EE319

Building a Cost-Effectiveness Model for Hypertrophic Cardiomyopathy: A Literature Review

Babak Nazer,[1] Jasimran Jandu,[2] Romita Das,[2] Caity Patrick,[2] Laura Elliot,[2] Michael Butzner,[3] and Ahmad Masri[1]

[1]Hypertrophic Cardiomyopathy Center, Knight Cardiovascular Institute, Division of Cardiology, School of Medicine, Oregon Health and Science University, Portland, OR, USA; [2]FIECON Ltd, St Albans, UK; [3]Cytokinetics, Incorporated, Health Economics and Outcomes Research, South San Francisco, CA, USA

BACKGROUND

- There is a lack of published data and relevant studies on the clinical and economic aspects of obstructive hypertrophic cardiomyopathy (oHCM).
- A targeted literature review (TLR) was undertaken to collect data inputs and assumptions required to develop a cost-effectiveness model (CEM) for oHCM.

METHODS

- The scope of the TLR included searching databases, during the timeframe 2010–2021, for clinical and economic data relevant to clinical effectiveness, cost and resource use, and utilities to inform data inputs and assumptions required to parameterize a CEM.
- PubMed and EMBASE were searched using key terms — including HCM, quality-of-life, cost-effectiveness, cost and resource use, and mortality — and eligibility criteria were applied (**Table 1**).
- Pharmacologic therapies for oHCM were searched on Clinicaltrials.gov and clinical evidence was included from associated publications.
- To address any oHCM-specific data gaps, relevant analogs (comparable diseases) were searched.
  - These included heart failure and transthyretin amyloidosis cardiomyopathy, both of which use the New York Heart Association (NYHA) Functional Classification as a measure of disease progression.

Table 1. Eligibility Criteria for Studies

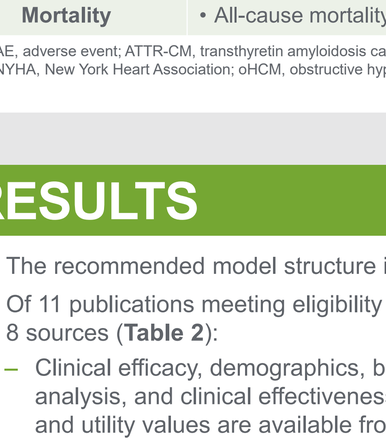
Section	Inclusion	Exclusion
Population		
Population settings	• oHCM demographics (including percent male, age, prior treatment, NYHA class)	• Demographics outside of oHCM
Economic evidence		
Quality of life	• Utility values – specific to NYHA class (within HCM or relevant analog) • Disutility values associated with CV AEs (across different disease areas)	• Utility values outside of CV diseases • Disutility values outside of CV AEs
Model structure	• HCM cost-effectiveness models • HCM cost-effectiveness models for HCM analogs (limited to HF and ATTR-CM)	• Analogs outside of HCM, HF, or ATTR-CM
Cost and resource use	• Costs specific to HCM • Costs relevant to CV AEs	• Costs and resource use outside of CV diseases
Clinical evidence		
Clinical effectiveness	• Transition probabilities or proportion of patients in each NYHA state in comparative studies, including: mavacamten, SoC (beta-blockers and calcium-channel blockers monotherapy or dual therapy), and disopyramide • RWE studies in HCM	• Comparators not of interest • Outcomes not of interest • Clinical trials outside of HCM • Clinical trials of invasive therapies, single-arm trials, or those not including SoC
Mortality	• All-cause mortality in HCM	• Mortality in indications not of interest

AE, adverse event; ATTR-CM, transthyretin amyloidosis cardiomyopathy; CV, cardiovascular; HCM, hypertrophic cardiomyopathy; HF, heart failure; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; RWE, real-world evidence, SoC, standard of care

RESULTS

- The recommended model structure is shown in **Figure 1**.
- Of 11 publications meeting eligibility criteria (**Figure 2**), the best evidence to inform a CEM was provided by 8 sources (**Table 2**):
  - Clinical efficacy, demographics, baseline characteristics of patients with oHCM, utility values for scenario analysis, and clinical effectiveness of standard-of-care therapy have been reported in clinical trials,[1-3] and utility values are available from a CEM study.[4]
  - Adverse event disutilities were derived from a study on atrial fibrillation.[5]
  - A 5-state Markov model (NYHA I–IV, death) was derived from an appraisal of tafamidis,[6] which allows for modeling between disease progression and clinical outcomes (**Figure 1**).
  - Cost and resource use in a real-world oHCM population were found, but costs were not broken down by NYHA class.[7-9]
  - Mortality data were derived from a recent abstract reporting a difference in all-cause mortality by NYHA class, although impact of therapies on NYHA class and associated outcomes was not assessed.[10]
- The published literature has major gaps in the evidence needed to build a robust CEM for oHCM (**Table 3**).

Figure 1. Recommended Model Structure



Key Model Points and Justification

- As there are no pre-existing models for oHCM, the model structure was based on the closest proxy, tafamidis in ATTR-CM.[6]
- Health states are stratified using NYHA functional class; a scoring system that classifies oHCM patients based on their limitations during physical activity due to symptoms.
  - Functional classification places patients in 1 of 4 categories (I–IV) based on their limitations.
  - A reduction in NYHA category by ≥1 class represents a clinically meaningful improvement.
  - NYHA classes are deemed a patient-relevant mechanism that has been observed as a statistically significant predictor of both QoL and survival.
  - This structure allows patients to either decline or improve in NYHA class, explicitly modeling the relationship between disease progression based on the functional ability of the patient and clinical outcomes.
  - At the end of each model cycle, patients may remain in the same health state, transition between NYHA classes, or die.
- This model structure has been ratified by a US clinician specializing in HCM.

ATTR-CM, transthyretin amyloidosis cardiomyopathy; HCM, hypertrophic cardiomyopathy; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; QoL, quality of life

Figure 2. Types of Publications Identified

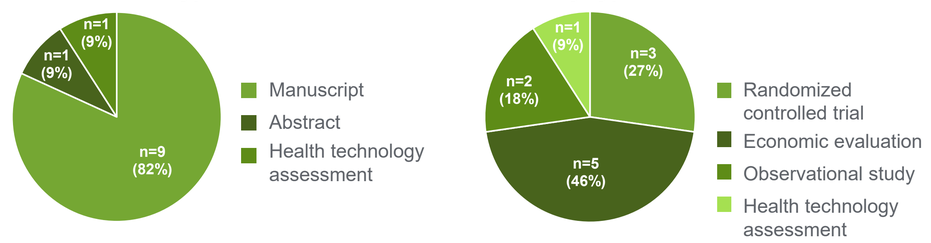


Table 2. Data to Inform the oHCM Cost-Effectiveness Model

Category/Data	Source	Justification
Population settings		
B/L distribution, age, % male	EXPLORER-HCM[1]	EXPLORER-HCM trial represents a trial population of oHCM patients.
Quality of life		
Utility values	King et al. 2016[4]	Includes a value for each NYHA class health state from I–IV; not differentiated by treatment arm. EXPLORER-HCM utility values were used as a scenario analysis; however, this source does not differentiate between NYHA III and IV.
AE disutility	Steg et al. 2012[5]	In the absence of AE disutility from EXPLORER-HCM or any other relevant CV diseases, atrial fibrillation was the closest available evidence due to its chronic nature.
Model structure		
NYHA class I–IV, death	Informed by structures published in HTAs	A 5-state Markov model was chosen as it allows patients to either decline or improve in NYHA class. Further, this structure allows for explicitly modeling the relationship between disease progression based on the patient's functional ability and clinical outcomes.
Cost and resource use		
Drug costs	BNF or eMIT	Treatment costs for SoC were sourced from the BNF. Where not available, costs were sourced from the eMIT.
Resource use	Clinician validation	Resource use was provided and validated by US clinicians.
Clinical effectiveness		
Transition probabilities	Desai et al. 2022[2]	Treatment effect (measured by transitions across NYHA classes I–IV) for both mavacamten and *aficamten* was based on data from the EXPLORER-HCM mavacamten arm. Similarly, treatment effect for SoC was taken from the SoC arm of the EXPLORER-HCM trial. AE rates from EXPLORER-HCM were used due to the small number of patients included in REDWOOD-HCM.
AE probability	EXPLORER-HCM[1]	To address the absence of data for *aficamten* and SoC.

AE, adverse event; B/L, baseline; BNF, British National Formulary; CV, cardiovascular; eMIT, Electronic Market Information Tool; HCM, hypertrophic cardiomyopathy; HTA, Health Technology Assessment; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; SoC, standard of care

Table 3. Evidence Gaps for the oHCM Cost-Effectiveness Model

Section	Evidence Gaps
Population	
Population settings	• Lack of population demographics that are generalizable and diverse
Economic evidence	
Quality of life	• No evidence on utility values for NYHA I–IV separately in oHCM • No disutility values within oHCM were identified for adverse events
Model structure	• Recent studies in oHCM have been published with a 3-state Markov model: NYHA class I, II, III/IV; these studies have not yet been submitted in a formal HTA assessment and therefore no limitations have been raised; however, similar model structures have been accepted in analogs
Cost and resource use	• Costs and resource disaggregated by NYHA class • There are currently limited data about healthcare-related and non–healthcare-related resource use and costs
Clinical evidence	
Clinical effectiveness	• Limited evidence on the clinical effectiveness of SoC in its disaggregated form (beta-blockers vs calcium-channel blockers vs disopyramide vs invasive therapies) • Lack of long-term data
Mortality	• One study was identified that evaluated the impact of NYHA class on mortality; however, it did not separate NYHA class III and IV • The impact of therapies on NYHA functional class and associated outcomes has also not been identified

HF, heart failure; HTA, health-technology assessment; NYHA, New York Heart Association; oHCM, obstructive hypertrophic cardiomyopathy; SoC, standard of care

CONCLUSIONS

- Data from this targeted literature review will be used to develop a CEM for oHCM.
- For identified gaps, research is warranted to generate evidence to help build robust CEMs for newer HCM pharmacotherapies, such as cardiac myosin inhibitors.

References

1. Olivotto I, et al. *Lancet* 2020;396:759-69. **2.** Desai N, et al. *Clin Ther* 2022;44:52-66.e2. **3.** Dybro AM, et al. *J Am Coll Cardiol* 2021;78:2505-17. **4.** King JB, et al. *JACC Heart Fail* 2016;4:392-402. **5.** Steg PG, et al. *Heart* 2012;98:195-201. **6.** Tafamidis for treating transthyretin amyloid cardiomyopathy. Available at: https://www.nice.org.uk/guidance/ta696/documents/committee-papers-2 [Accessed February 21, 2022.] **7.** Jain SS, et al. *J Med Econ* 2021;24:1115-23. **8.** Owens AT, et al. *Cardiol Ther* 2022;11:249-67. **9.** Butzner M, et al. *AHJ Plus: Card Res Practice* 2022;13:100089. **10.** Lakdawala N, et al. Presented at HFSA, September 10-13, 2021.

Acknowledgments and Disclosures

This study was funded by Cytokinetics, Incorporated. Editorial support for this poster was provided by Geraldine Thompson on behalf of Engage Scientific Solutions, Horsham, UK, and was funded by Cytokinetics, Incorporated. **BN** reports consulting fees from Biosense Webster, Boston Scientific, and Edwards Life Sciences, and investigator-initiated research funding from Biosense Webster, Galaxy Medical, and the NIH. **JJ**, **RD**, **CP**, and **LE** are employees of FIECON, who were consultants for Cytokinetics for this study. MB is an employee of Cytokinetics and holds stock in the company. **AM** has received consultant/advisor fees from Attralus, Bristol Myers Squibb, Cytokinetics, Ionis, and Tenaya, and research grants from Akcea, Ionis, Pfizer, Ultromics, and Wheeler Foundation.

Presented at the International Society for Pharmacoeconomics and Outcomes Research Europe (ISPOR-EU) Meeting | Vienna, Austria | November 6–9 2022

Cytokinetics