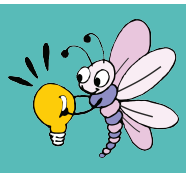
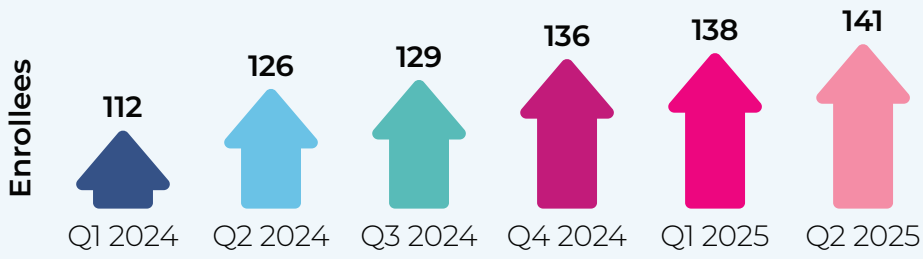
CASK: What Do We Know From Our Registry?

Registry overview



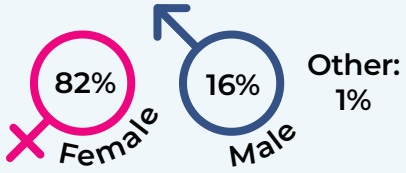
An increase in registry sign-ups has improved our understanding of the characteristics of people with CASK-related disorders

Increase in enrolment[1]



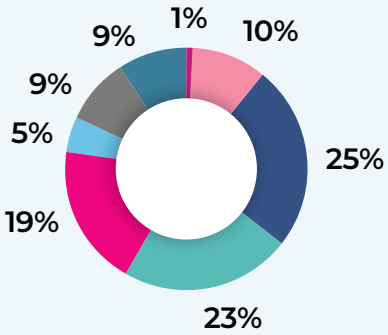
Gender[2]

(n=141)



Age range (years)[2]

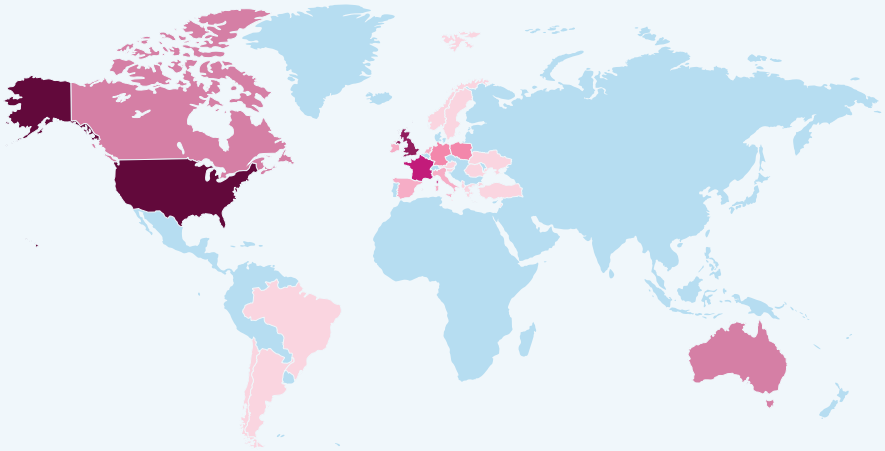
(n=141)



0–2 · 3–5 · 6–10 · 11–15 · 16–18 · 19–29 · 30–49 · 50+

Worldwide spread[2]

(n=143)



Enrollees: 1 · 2 · 5 · 7 · 20 · 22 · 54

Are you the parent or guardian of someone diagnosed with a CASK gene mutation? Join the RARE-X registry here!

References: **1.** RARE X Dataset. Data cut off: April 2025; **2.** RARE X Dataset. Data cut off: June 2025.

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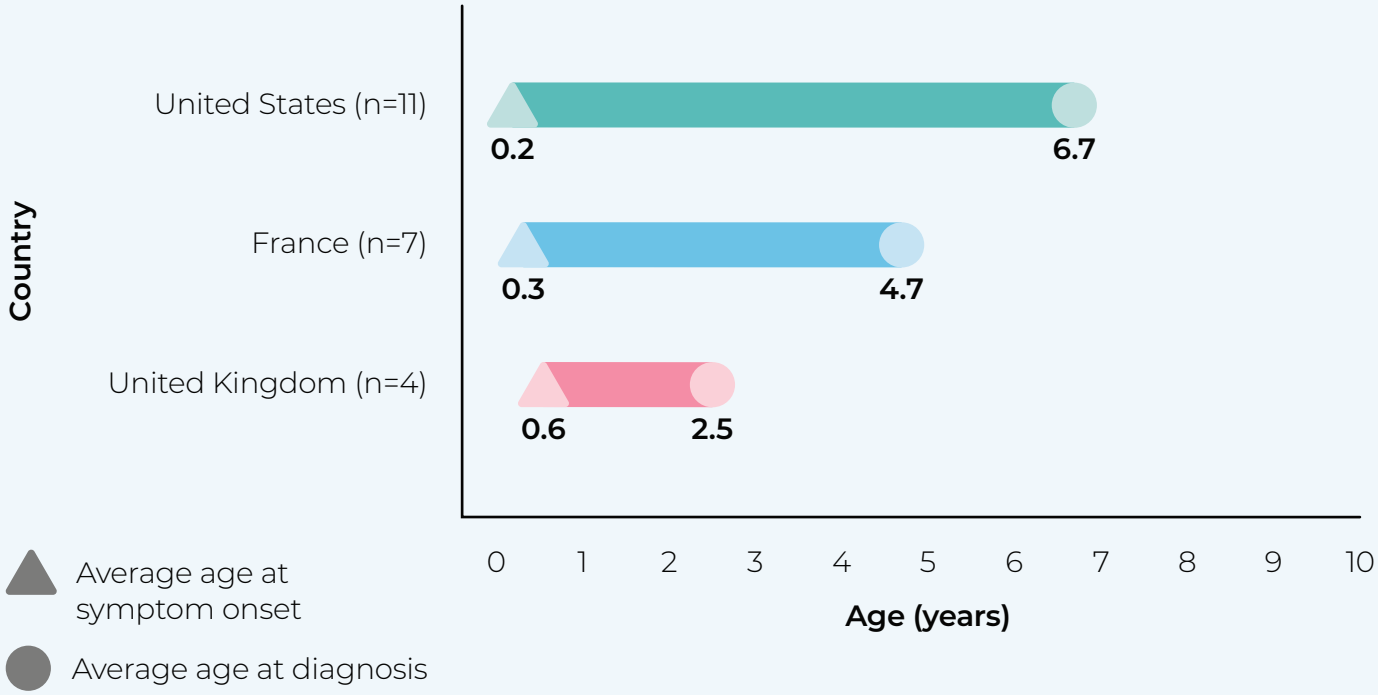
Diagnosis delay

How long does it take to get a diagnosis?[1]



Australia (n=2), Germany (n=1), Argentina (n=1), Netherlands (n=1), Spain (n=1), Canada (n=1) and Poland (n=1) were not included in this chart due to the low number of people from these geographies responding to this question.

The US

has the biggest gap between noticing symptoms and getting a diagnosis, with an average diagnosis age of

6.7 years

If gene therapies become available in the future, they will likely be most effective when given as soon as possible after birth. The current diagnosis delay is crucial to address!

References: **1.** RARE X Dataset. Data cut off: April 2025.

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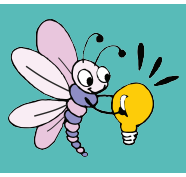
Symptoms

What are the most common symptoms?[1]

Difficulty with nonverbal behaviours
Undergrowth
Unusual eye gaze
Abnormal electroencephalogram (EEG)
Issues with arm and leg muscles
Feeding difficulties
Unusual movements
Hypotonia
Cognitive impairment
Seizures
Coordination issues
Short stature
Constipation
Hypertonia
Abnormal eye movement
Oral dysphagia
Visual impairment
Esophagus issues
Abnormal facial muscles

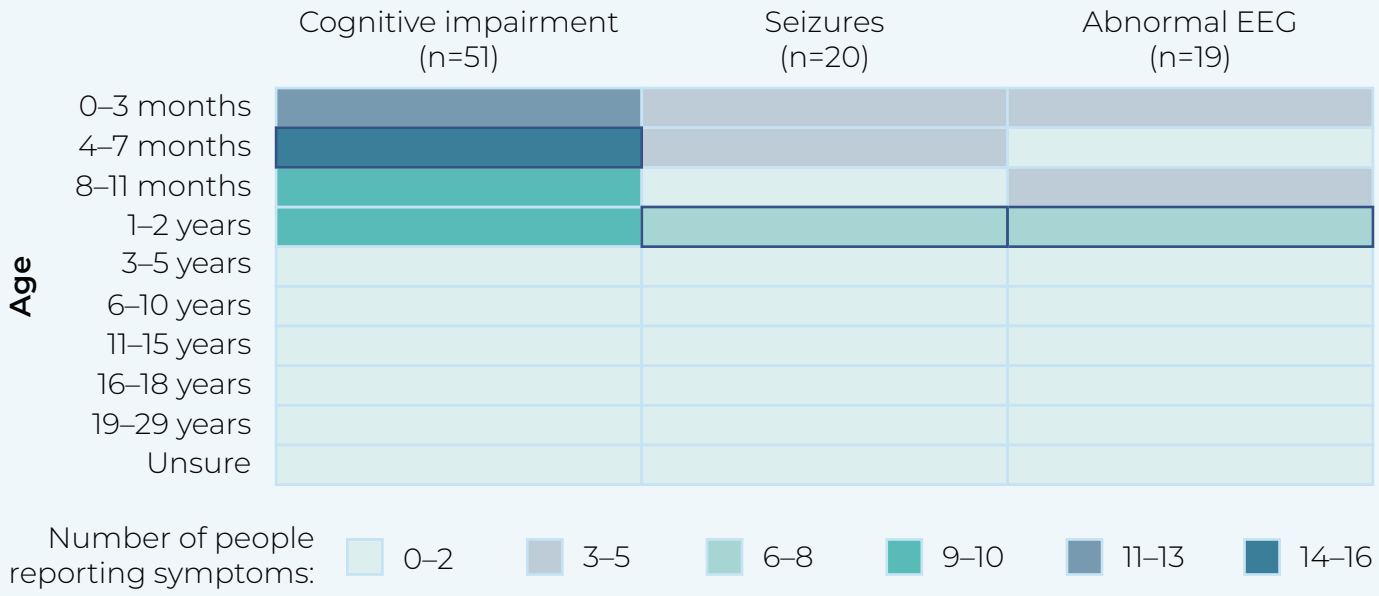
● Brain and nervous system ● Muscles ● Digestive ● Eyes and vision
● Growth ● Head, face, and neck ● Behaviour survey

The sample size for each survey used to determine symptom prevalence varied. Excludes 'abnormal muscle function'.



Symptoms related to the brain and nervous system are the most common[1]

Key symptoms occur relatively early in childhood[1]



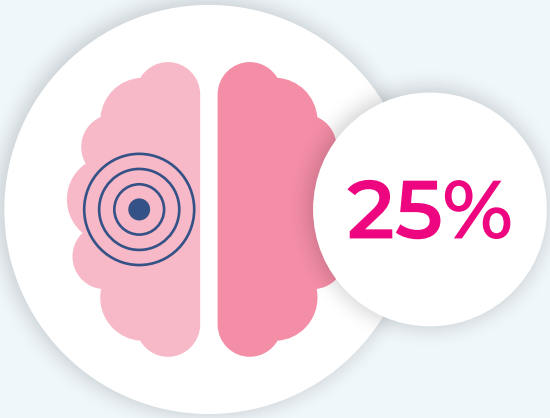
– Represents the most frequent age range at which each symptom appeared.

References: **1.** RARE X Dataset. Data cut off: April 2025.

Epilepsy

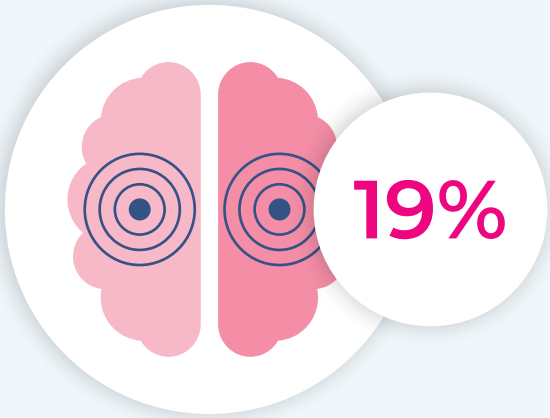
Types of epilepsy reported[1]

(n=16)



Focal

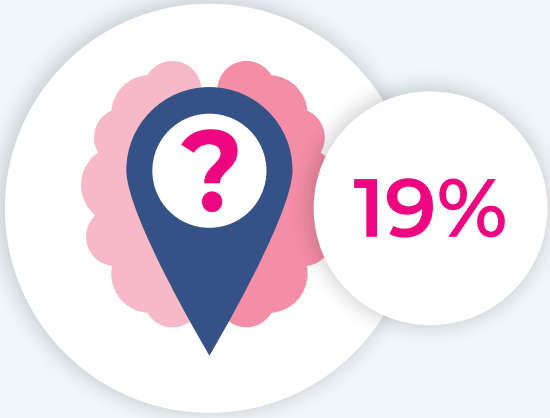
Starts in one part of the brain[2]



Generalised

Starts in the left and right sides of the brain[3]

Combined focal and generalised



Unknown epilepsy

Includes nonsyndromic epilepsy and cases where the condition is unknown or too early to determine[4]

This is the most common type of epilepsy reported

Considering only those who reported having epilepsy.

Explore our website for more information

References: **1.** RARE X Dataset. Data cut off: April 2025; **2.** Epilepsy Action. Focal Seizures. Available at: https://www.epilepsy.org.uk/info/seizures/focal-seizures; **3.** Johns Hopkins Medicine. Generalized Seizures. Available at: https://www.hopkinsmedicine.org/health/conditions-and-diseases/epilepsy/generalized-seizures; **4.** International League Against Epilepsy. Unknown Epilepsy. Available at: https://www.epilepsydiagnosis.org/epilepsy/unknown-epilepsy-groupoverview.html.

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Epilepsy

Syndromes

Infantile epileptic spasms syndrome (IESS)[1]

- Involves regular clustered spasms, with several spasms happening one after the other

Lennox-Gastaut syndrome (LGS)[2]

- Multiple seizure types, developmental delays, and distinctive brainwave patterns

Other epilepsy syndrome[3]

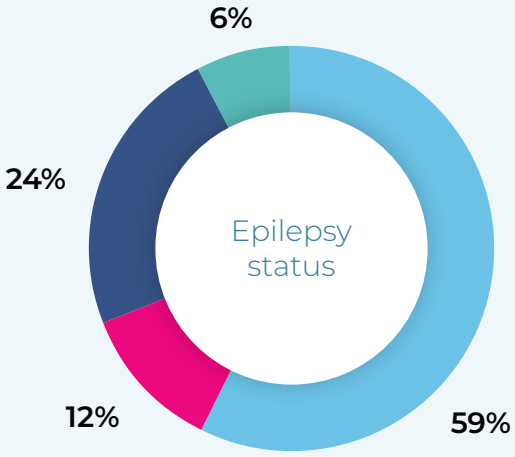
- An epilepsy syndrome is a group of signs and symptoms that tend to happen together, including particular types of seizures

Not a syndrome[4]

- Defined when it is uncertain or too early to tell

59% of individuals reported that their child's epilepsy does not constitute a specific syndrome (n=17)[5]

- IESS
- LGS
- Other epilepsy syndrome
- Not a syndrome



Considering only those who reported having epilepsy.

Treatment resistance

Treatment-resistant epilepsy is the resistance people can develop to medications that prevent seizures[6]

52% of patients have treatment-resistant epilepsy (n=21)[5]

Considering only those who reported having epilepsy.

References: **1.** Epilepsy Action. Infantile Epileptic Spasm Syndrome (West Syndrome). Available at: https://www.epilepsy.org.uk/info/syndromes/west-syndrome-infantile-spasms; **2.** National Institute of Neurological Disorders and Stroke. Lennox-Gastaut Syndrome. Available at: https://www.ninds.nih.gov/health-information/disorders/lennox-gastaut-syndrome; **3.** Epilepsy Foundation. What Is an Epilepsy Syndrome? Available at: https://www.epilepsy.com/what-is-epilepsy/syndromes; **4.** American Society of Gene + Cell therapy. Sail For Epilepsy, Part 2: An Overview of Syndromic and Monogenic Non-syndromic Epilepsies. Available at: https://www.asgct.org/publications/news/may-2022/sail-for-epilepsy-part-2; **5.** Epilepsy Foundation. Drug Resistant Epilepsy. Available at: https://www.epilepsy.com/treatment/medicines/drug-resistant-epilepsy; **6.** RARE X Dataset. Data cut off: April 2025.

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Seizures

Epilepsy involves a pattern of repeated seizures that are not caused by identifiable factors like injury or infection[1]

A seizure is a sudden surge of electrical activity in the brain that can affect behaviour, movements and consciousness[1]

Generalised tonic-clonic seizures
Muscles become stiff, followed by rhythmic shaking or jerking movements[2]

Motor seizures
Involves changes in muscle activity[3]

Non-motor seizures
Involves no movement but may involve staring spells or changes to senses, emotions and cognition[4]

Time since last seizure, by seizure type[5]

Time since last seizure	Generalised tonic-clonic seizures (n=10)	Motor seizures (n=12)	Non-motor seizures (n=7)
Today	3	4	2
1–6 days ago	1	3	1
1–4 weeks ago	2	2	3
5–12 weeks ago	1	1	1
13–26 weeks ago	0	1	0
6–12 months ago	1	0	0
13–24 months ago	0	0	0
>2 years ago	2	1	0

Considering only those who reported having seizures.

Among those who experience seizures, these events generally occur on at least a monthly basis, suggesting a relatively regular pattern[5]

References: **1.** Citizens Specialty Hospital. Difference between convulsions, seizures and epilepsy. Available at: https://www.citizenshospitals.com/blogs/difference-between-convulsions-seizures-and-epilepsy; **2.** Epilepsy Society. Epileptic Seizures. Available at: https://epilepsysociety.org.uk/about-epilepsy/epileptic-seizures; **3.** International League Against Epilepsy. Motor Seizure. Available at: https://www.epilepsydiagnosis.org/seizure/motor-overview.html; **4.** Epilepsy Foundation. Types of Seizures. Available at: https://www.epilepsy.com/what-is-epilepsy/seizure-types; **5.** RARE X Dataset. Data cut off: April 2025.

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Sleep

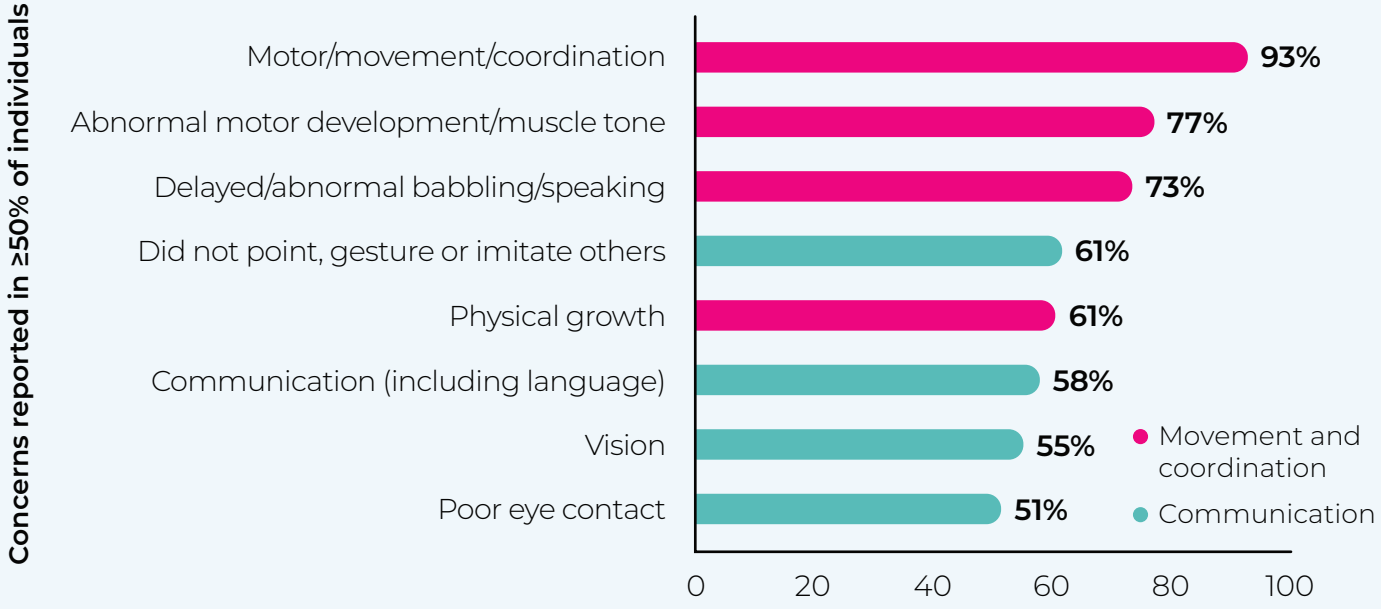
55% of children fall asleep within 20 minutes of going to bed (n=64)[1]

The most commonly reported number of minutes awake during the night was **60 minutes** (n=24)[1]

Development

Most of the concerns expressed regarding development are related to movement & coordination and communication[1]

(n=109)



Abnormal motor development/muscle tone refers to participants who are unusually stiff or floppy.

References: **1.** RARE X Dataset. Data cut off: April 2025.