Patient Data Sharing of Genetic and Health information Informs Genetics Discovery and Fuels Research

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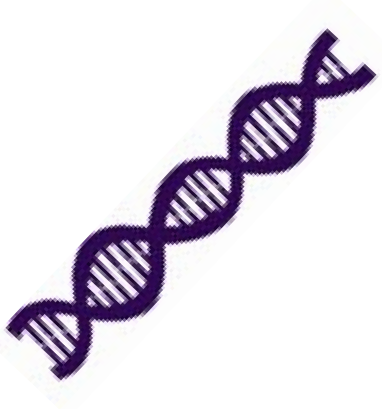
Overview

Discuss how advocacy groups including cureCADASIL and members of the GenomeConnect team from Geisinger are working to enable patients to broadly share de-identified genetic and health data

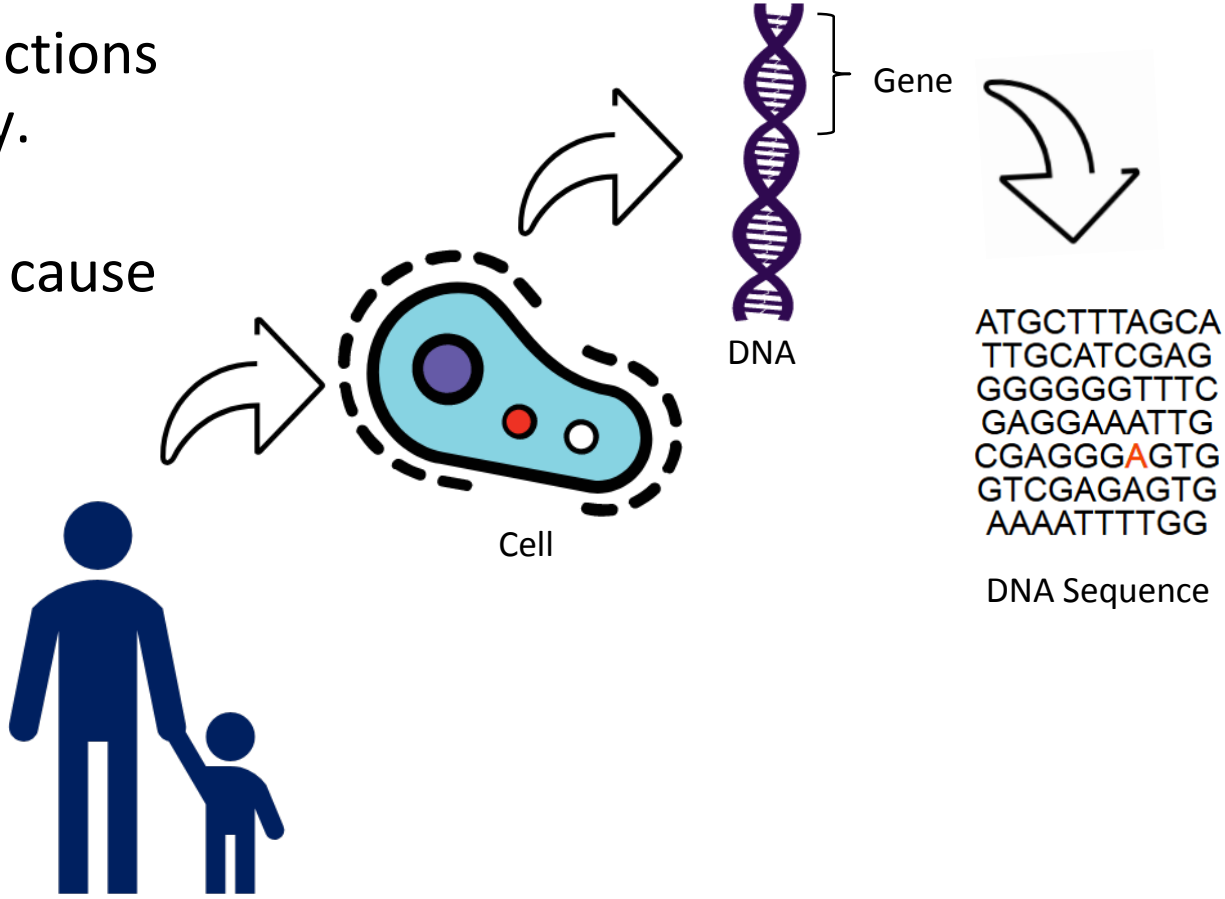
- Overview of genetics and rare disease
- ClinGen and GenomeConnect
- cureCADASIL
- Patient Data Sharing Program

Genetics and Rare Disease



Our DNA provides instructions for the human body.

Changes in our DNA can cause medical concerns.

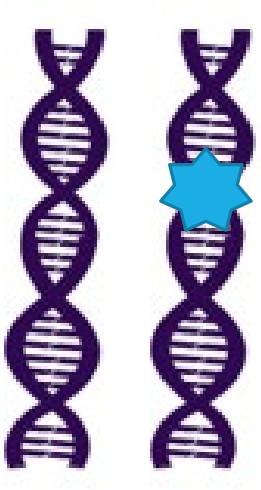


CADASIL - **C**erebral **A**utosomal **D**ominant **A**rteriopathy with **S**ubcortical **I**nfarcts and **L**eukoencephalopathy

- Caused by a genetic variant that affects the NOTCH3 gene. Changes in the NOTCH3 gene impact the muscle around the small blood vessels in the brain.

- CADASIL is associated with:
  - Stroke
  - Migraine with aura
  - Dementia
  - Changes in mood
  - Leukoencephalopathy or a change in the brain tissue that can be see on MRI

- Affects 2-4/100,000 people



NOTCH3 Gene

Genetic testing technology has increased our ability to detect genetic changes (variants).

We still have a lot to learn about the relationship between genetics and health.

ClinGen and GenomeConnect

ClinGen is one project working to increase understanding of genetics and genetic conditions.

ClinGen is a National Institutes of Health (NIH)-funded research project that is working to better understand the relationship between genes, genetic variants, and health.

ClinGen relies on

public data sharing

ClinGen
Clinical Genome Resource

To learn more about ClinGen: https://www.clinicalgenome.org/

ClinGen Expert Panels

Cardiovascular

- Brugada Syndrome Gene Curation
- Cardiovascular Dilated Cardiomyopathy
- Cardiovascular Familial Hypercholesterolemia Variant Curation Cardiovascular KCNQ1 Variant Curation
- Cardiovascular LQTS Gene Curation
- Familial Thoracic Aortic Aneurysm and Dissection Gene Curation
- Hypertrophic Cardiomyopathy Gene Curation
- Inherited Cardiomyopathy Variant Curation

Hearing Loss

- Hearing Loss Gene Curation
- Hearing Loss Variant Curation

Inborn Errors of Metabolism

- Aminoacidopathy Gene Curation
- Fatty Acid Oxidation Gene Curation
- Mitochondrial Disease Gene Curation
- Mitochondrial Disease Variant Curation
- Monogenic Diabetes Variant Curation
- PAH Variant Curation
- Storage Diseases Variant Curation

Hereditary Cancer

- Breast and Ovarian Cancer Gene Curation
- CDH1 Variant Curation
- Colon Cancer and Polyposis Gene Curation
- Hereditary Breast Ovarian and Pancreatic Cancer Variant Curation
- Hereditary Cancer Gene Curation
- Myeloid Malignancy Variant Curation
- PTEN Variant Curation
- Somatic/Germline Variant Curation
- TP53 Variant Curation
- VHL Variant Curation

Neurodevelopmental Disorders

- Autism and Intellectual Disability Gene Curation
- Brain Malformations Variant Curation
- Epilepsy Gene Curation
- Rett Angelman Variant Curation

RASopathy

- RASopathy Gene Curation
- RASopathy Variant Curation

Hemostasis/Thrombosis

- Coagulation Factor Deficiency
- Platelet Disorders

Sharing data with public databases helps experts learn more about the genetic basis of disease!

Laboratories

Patients & Patient Groups

Clinicians

Publicly available databases

Healthcare providers, researchers, and genetic testing laboratories use these databases to learn more about genetics and health.

GenomeConnect – ClinGen Patient Registry

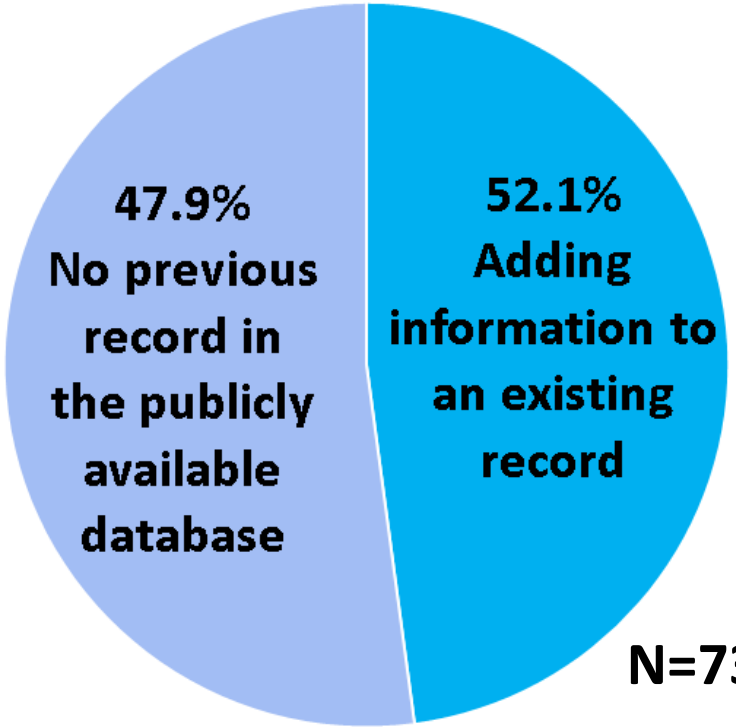
GenomeConnect
The ClinGen Patient Portal

GenomeConnect – ClinGen Patient Registry

GenomeConnect
The ClinGen Patient Portal

Patients serve as an important source of:

- Novel genetic information
- Additional details to inform our understanding of the genetics of health

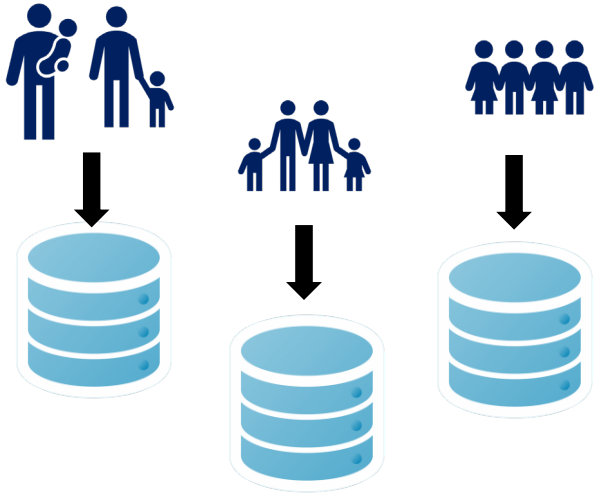


Data as of 11/2018

Patient Registries

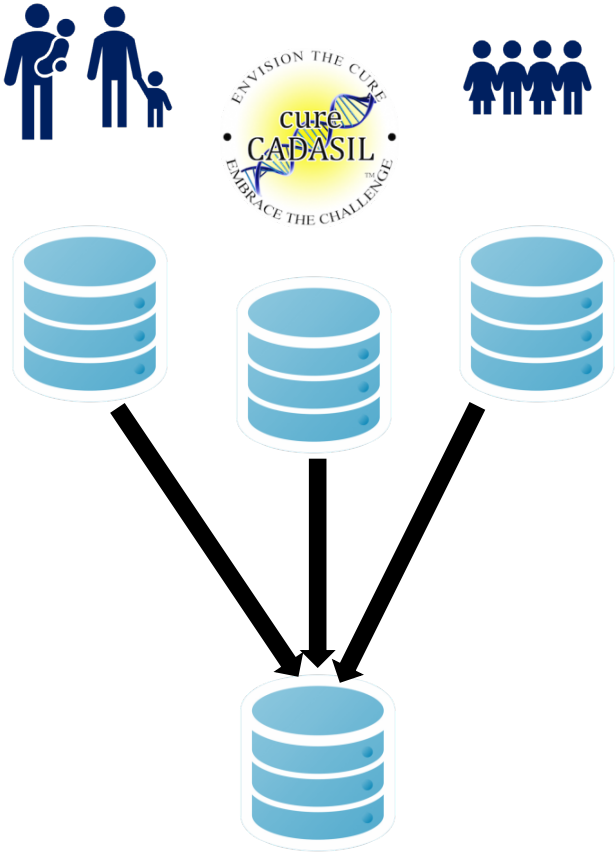
- A number of gene and condition specific registries exist and advocacy groups continue to establish new registries.

- Registries are and will be collecting valuable data that is may not be publicly shared.



Patient Data Sharing Program

Given the GenomeConnect team's experience, we wanted to begin a pilot to work with external registries and advocacy organizations to give more patients the option to share data.



cureCADASIL and CADASIL Family Registry

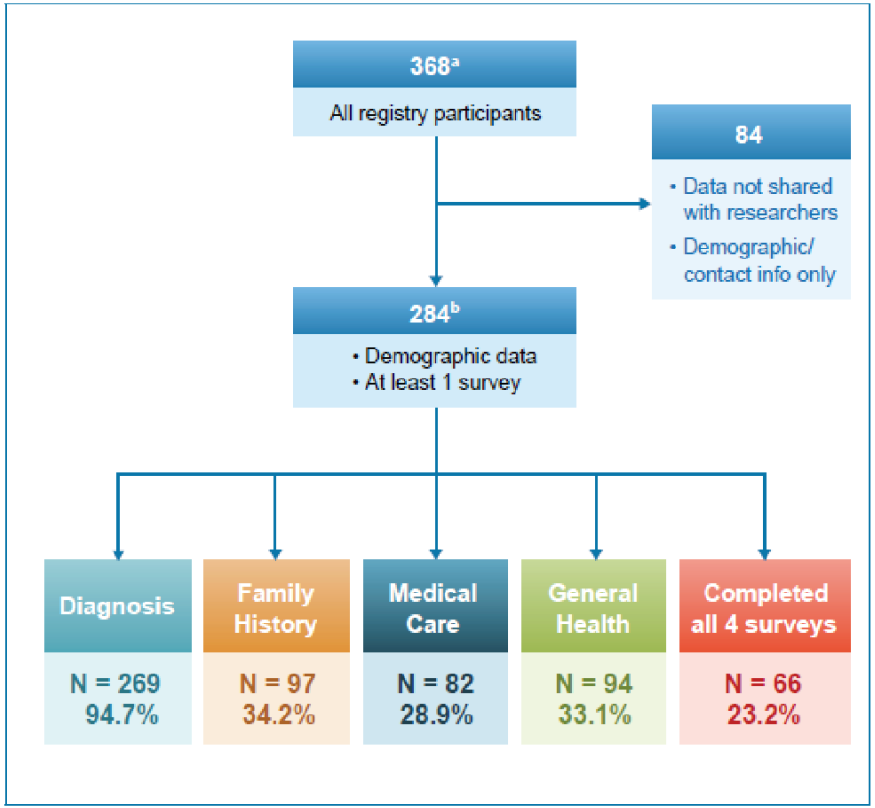
cureCADASIL Family Registry

Launched in August 2015

- Longitudinal, patient-reported registry that collects de-identified (anonymous) personal, medical, and genetic test information
- Online registry, through Invitae that provides a secure, HIPAA-compliant way of collecting information while keeping the patient anonymous; online consent

  www.curecadasilfamilyregistry.com
- 4 surveys: Diagnosis, Family History, Medical Care, General Health
- Global registry in English, Spanish, Portuguese, German, Chinese, Japanese (Google translate for other languages)

Figure 2. Survey Response Rates



[a] As of August 13, 2018.
[b] As of June 8, 2018.

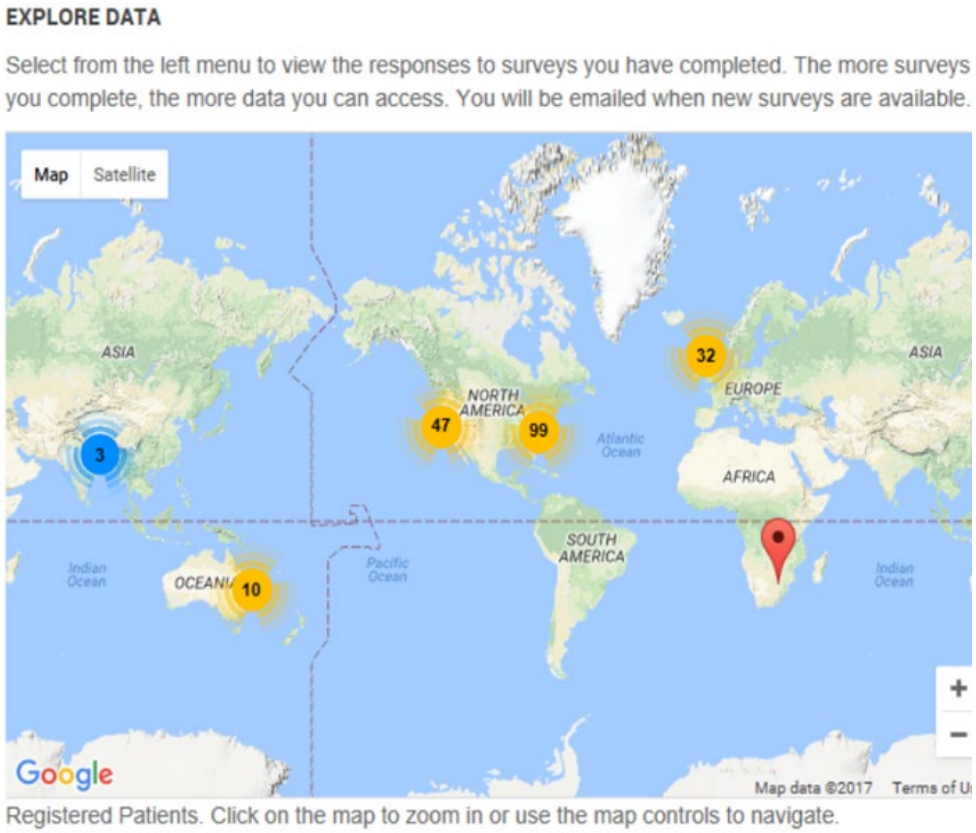
Global Registry

Participation

- Over 360 patients worldwide with available contact information, 284 with survey data (Talbird et al., 2018)
- Patients from over 15 countries
- 219 patients in the US

As of May 2019

- N = 426 worldwide



Registry Overview

Who can join?

- Adults aged 18 or older with a positive CADASIL diagnosis (either genetic diagnosis or medical diagnosis)
- Adults with a family history of CADASIL (at-risk but currently not diagnosed)
- Legal guardian on behalf of someone with CADASIL

How do CADASIL patients participate?

- Complete surveys and update surveys annually
- Upload genetic test results
- Benefits: See how CADASIL affects other patients, contacted about future studies

How do clinicians participate?

- Patient materials distributed to ~20 academic medical centers and ~60 physician offices throughout US
- Upon request, give patients a copy of genetic test results

Why is a CADASIL Registry Important?

To collect and share valuable information on CADASIL

- with each other and with the medical and research communities
- in order to gain a better understanding of the disease and accelerate CADASIL research

Accelerate research Recruitment for CADASIL studies

- cureCADASIL has successfully sped recruitment for 3 CADASIL studies to date: UCSF, Mayo Clinic Florida, NIH/NHLBI CADASIL Disease Discovery Study
- Inform future studies or clinical trials on meaningful patient outcomes
- Patient-reported data is being requested by the FDA more frequently

Empower patients

- Avenue to share experiences with CADASIL
- Avenue to participate in research

Patient Data Sharing Program Recruitment Strategies

- Patient materials
- Website, newsletters via email, social media
- CADASILcare webinars and other unique strategies being considered

Patient Data Sharing Program

Why is Data Sharing Important?

Helps increase of understanding of genetic conditions.

This may help identify possible interventions and treatments

Help doctors and genetic testing laboratories better understand genetic changes that cause disease.

This can help individuals get clearer genetic test results and better understand their risks.

The more information collected, the better researchers will understand how genes affect health and, ultimately, how best to care for patients!

Step 1 – Participants Choose to Participate

Allows the GenomeConnect team to access their genetic and health information in their registry account.

Their information is be de-identified and shared.
Information shared could include:

- Age
- Gender
- Race/ethnicity
- Health History
- Test Results
- Reason for test

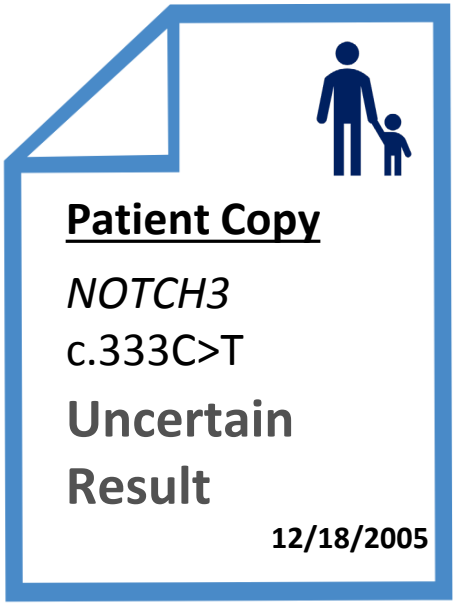
Step 2 – Upload a Copy of Their Genetic Test Results

If the participant has not already uploaded a copy of their genetic testing report, the are asked to do so.

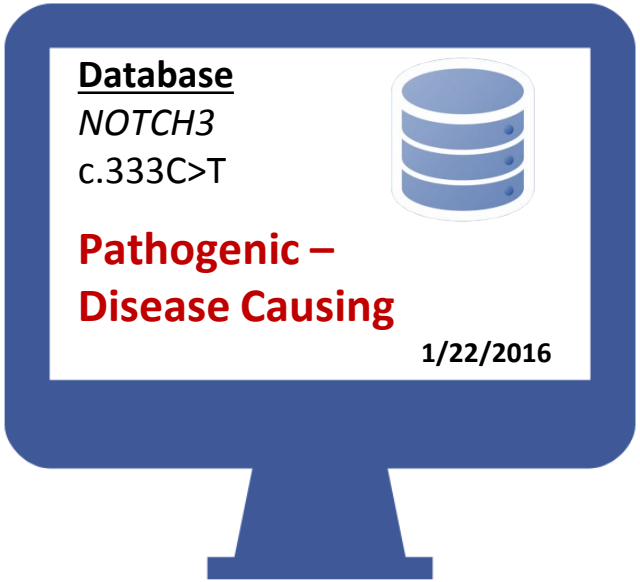
Genetic counselors review the genetic test results to ensure standardized data collection.

Genetic and health information is then de-identified and shared with publicly available databases including ClinVar

Participant Report



Database Entry from Reporting Lab



Participant has opted in to updates

Email to the participant informing them there may be an update to their results.

What about Privacy Concerns?

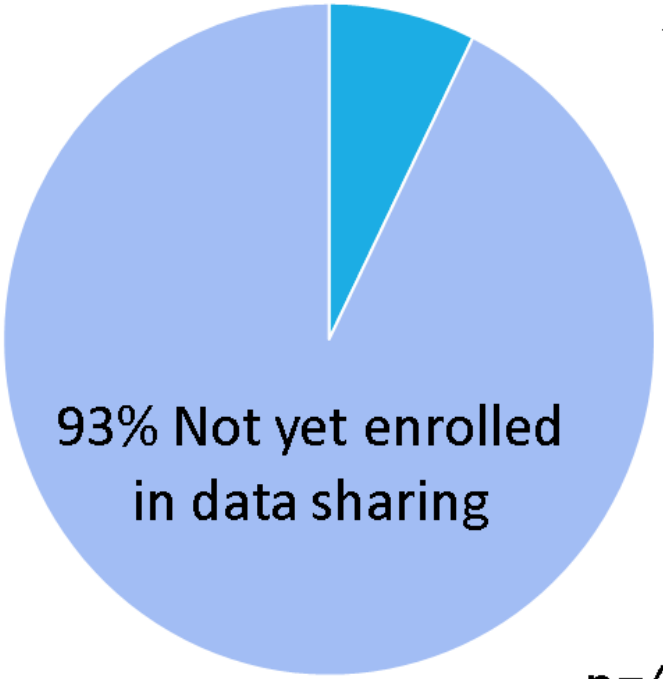
The GenomeConnect team and CureCADASIL take privacy seriously. As a result, there are a number of safeguards to protect privacy.

- HIPAA and FISMA compliant registry platform
- IRB governed consent and data sharing
- Only de-identified data is shared

Other Data Sharing Considerations

- Changing landscape of data sharing regulations

- Options to share data for a relative or deceased family member



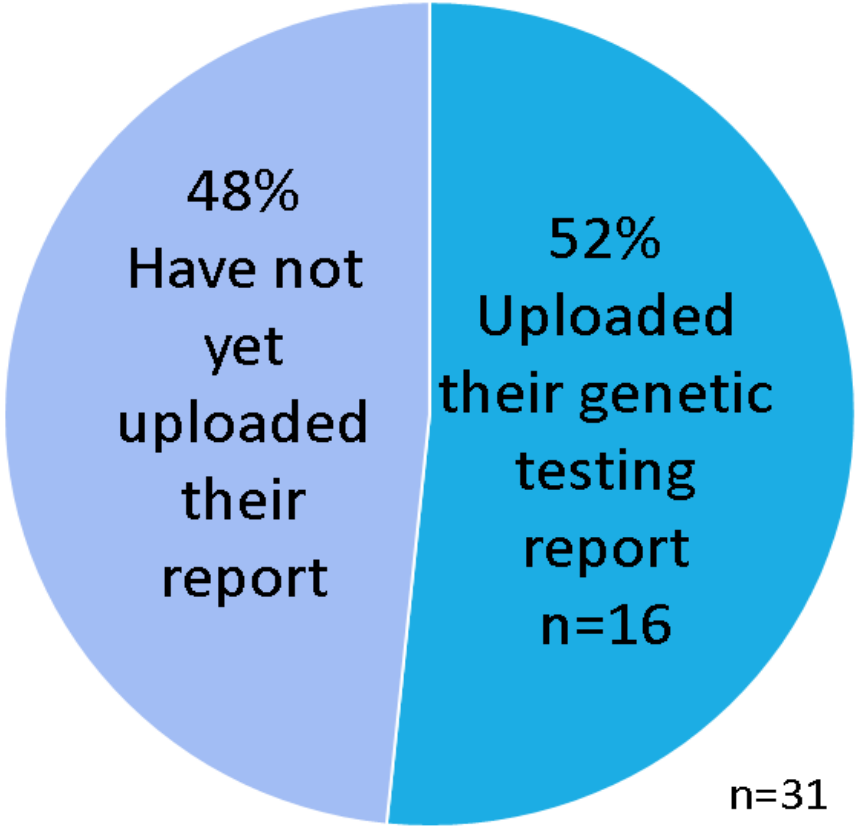
7% Enrolled in data sharing n=31

n=426

YES

The cureCADASIL Family Registry launched the program in February 2019

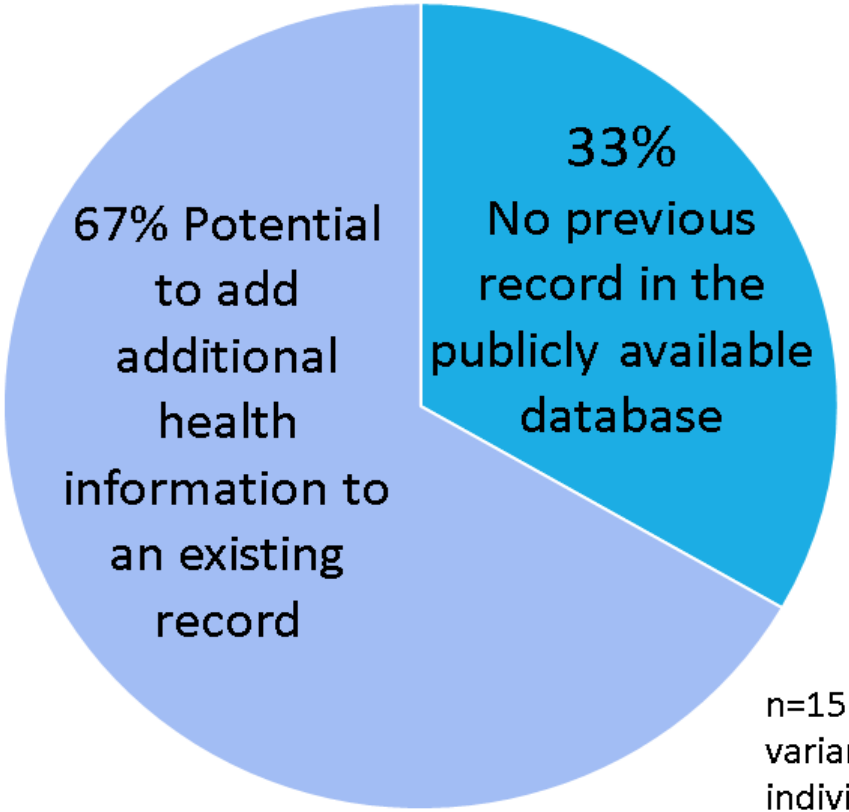
Data as of May 2019

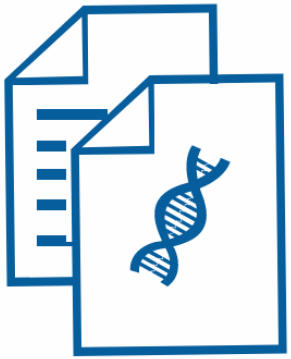


n=31

Compared to 30% of participants in enomeConnect that have uploaded their report.

Data as of May 2019

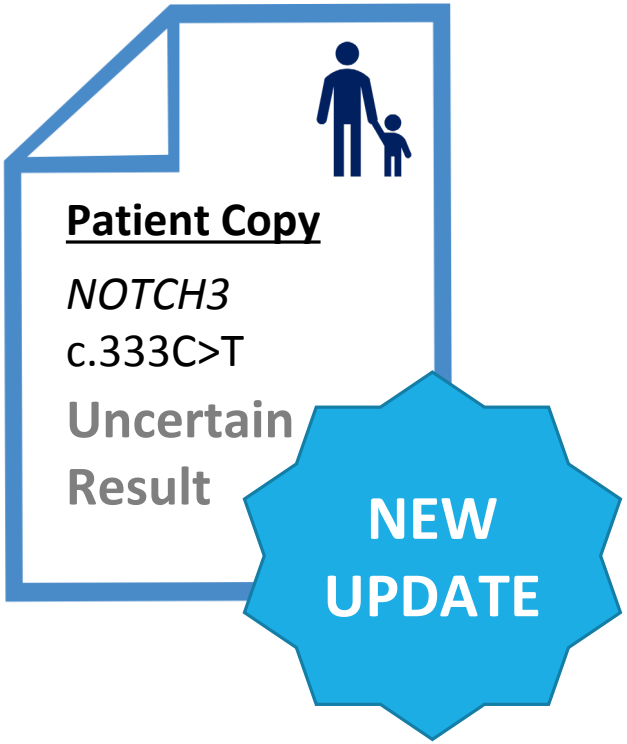




n=15 unique variants in 16 individuals

Data as of May 2019

2 participant reports are out of date compared to the genetic testing laboratory's current classification



Data as of May 2019

Conclusions

1. **The GenomeConnect team at ClinGen is working with advocacy groups including CureCADASIL to offer patients a structured way to share their genetic and health information.**
   - This data can be used to inform our understanding of genetic variants, genes, and genetic conditions. Ultimately, the goal is to improve patient care!

2. **From our experience so far with data sharing from the CADASIL Family Registry, we have learned:**
   - Patients are an important source of novel genomic data. 33% of variants shared from CureCADASIL participants have not been shared with the database before.
   - Participating in data sharing gives patients the option receive up to date variant interpretation with two updates already identified.

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- Melissa Landrum, PhD (ClinVar)
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- ClinGen Education WG
- The ClinVar Team

Invitae

- Vanessa Rangel Miller, MS, MBA (Invitae)
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- Jo Anne Vidal, BS (Invitae)

cureCADASIL

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