

Background

- Variant classification methods in cardiomyopathy have improved and the validity of gene-disease relationships have been assessed.
- These updates in curation methods have prompted the need for contemporary data on the cardiomyopathy genetic landscape.

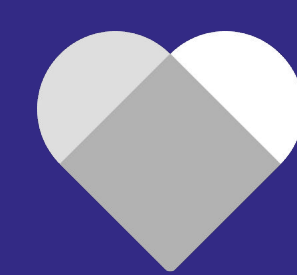
Aim

To describe genetic testing results in a nationwide cohort of affected and unaffected patients with cardiomyopathy-causing genotypes.

Methods



Retrospective chart review of affected and unaffected patients referred to a nationwide telehealth genetic counseling practice between 2019 and 2025.



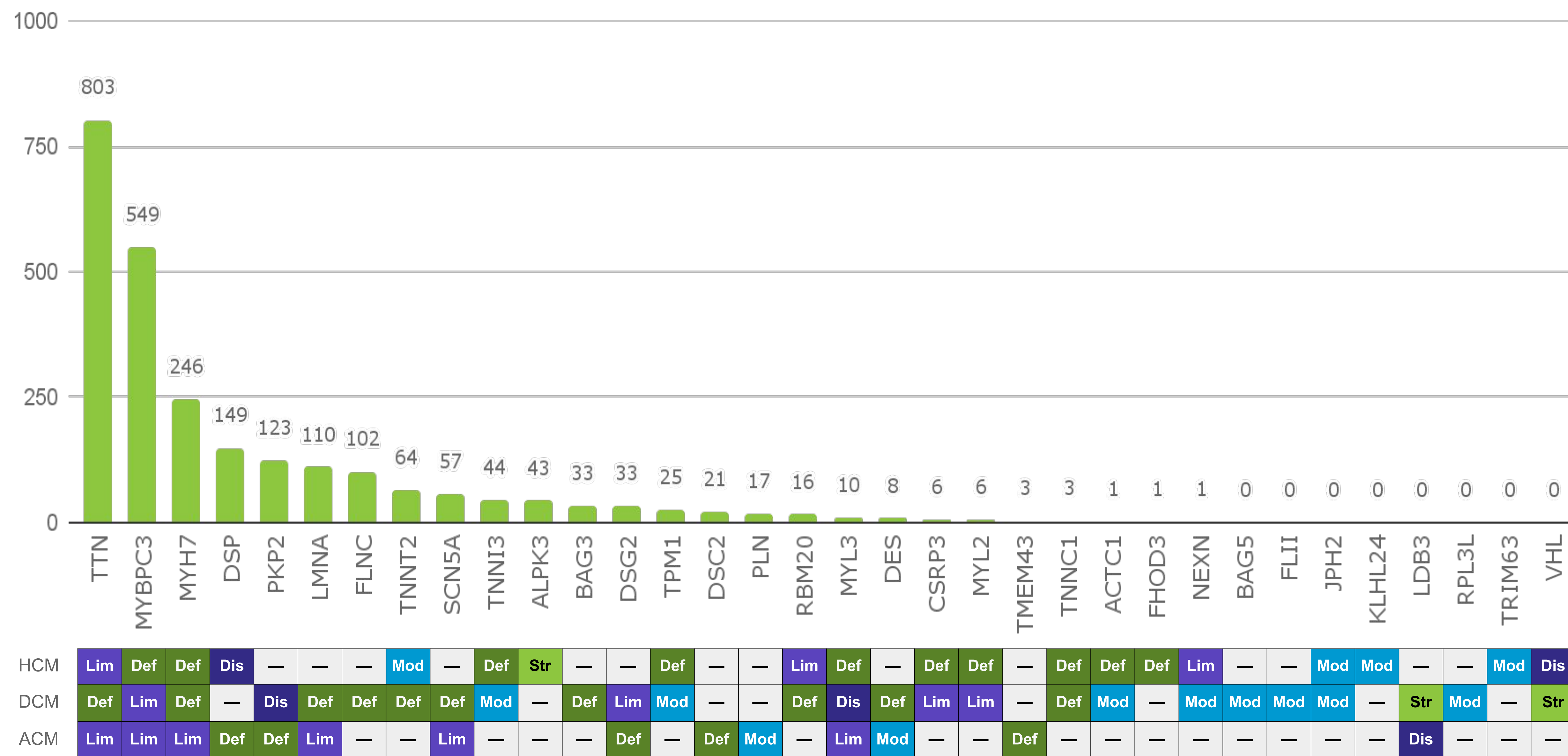
Inclusion Criteria: Disease-causing genotype in 34 cardiomyopathy genes curated by ClinGen with moderate, strong, or definitive evidence for hypertrophic (HCM), dilated (DCM), arrhythmogenic cardiomyopathy (ACM).



Exclusion Criteria: Genotype associated with a phenotype other than non-syndromic cardiomyopathy.

Genetic testing outcomes in a real-world nationwide cohort of 2478 patients with disease-causing genotypes in ClinGen-curated cardiomyopathy genes.

Disease-causing variants observed in cardiomyopathy genes



ClinGen gene-disease validity curations

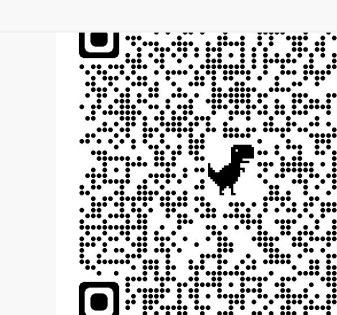
Legend: **Def** Definitive **Str** Strong **Mod** Moderate **Lim** Limited **Dis** Disputed **-** Not curated

Patient Characteristics and Genetic Testing Results of a Contemporary Nationwide Cohort of 2478 Patients with Disease-Causing Genotypes in ClinGen-Curated Cardiomyopathy Genes

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Presenting author & lead investigate disclosures: Colleen Caeshu is an employee of Genome Medical

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Results

N	Median Age	Sex
2478 patients	50y (IQR 26y)	52.1% Female (1291/2477)

Patients from **all 50** US states, most frequently:



- Georgia (25.3%)
- California (20.9%)
- Florida (19.8%)
- Texas (18.3%)
- Tennessee (15.6%)

Patients with ACM genotypes were younger at genetic testing than those with HCM or DCM genotypes

p < 0.005

0.9% (23/2478) of patients had two variants:

- 17.4% (4/23) in same gene
- 82.6% (19/23) in different genes
 - ↳ 57.9% (11/19) associated with two different phenotypes:
 - 54.5% (6/11) HCM/DCM
 - 36.4% (4/11) HCM/ACM
 - 9.1% (1/11) DCM/ACM

Four genes not in the cohort are not on genetic testing panels:

BAG5, FLII, KLHL24, RPL3L

Conclusions

- Rate of multiple variants is lower than prior reports; may be due to inclusion of unaffected patients, or improvements in variant classification.
- Clinical panels need to be updated to include newly identified genes.