



CADASIL Community Natural History Study

Initial Overview of Registry Activity and Survey Results

Introducing the CADASIL Community Natural History Study

- cureCADASIL with the National Organization for Rare Disorders (NORD®) created a CADASIL Community Natural History Study to track disease progression over time
- cureCADASIL transitioned from the previous Invitae CADASIL registry, which was “one and done” and provided little information about progression and outcomes

Natural History Study vs. Registry

Natural History Study

- Captures data from individuals to track the course of a disease over time
- Can also include those at-risk for the disease
- Targeted data collection

Registry

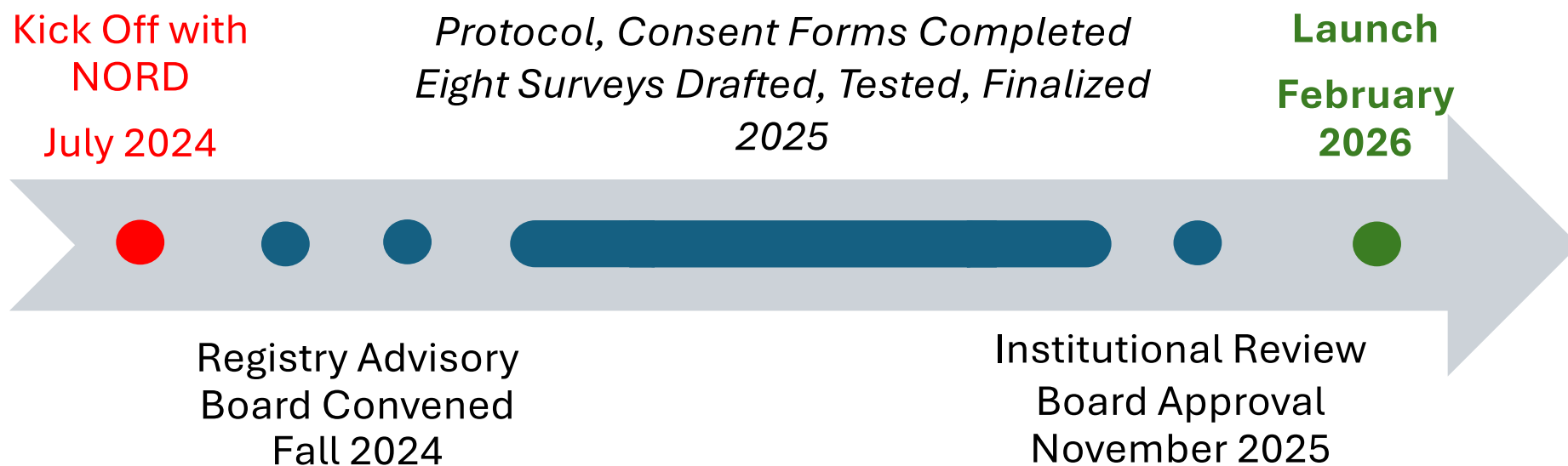
- Captures data from individuals with a disease at one point in time
- Primarily serves as a directory of patients
- Data collection is often broad in scope, not specific to the disease

We often refer to our natural history study as a registry, as short-hand

Purpose of Natural History Study

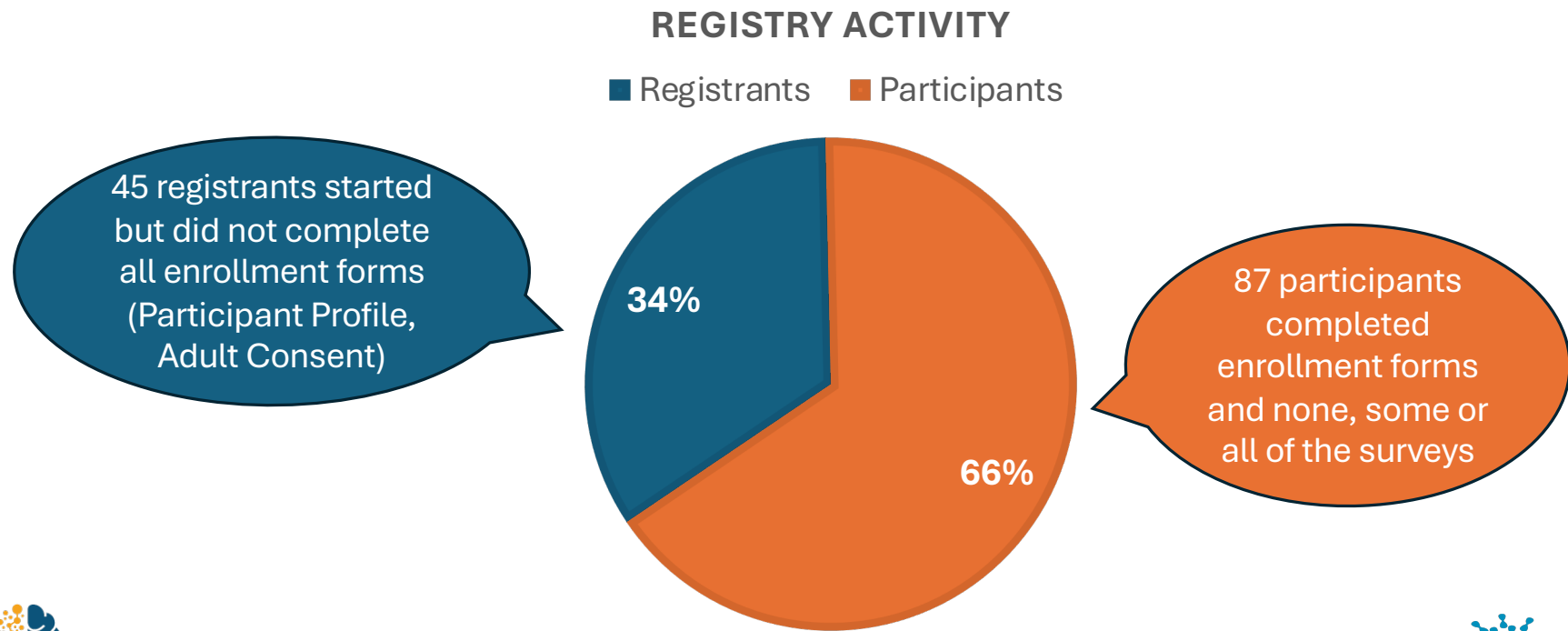
- Recruit individuals for research studies and clinical trials
- Better understand disease burden and progression
- Define potential entry criteria for research studies
- Define potential treatment targets
- Sell ourselves to Pharma to facilitate drug development and clinical trials – “We are ready”

Natural History Study Development Timeline

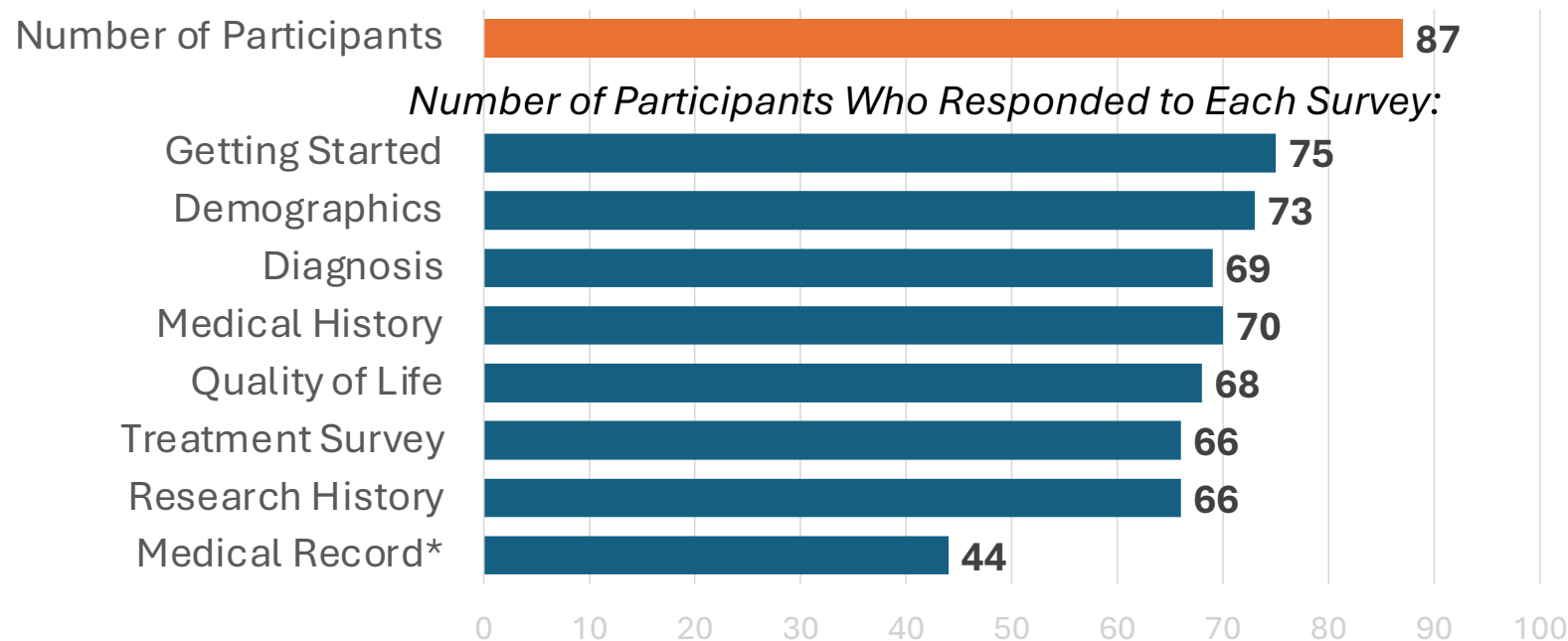


Registry Activity

Registry activity as of April 2, 2026



Registry Participants – Survey Completion



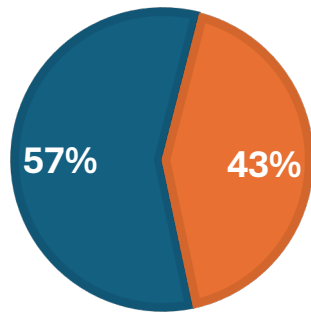
* Uploaded genetic test result for participants who received a genetic test

Demographics

PARTICIPANT GENDER



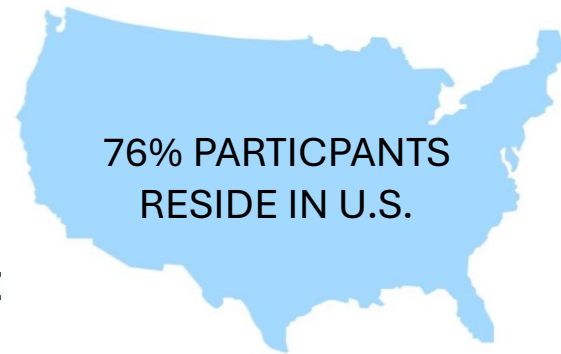
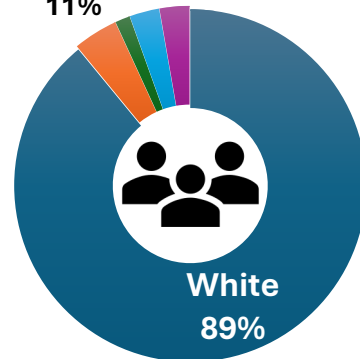
■ % Female ■ % Male



PARTICIPANT RACE

Other or Unreported

11%



24% from Canada, Mexico,
Europe, S America, etc.

*Natural history study is
international*



77% of participants able
to live independently

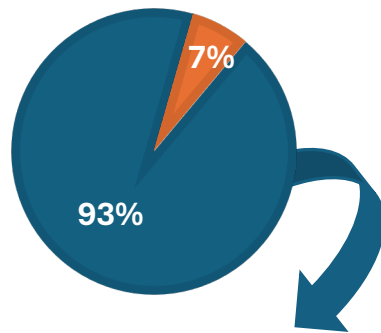


Employment for 33%
of participants
affected by disease

Diagnosis

PARTICIPANT ELIGIBILITY

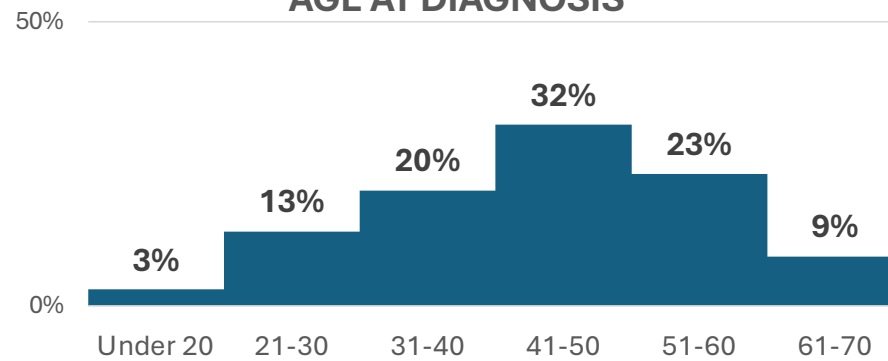
■ % Diagnosed with CADASIL ■ % Blood Relative



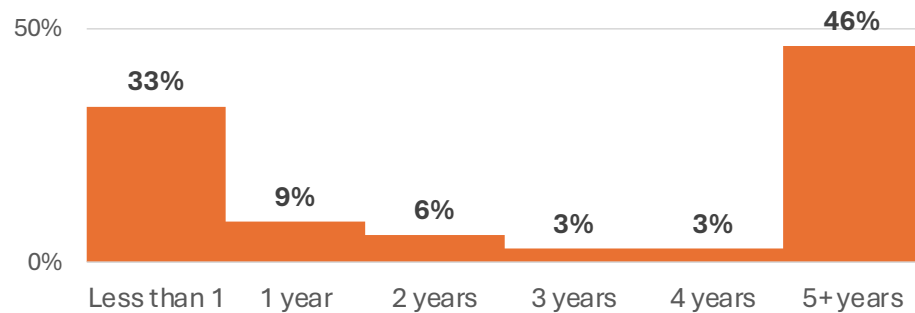
Almost 90% received a genetic test



AGE AT DIAGNOSIS



TIME FROM FIRST SYMPTOMS TO DIAGNOSIS (YEARS)



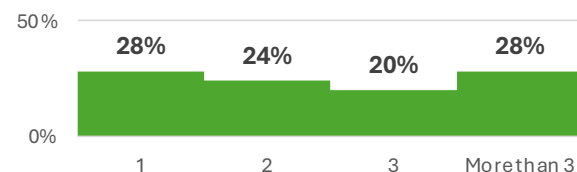
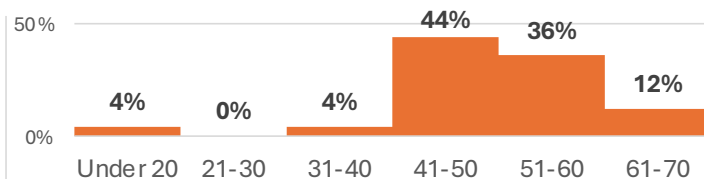
Medical History

PREVALENCE OF KEY SYMPTOMS

AGE AT TIME OF FIRST EVENT

NUMBER/FREQUENCY

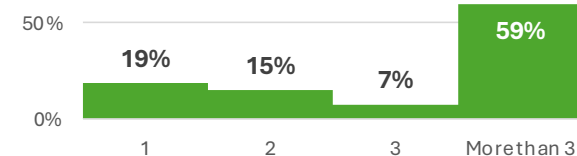
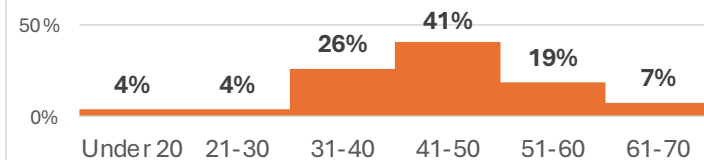
STROKE



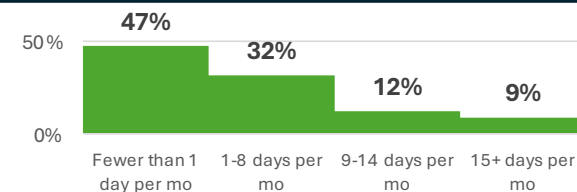
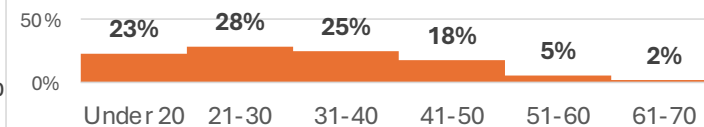
TIA



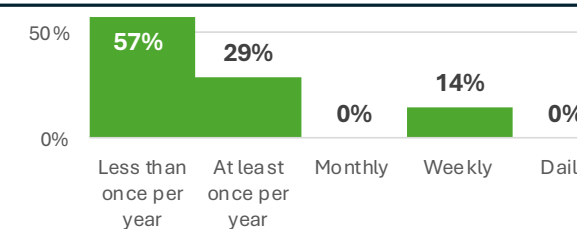
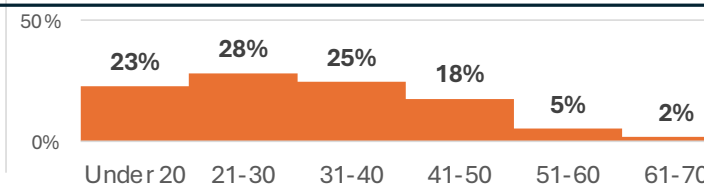
(TIA = Transient Ischemic Attack)



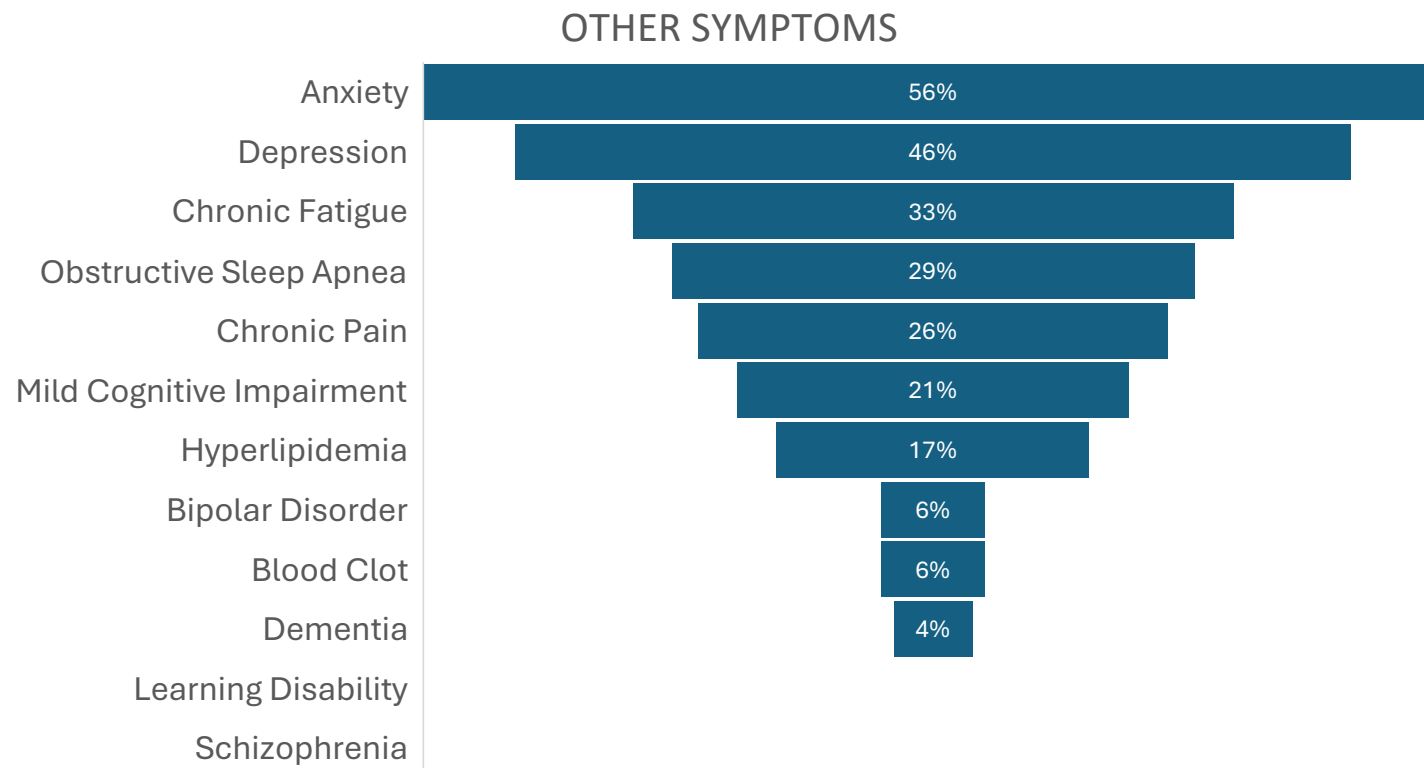
MIGRAINE



SEIZURE

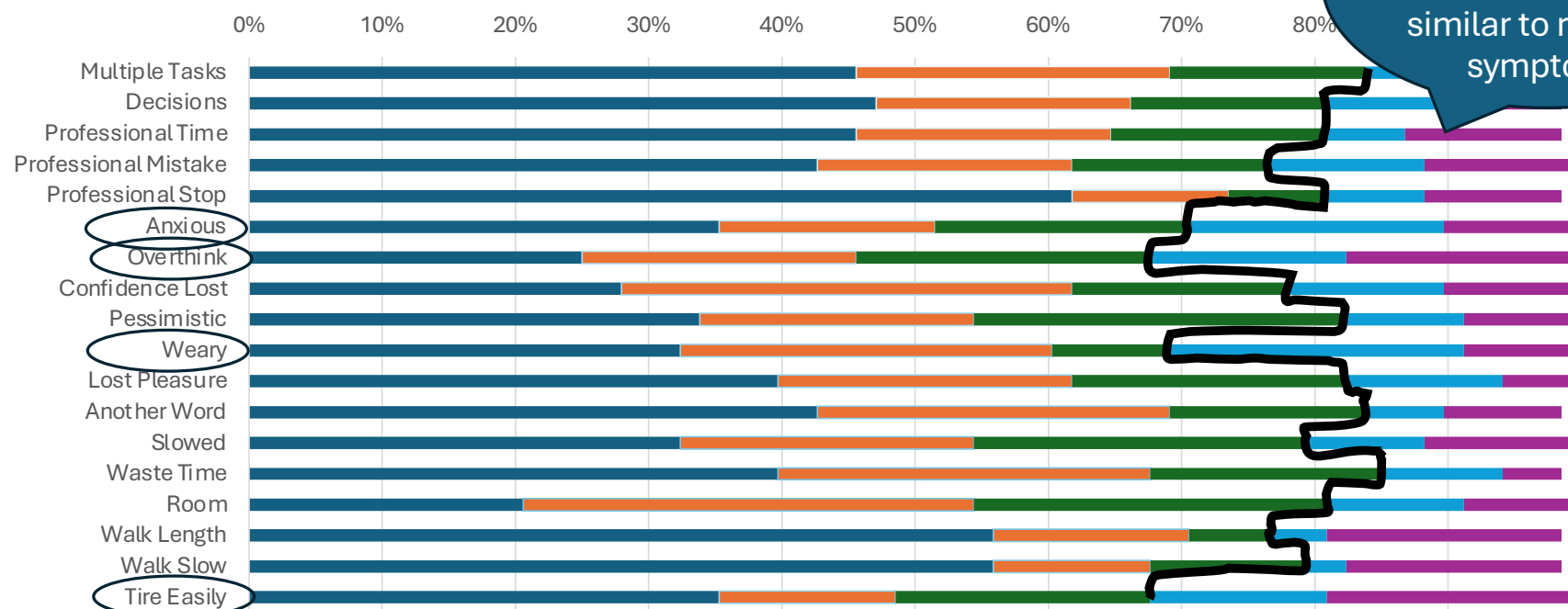


Medical History



CADASIL Patient-Reported Outcomes (CADA-PRO)

CADA-PRO Questionnaire Measuring Cognitive, Motor, Emotional and Behavioral Outcomes

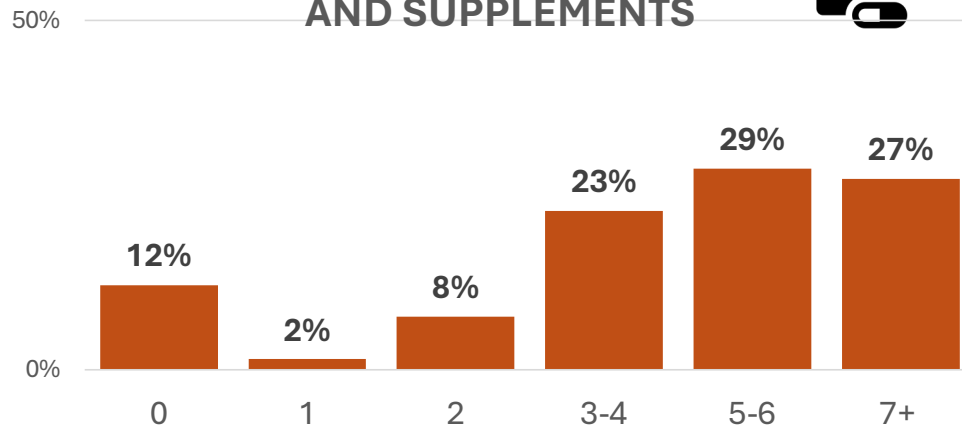


See Appendix for questions that link to CADA-PRO outcomes

■ Never ■ Rarely ■ Sometimes ■ Frequently ■ Very Often

Treatment Survey

NUMBER OF MEDICATIONS AND SUPPLEMENTS



42% of participants
hospitalized for stroke, TIA,
migraine, or seizure



8% of participants use an
assistive device (cane, walker,
wheelchair)

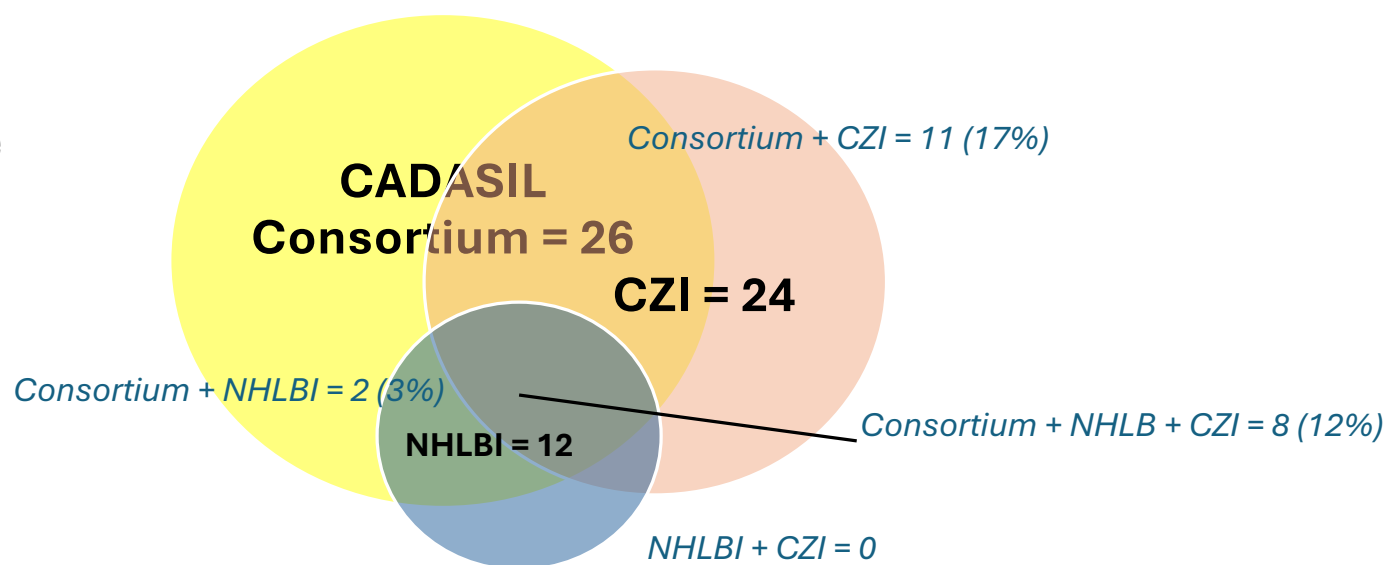
Participation in Other CADASIL Research Studies

Other Research Studies

CADASIL Consortium

CZI = Chan Zuckerberg Initiative

NHLBI= National Heart, Lung & Blood Institutes of the National Institutes of Health (NIH)



In **None** of the Three Studies = 33 (50%)

In **One** Study Only = 12 (18%)

In **More than One** Study = 21 (32%)

Next Steps

In light of the above findings, cureCADASIL will pursue several steps:

- Continue to promote this study to boost enrollment overall and among individuals from minority groups
- Encourage Registrants to complete enrollment process and Participants to complete all applicable surveys
- Continue to disseminate summaries of survey results
- As participation grows, conduct analyses of diagnostic details, reported symptoms, treatment and outcomes and report interesting findings

Appendix

Key Linking Patient Questions to CADA-PRO Outcomes*

Multiple Tasks	I find it difficult to carry out an activity with multiple tasks; I might forget a step and/or do a step out of order.
Decisions	I find it hard to make decisions, whereas I didn't have a problem with this before.
Professional Time	I have difficulties in my everyday and/or professional activities; It takes me more time to complete them.
Professional Mistake	I have difficulties in my everyday and/or professional activities; I need to check that I haven't made any mistakes.
Professional Stop	I have had to give up some or all of my daily and professional activities.
Anxious	I feel anxious, nervous, and have difficulty relaxing.
Overthink	I tend to overthink and worry.
Confidence Lost	I've lost self-confidence.
Pessimistic	I have pessimistic ideas, I'm discouraged about my future.
Weary	I feel weary, it takes more effort to get started, and I tend to put things off until tomorrow.
Lost Pleasure	I've lost pleasure or interest in certain things I would ordinarily enjoy.
Another Word	I sometimes use one word when I mean another.
Slowed	I feel slowed down in the way I think and/or do things.
Waste Time	I waste a lot of time looking for small everyday objects.
Room	Sometimes I enter a room and forget what I came in to do.
Walk Length	I can't walk for as long as I used to.
Walk Slow	I walk more slowly than before.
Tire Easily	I get tired more easily.