Data sharing in Canada through the Canadian Open Genetics Repository

COGR
Canadian Open
Genetics Repository

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opengenetics.ca

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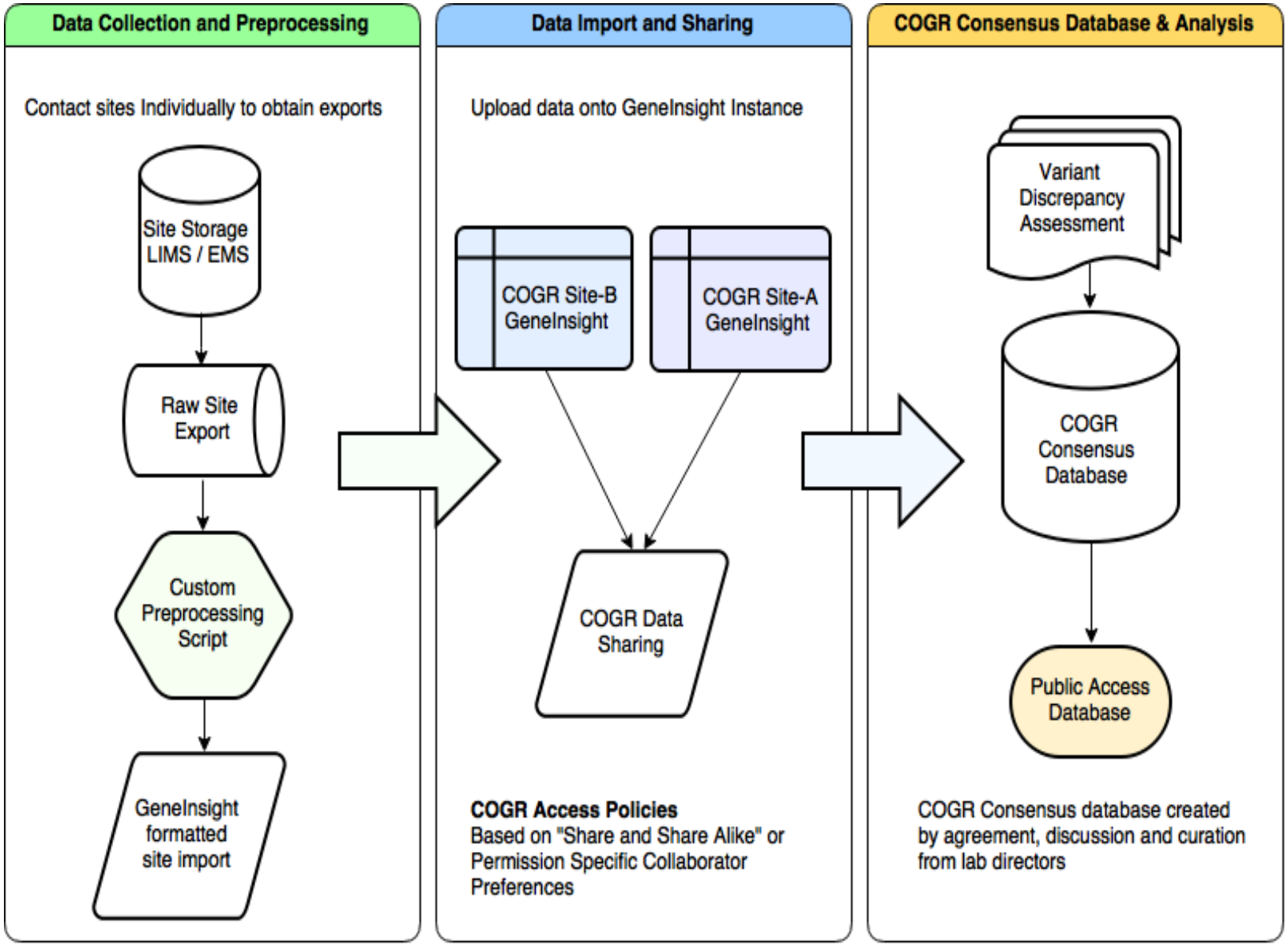
OntarioGenomicsInstitute

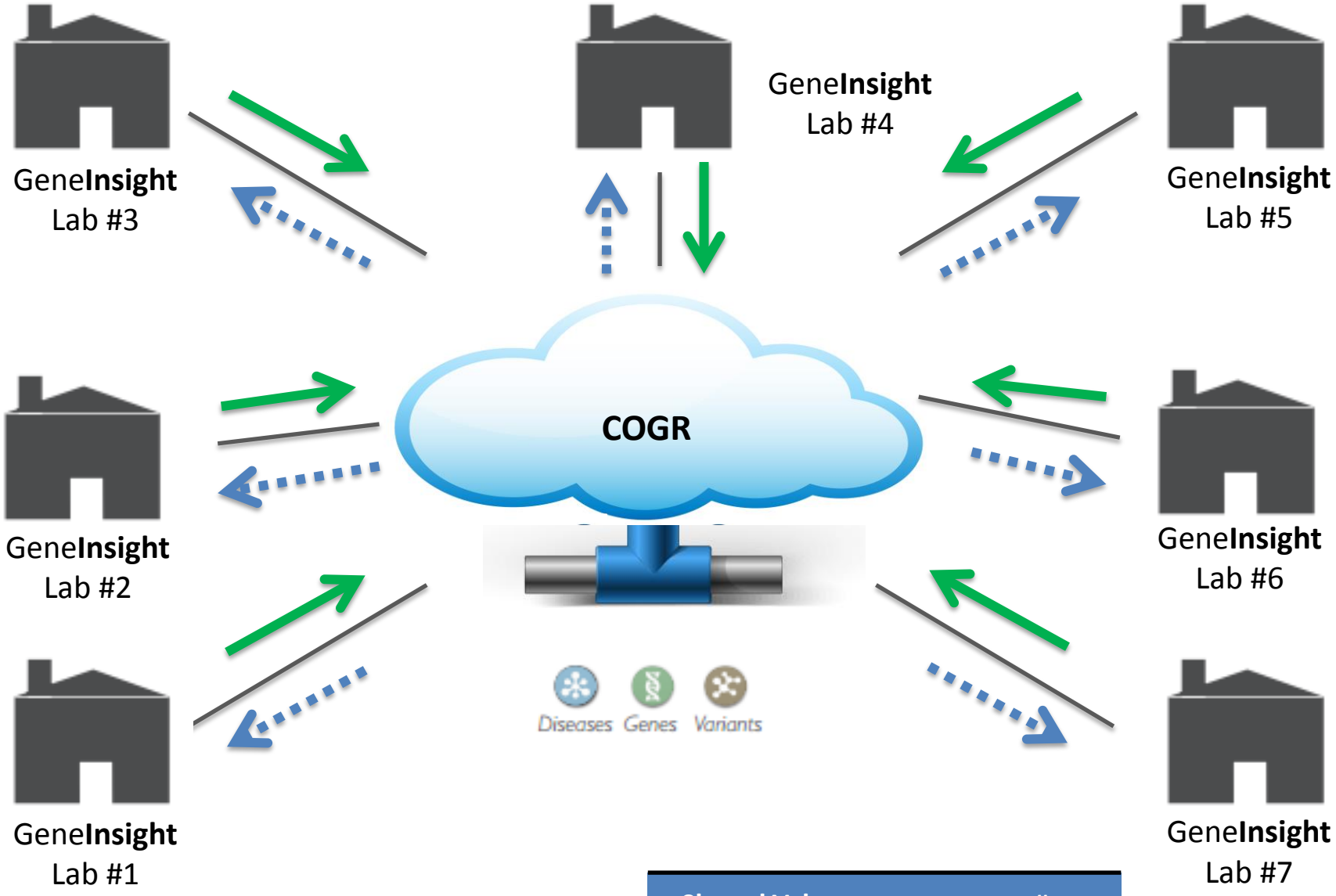
GenomeCanada

Objectives

- To create Canada's unified, open-access, clinical-grade genetic database using a commonly shared platform
- Standardize variant assessment procedures
- Data extraction and variant classification consensus building
- Data Access and Disseminate results to a large public repository

Workflow Overview





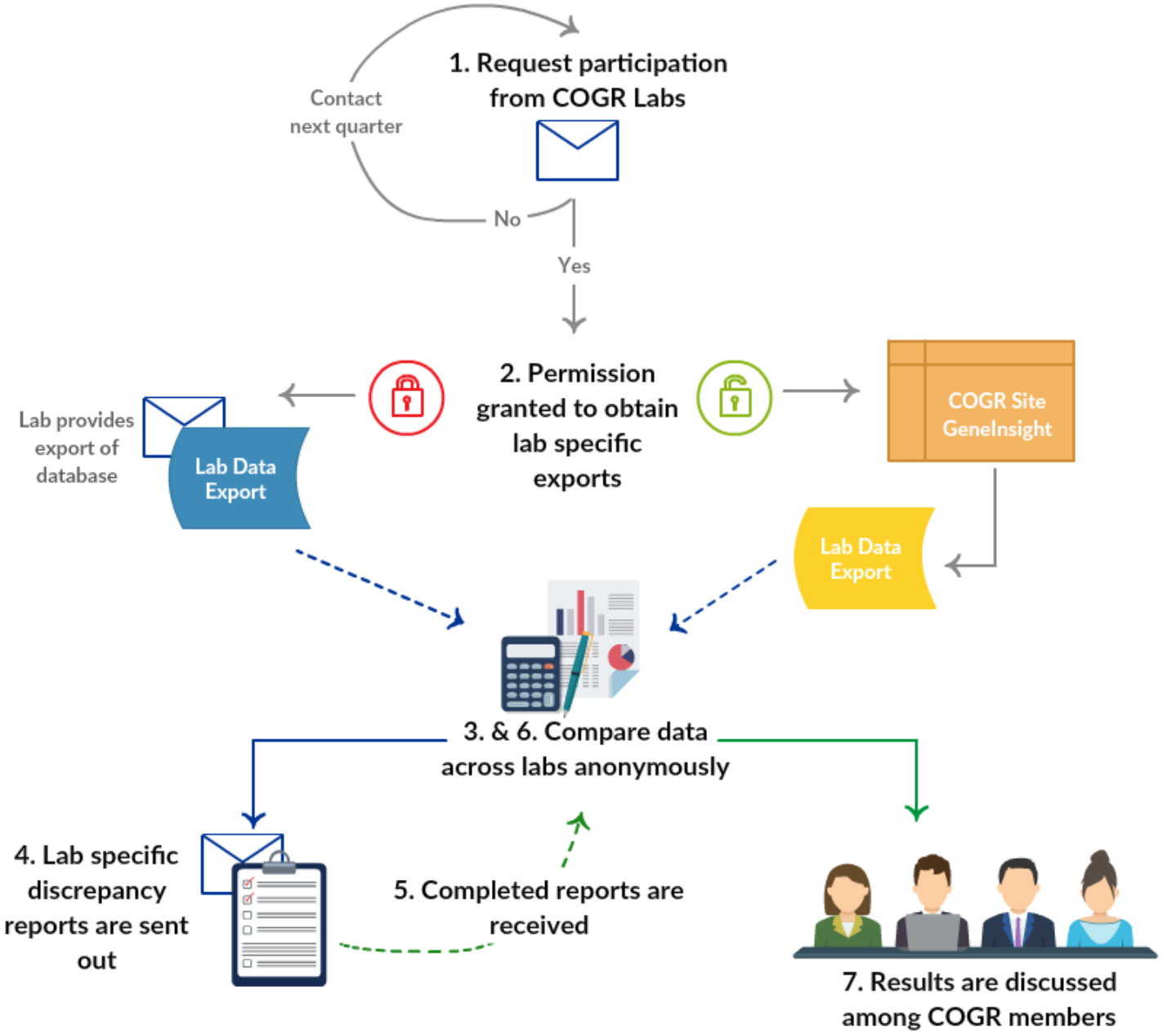
Shared Values	#
Interpreted Variants	~20,000
Genes	1,266
Diseases	66

Clinically validated, de-identified, and approved data

Read-only viewing with ability to validate and import

COGR - BRCA Participating Institutions

- **A. Alberta Children's Hospital (Calgary, AB)**
- B. Atlantic Cancer Research Institute (Moncton, NB)
- **C. British Columbia Cancer Agency (Vancouver BC)**
- D. Children's & Women's Health Centre of BC (Vancouver BC)
- **E. Children's Hospital of Eastern Ontario (Ottawa ON)**
- **F. Credit Valley Hospital, Trillium Health Centre (Mississauga ON)**
- **G. Dept of Medical Genetics, University of Alberta (Edmonton, AB)**
- **H. Hamilton Health Sciences, McMaster University (Hamilton, ON)**
- I. Impact Genetics Inc. (Bowmanville, ON)
- J. Izaak Walton Killam Health Centre (Halifax, NS)
- **K. Kingston General Hospital, Queen's University (Kingston, ON)**
- L. McGill University Health Complex (Montréal, QC)
- M. Memorial Health University Medical Center (St. John's, NL)
- **N. Mount Sinai Hospital, University of Toronto (Toronto, ON)**
- **O. North York General Hospital (Toronto ON)**
- P. Ontario Institute of Cancer Research (OICR) (Toronto, ON)
- **Q. Regional Health Authority, University of Manitoba (Winnipeg, MB)**
- R. Sainte-Justine Hospital, University of Montreal (Montréal, QC)
- S. SickKids Hospital and McLaughlin Centre (Toronto, ON)
- T. University Hospital, Western University (London, ON)
- **U. Women's College Hospital, University of Toronto (Toronto, ON)**
- V. Jewish General Hospital, Montreal (Montréal, QC)

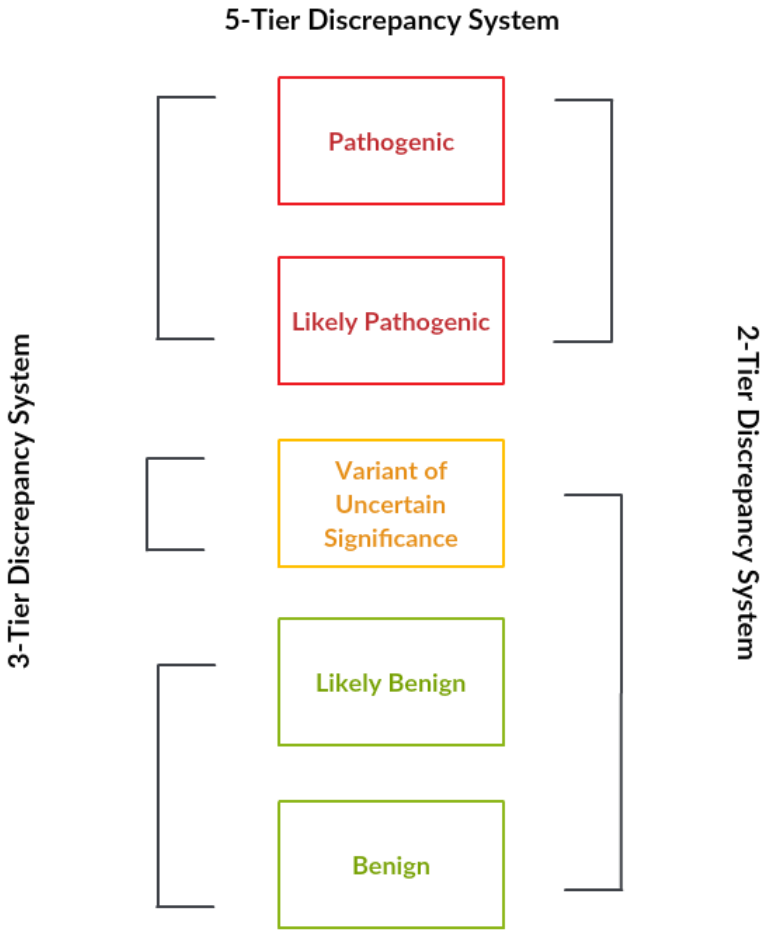

1. Request participation from COGR Labs
Contact next quarter
No
Yes
2. Permission granted to obtain lab specific exports
Lab provides export of database
Lab Data Export
COGR Site GeneInsight
Lab Data Export
3. & 6. Compare data across labs anonymously
4. Lab specific discrepancy reports are sent out
5. Completed reports are received
7. Results are discussed among COGR members

Discrepancy Report Results Overview

- **11** participating labs across 4 provinces
  - ON, BC, AB, MB

- Received total of **5,554** *BRCA1/2* variants
  - 3014 unique variants
    - 1,148 seen in >2 labs
  - 110 to 1072 variants per lab (505 on average)

Tiered Discrepancy Models



5-tiered

- Initially implemented

3-tiered

- Recommended by participants

2-tieried

- Clinical management

Data Received

5-tier

- 900 variants had 2 or more classifications
- 350 (38.9%) were discordant
  - 1410 observations of these variants

3-tier

- 240 (26.7%) discordant

2-tier

- 45 (5%) discordant

After analysis

330 (23.8%) discordant variant observations changed classification after analysis

5-tier

- Number of discordant variants decreased from 38.9% to 30.7%

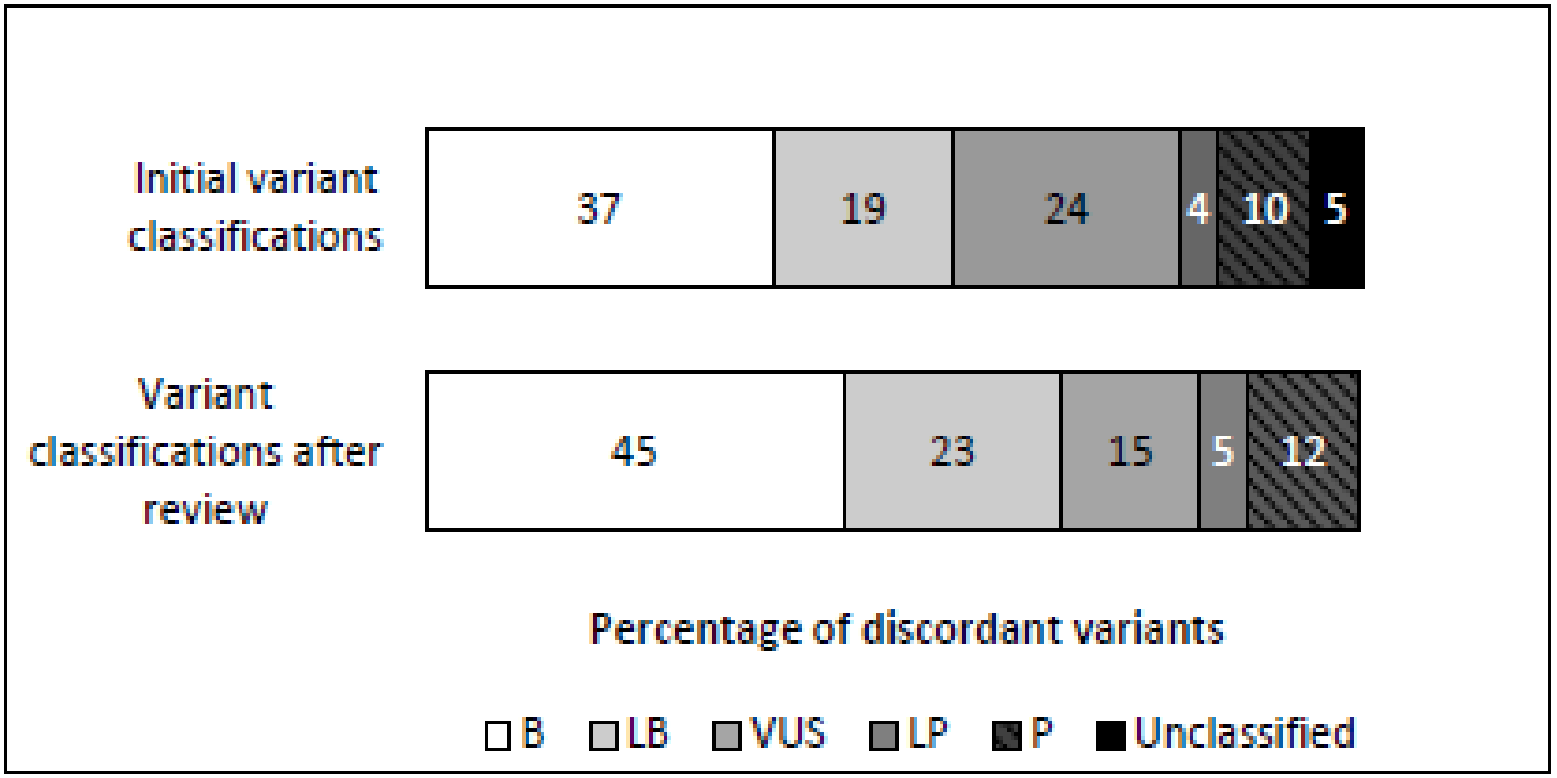
3-tier

- Decrease from 26.7% to 12.45%

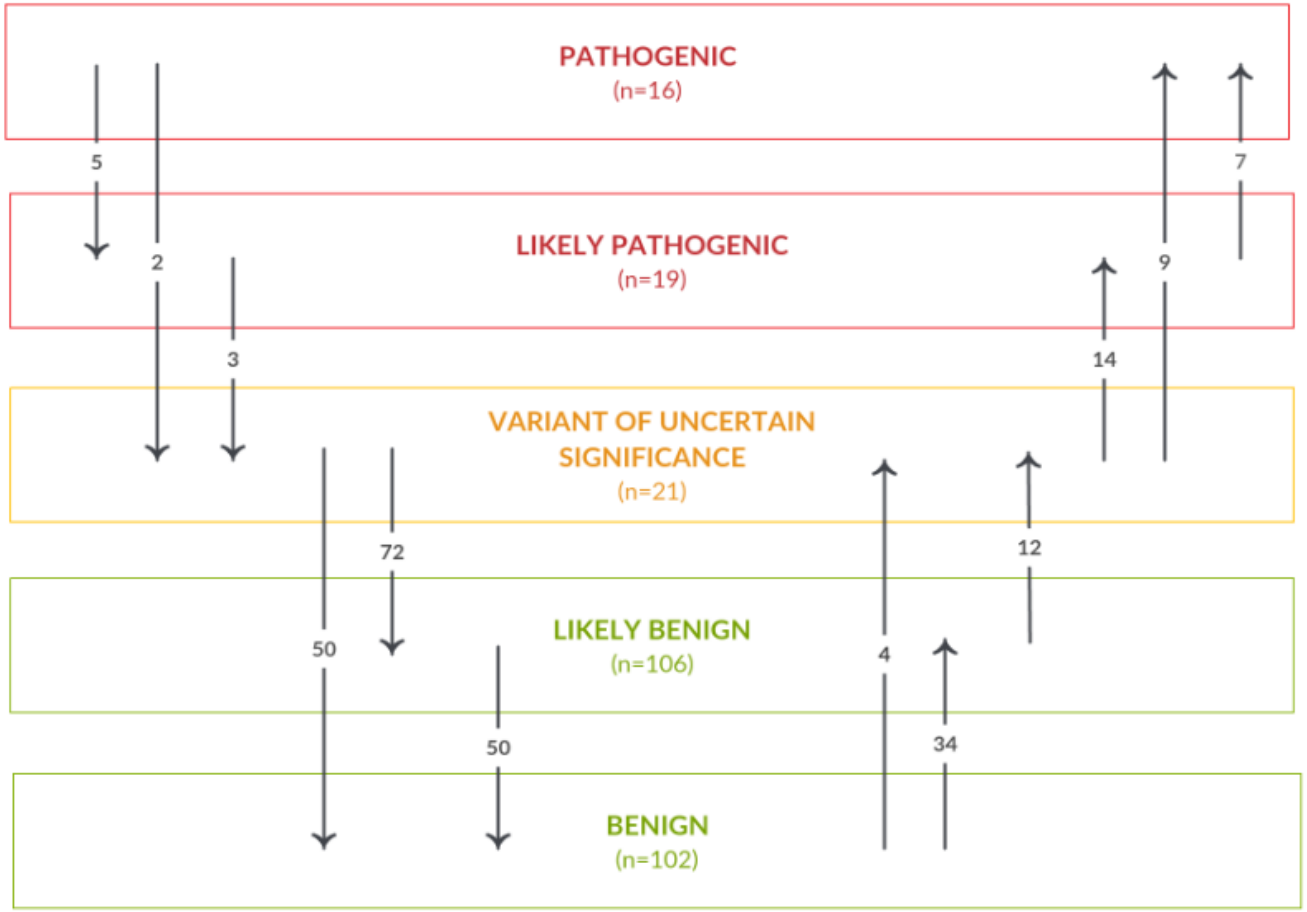
2-tier

- Decrease of from 5% to 1%

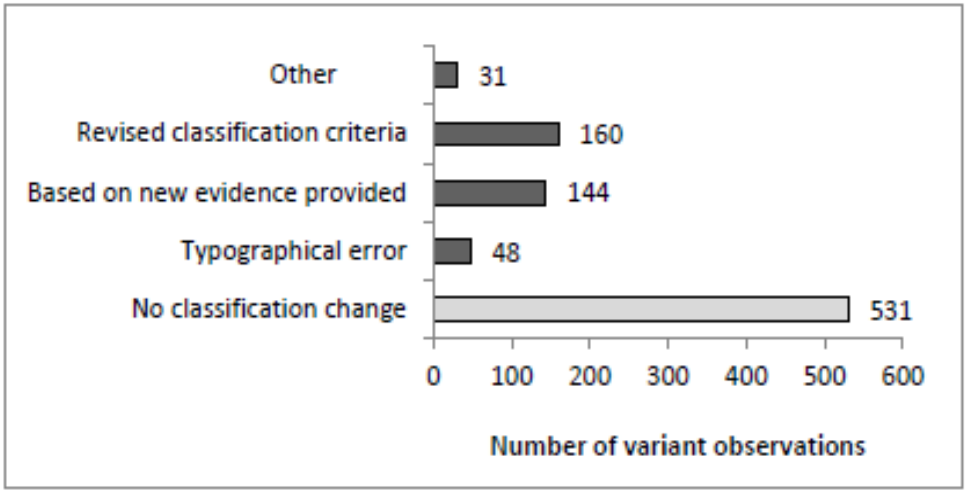
Classification Changes

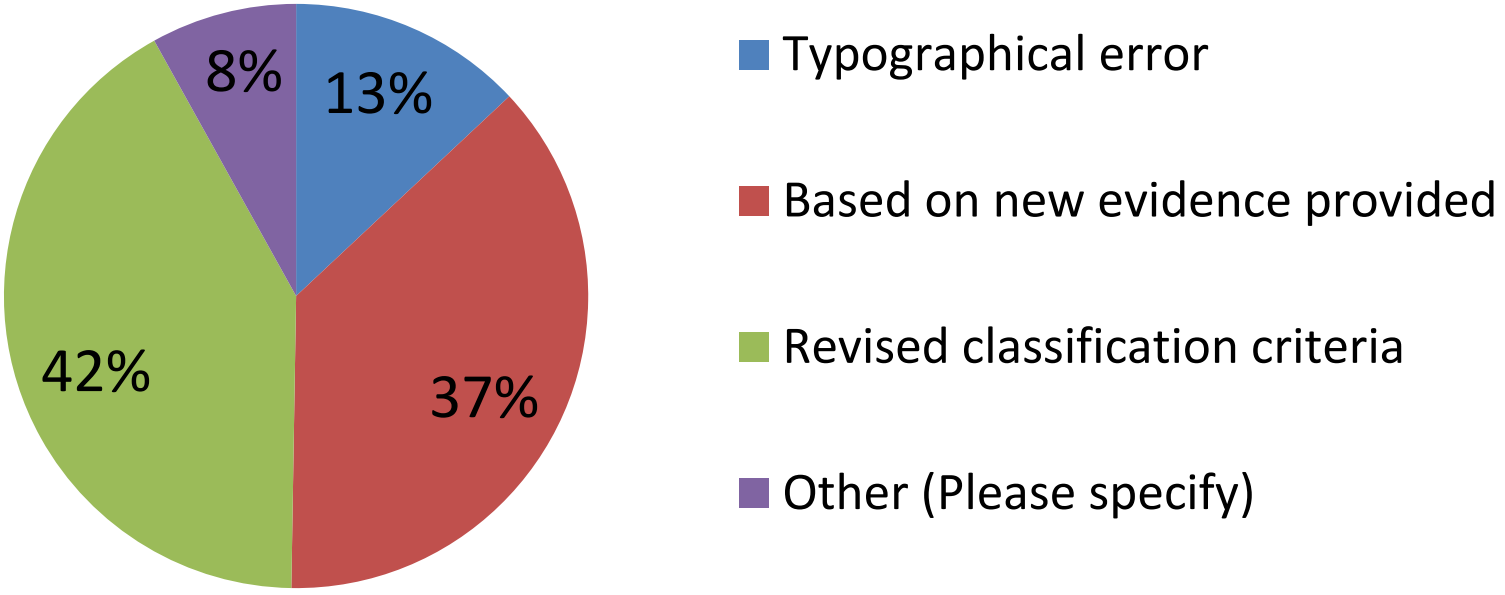


Direction of Classification Changes

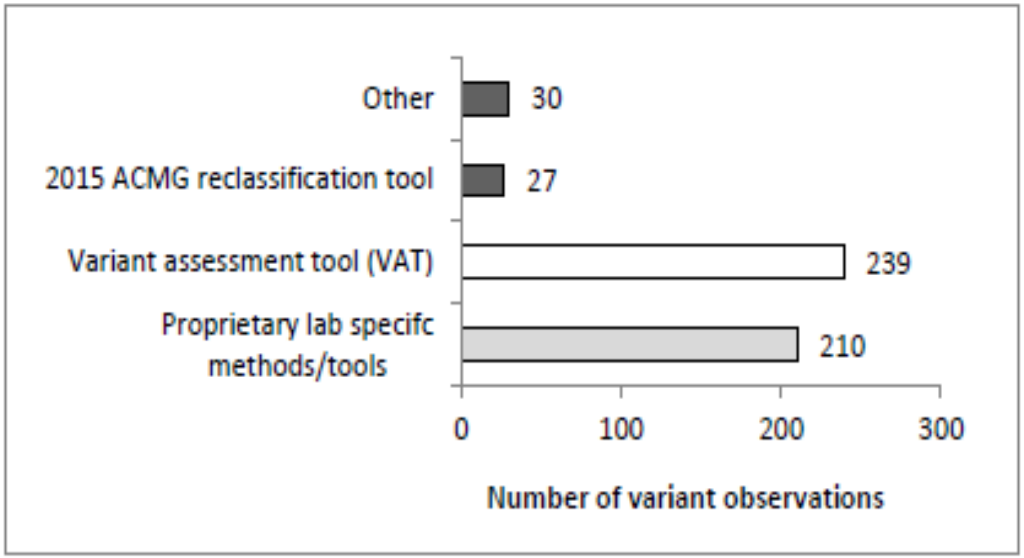


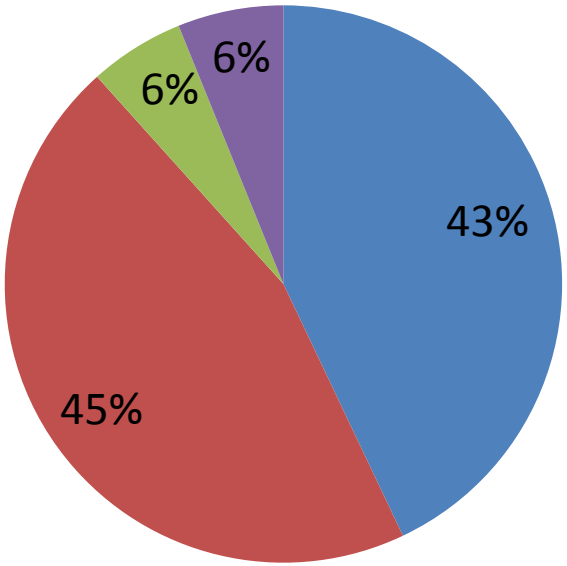
Reason for Reclassification





Methods for Reassessment





- We used our own methodology or tools to reassess
- We used the COGR variant assessment tool (VAT)
- We used the ACMG reclassification tool provided

Take Home

- A Canadian inter-institutional quality improvement program
- Importance of periodic review, tracking and maintaining versioned variant information including for variant classification
- mandatory data submission - proficiency testing, laboratory accreditation
- Real-time reporting of variant data - quality assessment program
- We encourage individual institutions to share their data holdings – generate, maintain and preserve knowledge

Collaborating Organizations

COGR
Canadian Open
Genetics Repository

GenomeCanada

CanSHARE

OntarioGenomicsInstitute

Beacon Network

ClinGen
Clinical Genome Resource

DNASTACK

BRCA
EXCHANGE

THE
HUMAN VARIOME
PROJECT

VARIANTWIRE

Global Alliance
for Genomics & Health