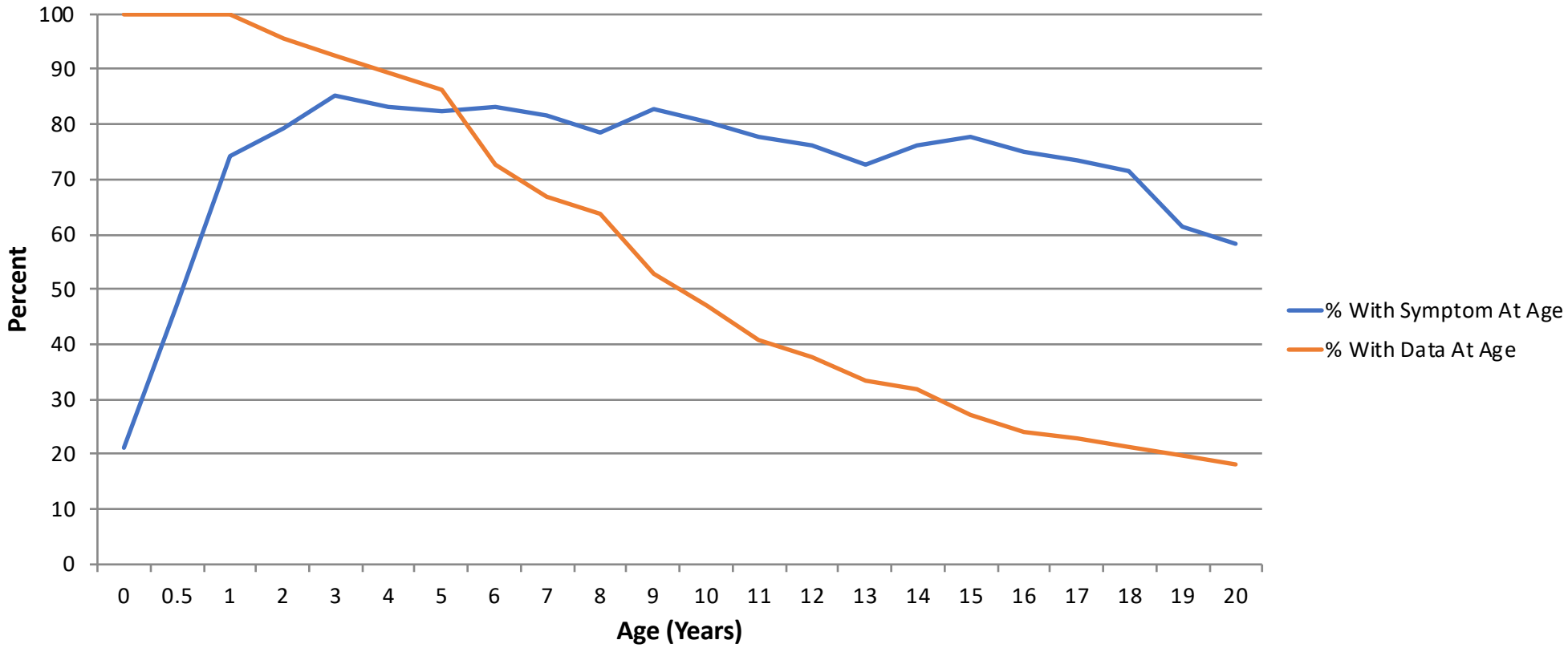

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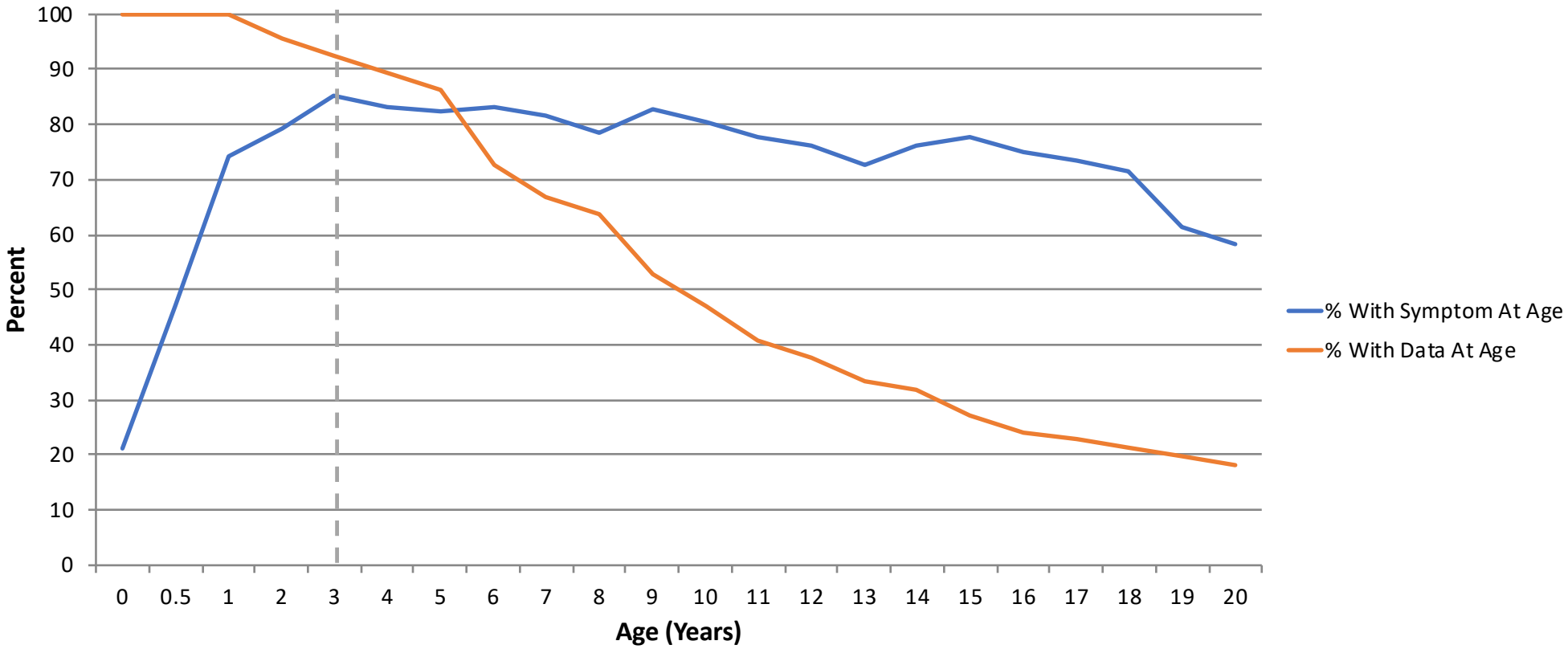
n=66

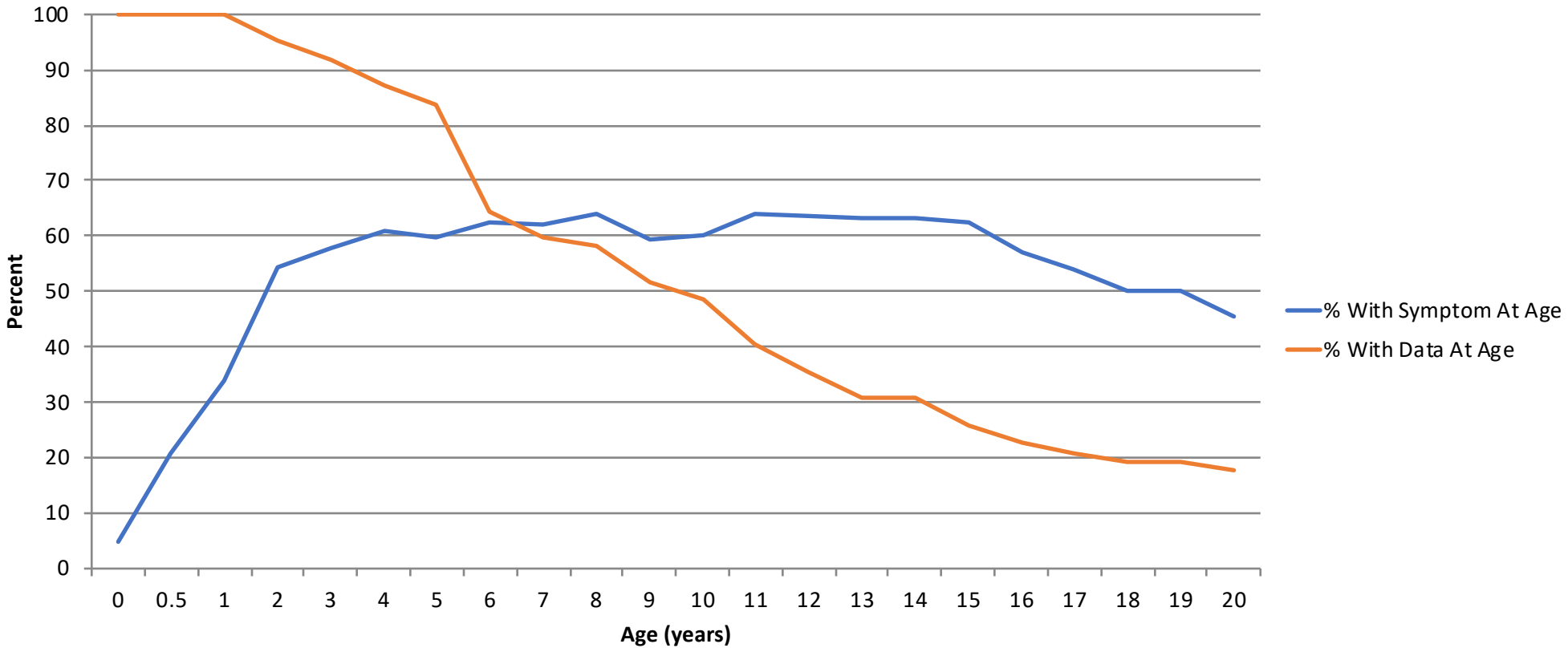
Hypotonia by age



Caroline Mebane

n=66

Clumsiness/discoordination by age



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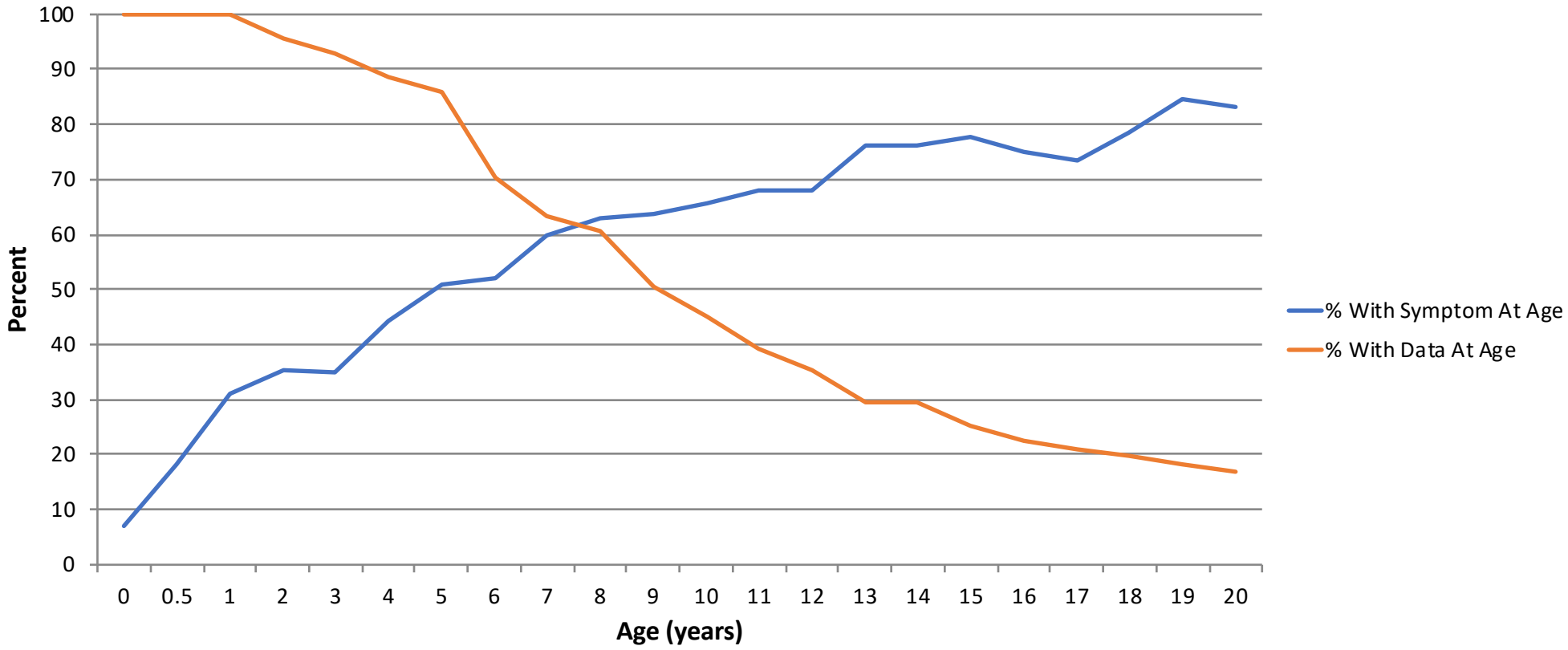
n=62

Optic nerve atrophy by age



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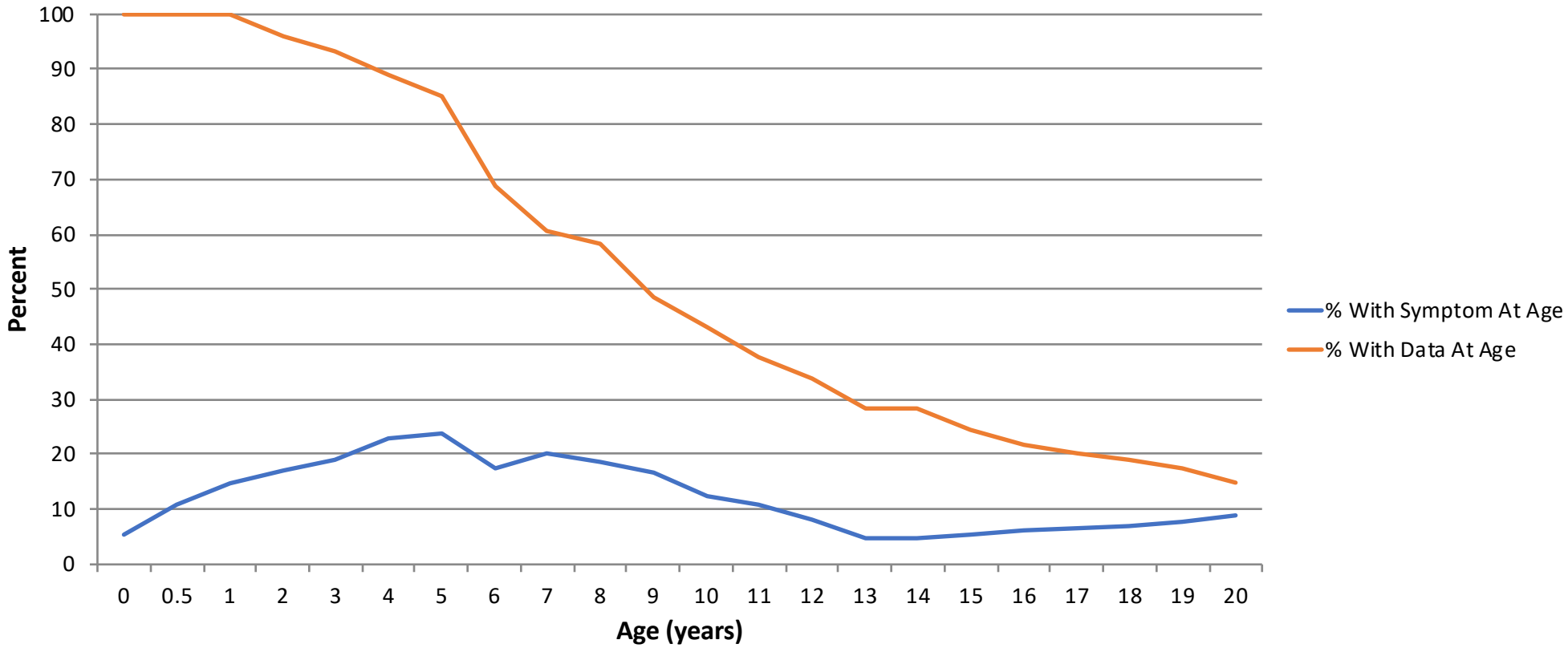
n=71

Cortical visual impairment by age



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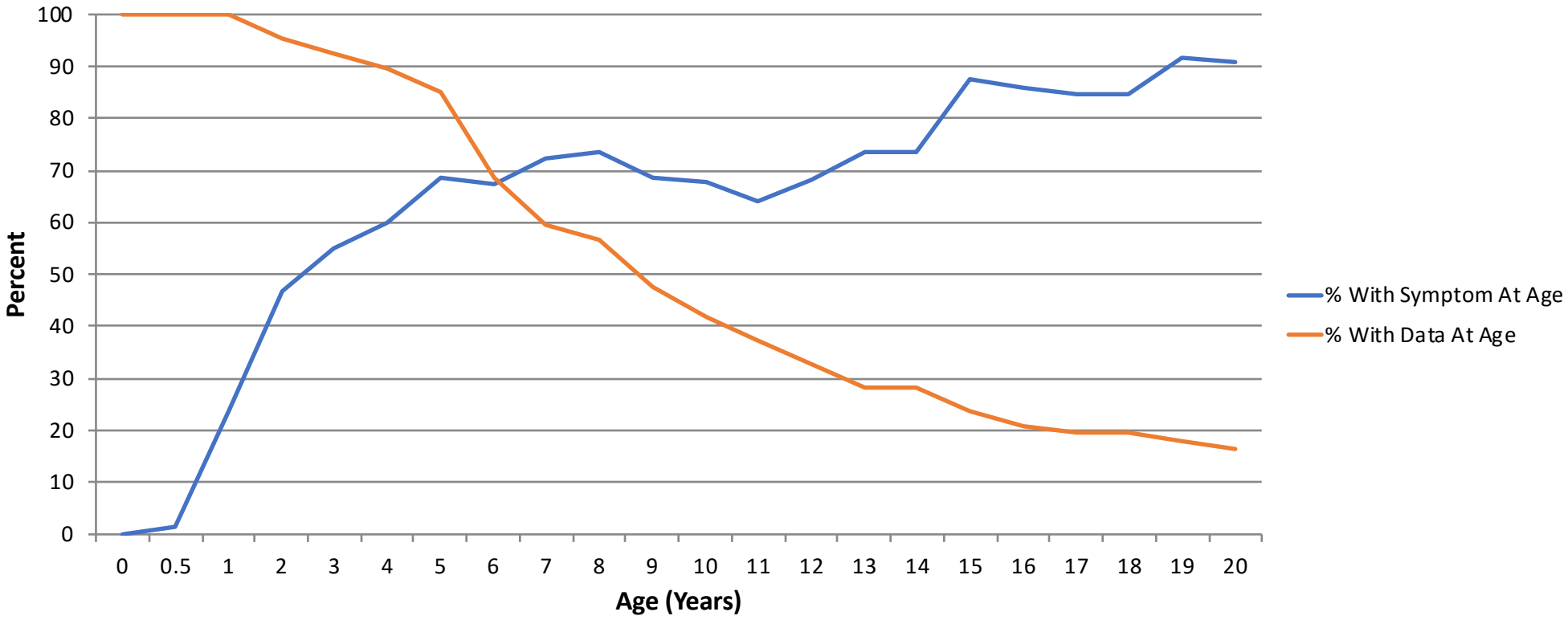
n=74

Abnormal neuroimaging by age



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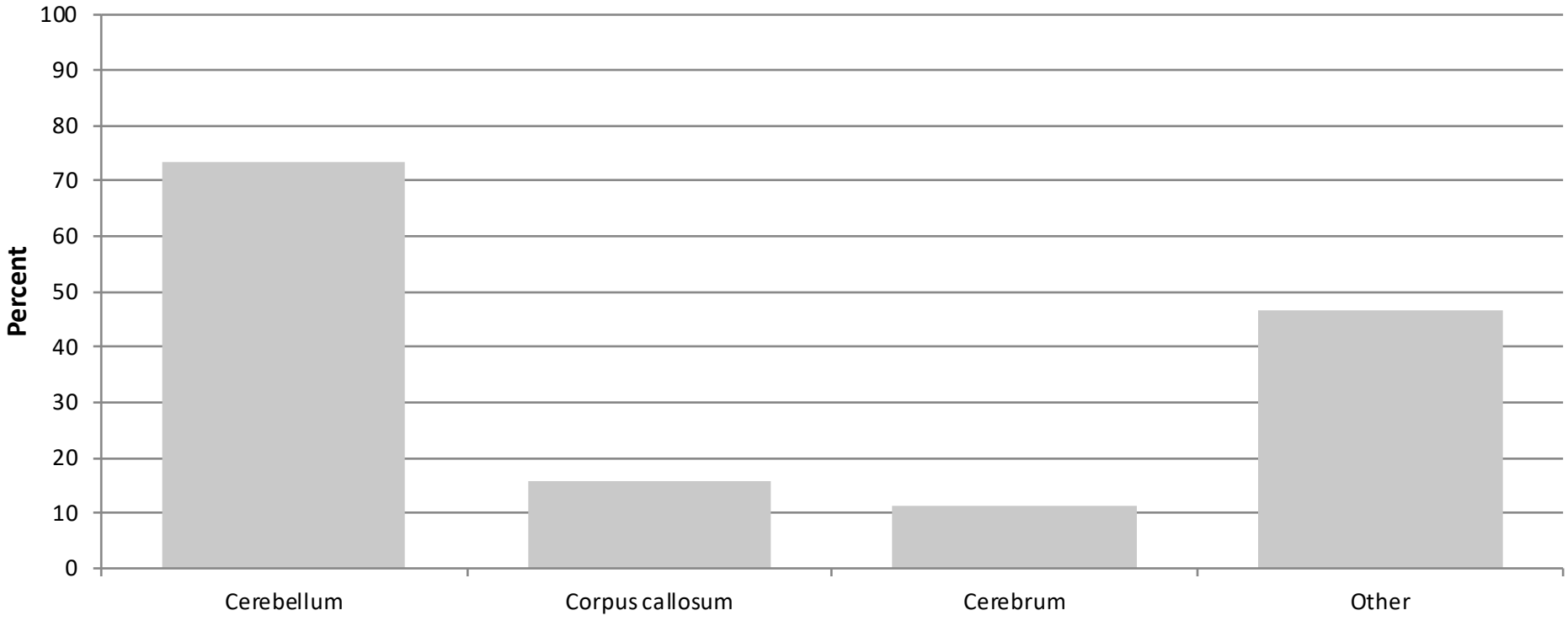
n=67

Type of neuroimaging abnormalities



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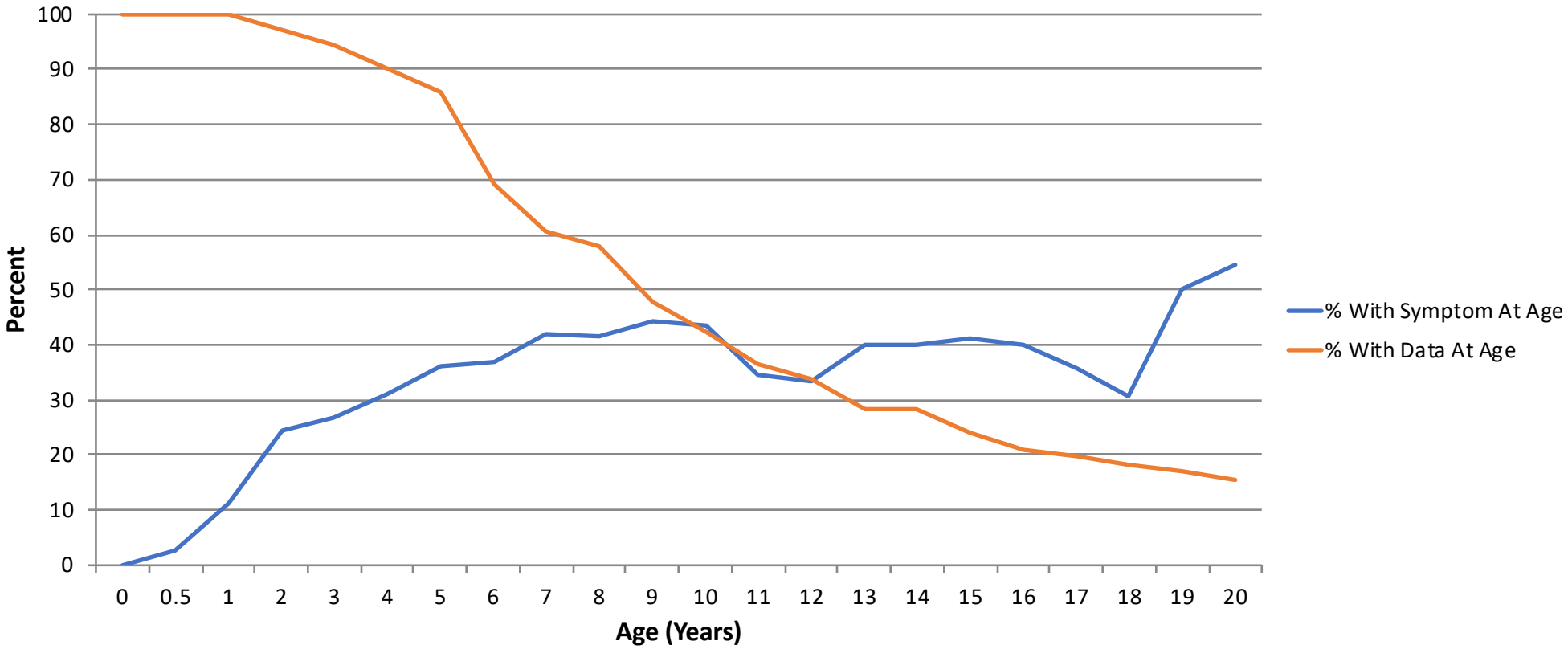
n=45

Seizure history by age



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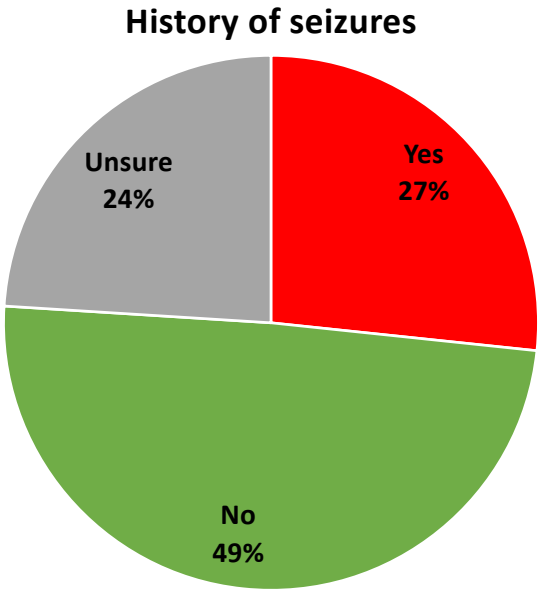
n=71

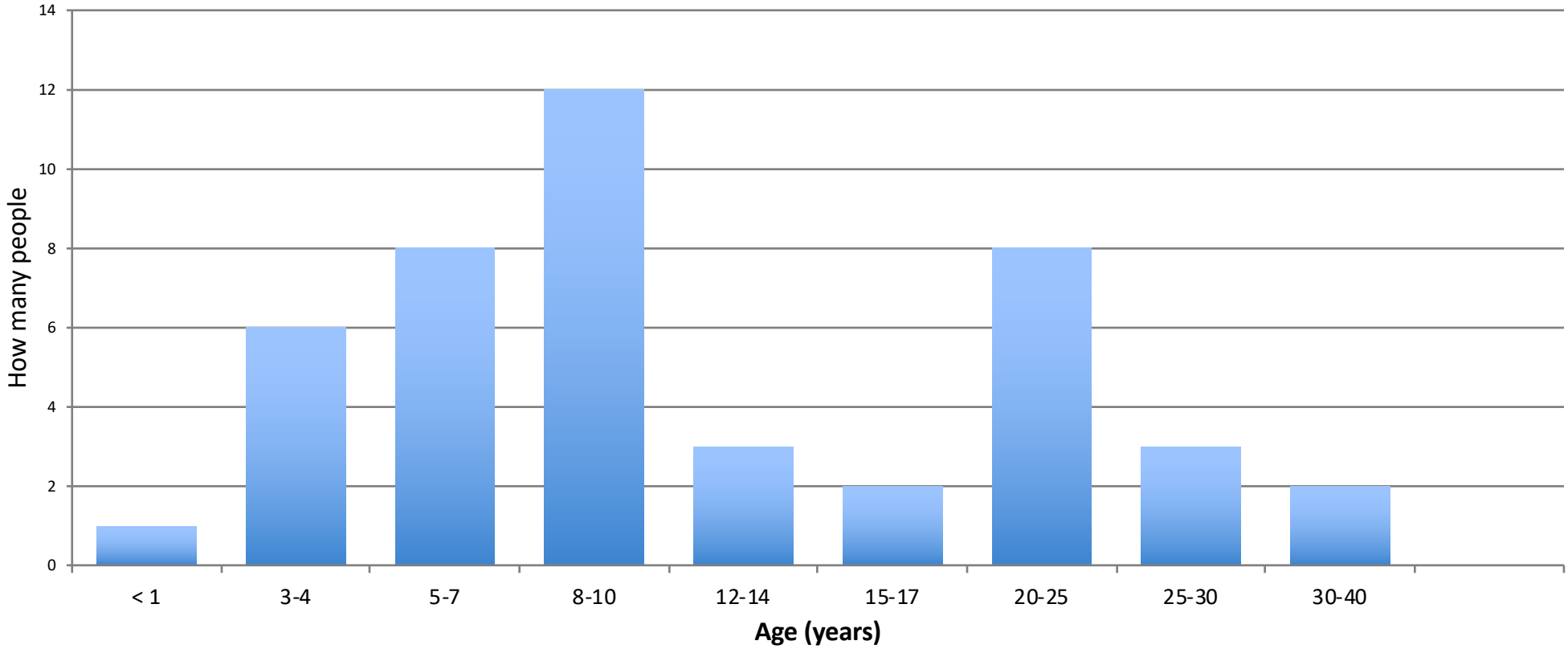
Seizures in KAND: Rare Epilepsy Network survey

- Survey designed by Rare Epilepsy Network (REN) to better characterize rare epilepsies
- 101 participants (95% response rate!)
- 45% of participants reported at least one seizure



Jennifer Bain, MD, PhD

Who gets seizures?



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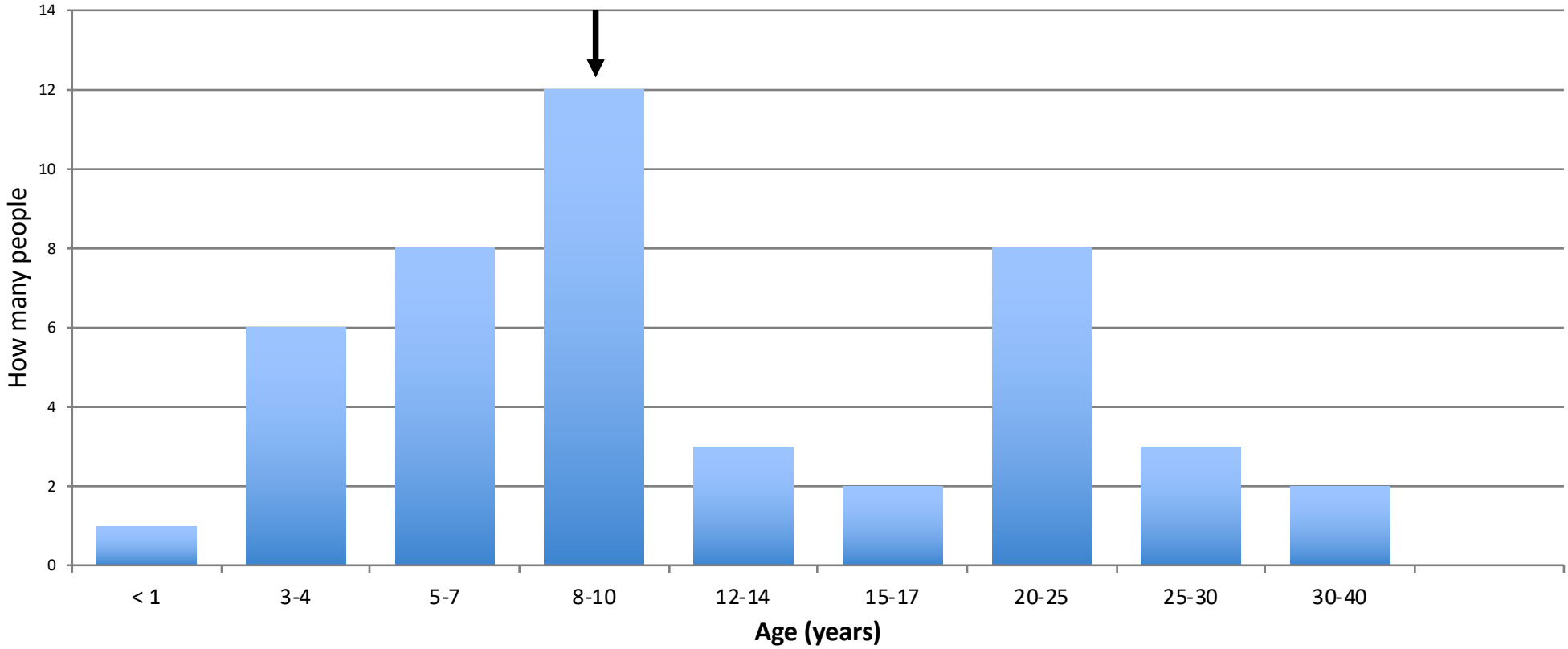

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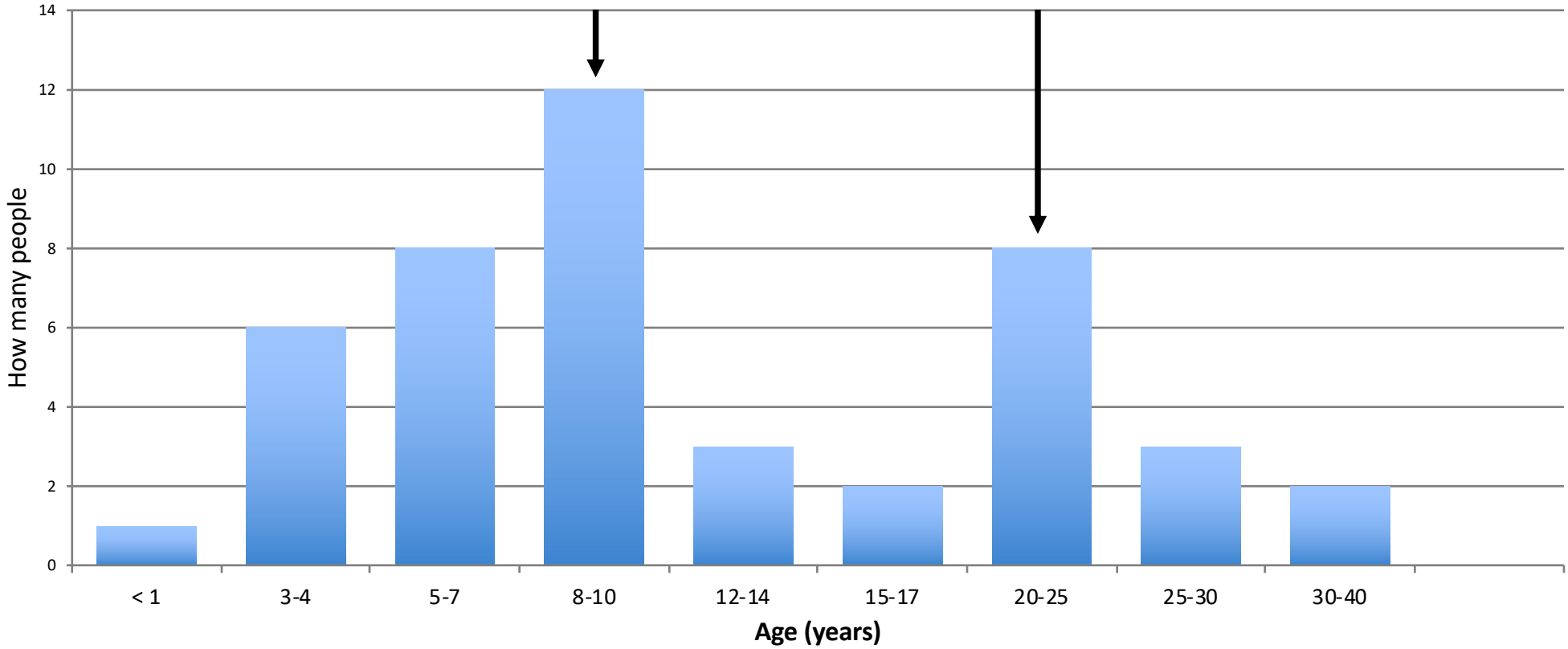
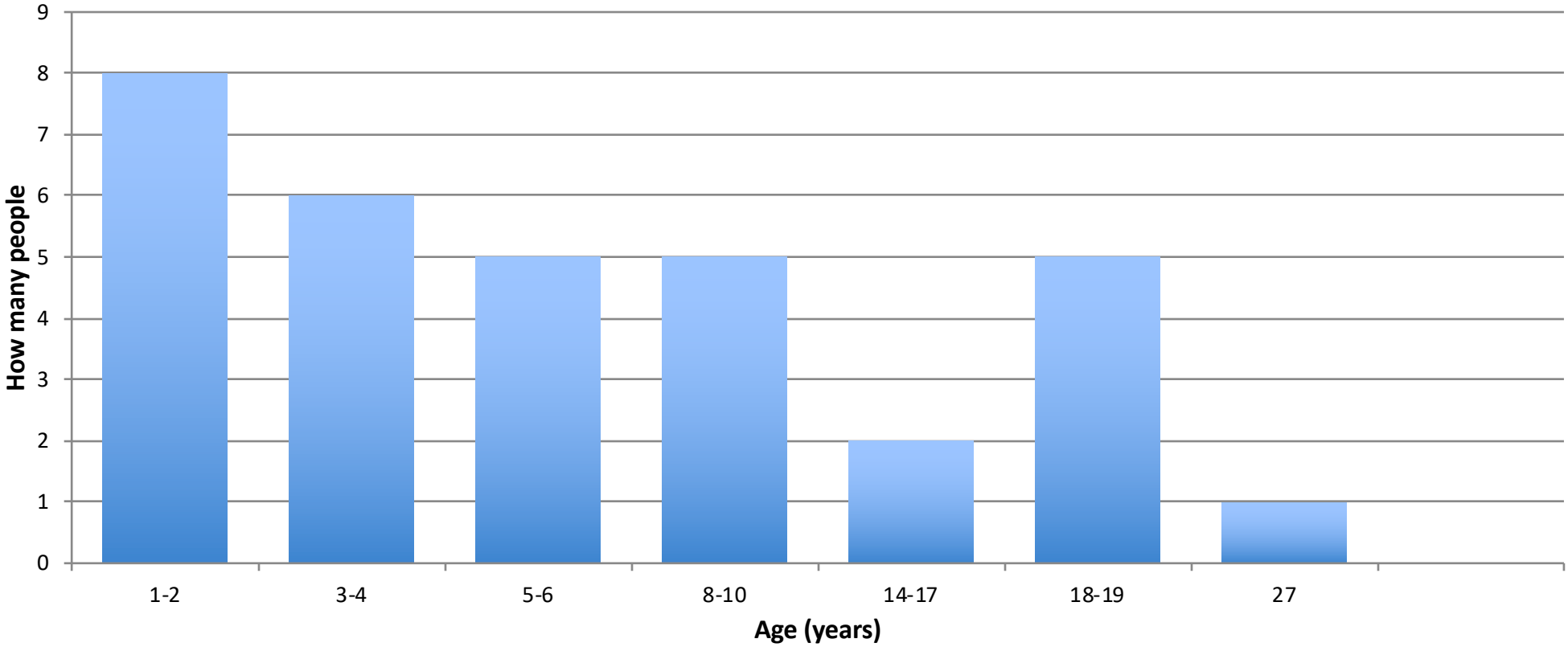


Jennifer Bain, MD, PhD

Age at first seizure



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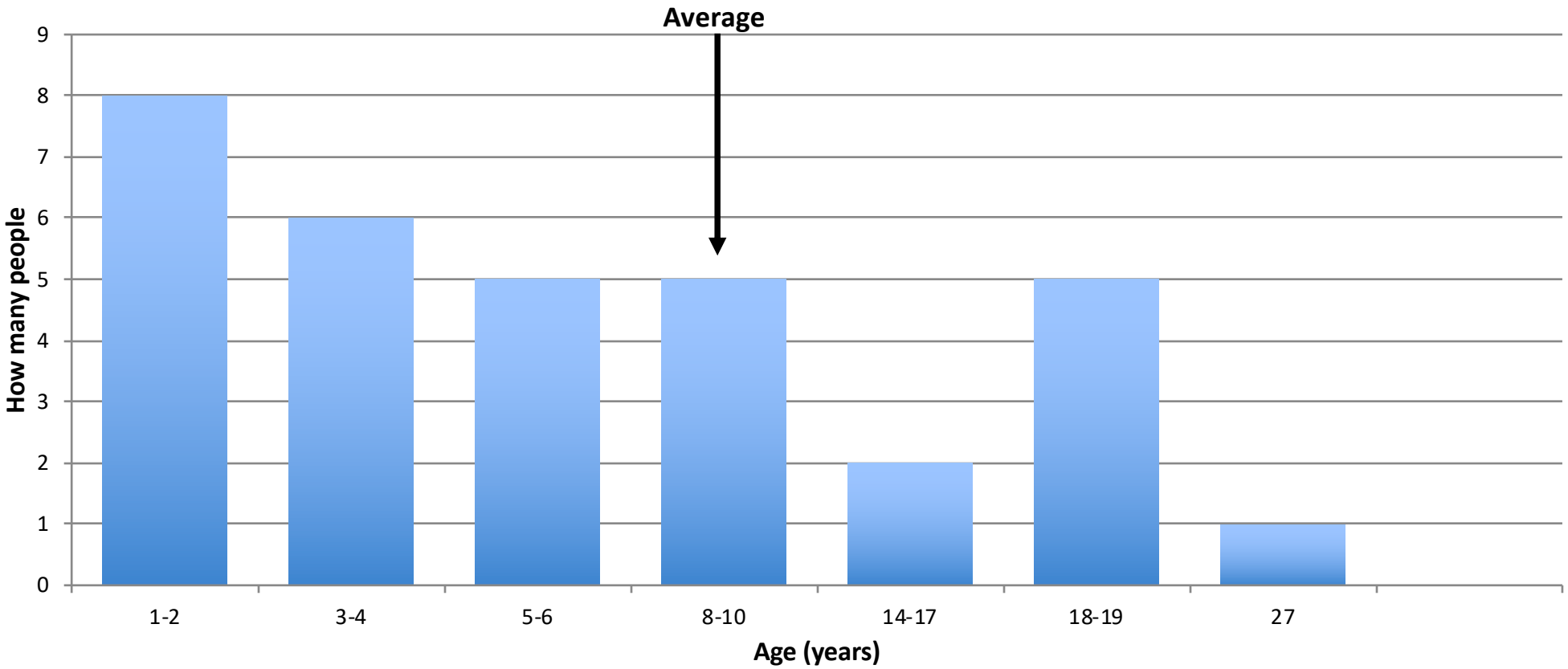

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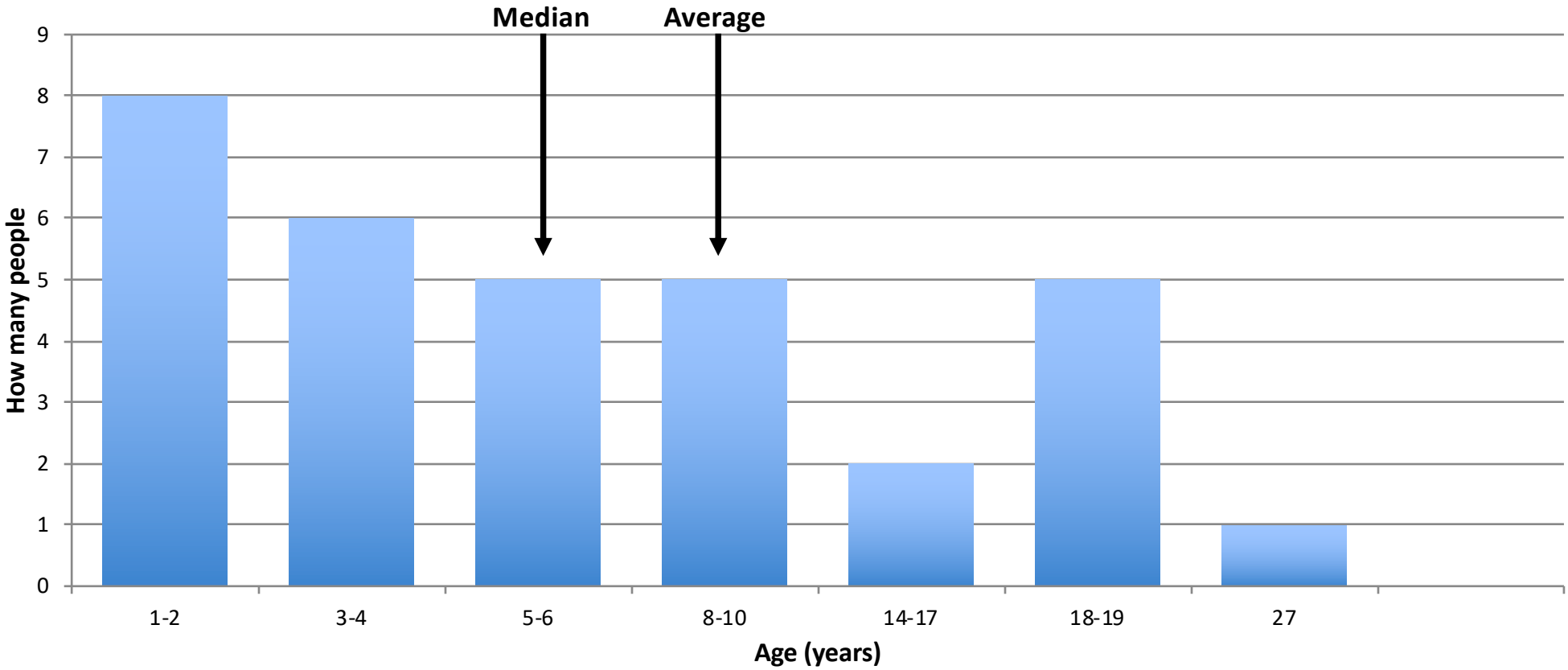

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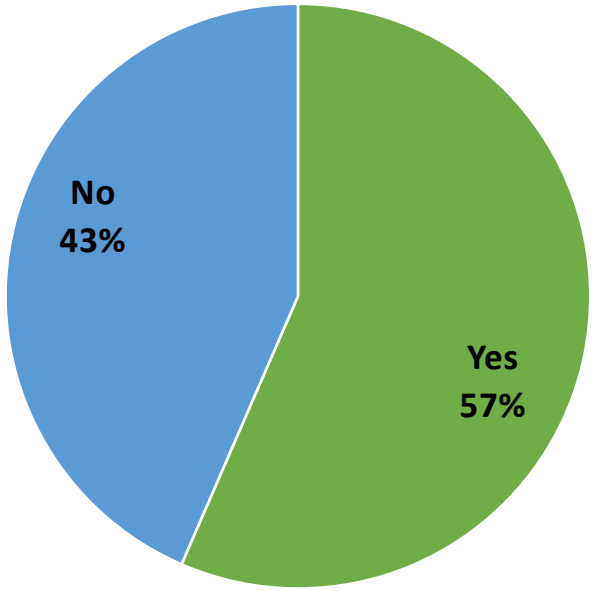
How many had a seizure in the last 6 months?

- Out of the participants with any seizure history, 54% had at least one seizure in the last 6 months



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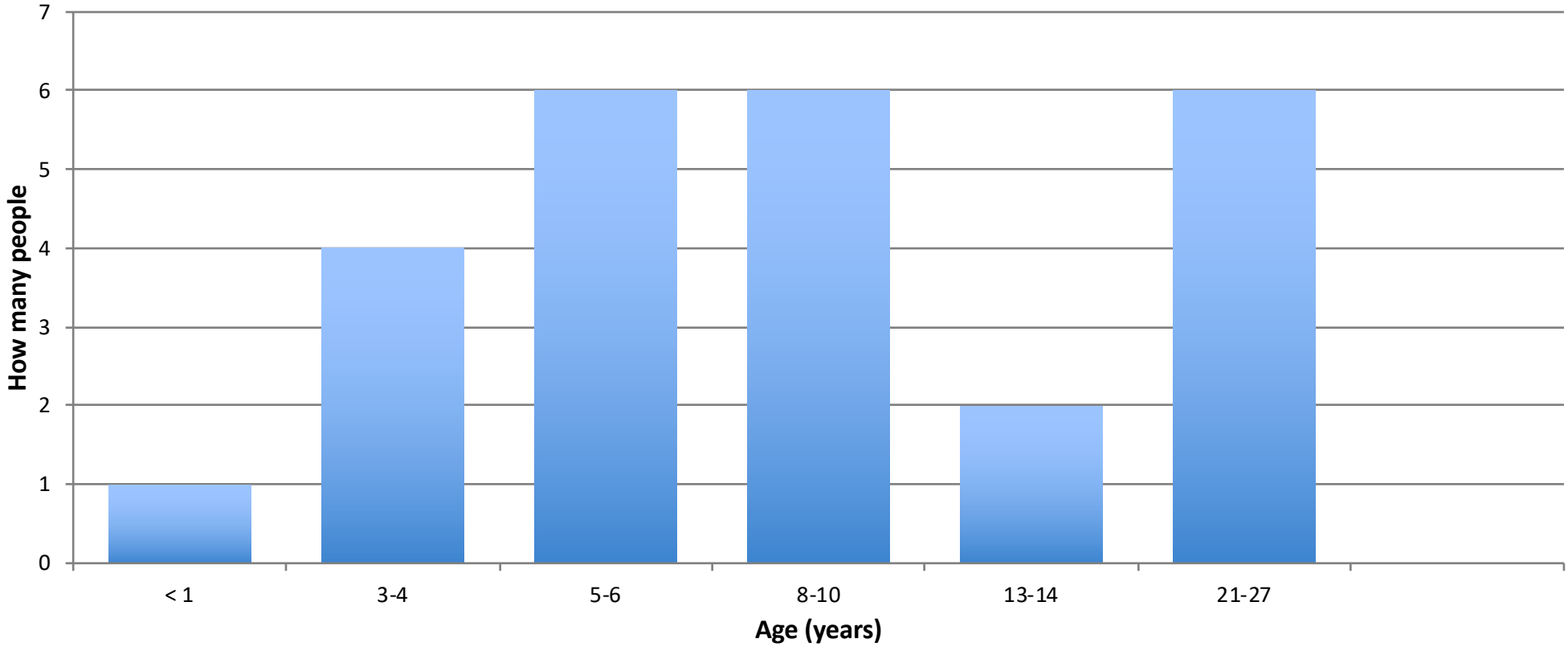

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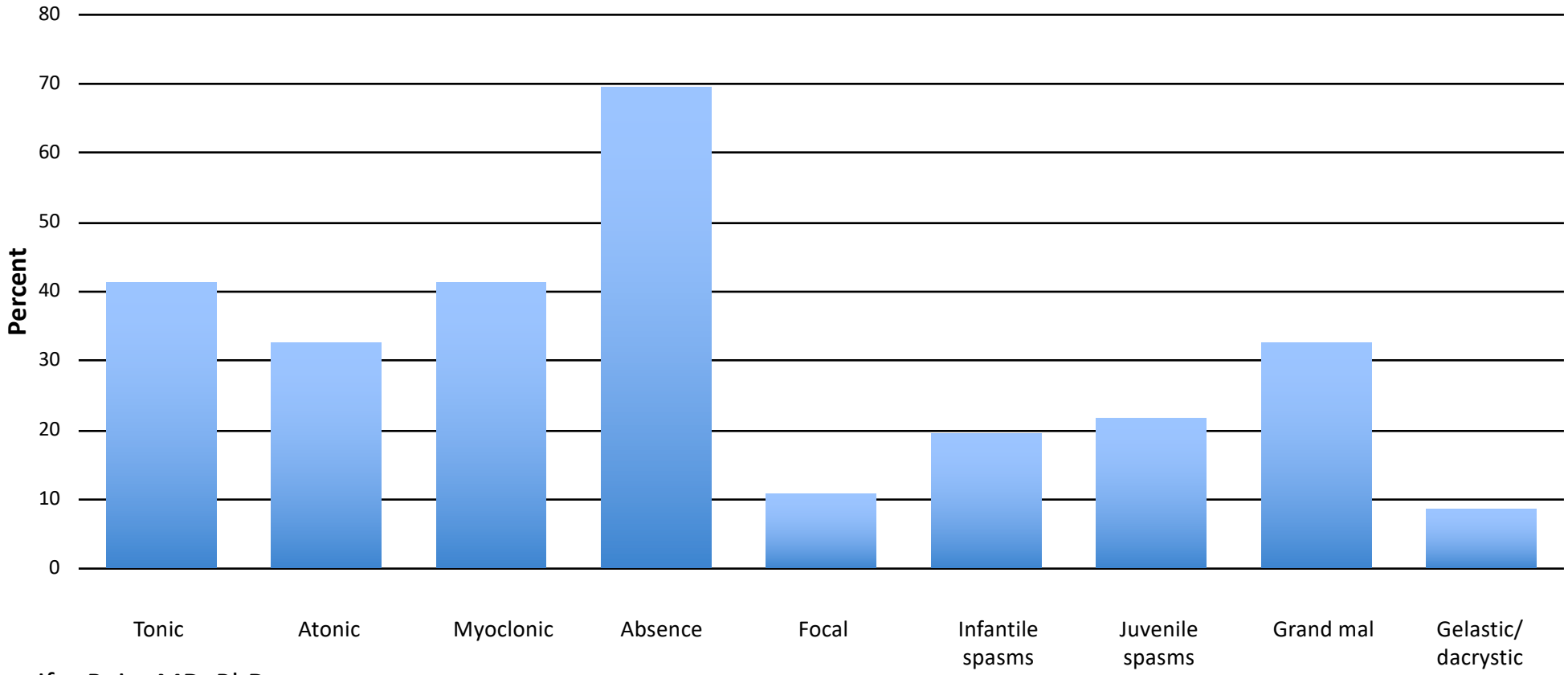
What types of seizures do we see?



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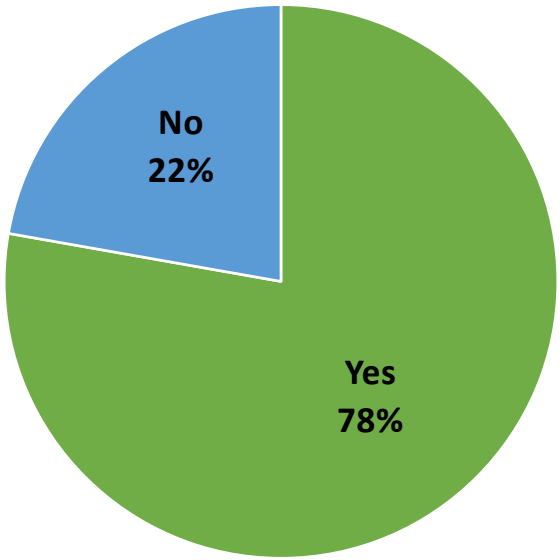
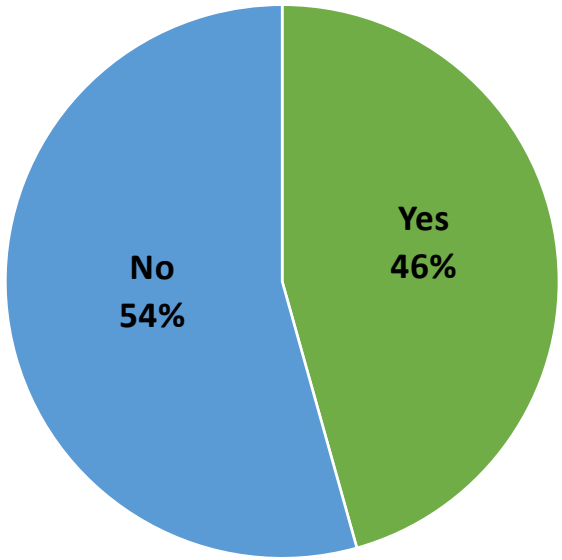
Anti-seizure medication use

Maintenance medication



Rescue medication



Anti-seizure maintenance medications

Levetiracetam *(Keppra)*	**69**
Clobazam *(Onfi)*	**33**
Lamotrigine *(Lamictal)*	**28**
Carbamazepine *(Tegretol)*	**22**
Valproic acid/Valproate	**22**
Medical marijuana/Cannabis/Cannabanoid/CBD/THC	**19**
Clonazepam *(Klonopin)*	**14**
Phenytoin *(Dilantin)*	**14**
Lorazepam *(Ativan)*	**11**
Topiramate *(Topamax)*	**11**

Others: lacosamide, oxcarbazepine, vigabatrin, zonisamide ACTH, eslicarbazepine, gabapentin, phenobarbital, prednisone, pregabalin, perampanel

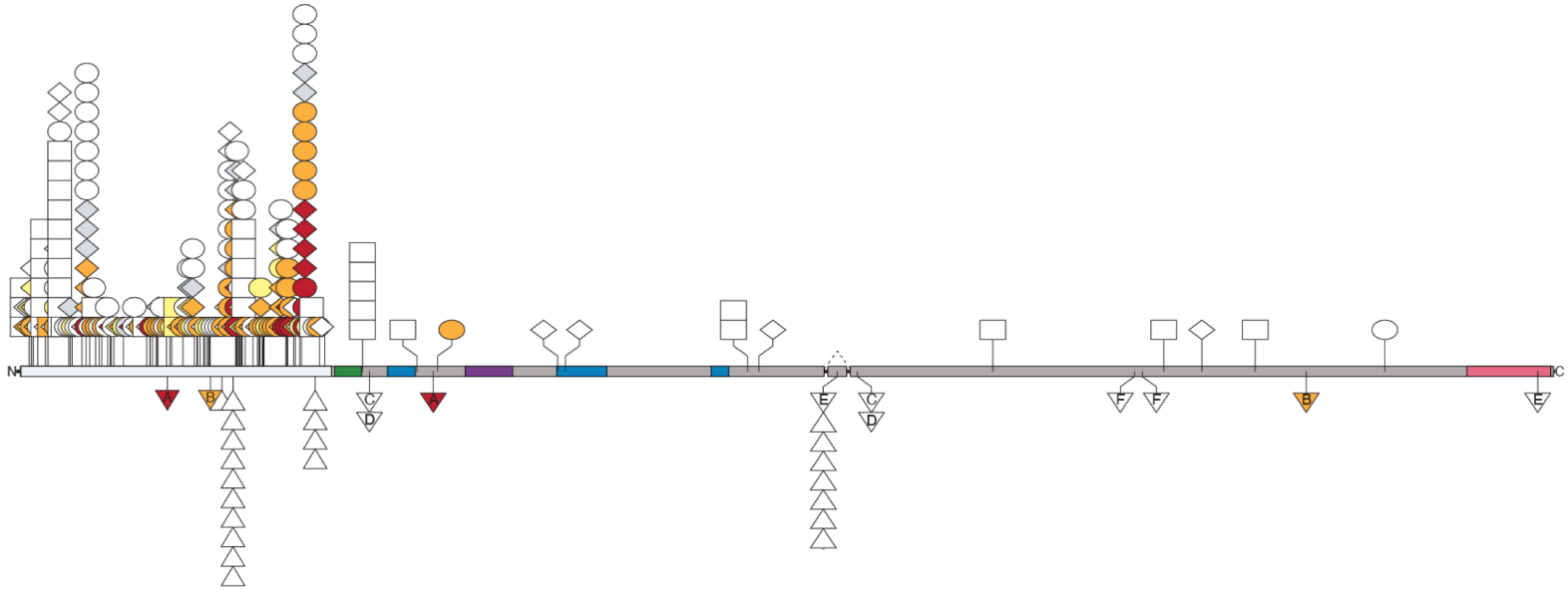
Jennifer Bain, MD, PhD

What this tells us

- Not everyone with KAND has the same challenges
- Some symptoms (e.g., hypertonia) are more common than others (e.g., cortical visual impairment)
- Different symptoms arise at different times
- We still have a lot to learn

Still to learn

- How does the condition change over time?
- Does this differ by genetic variant?
- What treatments do or do not work?



What we need from you

- Keep us updated: fill out your Year 3 Follow Up Survey
  - Survey sent out September 7th, 2021
  - Sent to people in the study for more than 6 months
  - Medical history update as well as Vineland Adaptive Behavior Scale update
- Send us your records
  - Reports: MRI reports, EEG reports, OCT reports
  - Original images and data: MRIs, EEGs
- Help us keep in touch
  - Give us your updated contact information
- Keep an eye out for more opportunities in the future, both virtual and in person…

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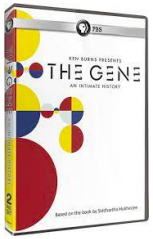
Contact us at kif1a_study@cumc.columbia.edu !

Acknowledgments



For more on KAND check out

Chung lab

Natural history study team

Caroline Mebane
Scott Robinson
Laura Hamm

Jennifer Bain, MD, PhD

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