EPH59

An Evidence Gap Analysis of the Epidemiology and Burden of Obstructive Hypertrophic Cardiomyopathy

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BACKGROUND

- Hypertrophic cardiomyopathy (HCM), which has an obstructive (oHCM) and nonobstructive (nHCM) subtype, is a chronic, progressive myocardial disorder defined by left ventricular (LV) that is not solely explained by abnormal loading conditions.[1]
- oHCM is characterized by dynamic LV outflow tract obstruction resulting from ventricular hypertrophy and mitral valve systolic anterior motion and by elevated LV filling pressures.[2]
- Due to the array of symptoms and complications associated with oHCM, the disease has a substantial clinical, economic, and humanistic burden. There is a need to identify available evidence and understand key evidence gaps to inform future research.

Objective

- To assess evidence gaps related to the epidemiology, burden, and treatment of oHCM in Europe, North America, and Japan.

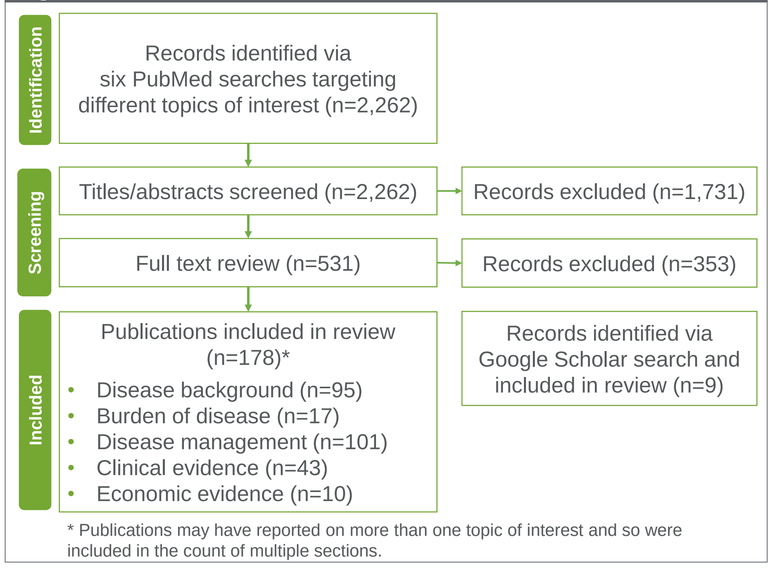
METHODS

- A targeted literature review was conducted using PubMed to identify HCM/oHCM studies published between 2012 and 2022.
- Outcomes of interest included epidemiology, natural history, pathophysiology, management, and clinical (e.g., clinical trials, observational studies), economic (e.g., healthcare resource use, cost), and humanistic burden.
- Original research articles, review articles, and congress abstracts focusing on adult patients in France, Germany, Italy, Spain, United Kingdom (UK), United States (US), Canada, and Japan were included.
  - Studies were excluded if they included non-adult patients and/or healthy volunteers; were animal or in vitro studies; assessed another disease area; focused on treatments or outcomes not related to HCM; were study protocols, case reports, or grey literature; or were not available in English.
- Identified studies were reviewed in full to qualitatively identify evidence gaps.

RESULTS

- The PubMed search identified 2,262 unique articles, of which 178 unique articles were included in the review (**Figure 1**).
- Most studies evaluated HCM broadly, with limited information specifically for oHCM.
- Therefore, a supplementary Google Scholar search was used to identify additional oHCM articles (n=9).
- Disease natural history, pathophysiology, and management were reviewed at the global level by multiple studies; however, significant evidence gaps were noted for disease epidemiology, burden, and treatment (**Figure 2**).

Figure 1. Article Inclusion Criteria

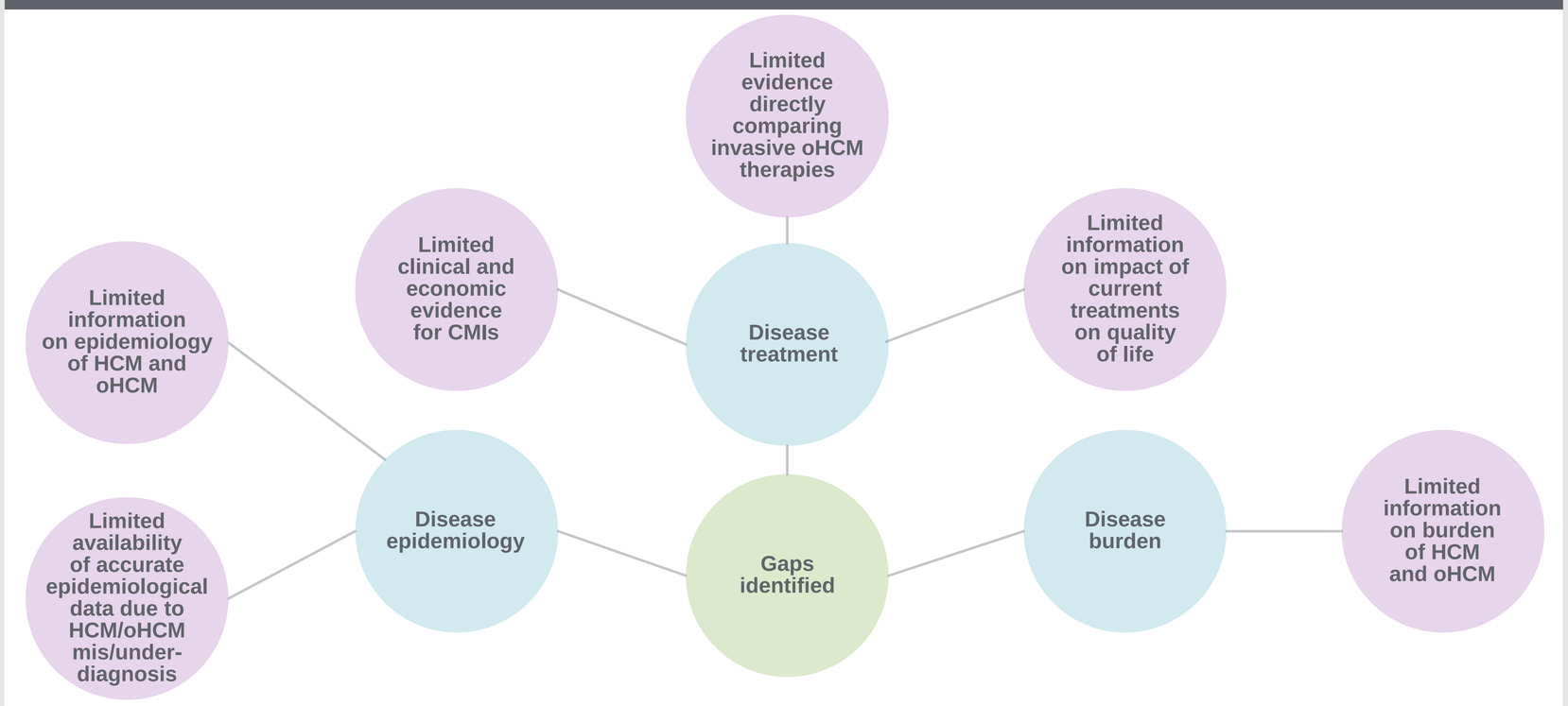


* Publications may have reported on more than one topic of interest and so were included in the count of multiple sections.

Disease Epidemiology

- The global prevalence of HCM was reported by various clinical reviews and guidelines.[2-6]
  - Global HCM prevalence estimates were consistently reported to be 1:200 (when considering familial transmission, subclinical cases, and pathogenic sarcomere mutations) to 1:500 (based on disease phenotype characterized using echocardiography).[2-6]
- Included studies reported HCM prevalence estimates in the US,[7] Germany,[8] and the UK [8] (**Figure 3**); however, **estimates of HCM prevalence were not found for France, Italy, Spain, Canada, and Japan**.
  - Studies have shown that HCM prevalence is increasing in the US, UK, and Germany.[7,8]
- In contrast to HCM, global epidemiological data for oHCM were not found.
  - **No studies were identified reporting oHCM prevalence or incidence in France, Italy, Spain, or Canada.**

Figure 2. Identified Evidence Gaps in oHCM



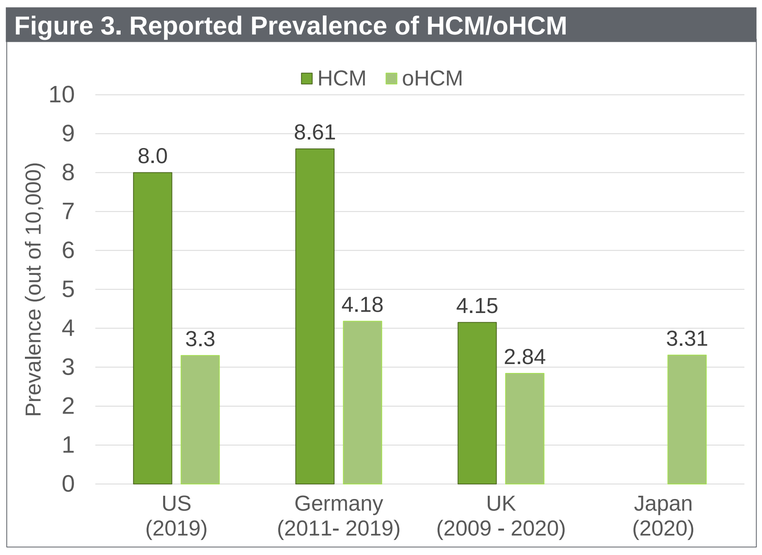
Topic	Global*	US	Canada	UK	France	Germany	Italy	Spain	Japan
oHCM epidemiology		■		■		■			■
oHCM burden		■							■

*If not otherwise specified, information obtained from review articles was assumed to represent global data.

No data | Data available

- Single studies of oHCM prevalence were found for the US (medical claims data),[7] Germany and the UK (retrospective study of patient data),[8] and Japan (retrospective study of hospital data)[9] (**Figure 3**).
- **A single study was identified that reported oHCM incidence**. Based on medical claims data, the incidence of clinically diagnosed oHCM in the US was 0.015% (1.5 in 10,000) in 2019.[7]

Figure 3. Reported Prevalence of HCM/oHCM



Note: The prevalence estimates presented are out of 10,000.

Disease Burden

- Several studies were identified describing the global clinical burden of HCM as well a single study for Italy.[10] However, **there was a lack of data specific to other countries of interest and limited information was identified for the global and country specific economic and humanistic burden of HCM**.
- An Italian single-center retrospective cohort study found that between 2010 and 2015 there were 187 hospitalizations in 92 patients with HCM, with approximately one in three hospitalizations (84.5%) being cardiovascular related.[10]
  - The hospitalizations were often unplanned and the result of acute disease-related complications.[10]
- Limited information was identified on the clinical, economic, and humanistic burden of oHCM**.** Although multiple US studies and one Japanese study were identified,[9] **there was a lack of burden studies for France, Germany, Italy, Spain, UK, and Canada**.

Based on the identified data for the US and Japan:

- **oHCM has a substantial humanistic and clinical burden due to an array of symptoms and complications**.
  - oHCM is associated with atrial fibrillation, ventricular or supraventricular arrhythmias, sudden cardiac arrest, stroke, and heart failure.[9,11]
  - Patients with oHCM tend to experience a greater number and more severe symptoms than patients with nHCM.[4,12]
- **oHCM has a substantial economic burden**.
  - Pharmacy utilization and physician visits increase after an oHCM diagnosis.[13]
  - Healthcare costs increase further for oHCM patients undergoing invasive septal reduction therapies (SRT) with either surgical septal myectomy (SM) or alcohol septal ablation (ASA). The increased cost is mostly driven by inpatient hospitalizations and surgical costs.[14]

- Prevalence and burden data were identified for HCM/oHCM, **burden and epidemiological estimates may be inaccurate as the disease is frequently misdiagnosed or underrecognized in clinical practice.**[2,6,15]

Disease Treatment

- The current pharmacological therapies for symptomatic oHCM recommended by US, UK, and Japanese guidelines are β-blockers (BBs), calcium channel blockers (CCBs), and disopyramide.[1,2,4]
  - However, only a minority of patients experience complete relief from obstruction with these therapies,[16] and often invasive SRT with SM or ASA is recommended.[17]
- Although BBs, CCBs, and SRT are common interventions for oHCM, no information was identified on the impact of these therapies on patient quality of life.
  - Furthermore, no head-to-head trials were identified directly comparing SM and ASA.
- Limited clinical and economic data were identified for cardiac myosin inhibitors (CMIs) mavacamten[18] and aficamten.[19]

Limitations

- Although the review was carefully designed and conducted, it was not systematic and was restricted to the last ten years which may have incompletely captured the topics of interest.

CONCLUSIONS

- Certain evidence gaps exist for country-level epidemiology and burden data of oHCM.
- Future research should address these gaps, with a specific focus on generating real-world evidence for Canada and European countries to quantify the burden and unmet need and support the evaluation of emerging evidence in these regions.
- Further evaluations are needed to understand the clinical and economic impact CMIs will have on the disease space.

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