Phenotypic Distribution and Clinical Burden of Pediatric Hypertrophic Cardiomyopathy: Insights From a Longitudinal US Claims Database

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BACKGROUND

- Pediatric hypertrophic cardiomyopathy (HCM) is rare and clinically heterogeneous.
- Contemporary real-world epidemiology data are severely limited but increasingly important as targeted therapies and clinical trials in pediatric HCM emerge.

OBJECTIVE

- Characterize the real-world epidemiology of pediatric HCM in the United States.

METHODS

Study Design

- Retrospective cohort study using patient-level administrative claims to identify pediatric patients with HCM in the United States from 2016 through 2024 (index date = first HCM diagnosis).

Database

- Symphony Health's Integrated Dataverse (IDV) includes longitudinal US claims data (Jan 2016–Mar 2024) spanning prescription, medical, and hospital records across all payer types.
- The database captures >10 billion deidentified prescription claims from >280 million patients (average ~5 years of history), linked to medical and hospital data for ~180 million patients.
  - It draws from 65,000 pharmacies, 1500 hospitals, 800 outpatient facilities, and 80,000 physician practices, covering ~75% of US prescriptions.
  - Patient distribution mirrors US census regions, though IDV represents a convenience sample.

Inclusion Criteria

- Evidence of HCM: Patients with HCM met the following selection criteria:
  - ≥2 medical claims with a diagnosis code for HCM (ICD-10: I42.1 or I42.2) in any position at least 30 days apart.
- Age between 1 to 17 years at index diagnosis date.
- Continuous enrollment with medical and pharmacy benefits for 12 months prior to and at least 12 months after (and including) the index date.
- oHCM was defined as ≥2 I42.1 diagnoses, evidence of septal reduction therapy (SRT), or a higher frequency of I42.1 vs I42.2 codes; confirmed nHCM was defined as ≥2 I42.2 diagnoses without SRT or a higher frequency of I42.2 vs I42.1 codes.

Exclusion Criteria

- Patients with evidence of Pompe disease, Danon disease (LAMP2 deficiency), Noonan syndrome, mitochondrial myopathy/disease, amyloidosis, or Fabry disease during the study period were excluded.

Study Outcomes

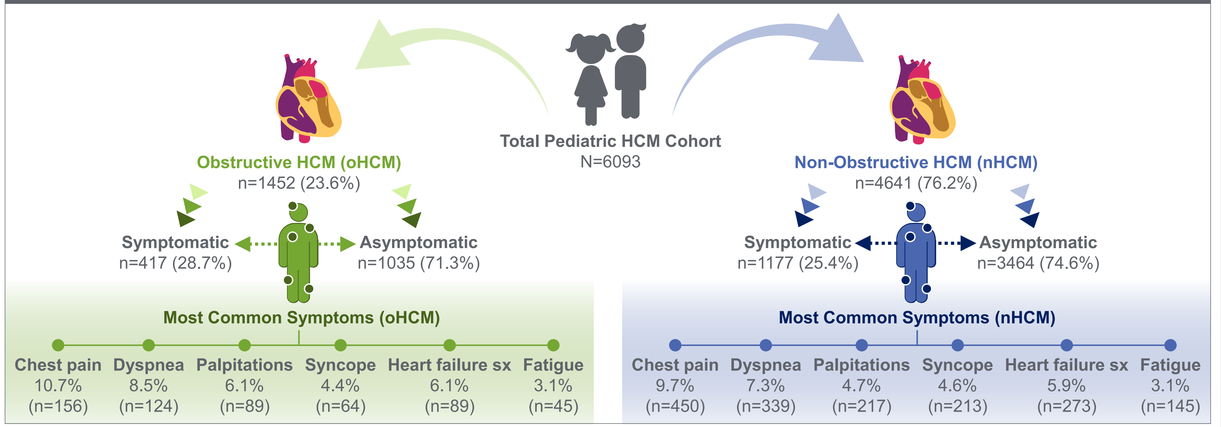
- **Disease phenotype:** We describe disease phenotype at presentation and symptomatology within ±3 months of the index encounter.
- **Baseline characteristics:** Age at index diagnosis (mean, median, and distribution), age group, sex, geographic region, insurance type, and length of follow-up.
- **Symptoms:** fatigue, chest pain, syncope, dyspnea, heart failure, and palpitations.
- **Comorbidities:** Hypertension, depression, obesity, and pulmonary circulation disorders.

RESULTS

Patient Population

- Among 6093 children and adolescents with HCM:
  - 1452 (24%) had obstructive HCM (oHCM).
  - 4641 (76%) had non-obstructive HCM (nHCM).
- Most patients were asymptomatic, though symptoms were slightly more frequent in oHCM vs nHCM (28.7% vs 25.4%; *P*=0.01).
- Most common symptoms in both groups, oHCM vs nHCM (**Figure**):
  - Chest pain (10.7% vs 9.7%).
  - Dyspnea (8.5% vs 7.3%).
  - Heart failure symptoms (6.1% vs 5.9%).
  - Palpitations (6.1% vs 4.7%).
  - Syncope (4.4% vs 4.6%).

Figure: Study design – pediatric hypertrophic cardiomyopathy cohort



HCM, hypertrophic cardiomyopathy; sx, symptoms

- Age at index diagnosis was slightly higher in oHCM vs nHCM (mean 11.0 ± 5.1 vs 10.5 ± 5.3 years; *P*=0.001), although median age was similar (12 years).
- Most patients were male (oHCM 66.9% vs nHCM 64.3%), with no meaningful sex difference between obstructive and non-obstructive disease (*P*=0.07).

Comorbidities

- Individual extracardiac conditions were uncommon among oHCM and nHCM groups, respectively:
  - Hypertension (4.5% vs 6.1%).
  - Chronic pulmonary disease (7.0% vs 7.5%).
  - Obesity (6.3% vs 5.4%).
  - Depression (2.1% vs 3.6%).

Limitations

- Real-world data in this study utilized ICD-10 coding for disease identification, study outcomes, and may be subject to inconsistencies without patient-level genetic and anatomical confirmation.
- Due to the descriptive nature of this study, these results only include unadjusted analyses.

CONCLUSIONS

- In this large, real-world US cohort, ~1 in 4 children with HCM had obstructive disease, and roughly 1 in 4 was symptomatic.
- These findings define the size and characteristics of the pediatric oHCM population most likely to be targeted by emerging disease-modifying therapies, and highlight a large, predominantly asymptomatic group in whom earlier intervention strategies may ultimately be evaluated.

Acknowledgments

This study was funded by Cytokinetics, Incorporated. Editorial support for this presentation was provided by David Sunter, PhD, on behalf of Engage Scientific Solutions and was funded by Cytokinetics, Incorporated.

Disclosures

JC, AD: No potential conflicts of interest with respect to the research, authorship, and/or publication. **EP, XL:** Employees of Putnam, who were consultants for Cytokinetics, Incorporated for this study. **MB, JG, SS:** Employees of and own stock in Cytokinetics, Incorporated.

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Presented at the 2026 European Society of Cardiology (ESC) Heart Failure Congress | Barcelona, Spain | May 9–12, 2026