genomics4rd

A data lake powering rare disease research across Canada

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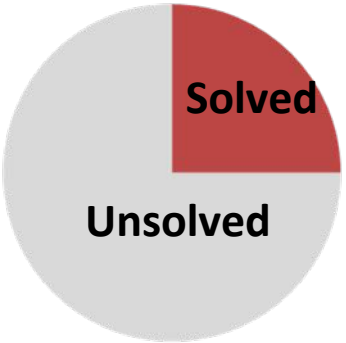
University of Ottawa

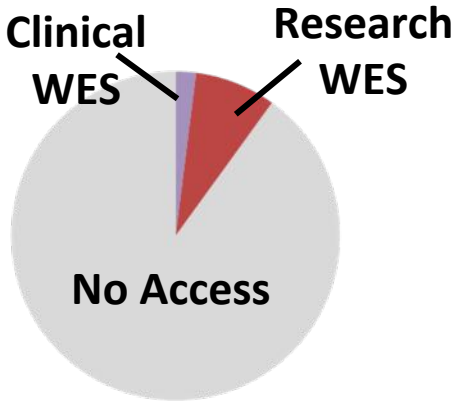
C4R-SOLVE

CARE forRARE

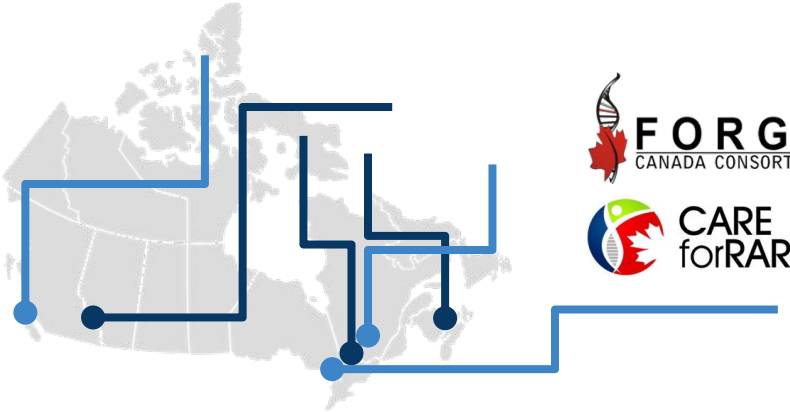
Fully understand the molecular pathogenesis of unsolved RDs



Facilitate timely diagnosis and optimal delivery



Our challenge



FORGE CANADA CONSORTIUM

CARE forRARE

14+ datasets scattered across country in silos

Much of the data is difficult to discover or share

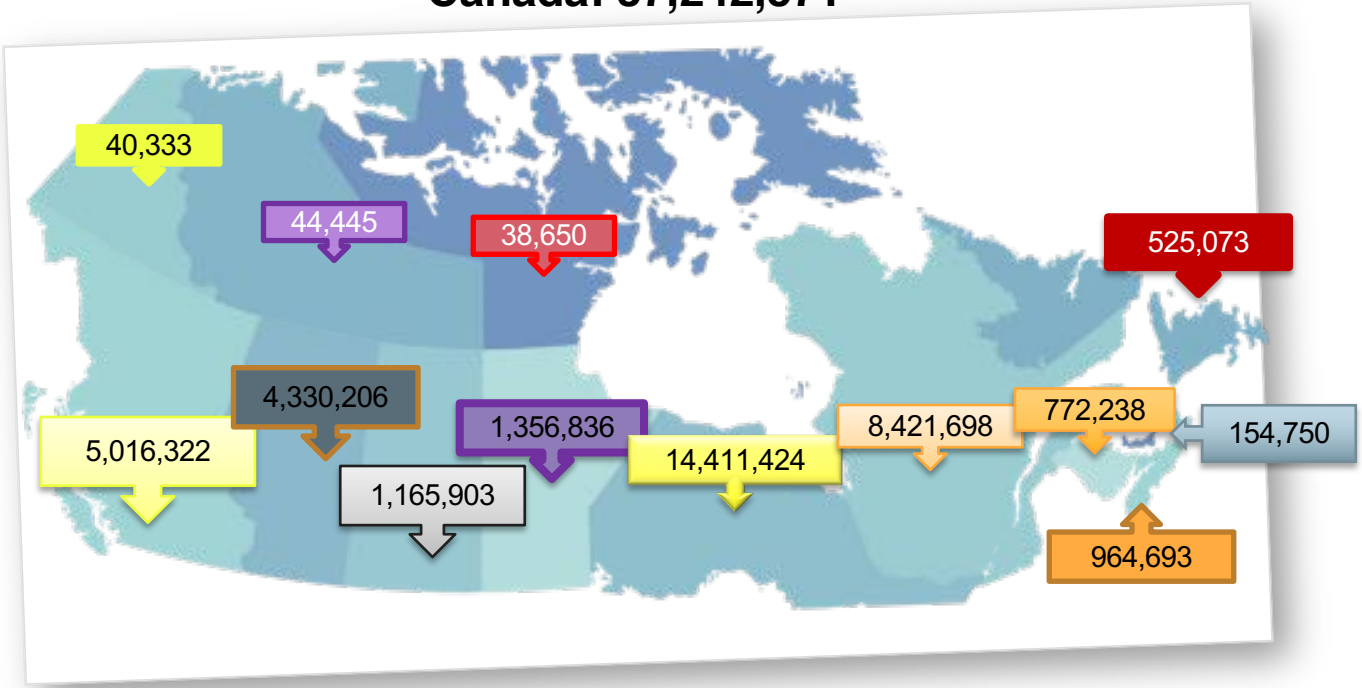
Over 50% are still **unsolved**

Joint analysis is difficult

Circa 2011; Toronto, Canada

Our opportunity

Canada: 37,242,571



Statistics Canada estimates Q4 2018

An estimated 10,000 rare disease patients meet criteria for GWS/year

Our goal

Diverse data types:

structured phenotype

family history data

2D and 3D facial photos

genomics + other 'omics (transcript/metabol/lipid-ome)

health services data

Linkages to data:

patient-reported data

administrative data

Lakes

2 million lakes in Canada

60% of the world's lake are found in Canada

Lake Louise, Alberta, August 2018 (photo courtesy of Francois Bernier)

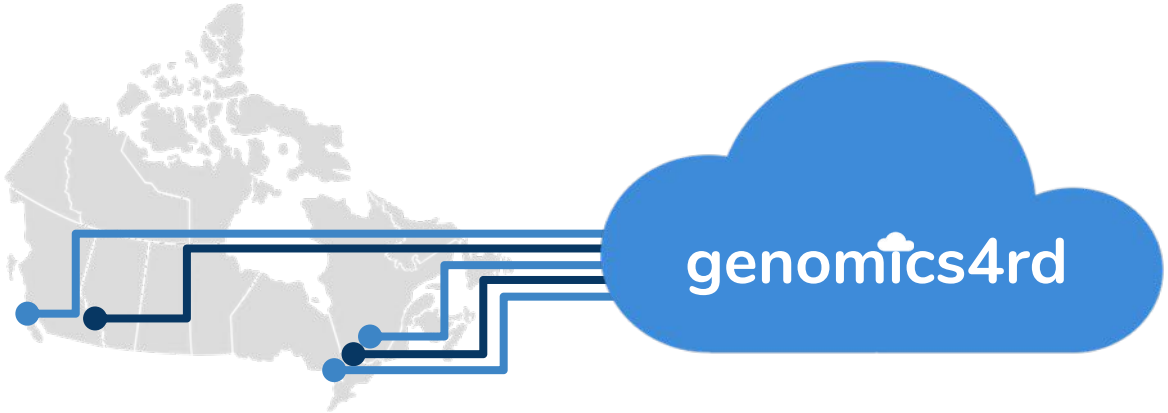
The solution?

A data lake for rare disease research

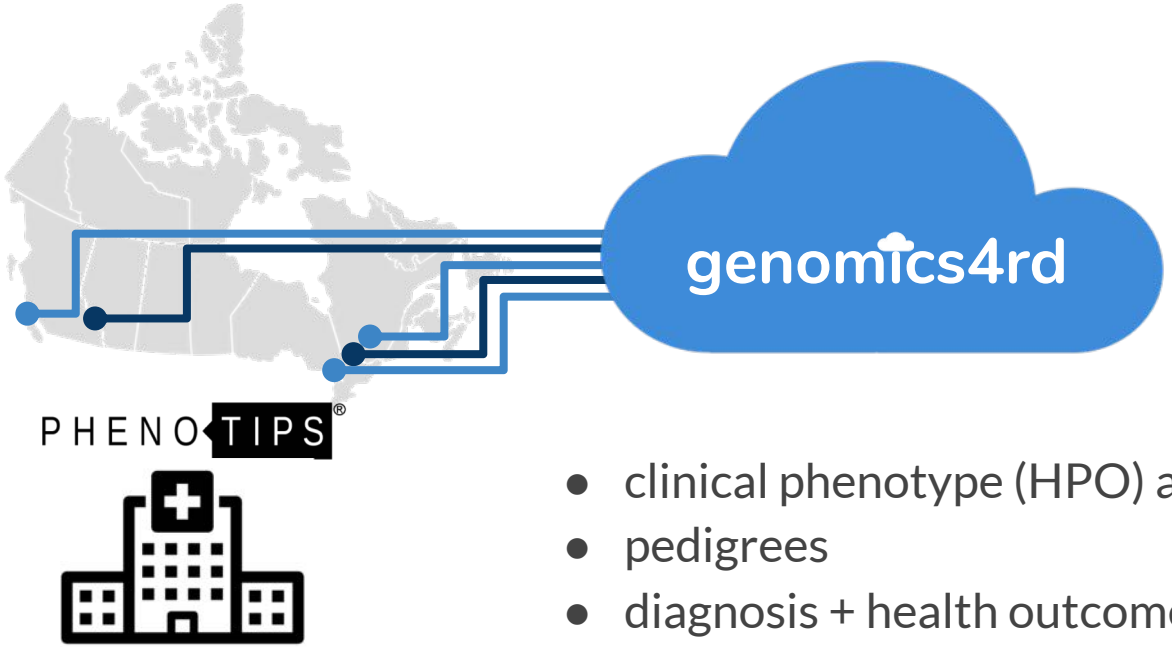
Genomics4RD

the first Canada-wide data lake for rare disease research

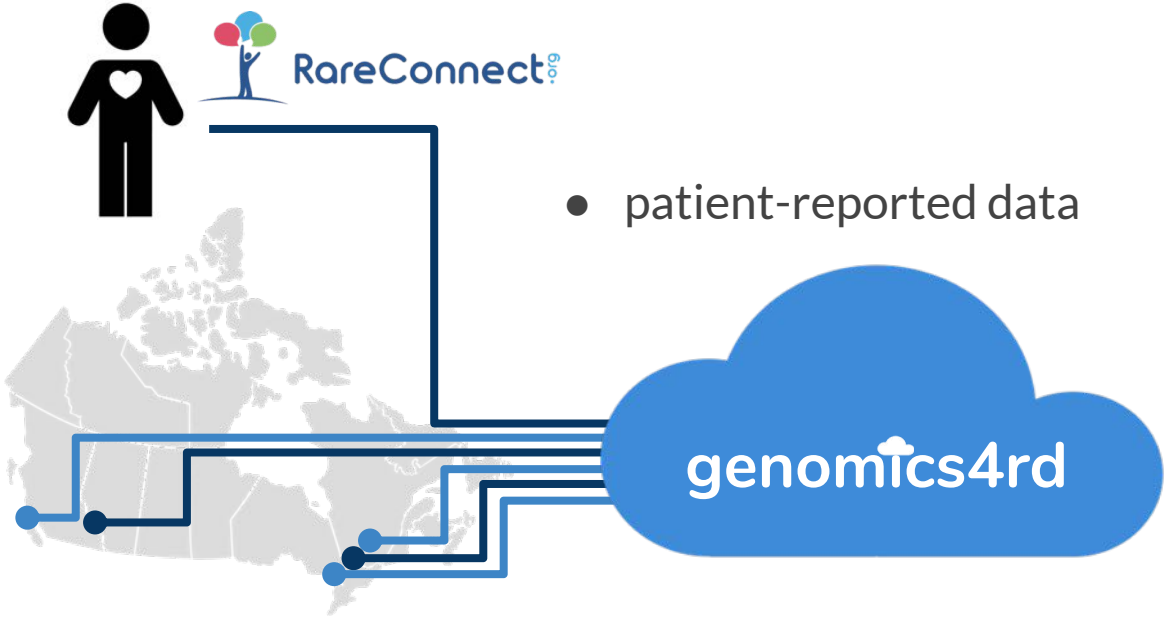
Genomics4RD launched Feb 2019



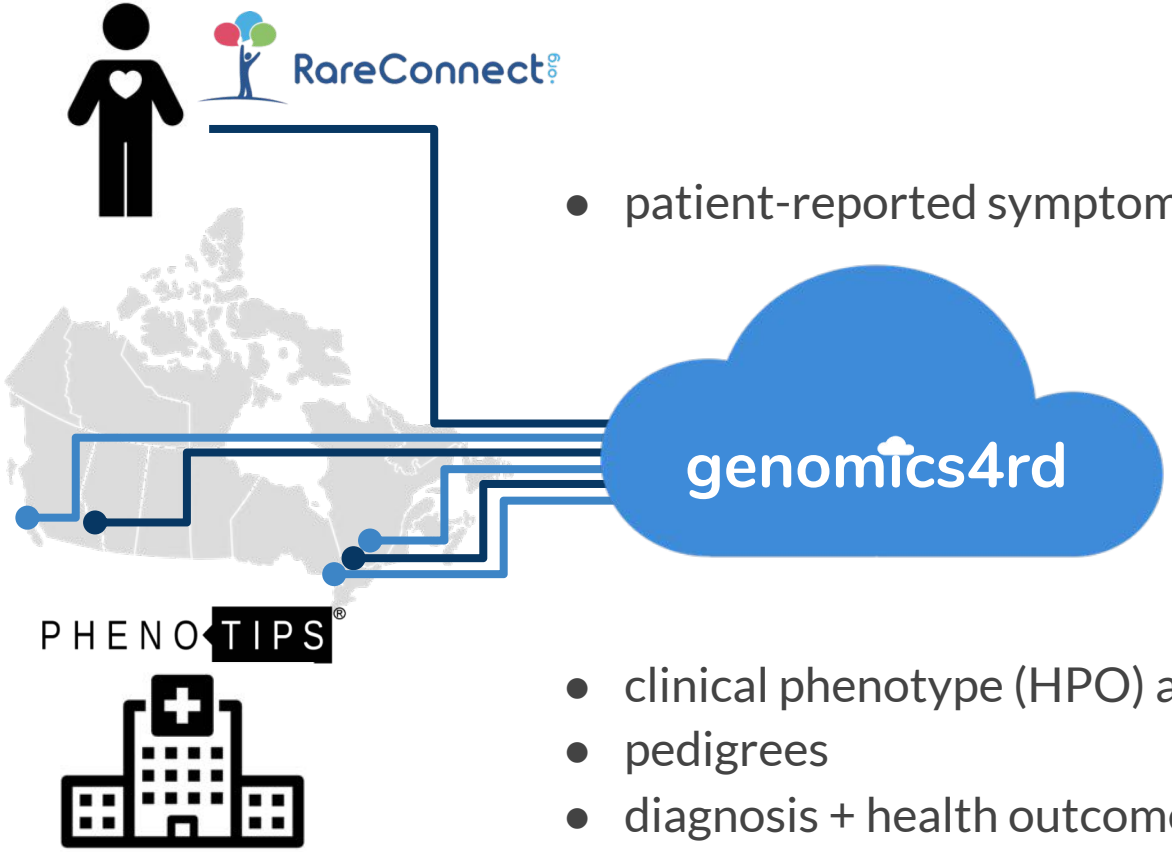
1. structured & unstructured data
2. tools for researchers
3. unified governance



- clinical phenotype (HPO) and dx (ORDO/OMIM)
- pedigrees
- diagnosis + health outcome surveys
- wes/wgs
- other ‘omics data



- patient-reported data



- patient-reported symptoms

computer-readable metadata to help researchers discover and access data

- clinical phenotype (HPO) and dx (ORDO/OMIM)
- pedigrees
- diagnosis + health outcome surveys
- wes/wgs
- other ‘omics data

Tools to

collect and **analyze**

these complex data

Clinical phenotyping through PHENOTIPS®

phenotype

Clinical symptoms and physical findings

GROWTH PARAMETERS

Weight for age
- ★ Decreased body weight (<-2SD)

Stature for age
- ★ Short stature (<-2SD)
- NO Tall stature (>+2SD)

CRANIOFACIAL

- Small face

EAR DEFECTS

- Preauricular pit
- Abnormality of the outer ear
- NO Abnormality of the inner ear

CUTANEOUS

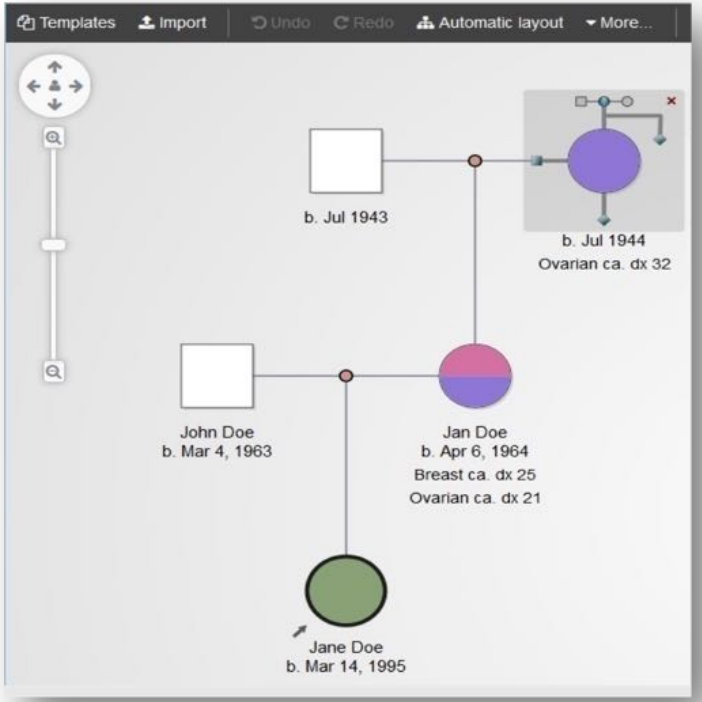
- Red hair

NEUROLOGICAL

- ★ Aggressive behavior

hpo

family history



Tagging HPO terms for data analysis

Clinical symptoms and physical findings

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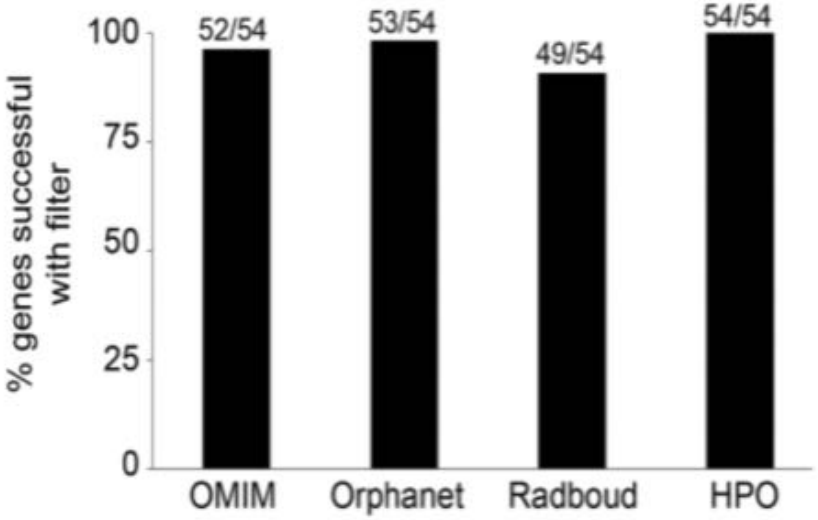
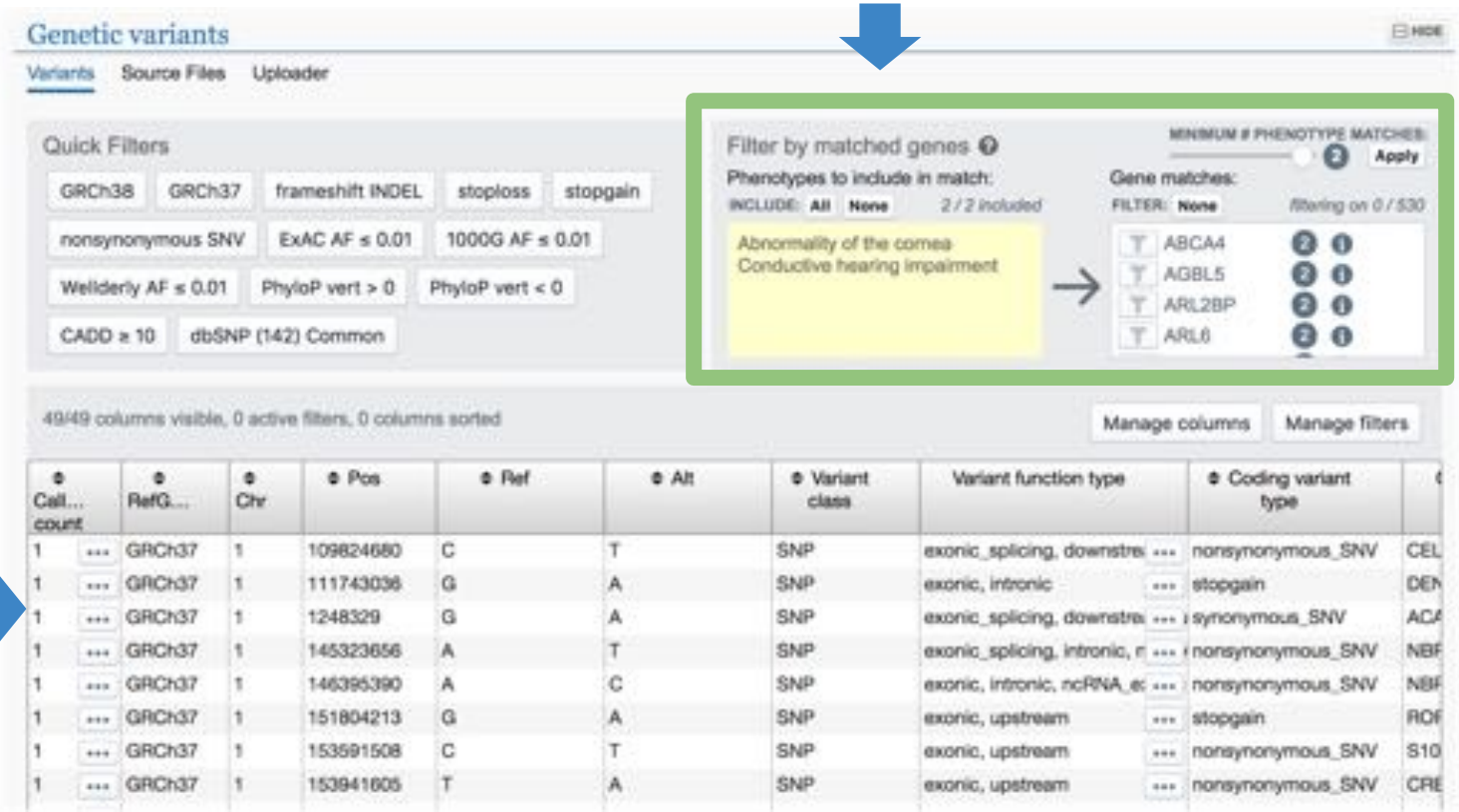


Kernohan et al., Hum Mutat 2018;39:197-201

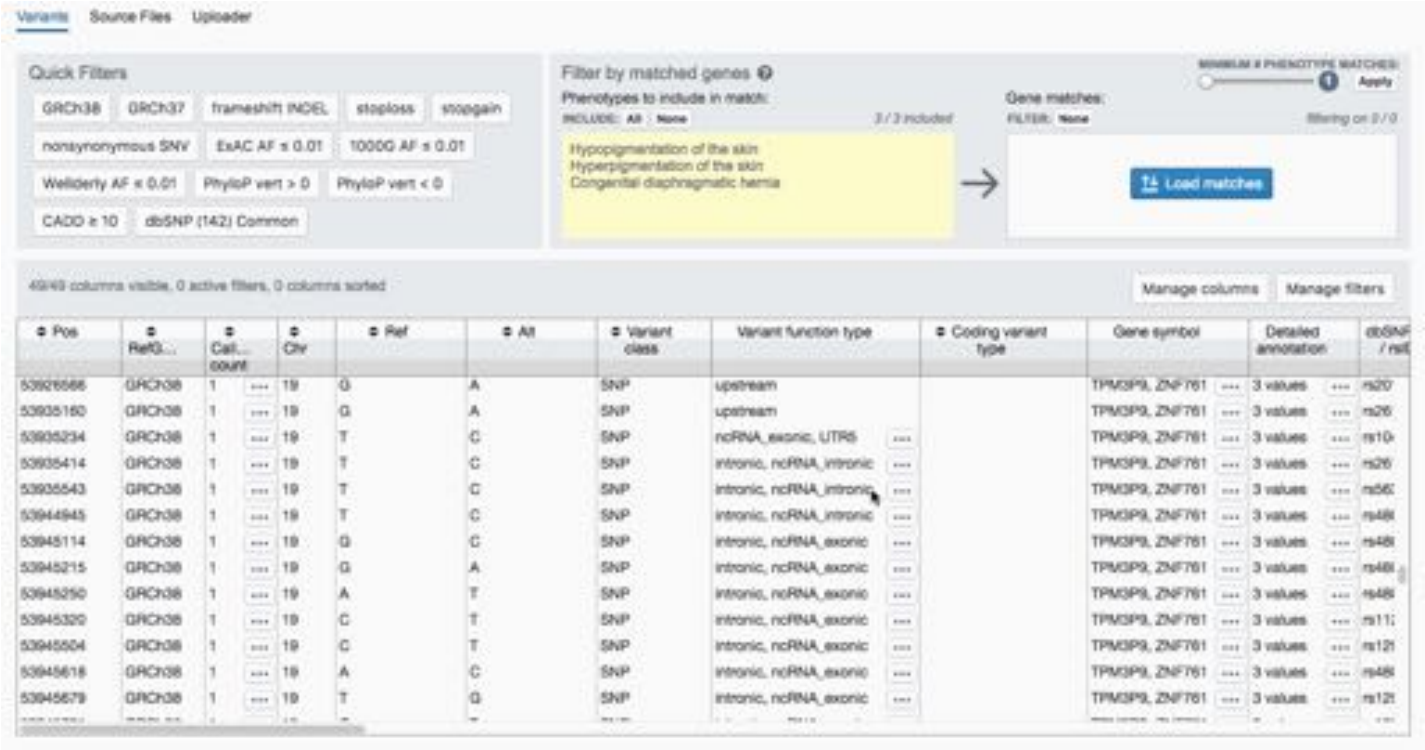
Genomic investigation

phenotype

exome/ genome results



Genomic investigation



scalable variant store and virtual phenotype-based panels

Outcomes and utilization surveys

Enrollment Site for Patient

Ontario

CHEO | Hamilton Neurology | SickKids | Stollery | Toronto General Hospital (UHN) | Credit Valley Hospital | Health Sciences North | Kingston General Hospital | London Health Sciences Centre | North York General Hospital | Mount Sinai Hospital

Which clinical presentation criteria applies to this patient? (check 2 or more items)

Please select at least 2 options: ✔

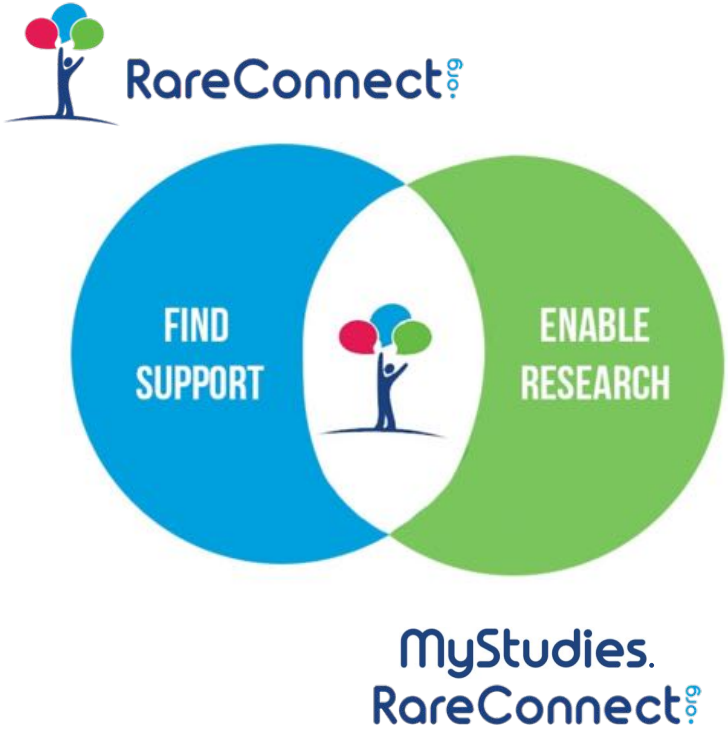
- [ ] Moderate to severe developmental or functional impairment
- [x] Multisystem involvement
- [x] Progressive clinical course
- [ ] Differential diagnosis includes ≥ 2 well defined conditions requiring evaluation by multiple targeted gene panels
- [ ] Suspected severe genetic syndrome NYD for which multiple family members are also affected, or where parents are consanguineous

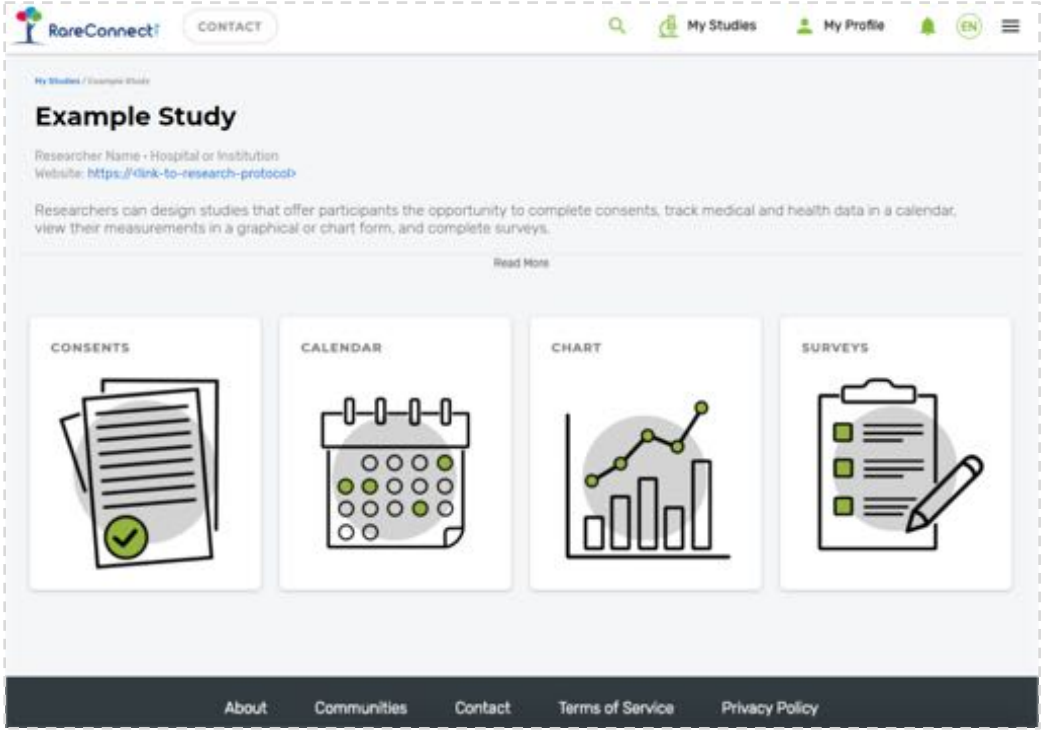
Which management impact criteria applies to this patient? (check 1 or more item)

Please select at least 1 option: ✔

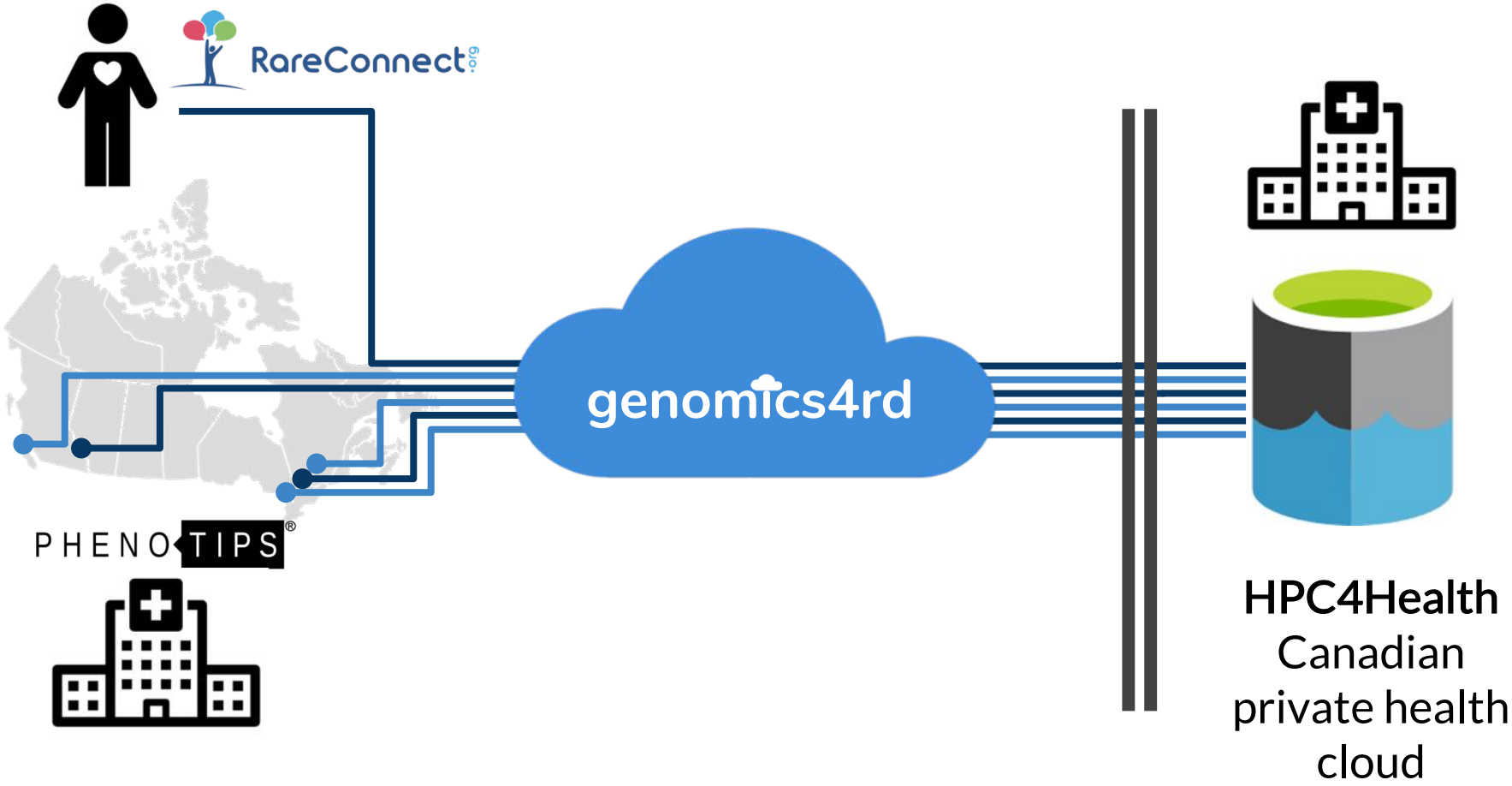
- [x] Will limit further invasive diagnostic investigations
- [ ] Results allow for specific and informed reproductive decision making (for patient or parents)
- [ ] Will enable identification of at risk family members and facilitate early intervention

Patient self-reporting through RareConnect



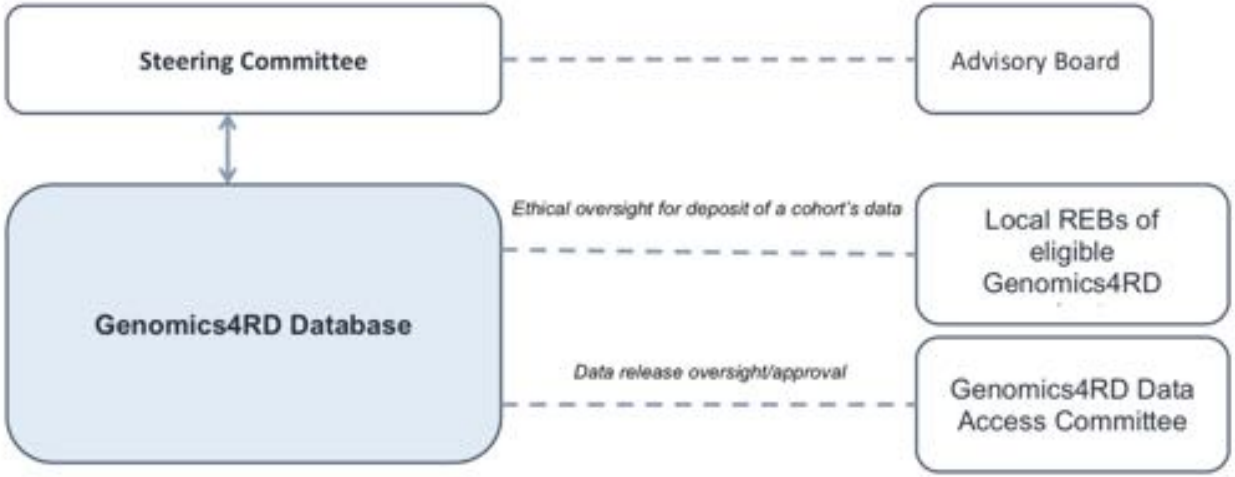


How is access managed?


RareConnect.org
genomics4rd
PHENOTIPS®
HPC4Health
Canadian
private health
cloud

Governance and data access

- CHEO Research Institute is data custodian
- Platform is managed by Steering Committee + Advisory Board
- Data Access requests are evaluated by Data Access Committee
- Rare disease patient/advocate representation



level 1

“open”

Public access

Aggregated variants, genes of interest, and coded phenotypes

level 2

“registered”

Consortium members

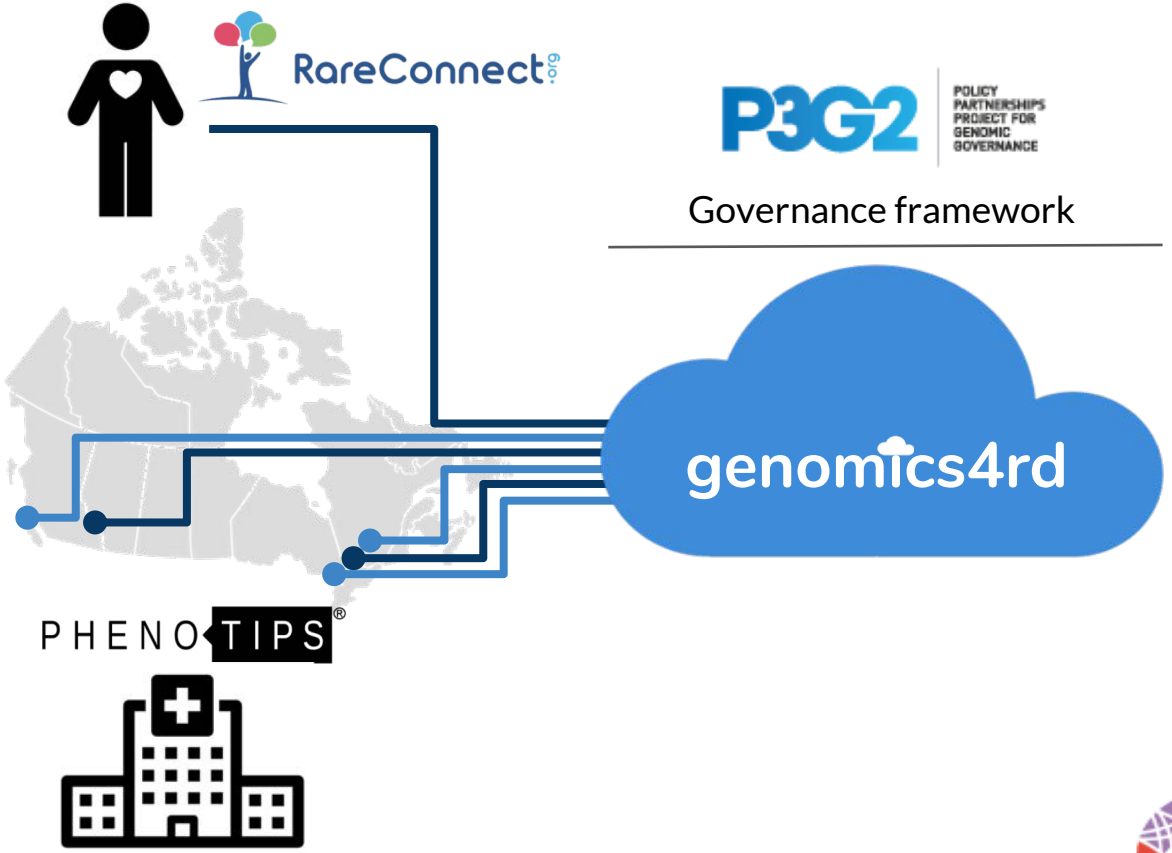
Individual-level variants, processed -omics data, phenotype descriptions, and family history

level 3

“controlled”

Approved research projects

Full access to structured and unstructured data, raw sequence, health administrative data

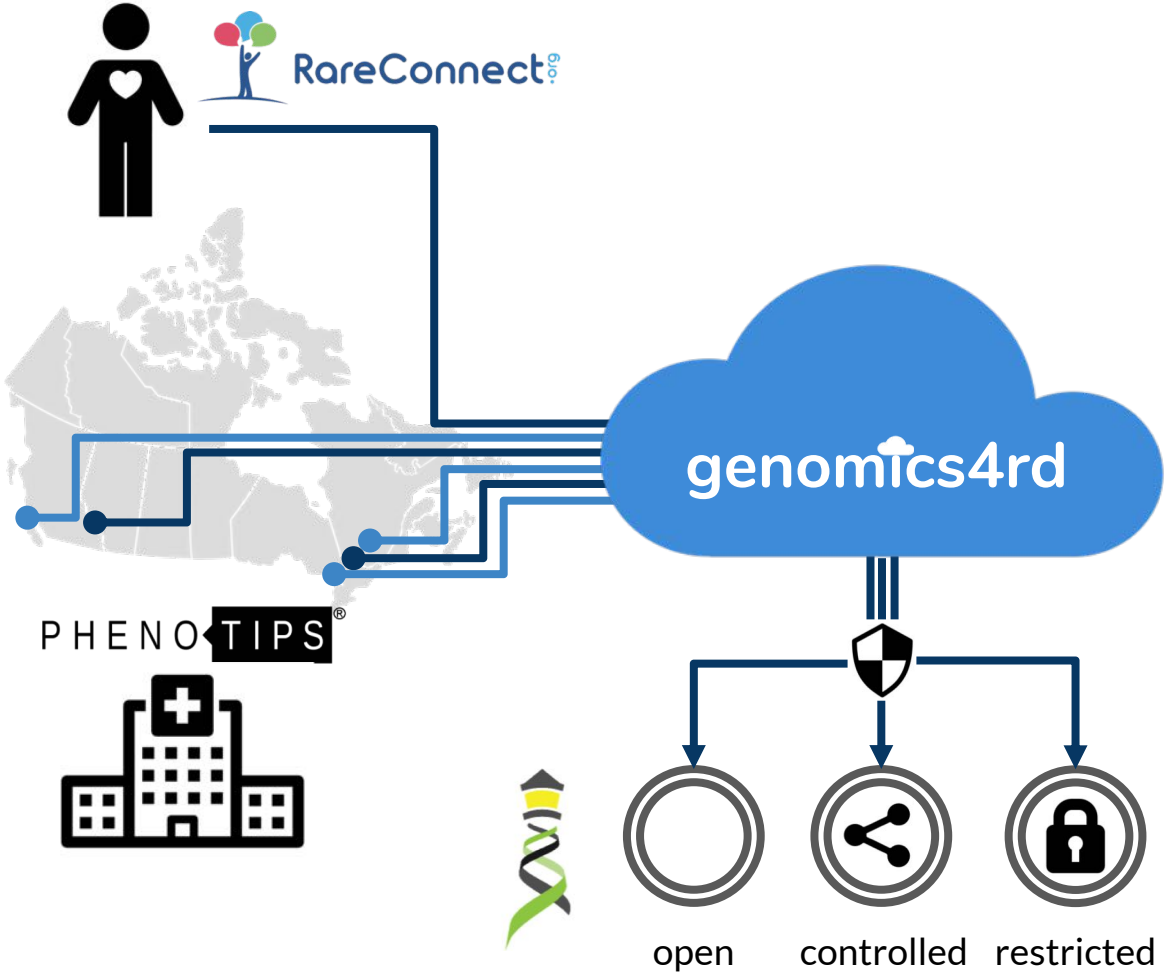


evaluate consent forms

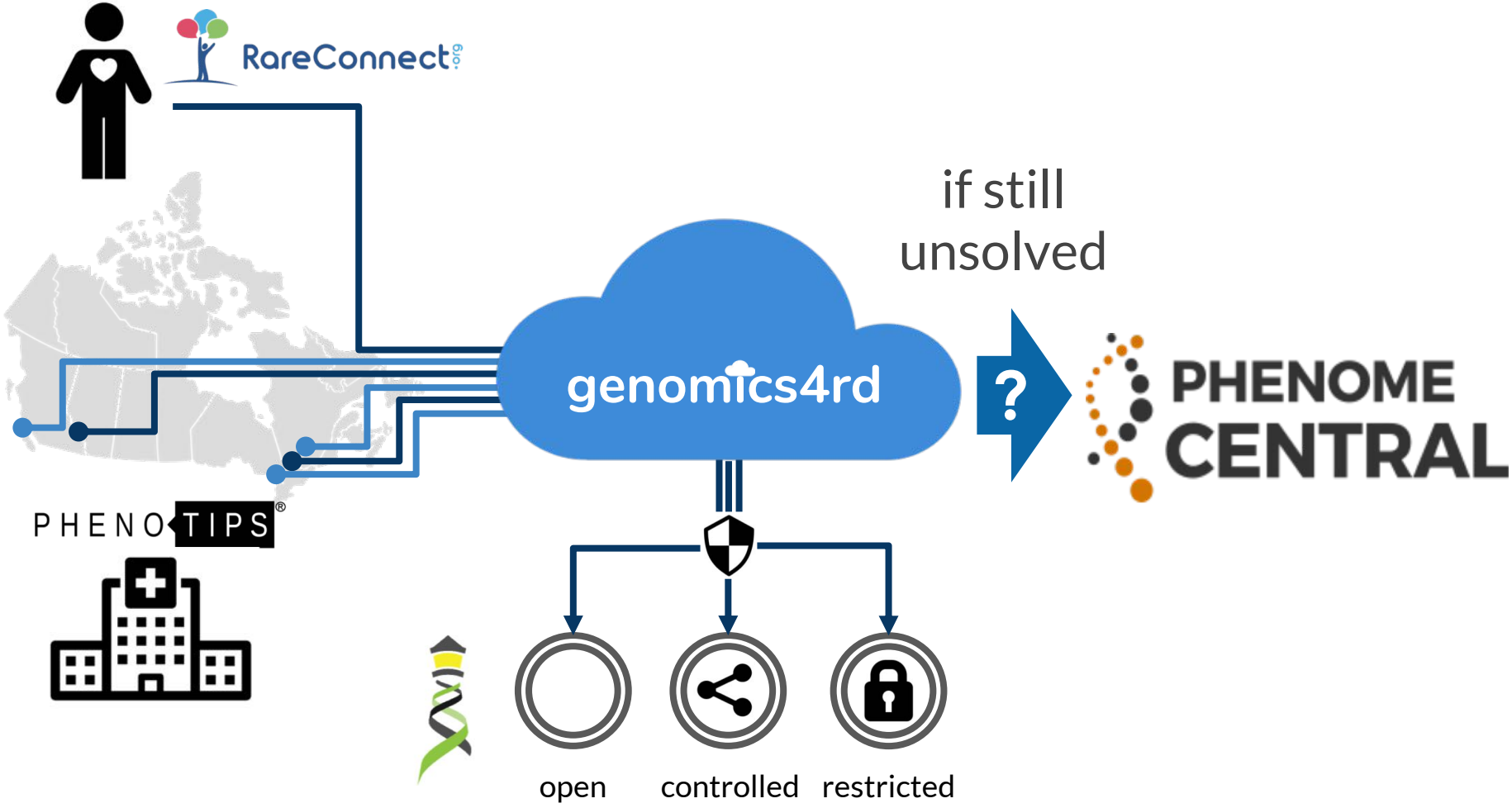
computable consent and data use conditions:

- DUO
- ADA-M

Global Alliance for Genomics & Health


RareConnect.org
genomics4rd
PHENOTIPS®
open
controlled
restricted

Still unsolved?

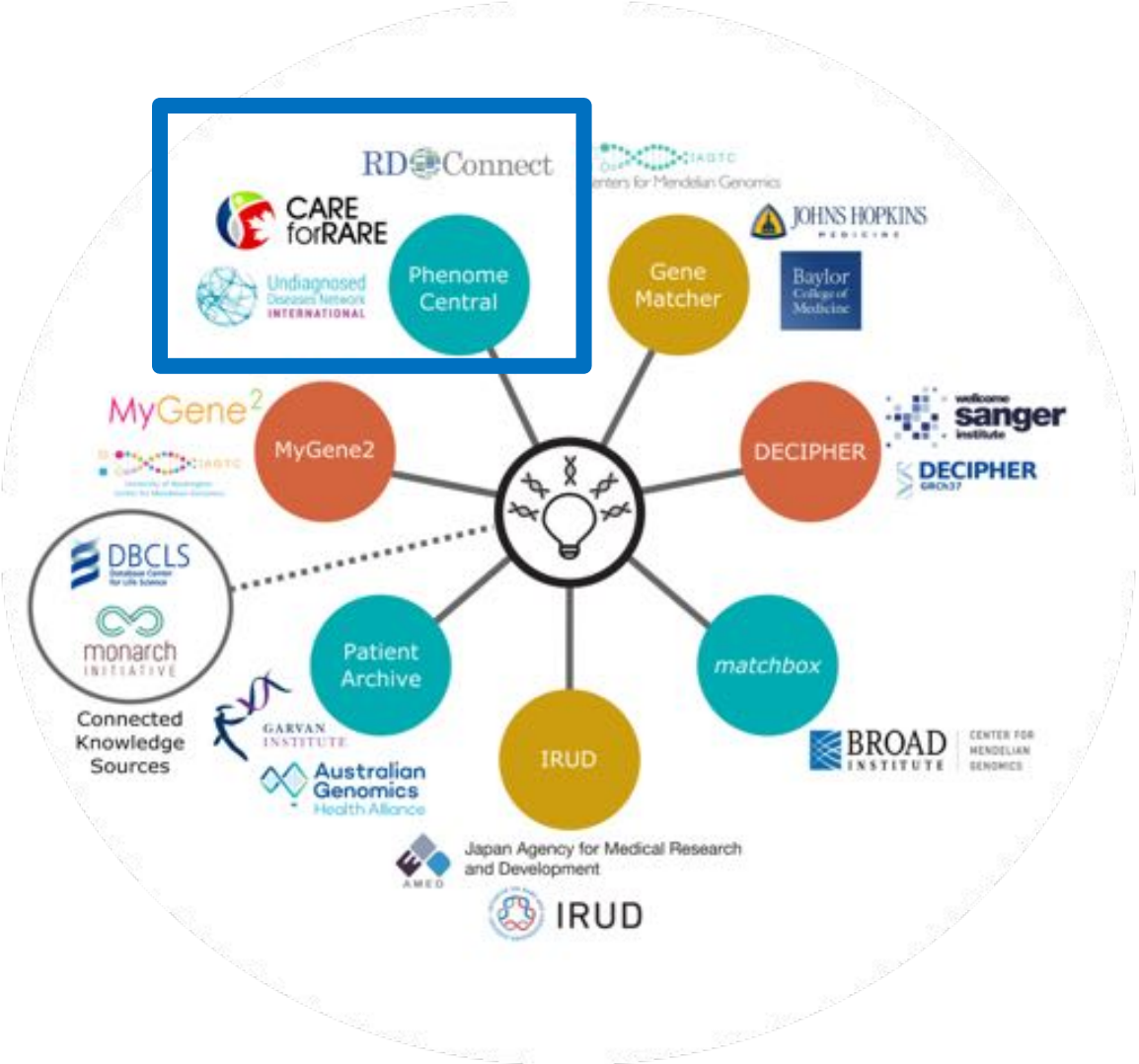

RareConnect.org
PHENOTIPS®
genomics4rd
if still
unsolved
?
PHENOME
CENTRAL
open
controlled
restricted

Matchmaker Exchange

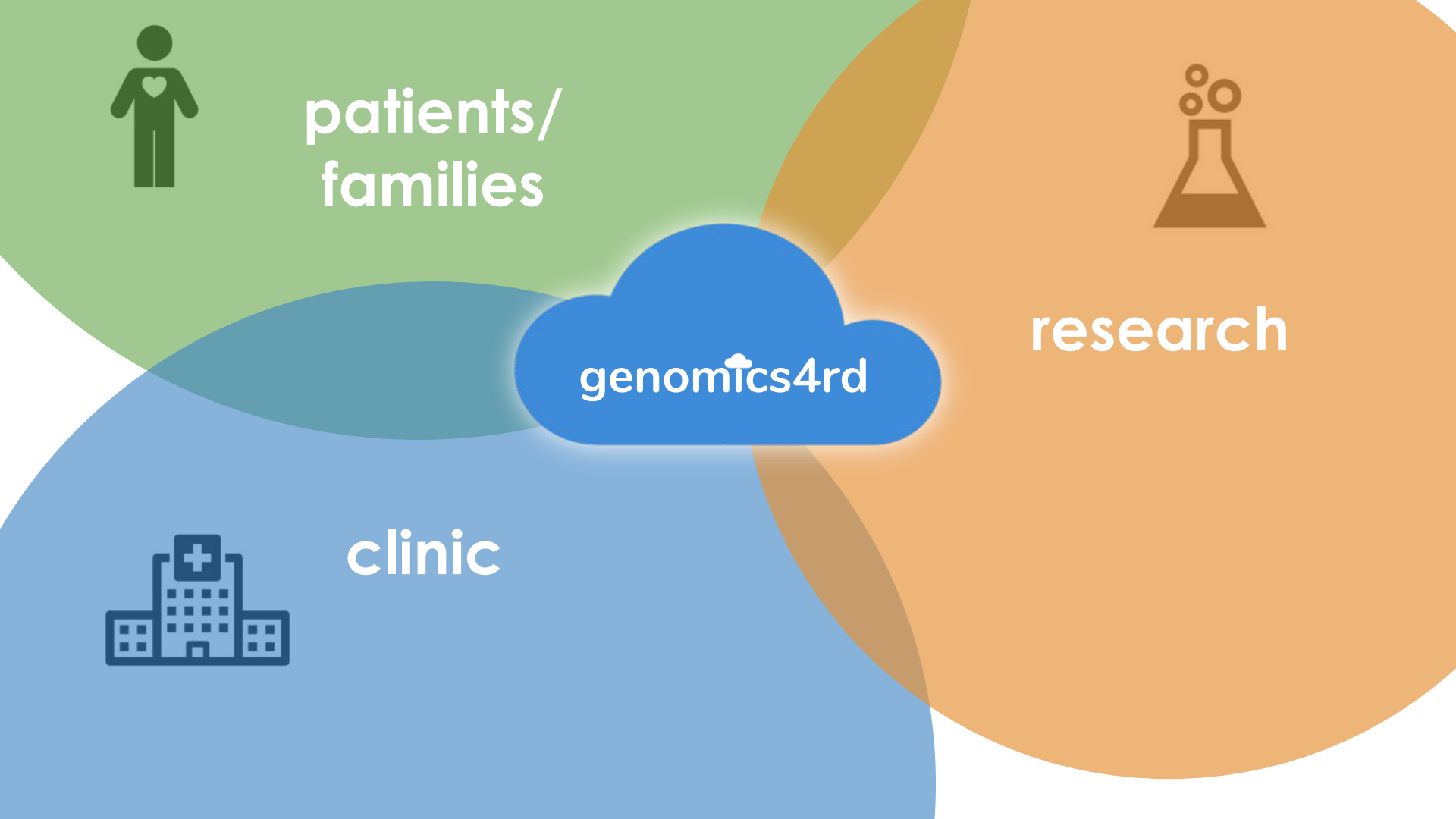
86 countries

130k+ patients

11k+ unique genes



Global Alliance for Genomics & Health


patients/
families
research
genomics4rd
clinic

Thank you

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Ian Stedman

Robin Hayeems
Christian Marshall

Orion Buske
Pawel Buczkowicz
Alina Gvozdik
Daniel Gross
Sebastian Stanisor
Teyden Nguyen

and especially **funders**, **partners**, and **participants**

genomics4rd.ca