

# Data sharing in Canada through the COGR:

a unified clinical genome database as a community resource for standardizing and sharing genetic interpretations



**COGR**  
Canadian Open  
Genetics Repository

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the Canadian Open Genetics Repository Working Group*



Ontario **Genomics** Institute



BRIGHAM  
AND  
WOMEN'S  
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HARVARD  
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PERSONALIZED MEDICINE



**Genome**Canada

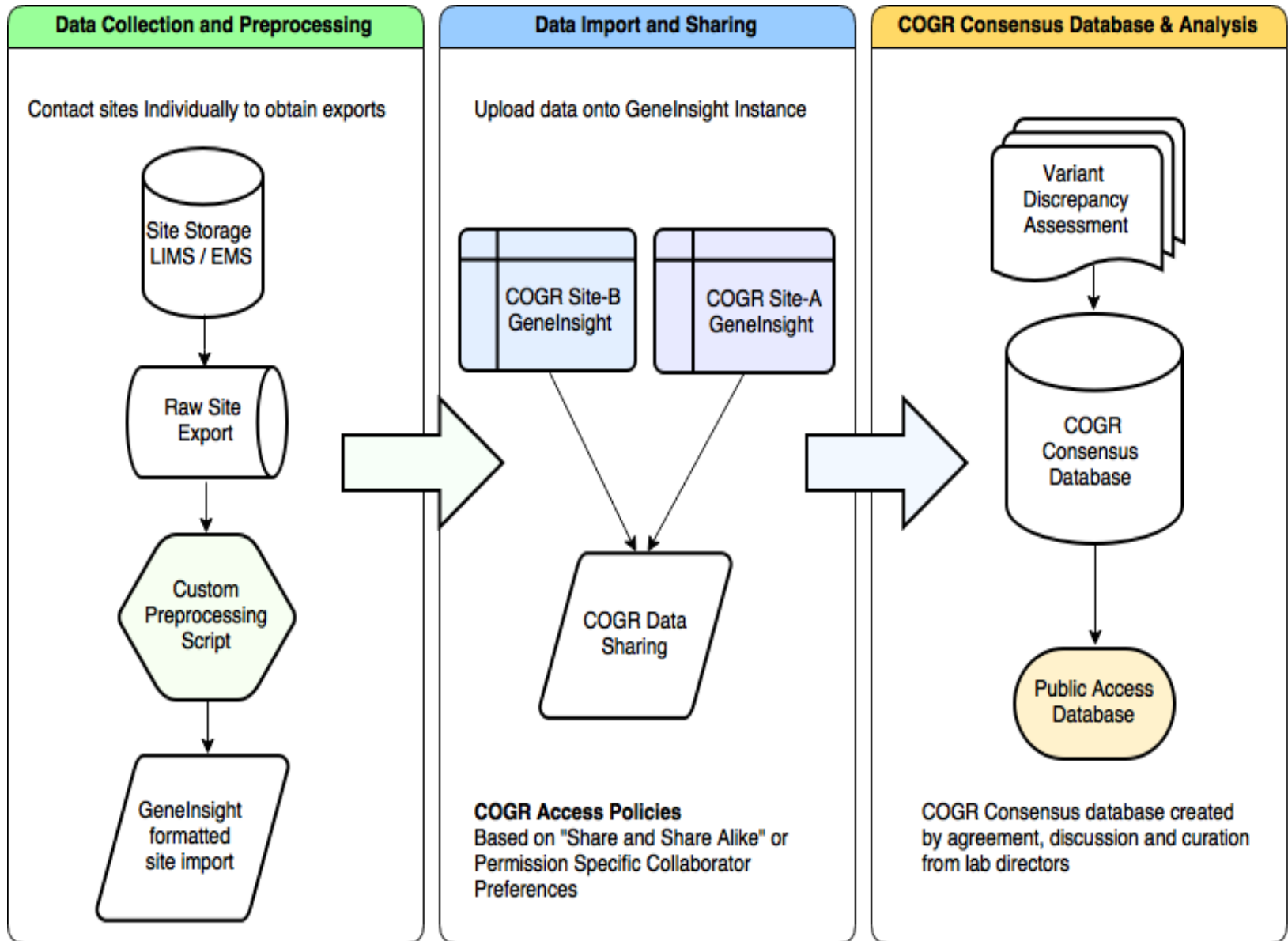
# Overview

- Grant funded by Genome Canada
- Collaborative effort for the collection, sharing and analysis of variants reported by medical diagnostic laboratories across Canada
- Collaborate with other global initiatives including ClinVar, BRCA Challenge, Human Variome Project

# Objectives

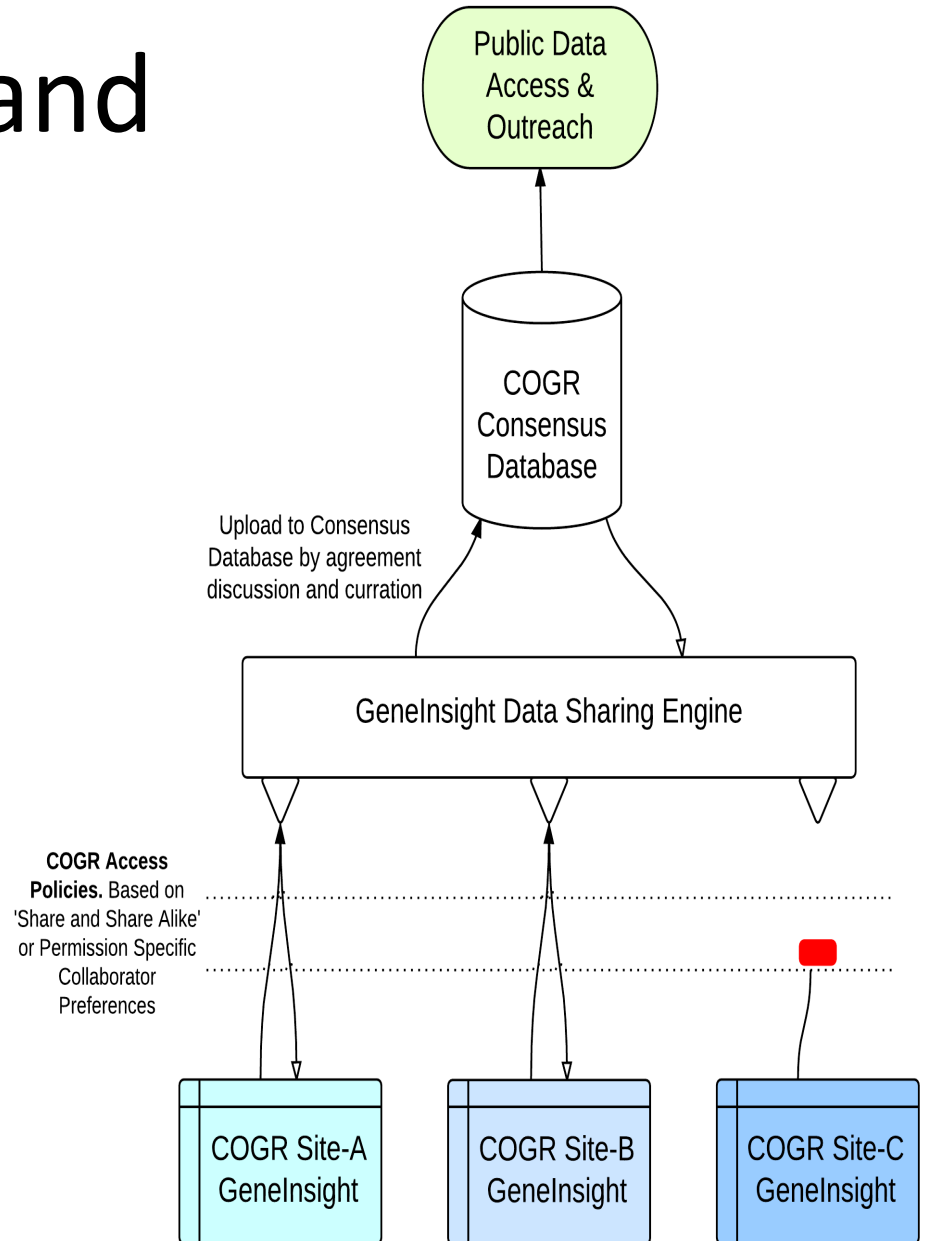
- To create Canada's unified, open-access, clinical-grade genetic database using a commonly shared platform
- **Standardize** variant assessment procedures
- **Data extraction** and variant classification **consensus** building
- **Data Access** and **Disseminate** results to a large public repository

# Workflow Overview



# COGR storage and sharing

- The COGR Consensus Database holds variants with consensus classifications across labs
- Sharing is optional at the discretion of the lab and only enabled upon request



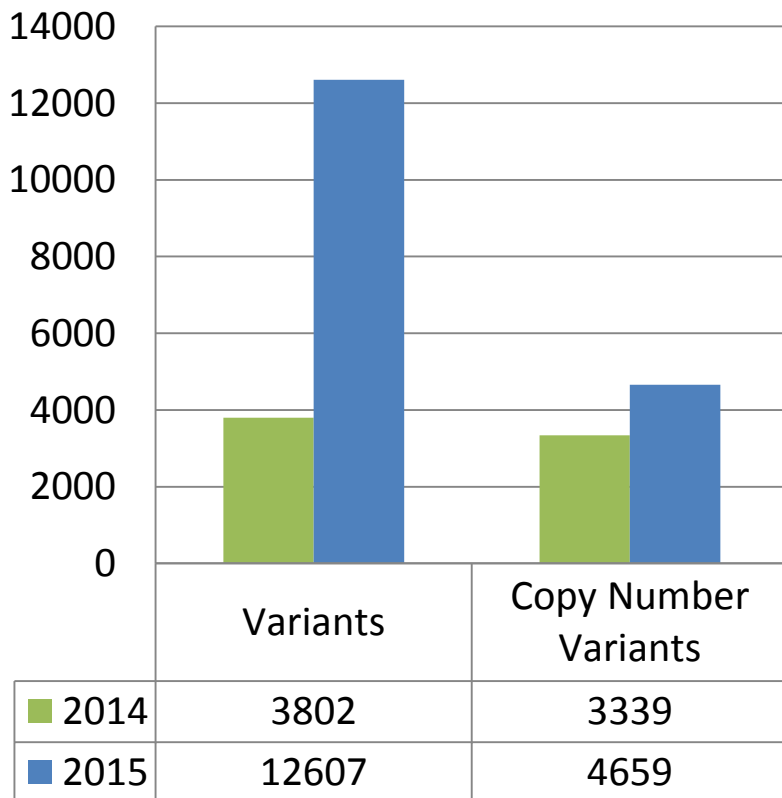
## 23 GeneInsight Instances Created

| Organization  | Upload Status | Sharing Status |
|---|---------------|----------------|
| Alberta Children's Hospital, Calgary AB                             | Uploaded      | Sharing        |
| Atlantic Cancer Research Institute, Moncton NB                      | Pending       | -              |
| British Columbia Cancer Agency, Vancouver BC                        | Uploaded      | Sharing        |
| Children's & Women's Health Centre of BC, Vancouver BC              | Uploading     | -              |
| Children's Hospital of Eastern Ontario, Ottawa ON                   | Uploaded      | Sharing*       |
| Credit Valley Hospital, Trillium Health Centre, Mississauga ON      | Uploaded      | Sharing        |
| Dept of Medical Genetics, University of Alberta, Edmonton AB        | Uploading     | -              |
| Hamilton Health Sciences, McMaster University, Hamilton ON          | Uploaded      | -              |
| Impact Genetics Inc., Bowmanville ON                                | Pending       | -              |
| Izaak Walton Killam Health Centre, Dalhousie University, Halifax NS | Uploading     | -              |
| Jewish General Hospital, Montréal QC                                | Uploading     | -              |
| Kingston General Hospital, Queen's University, Kingston ON          | Uploaded      | Sharing        |
| McGill University Health Complex, Montréal QC                       | Uploaded      | -              |
| Memorial Health University Medical Center, St. John's NL            | Pending       | -              |
| Mount Sinai Hospital, University of Toronto, Toronto ON             | Uploaded      | Sharing*       |
| North York General Hospital, Toronto ON                             | Uploaded      | Sharing        |
| Ontario Institute of Cancer Research (OICR), Toronto ON             | Uploaded      | Sharing        |
| Regional Health Authority, University of Manitoba, Winnipeg MB      | Uploading     | Sharing        |
| Sainte-Justine Hospital, University of Montreal, Montréal QC        | Uploading     | -              |
| SickKids Hospital and McLaughlin Centre, Toronto ON                 | Uploaded      | Sharing        |
| University Hospital, Western University, London ON                  | Pending       | -              |
| Women's College Hospital, University of Toronto, Toronto ON         | Uploaded      | Sharing*       |

**\*Also sharing with VariantWire**

# COGR Variant Numbers

## COGR Comparison 2014/2015

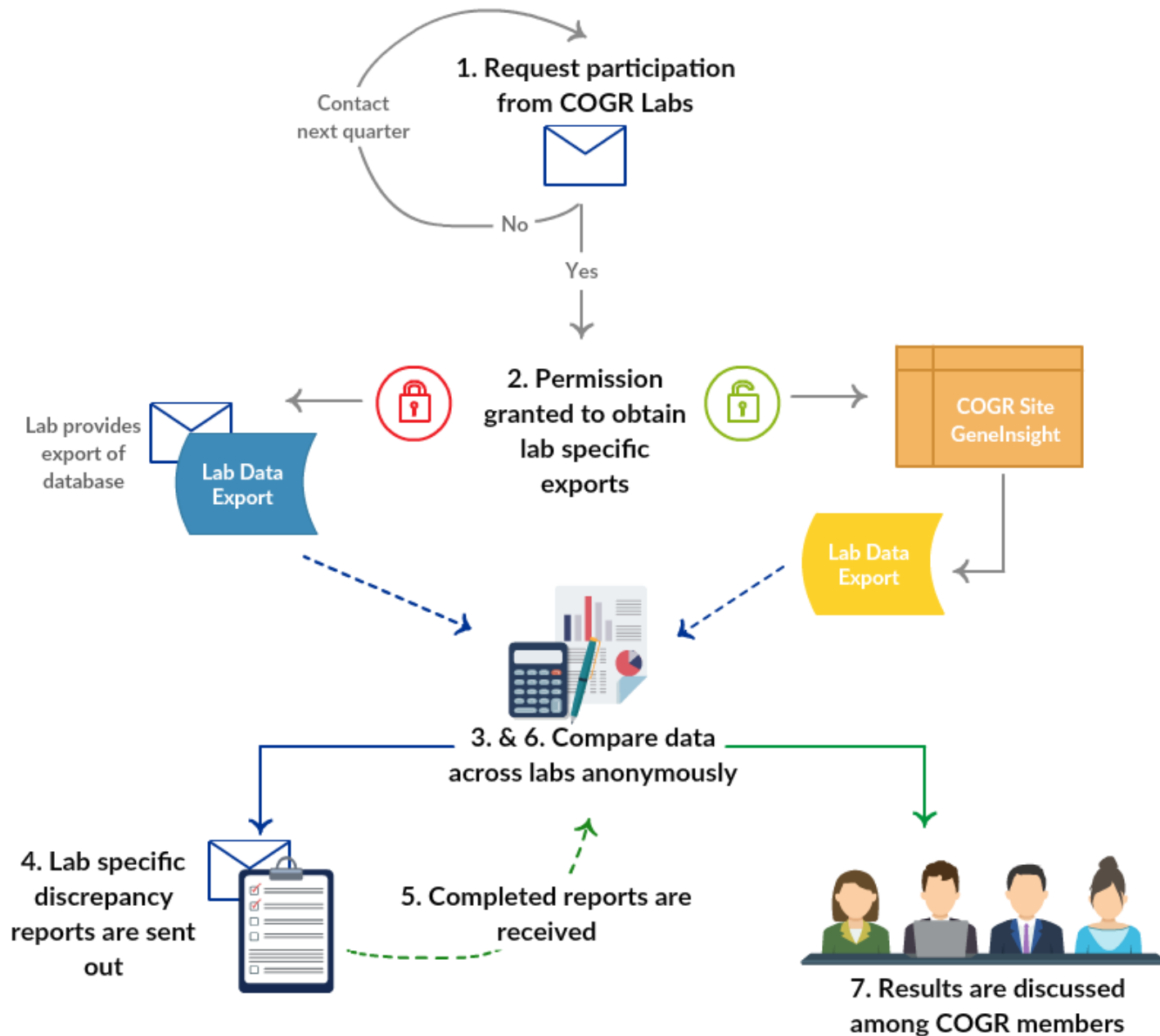


- >17,000 variants
- 1,266 genes
- 66 diseases

# The COGR Recent Initiative

- 2016 marks the COGR's 4<sup>th</sup> year
  - Focus to make data holdings both extremely accurate and readily accessible
- Focus on creating and dispersing lab specific discrepancy reports
  - Build consensus clinical interpretations on variants identified in Canadian diagnostic laboratories and academic medical centers
  - Initial project looked at *BRCA1/2*





# 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)**

# Discrepancy Report Results Overview

1. Overall discrepancy report results
  2. Total changes in classifications and reasoning
  3. Changes in discrepant variant classifications
  4. Methods for reassessment
- **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)

# Submission Data - Before Issuing Discrepancy Reports

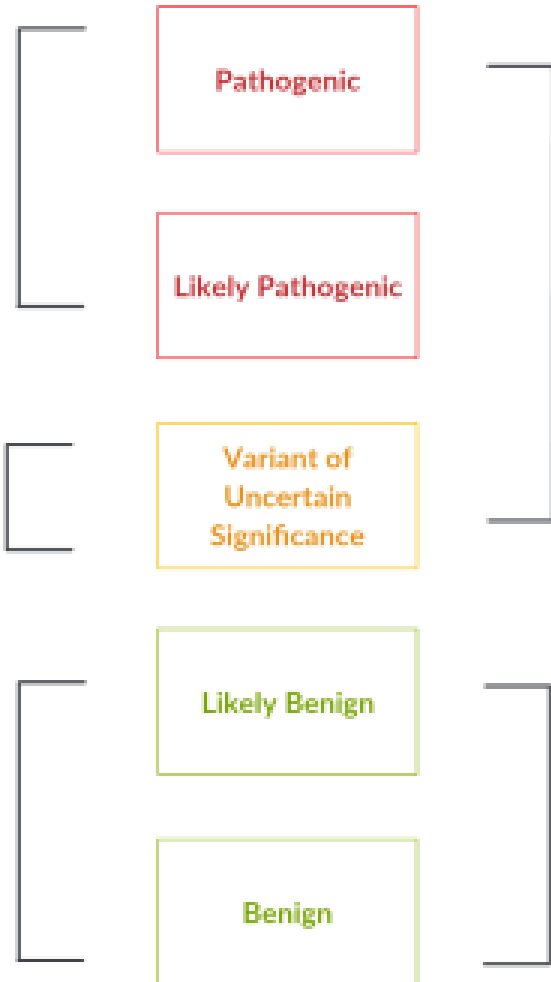
After data submission 1,148 unique variants were identified in more than one lab

- 550 (48%) of variants had concordant classifications
- 350 (30%) were discordant
- 248 (22%) were unclassified by all labs

\*According to 5-tier classification system

# Tiered Discrepancy Systems

5-Tier Discrepancy System



5-tiered

- Initially implemented

3-tiered

- Recommended by participants

2-tiered

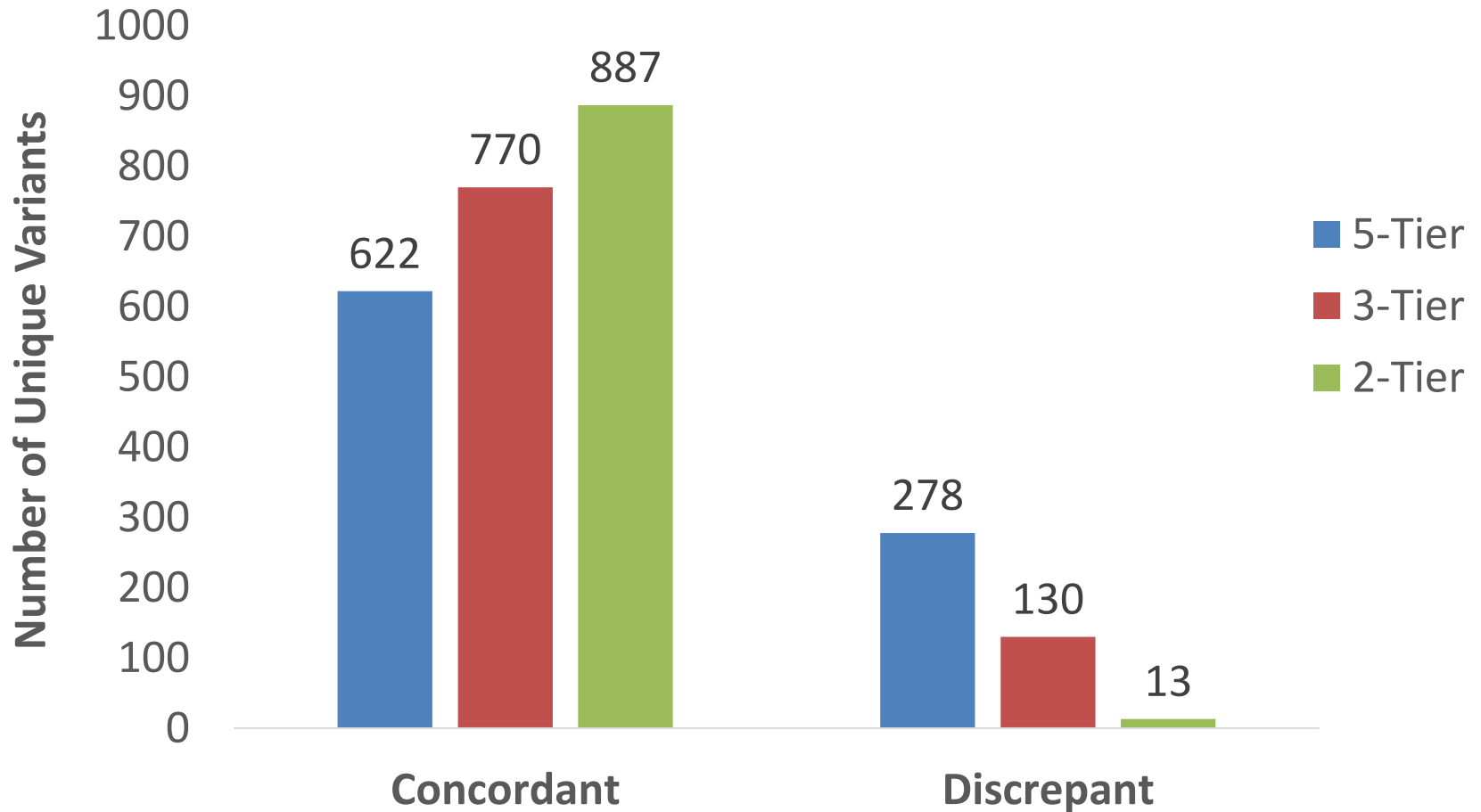
- Clinical management

# After Review of Discrepancy Report Results

- 42% of discordant variants changed classifications
- 28% did not change classifications
- 30% were not reassessed

| <i>Initial Interpretations</i> |                   |          | <i>Final Interpretations</i> |          |                       |
|--------------------------------|-------------------|----------|------------------------------|----------|-----------------------|
|                                | <b># Variants</b> | <b>%</b> | <b># Variants</b>            | <b>%</b> | <b>Overall Change</b> |
| <b>Benign</b>                  | 526               | 37%      | 637                          | 45%      | 111 (8%)              |
| <b>Likely Benign</b>           | 271               | 19%      | 321                          | 23%      | 50 (4%)               |
| <b>VUS</b>                     | 342               | 24%      | 211                          | 15%      | 127 (9%)              |
| <b>Likely Pathogenic</b>       | 60                | 4%       | 64                           | 5%       | 4 (>1%)               |
| <b>Pathogenic</b>              | 136               | 10%      | 170                          | 12%      | 34 (2%)               |
| <b>Unclassified</b>            | 75                | 5%       | 9                            | 1%       | 72 (5%)               |
| <b>Total</b>                   | 1410              |          | 1410                         |          | 398 (28%)             |

# Final Discrepancy Results



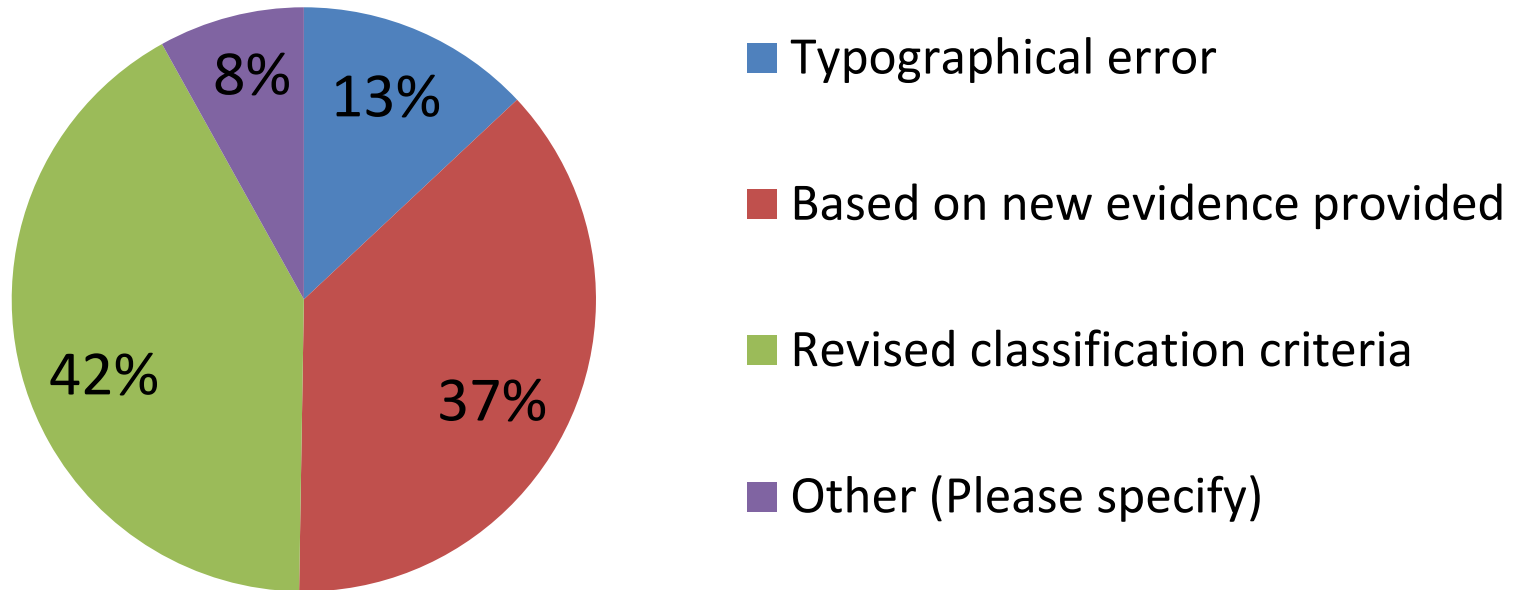
# After Review of Discrepancy Report Results

- Only 18% of the discrepant variants reached a consensus for 5-tier system
  - But most labs did not review minor discrepancies
    - Benign vs Likely Benign
    - Pathogenic vs Likely Pathogenic
- In total, for 5-tier system:
  - 69% (622/900) of all unique & classified variants were concordant
- In total, for 3-tier system (LB/B, VUS, LP/P)
  - 86% (770/900) of all unique & classified variants were concordant



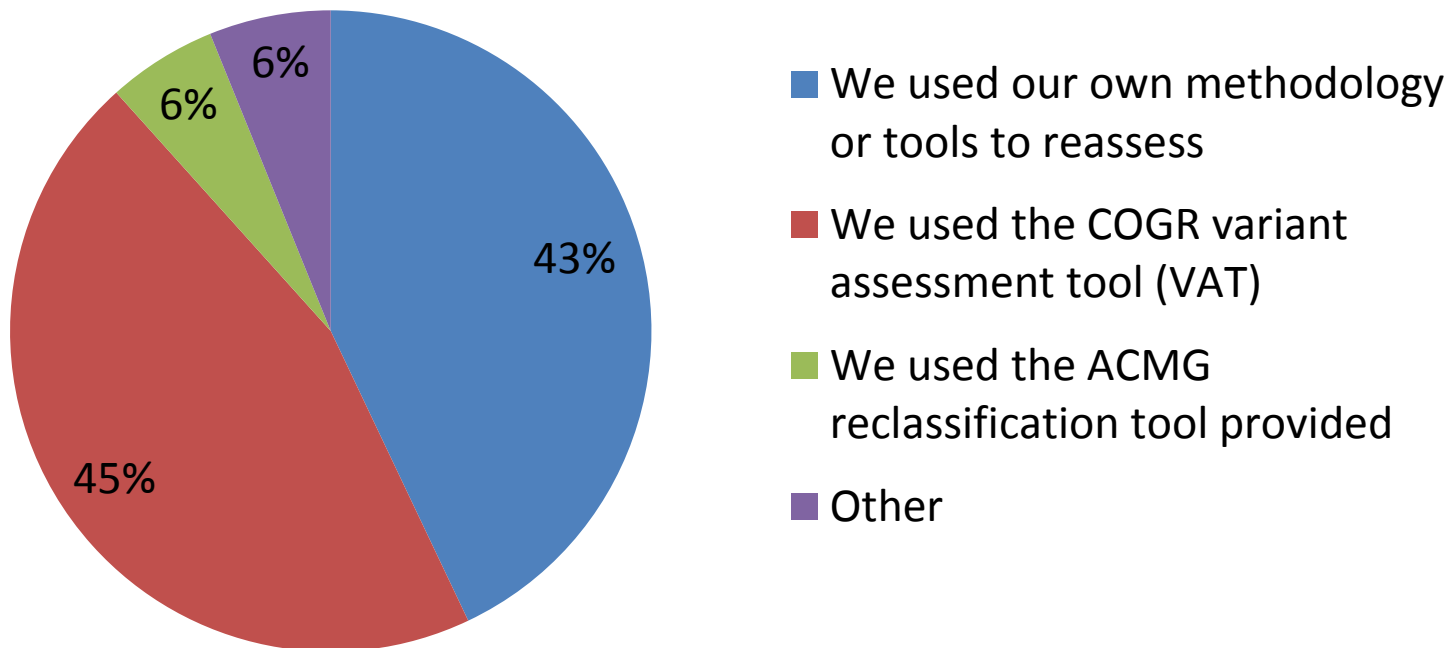
# Reasoning For Reclassification

- 9 out of 11 labs specified reasoning for some variants
- 64% of reassessed variants provided reclassification reasoning:



# Methods Used for Reassessment

- Most labs did not review variants through the COGR network
- 8 out of 11 labs specified their reassessment methods
- 34% of variants had specified reassessment methods:



# Summary

- Successful exercise with positive feedback within the COGR community
- Limited resources provide challenges for labs to do this without guidance and help
- Continuing initiatives:
  - Release quarterly discrepancy reports
  - Provide consensus variant interpretations through public database
  - Further collaboration with other international data-sharing efforts including ClinVar, the HVP and the GA4GH

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