



# Episode Triggers in AHC:

*An Analysis of Patient-Reported Data*

Nina Frost | September 15, 2025 | ATP1A3 Symposium

# Not just anecdotes: the lived experiences of patients provide impactful data

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# We are translating the patient experience into *data*

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Patient anecdotes,  
narratives, observations

Research questions to  
inform new/ongoing studies



Standardized, IRB-governed  
survey platform

SME input to refine questions  
and scope



Analysis of patient-reported  
data

Impact of age, genotype,  
sex on patient experience

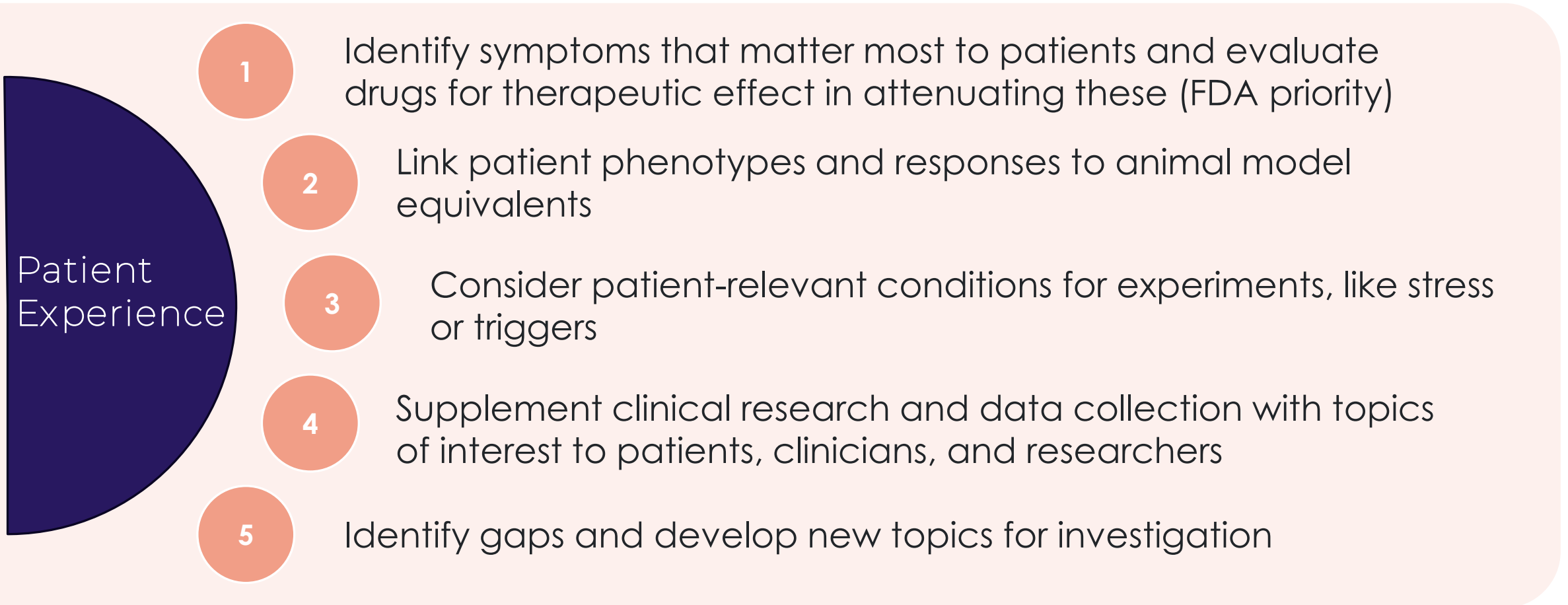
***Novel findings of episode  
triggers and precursors***

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# We use the patient survey to embed the patient experience in research

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Patient Centric *Analysis of patient-reported data allows us to:*



# Our second survey queried topics relevant to patients and researchers

 Sleep

 Triggers

 Medications

 Headaches

Section 1 of 11

## Sleep, Triggers, Medications, and Headaches: Insight into the AHC Patient Experience

**B** *I* U ↺ ✕

The purpose of this survey is to capture the AHC patient experience in four areas: sleep, triggers, medications, and headaches.

Understanding the experience of a large group of patients in each of these categories could inform research into the underlying disease mechanisms of AHC. It may also give caregivers and physicians information to refine strategies for disease management.

We want to understand these specific symptoms in the context of the patient's overall symptom profile.

This survey is intended to be completed by AHC patient caregivers. We encourage caregivers to consult their patient, if possible, to provide the most accurate responses. Some AHC patients over the age of 18 may choose to complete the survey themselves if they are able. If you are completing this survey for yourself, "the patient" refers to you, your symptoms, and your experiences for the remainder of this survey.

We estimate the survey should take approximately 15 to 20 minutes to complete.

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# Triggers in AHC

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Triggers and episode precursors were a priority because paroxysmal episodes were the most preferred target for elimination.

We wanted to offer insight into the relationship between triggers and paroxysmal episodes.

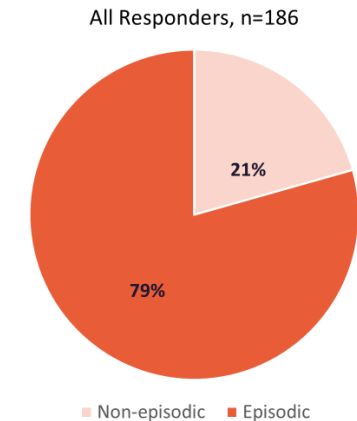
## Understanding the Patient Priorities

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“

Would you prefer to eliminate the episodic symptoms of AHC (such as hemiplegia, dystonia and seizures) OR the constant or non-episodic daily symptoms experienced by your patient (such as motor and speech difficulties)?

”



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*Across age, genotype, and sex groups, responders consistently prioritized the elimination of paroxysmal symptoms*

## Triggers in AHC: the Survey

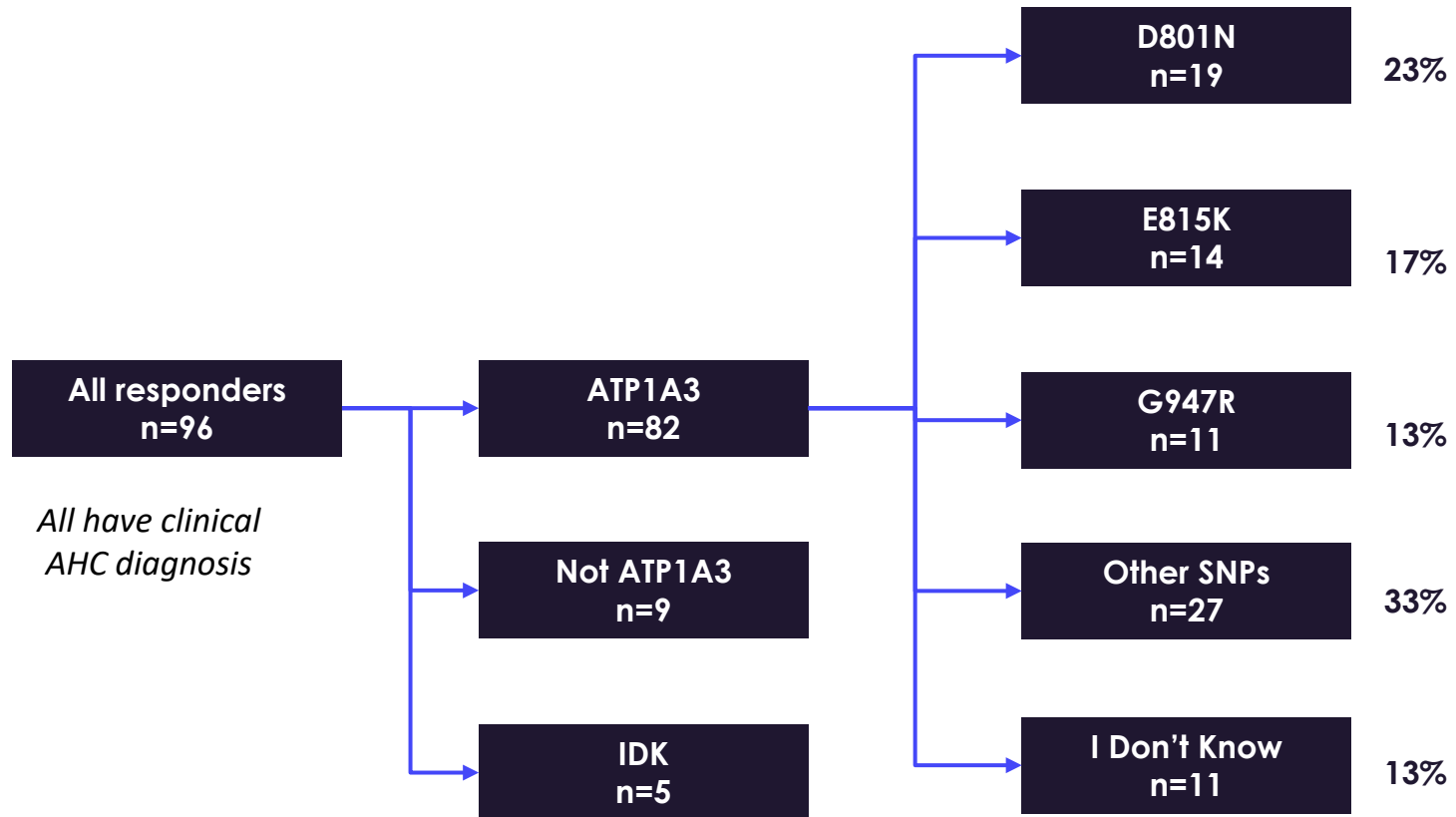
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*Who were the survey takers?*

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# Patient Genotype Data As Reported by Survey Respondents

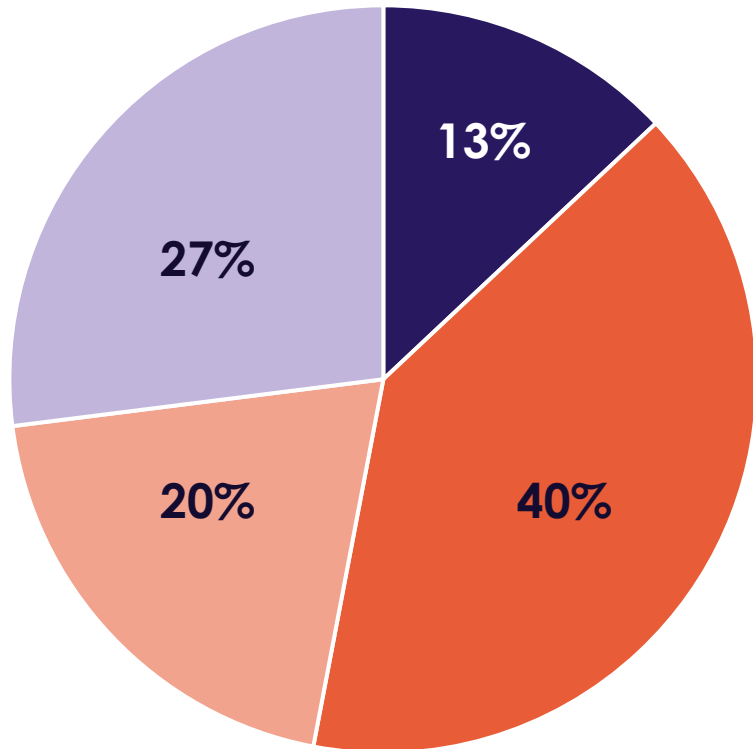
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**More than half of patients were 10 or younger; more than half were female.**

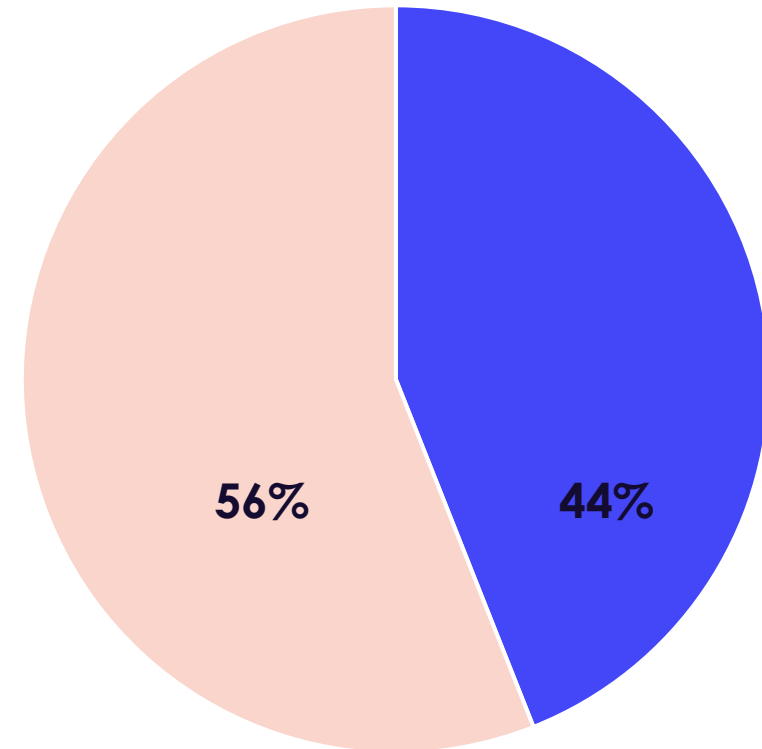
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**Age Distribution**



■ <=3 ■ 4-10 yo ■ 11-17 yo ■ >=18 yo

**Sex Distribution**



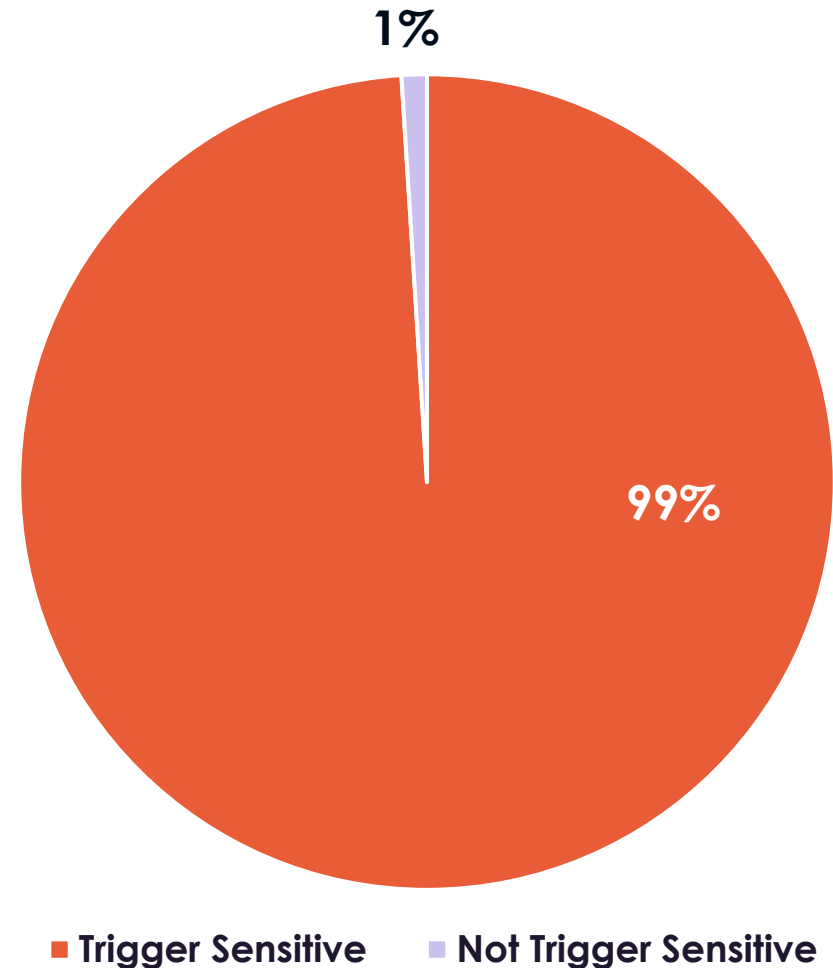
■ Male ■ Female

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## A sensitivity to triggers was nearly universal in AHC patients.

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*95/96 (99%) of responders indicated that a trigger could induce AHC episodes in their patient.*



# Most commonly-reported AHC triggers: excitement, fatigue, stress, exercise

“

Which triggers can cause AHC episodes in your patient, now and in the past?

”

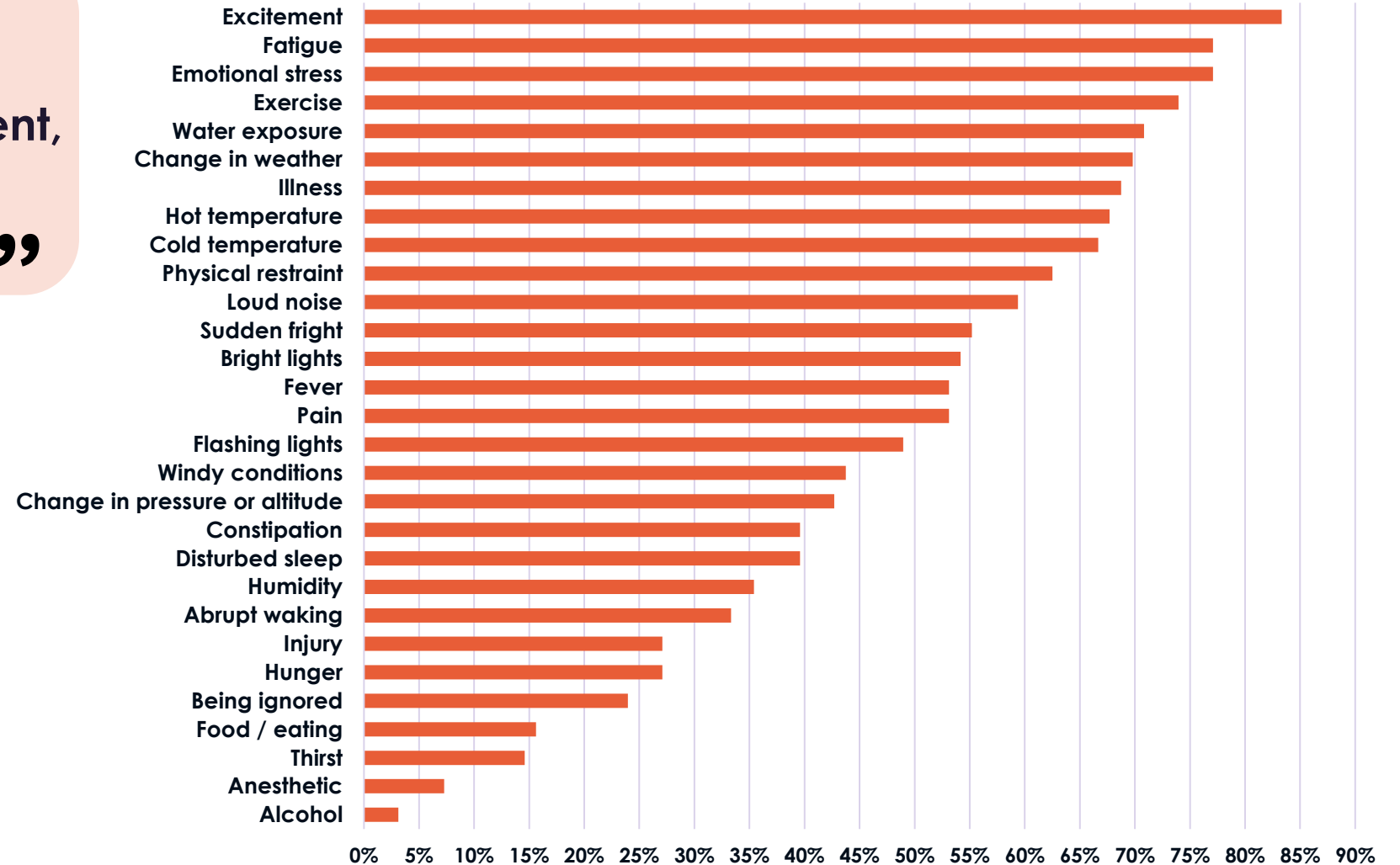
“Write-in” responses:

strong smells (including smoke) (5),  
visual overstimulation/screens (7),  
general commotion (3)

**Genotype, Sex, Age Effect?**

**No statistically significant differences**  
in reported triggers were present  
when respondents were stratified by  
genotype, sex and age.

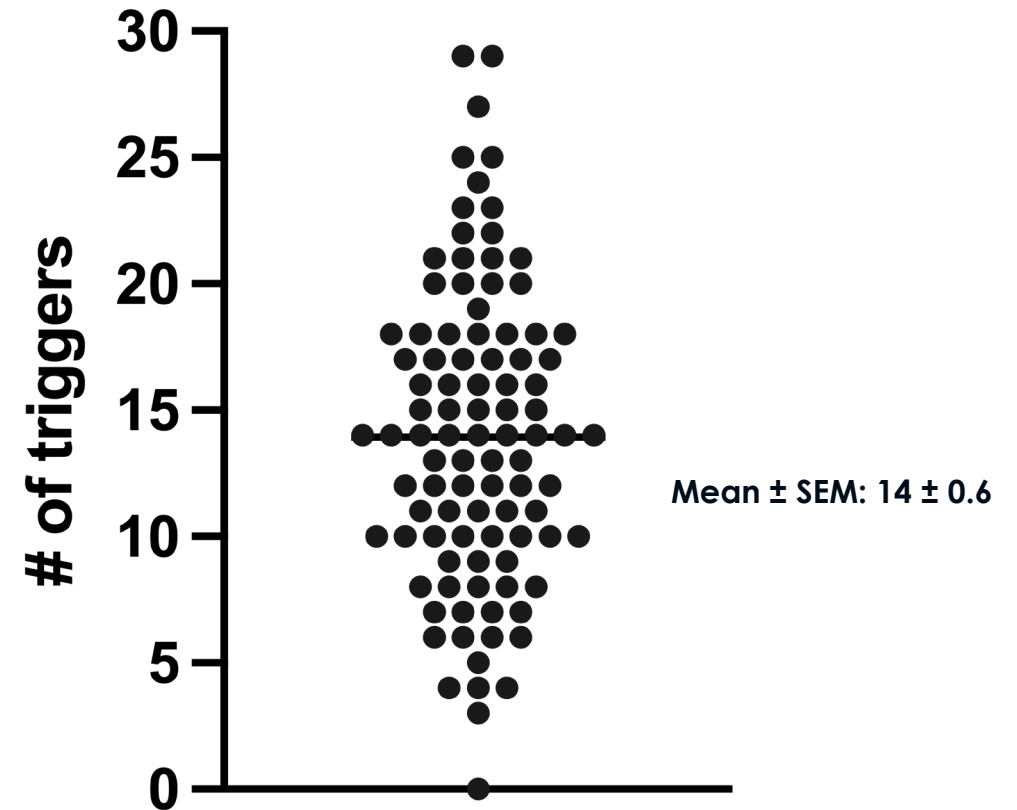
## AHC Triggers



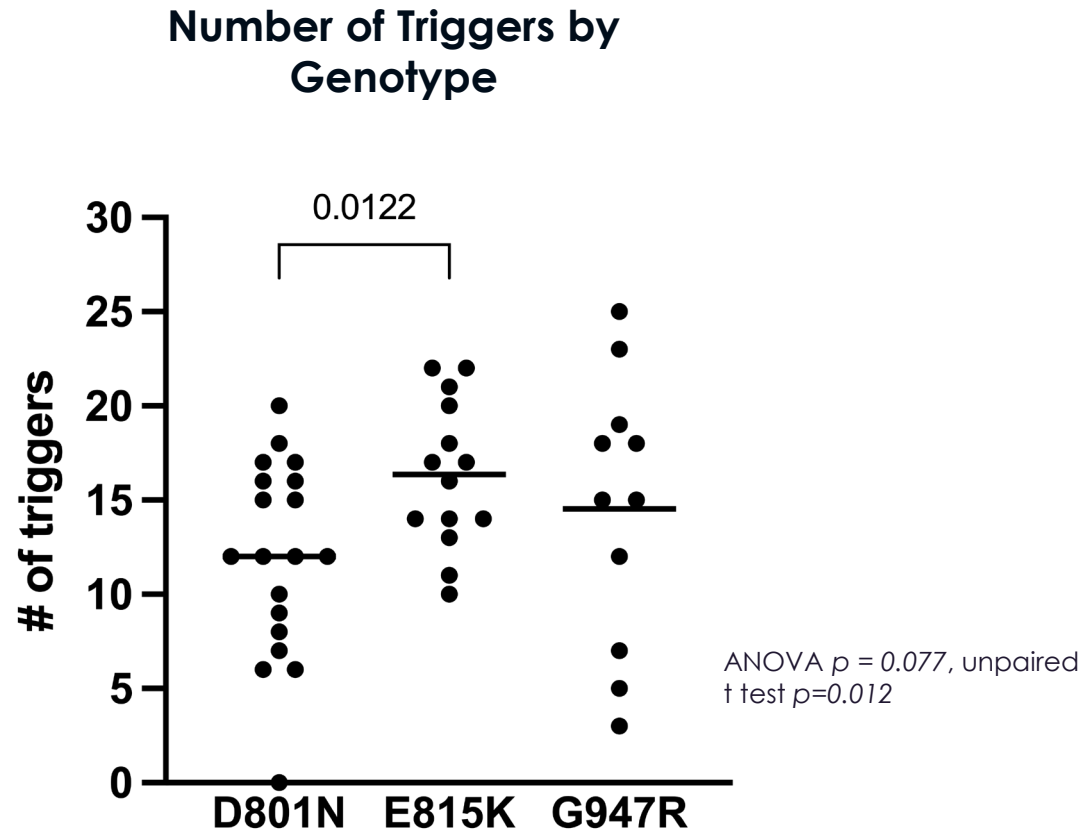
# Survey takers identified multiple triggers for each AHC patient

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*On average, respondents identified 14 triggers for each AHC patient.*



# E815K patients have a greater number of triggers than D801N patients.



	D801N	E815K	G947R
n	19	14	11
Minimum	0.000	10.00	3.000
Maximum	20.00	22.00	25.00
Range	20.00	12.00	22.00
Mean	12.00	16.36	14.55
Std.Dev.	5.110	3.915	7.160
SEM	1.172	1.046	2.159

There was no statistically significant difference in the number of triggers identified between male and female patients or between age groups.

Variability was highest in G947R respondents.

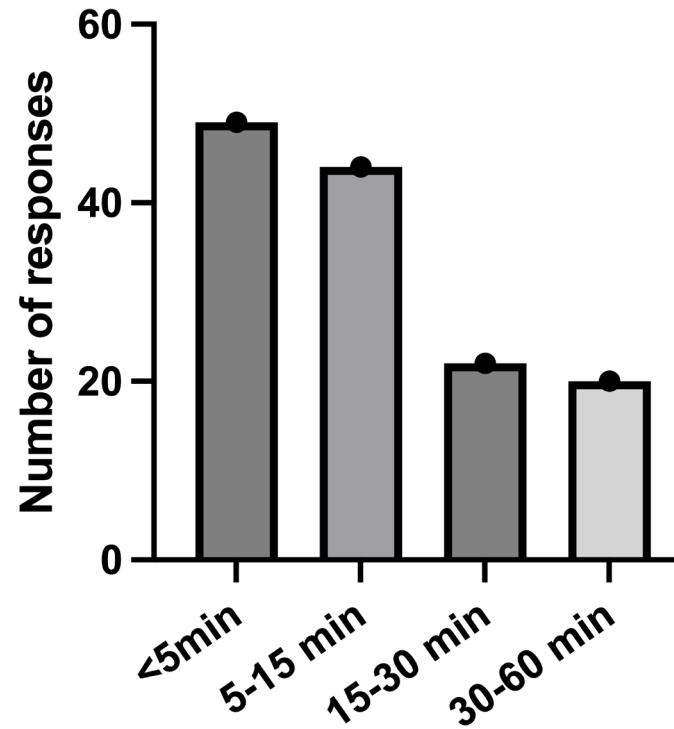
# Trigger to onset timing

“  
How long does it take, on average, for a trigger to provoke symptoms in your patient?  
”

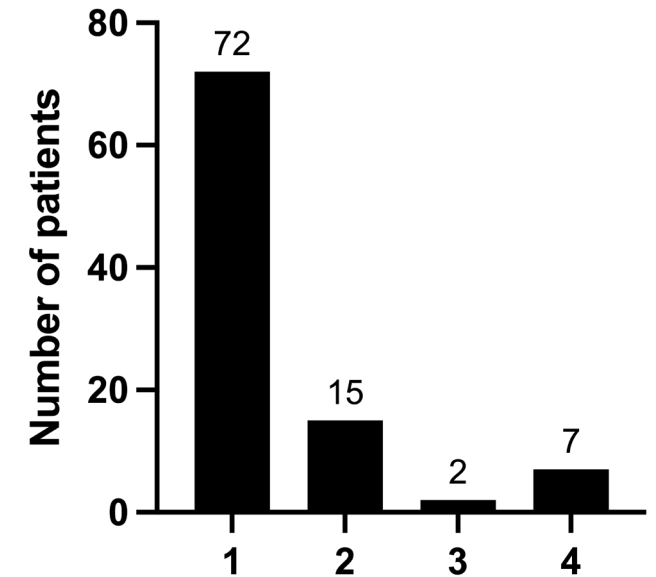
Most patients experience symptoms within 15 minutes of a trigger.

25% of respondents selected multiple categories, suggesting variability in response time for individual patients.

Trigger to Onset Time



How Many Respondents selected more than one category?



# Episode Precursors: Premonition or Prodrome?

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“

Do you think your patient can tell an episode is coming, before it starts?

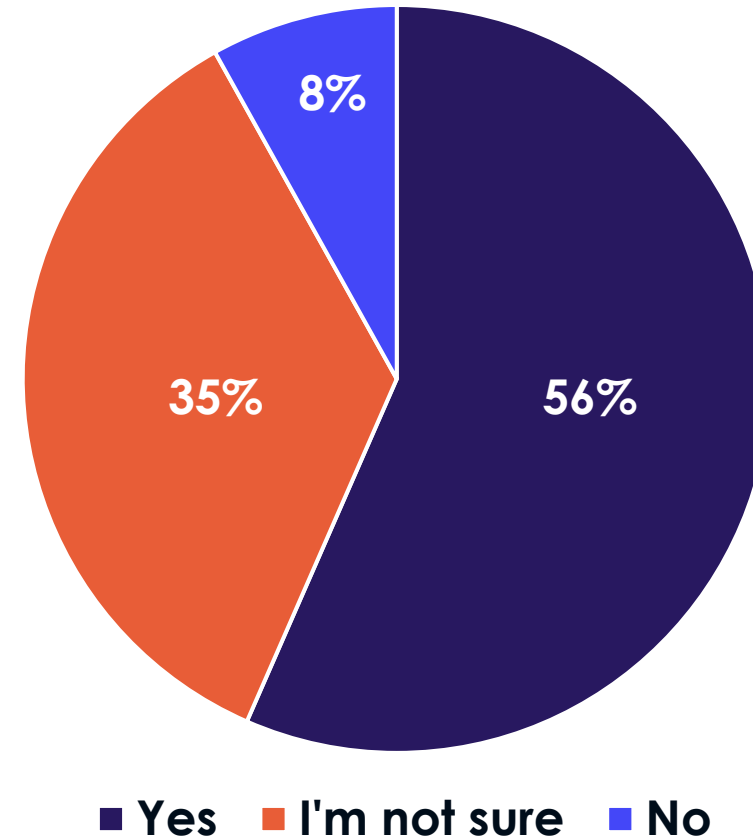
”

The majority of respondents reported that their patient can sense the onset of an episode before symptoms appear.

A significant minority were unsure.

Only 8% of respondents believed their patient could *not* feel an impending episode.

This pattern was consistent across genotype, sex, and age groups.



# Episode Precursors Observed by Caregivers

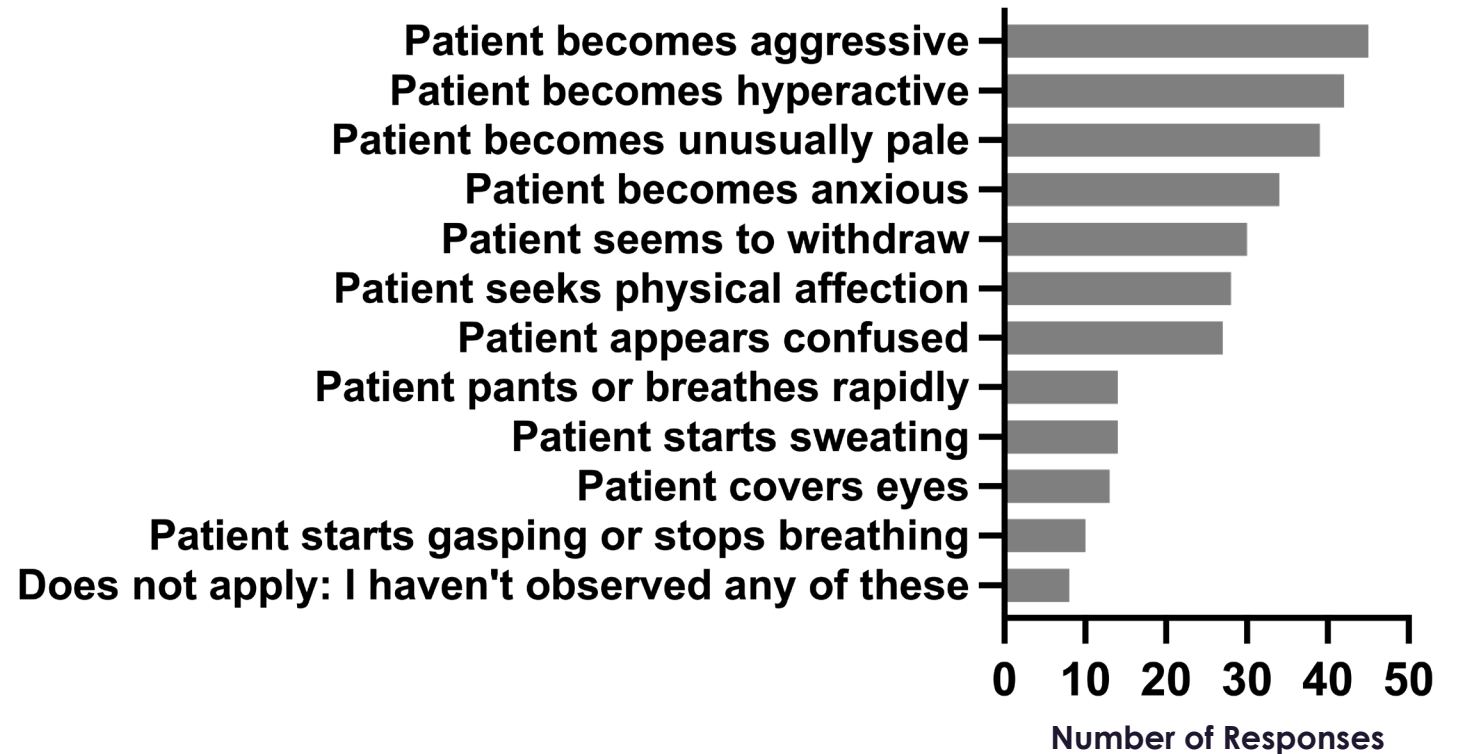
“

Do you observe any of the following before the start of an AHC episode? Please check all that apply

”

The three most commonly-reported phenotypes preceding paroxysmal episodes are **aggression**, **hyperactivity** and **pallor**.

## Behaviors Preceding an Episode





Terrey, M. *et al.* Alternating hemiplegia of childhood associated mutations in *Atp1a3* reveal diverse neurological alterations in mice. *Neurobiol. Dis.* **212**, 106954 (2025).

## Multiple triggers were reported to increase the **likelihood** of an episode

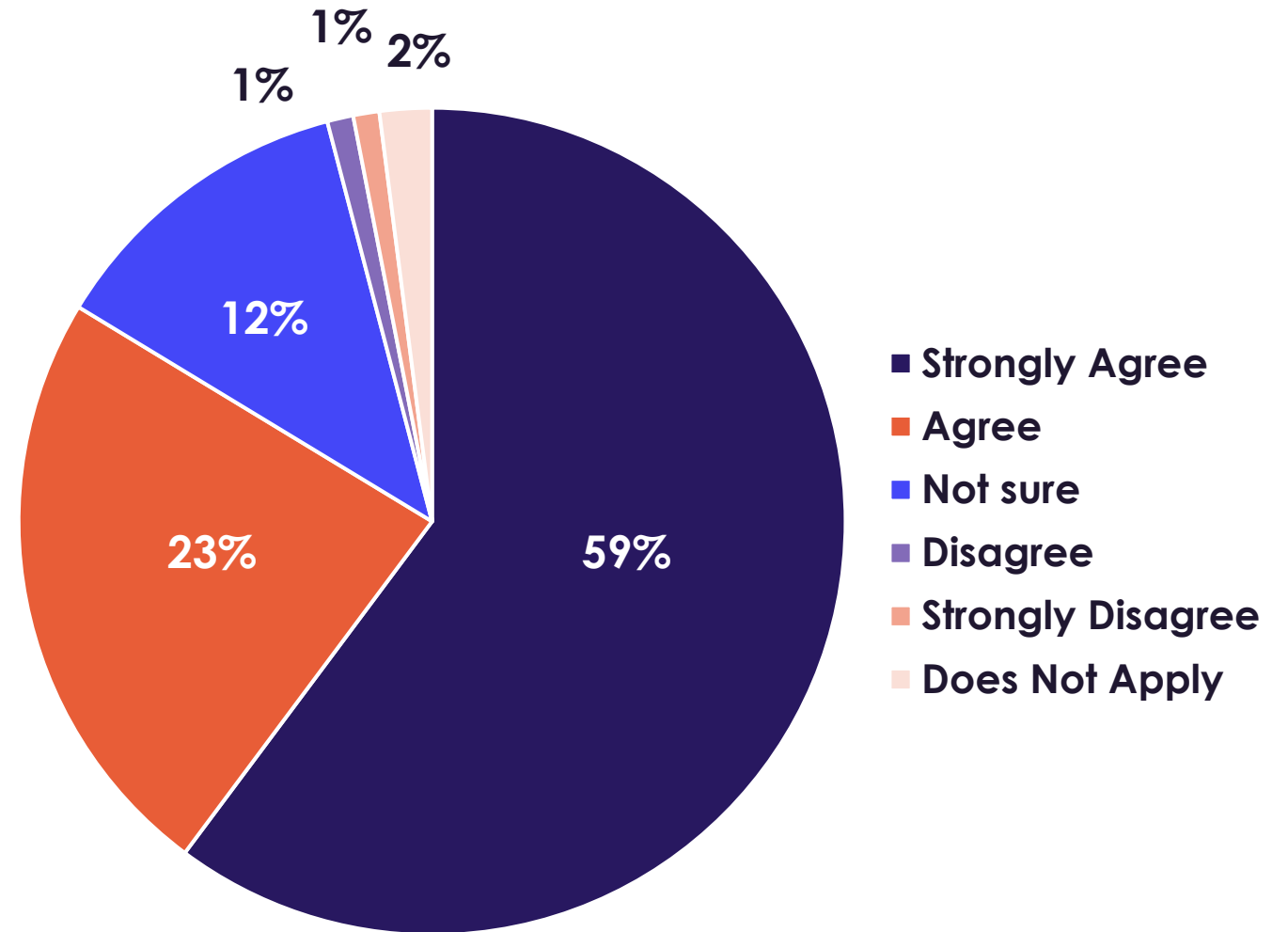
“

Do multiple triggers, experienced in the same day, make it more likely to experience an AHC episode?

”

**82% of respondents strongly agreed or agreed** that multiple triggers would raise the likelihood of a paroxysmal episode for their patient.

**Only 2% of respondents disagreed or strongly disagreed.**



# Multiple triggers were reported to increase the **severity** of an episode

“

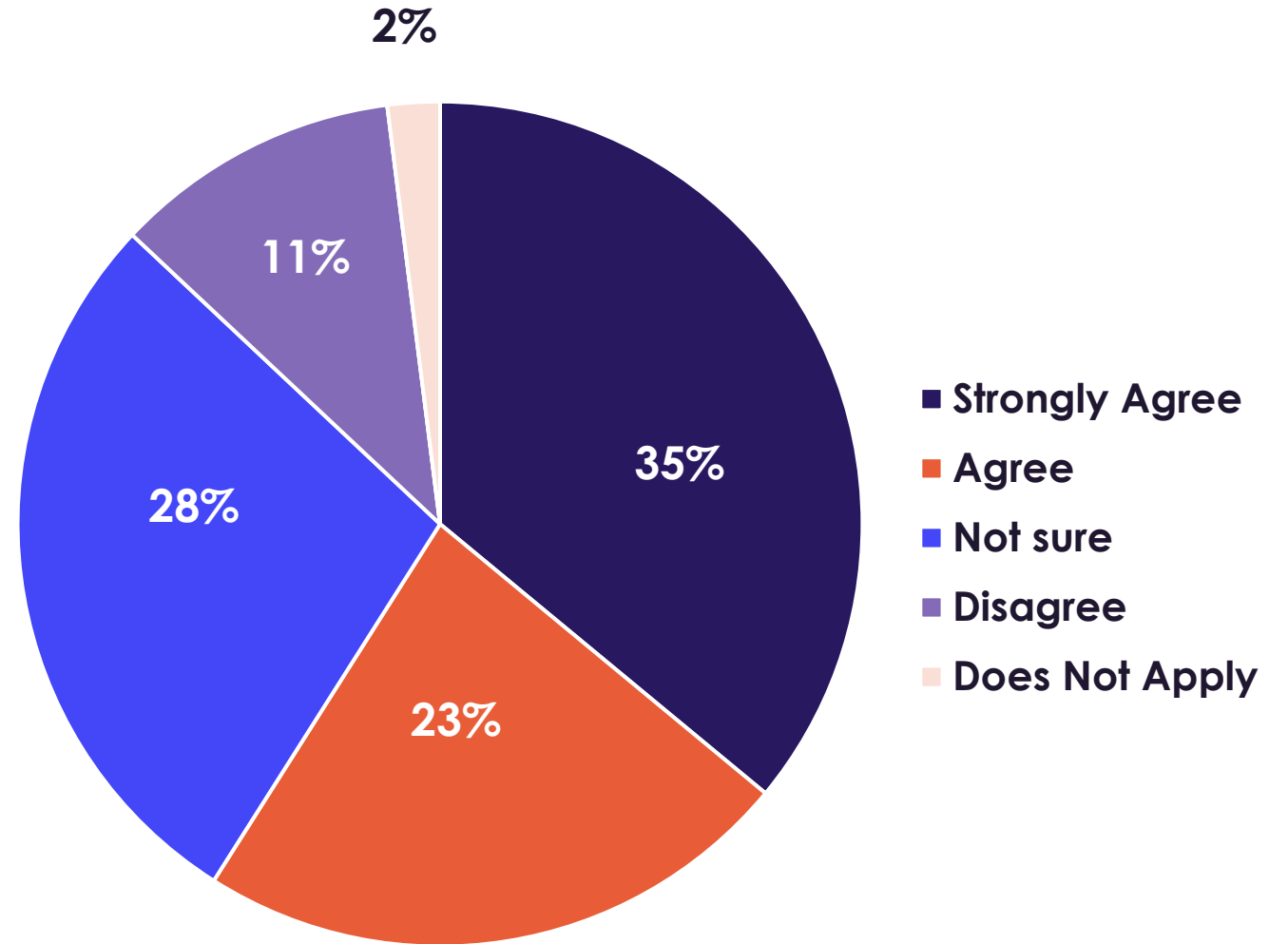
Do multiple triggers, experienced in the same day, cause a more severe AHC episode in the patient?

”

The majority of respondents agreed that multiple triggers would raise the severity of a paroxysmal episode for their patient.

There was more uncertainty with 28% of respondents unsure.

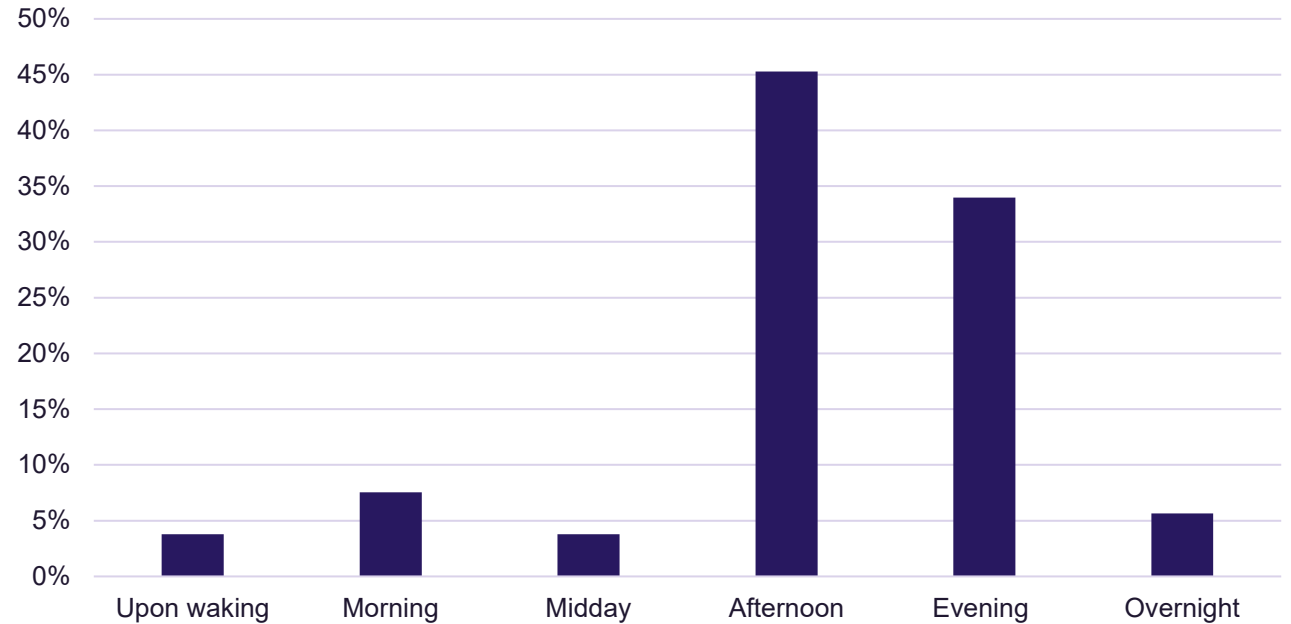
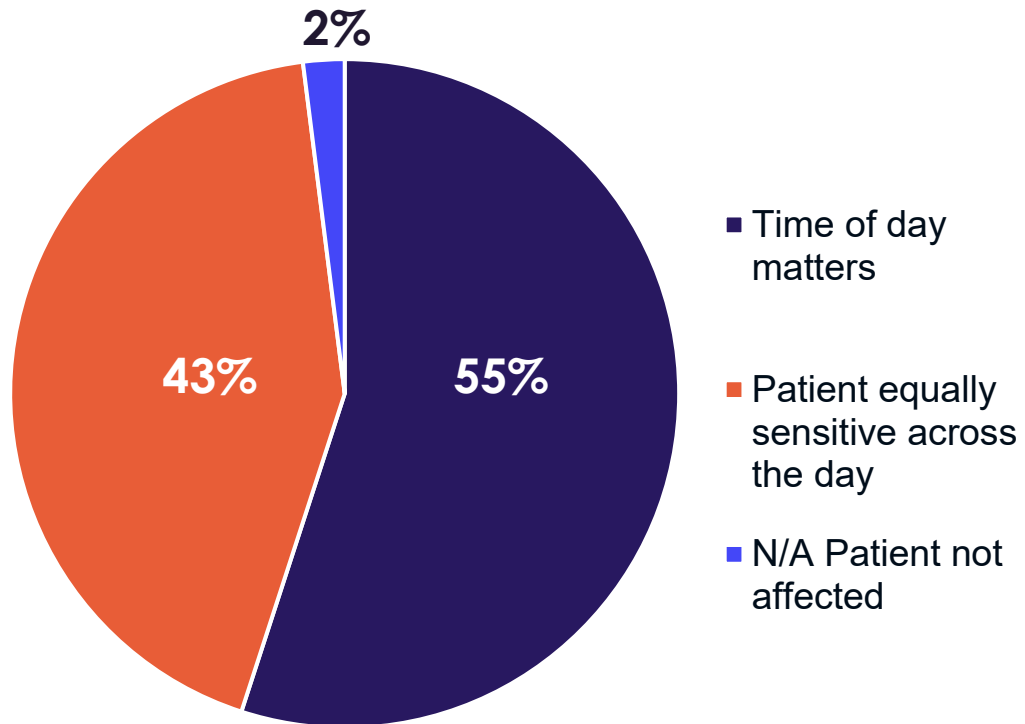
Only 11% “disagreed;” no respondents “strongly disagreed.”



# Trigger sensitivity is linked to time of day for a majority of patients

“

At what time of day is your patient most sensitive to triggers? ”



**43%** of patients are equally sensitive regardless of time of day.

**55%** report a sensitivity to triggers that correlates with time of day.

Increased sensitivity reported in the **afternoon and evening (79%)**.

# For most patients, trigger sensitivity declines or stays constant as they age

“

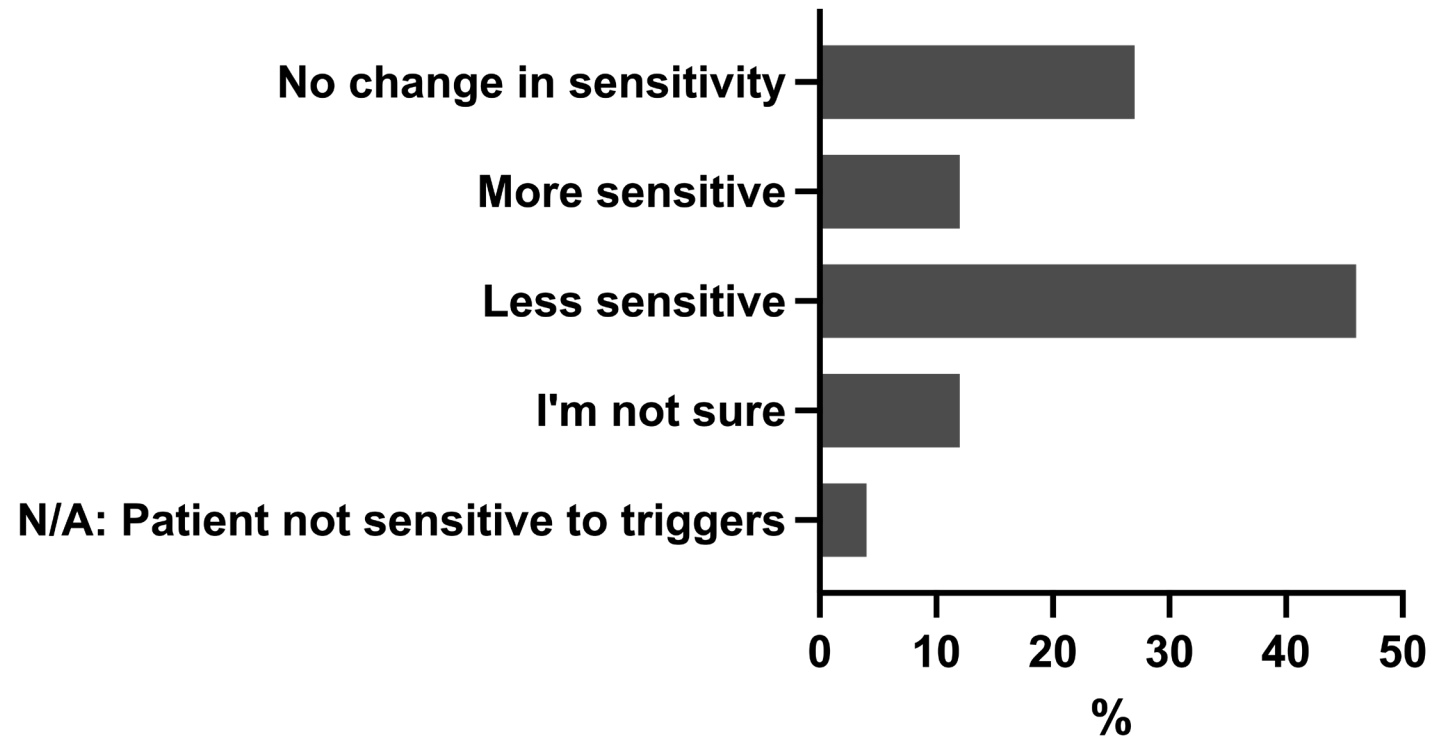
Is your patient becoming more or less sensitive to triggers as they get older? ”

**46%** of adult AHC patients are reported to become **less sensitive** as they get older.

A significant minority report no change in sensitivity.

12% report getting more sensitive to triggers with age.

>=18 y.o. patients, n=19



# Heightened trigger sensitivity was reported in early childhood, adolescence

“

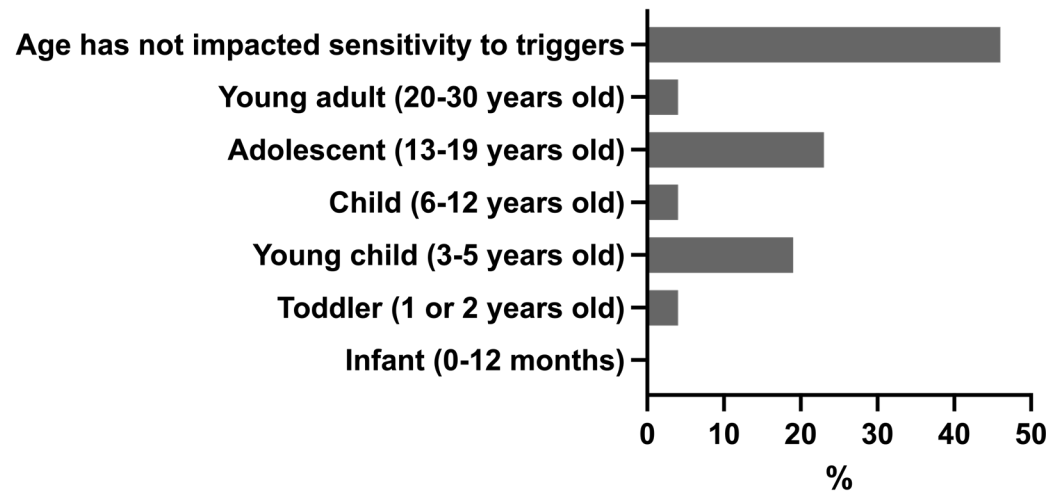
At what age has the patient been most sensitive to triggers?

”

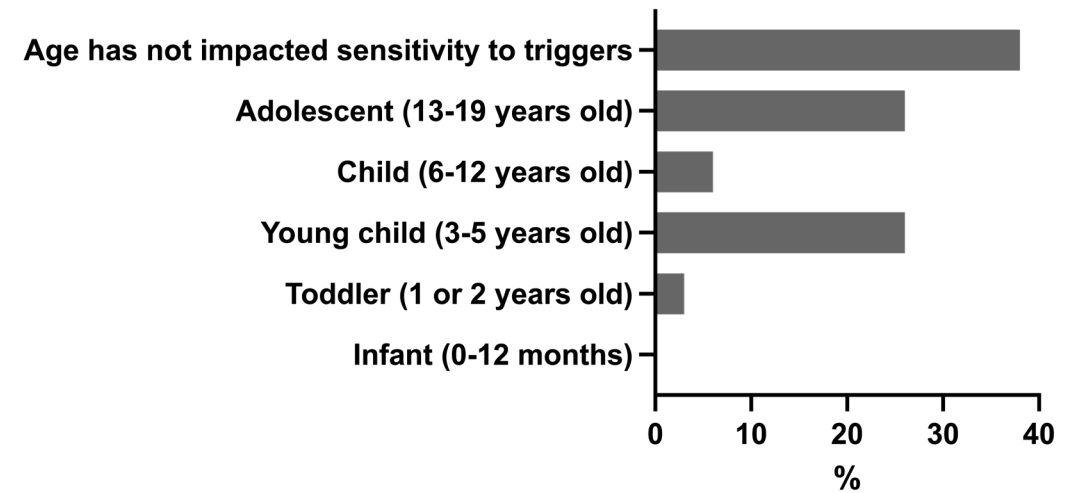
Nearly half of respondents for patients over age 18 (46%) report that **age does not impact sensitivity to triggers.**

The remaining half report that **young childhood** and **adolescence** are periods of **increased sensitivity to triggers.**

>=18 y.o. patients, n=19



>=15 y.o. patients, n=34



# AHC symptoms generally worsened or stayed the same with **puberty**

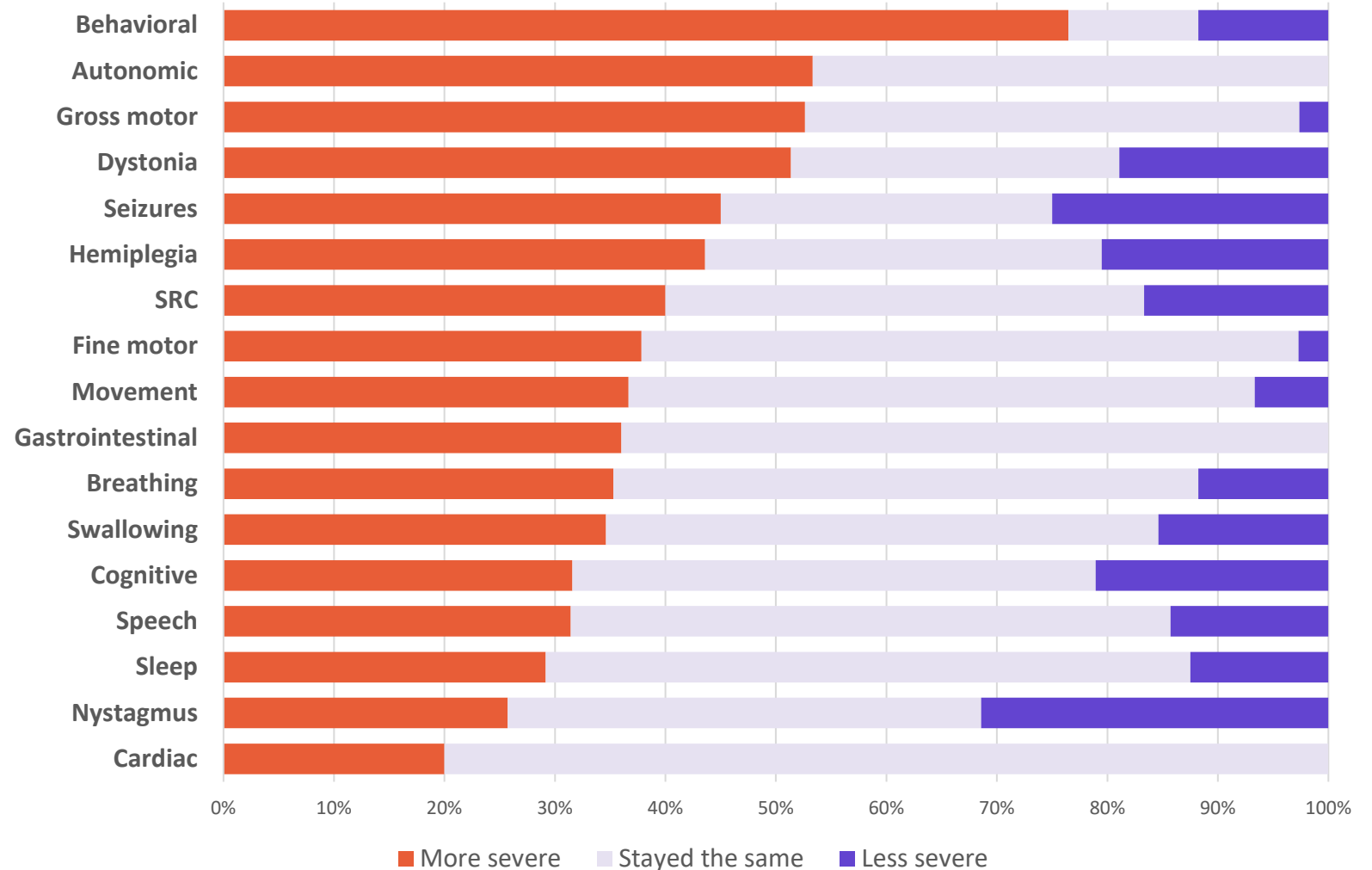
“

Did any symptoms become more severe or less severe for your patient with puberty? ”

Puberty appears to correlate with some changes in symptom severity.

Some symptoms worsen for a majority of patients after puberty: behavioral issues, autonomic dysfunction, gross motor deficits, dystonia and seizures.

All other symptoms “stayed the same” for the majority of patients.



## Looking forward to new applications...

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We have an IRB-governed platform to survey the patient population.

***What comes next?***

**We want to use our patient survey platform in support of your research.**

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**Not just data: We capture the  
relentless challenges of the  
patient experience**



Hannah Zimmer  
*with Archie*

# Thank you

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## Data Analysis:



*Dr. Natalia Morsci, Scientific  
Director for RARE Hope*

## Survey Team:

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Dr. Natalia Morsci*

Many thanks to the  
patient foundations from  
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## Advisors:

### Survey 1:

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Dr. Suzanne DeBrosse  
The joint Research Council  
The Boards of AHCF and Cure AHC  
The Medical Advisory Board of AHCF  
North Star Review Board*

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Dr. Ganesh Mochida  
Dr. Nutan Sharma  
Dr. Andrew Landstrom  
Dr. Sujay Kansagra  
Dr. Allison Brashear and team  
Dr. Simona Balestrini  
Irene de Boer  
North Star Review Board  
The joint Research Council  
The Boards of AHCF and Cure AHC*

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