

Assessing the Utility of Existing Hereditary Angioedema Disease Models for Health Economic Evaluation of Future Therapies

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Background

- Hereditary angioedema (HAE) is a rare, genetic disease characterized by debilitating swelling episodes in various parts of the body¹
- The chronic and unpredictable nature of HAE results in substantial burden for patients, caregivers, and health systems
- Over the last two decades, acute and long-term prophylactic treatments have become available for patients; however, these formats and requirements can be burdensome
- As new HAE treatments, such as oral therapies, emerge, it is important to consider whether existing HAE modeling frameworks are fit for assessing their potential value impact
- Payers and health technology assessment (HTA) bodies use economic models to help inform their decisions on population interventions and to make the best use of limited healthcare resources²
- This study identified existing HAE disease models and assessed their utility for evaluating the health economic value of future HAE therapies

Methods

- We conducted a prespecified literature search in PubMed and HTA databases to identify pertinent peer-review literature, congress proceedings, and agency assessments on HAE disease models
- We included studies involving patients with any type of HAE (type 1, 2, and HAE with normal C1-INH) reporting a disease model relating to HAE pharmaceutical treatment
- For each study, we extracted detailed information on:
 - Disease modeling approach
 - Impact of simulated interventions on disease progression
 - Health economic analysis specifications and outcomes
- We assessed the quality of reporting using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) II criteria—a 28-item checklist assessing the robustness of health economic evaluation reporting, where a higher score indicates more complete reporting³

References

- Radojicic C, Riedl MA, Craig TJ, et al. Patient perspectives on the treatment burden of injectable medication for hereditary angioedema. *Allergy Asthma Proc.* May 1 2021;42(3):S4-S10. doi:10.2500/aap.2021.42.210025
- O'Reilly D, Gaebel K, Xie F, Tarride JE, Goeree R. Health economic evaluations help inform payers of the best use of scarce health care resources. *Int J Circumpolar Health.* 2011 Sep;70(4):417-27. Epub 2011 Sep 14. PMID: 21924008.
- Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs A H, Carswell C et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMJ* 2022; 376 :e067975
- Bernstein JA, Tyson C, Relan A, Adams P, Magar R. Modeling Cost-Effectiveness of On-Demand Treatment for Hereditary Angioedema Attacks. *J Manag Care Spec Pharm.* 2020 Feb;26(2):203-210. doi: 10.18553/jmcp.2019.19217. Epub 2019 Dec 16. PMID: 31841366.
- CADTH Common Drug Review Pharmacoeconomic Review Report 2018. For the Treatment of Acute Attacks of Hereditary Angioedema (HAE) in Adults with C1 Esterase Inhibitor Deficiency.
- Helbert M, Pang F, Alvarez-Reyes M, Pearson I, Wolowacz S, Diwakar L. A Cost-Effectiveness Comparison of Icatibant and C1-Esterase Inhibitor Concentrate for the Symptomatic Treatment of Acute Attacks of Types I and II Hereditary Angioedema in the UK Setting. Presented on 6 November at ISPOR 2012, Berlin.
- Christopher Tyson, Anurag Relan, Philippe Adams, Angela Haynes & Raf Magar (2019) Cost-effectiveness model for on-demand treatment of hereditary angioedema (HAE) attacks, *Journal of Drug Assessment*, 8:sup1, 22, DOI: 10.1080/21556660.2019.1658300
- Drug Therapies for the Long-Term Prophylaxis of Hereditary Angioedema Attacks. Ottawa: CADTH; 2019 Dec. (CADTH Technology Review; no. 25)
- Prophylaxis for Hereditary Angioedema with Lanadelumab and C1 Inhibitors: Effectiveness and Value. *ICER* 2018.
- Lanadelumab for Preventing Recurrent Attacks of Hereditary Angioedema. *NICE* 2019
- Bertralstat for Preventing Recurrent Attacks of Hereditary Angioedema. *NICE* 2021
- Graham C, Machnig T, Knox H, Supina D, Krishnarajah G. Attacks Avoided and Cost Offsets Associated with Subcutaneous C1-Inhibitor (Human) Long-Term Prophylaxis of Hereditary Angioedema. *Ann Allergy Asthma Immunol* 119 (2017) S17-S96
- Federici C, Perego F, Borsoli L, Crosta V, Zanichelli A, Gidaro A, Tarricone R, Cicardi M. Costs and effects of on-demand treatment of hereditary angioedema in Italy: a prospective cohort study of 167 patients. *BMJ Open.* 2018 Jul 30;8(7):e022291. doi: 10.1136/bmjopen-2018-022291. PMID: 30061443; PMCID: PMC6067408.

Results

- We identified 10 HAE disease models; 5 were reported in peer-reviewed publications, and 5 were reported in HTA evaluations (Table 1)⁴⁻¹³

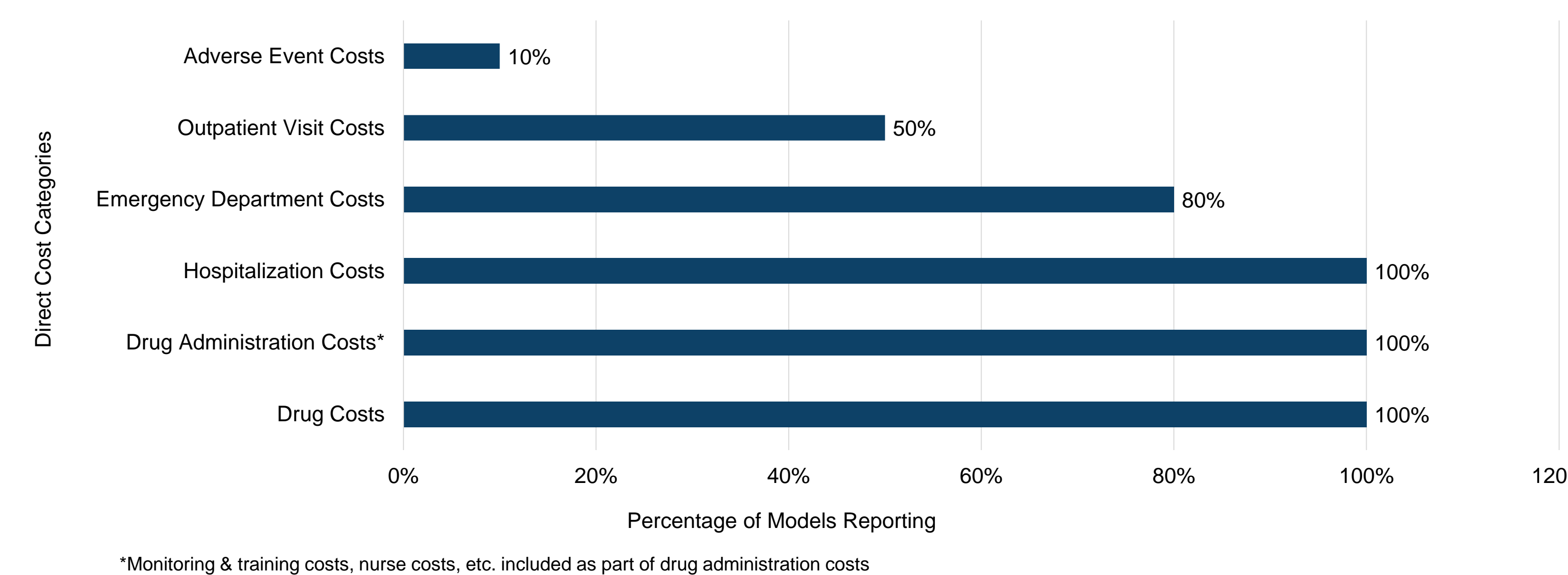
Table 1. Overview of Select Model Characteristics and Specifications

	N Studies		N Studies
Economic Analyses Used		Time Horizons Used	
Cost utility	6	Lifetime	4
Cost-effectiveness	3	1-year	3
Cost-minimization	1	1 HAE attack	3
HAE Therapies Studied		HAE Attack Characteristics Simulated*	
On-demand only	5	Location	5
Long-term prophylaxis (LTP) only	3	Severity	5
LTP with on-demand	2	Duration	9
Primary Modeling Approach Used		Key Intervention Effects Simulated	
State transition	5	Reduction of HAE attacks	5
Decision tree	4	Time to HAE attack resolution	5
Cost-effectiveness	1	Cost Types Simulated**	
		Direct	10
		Indirect	3

*Some models simulated multiple attack characteristics
**Some models simulated both direct and indirect costs

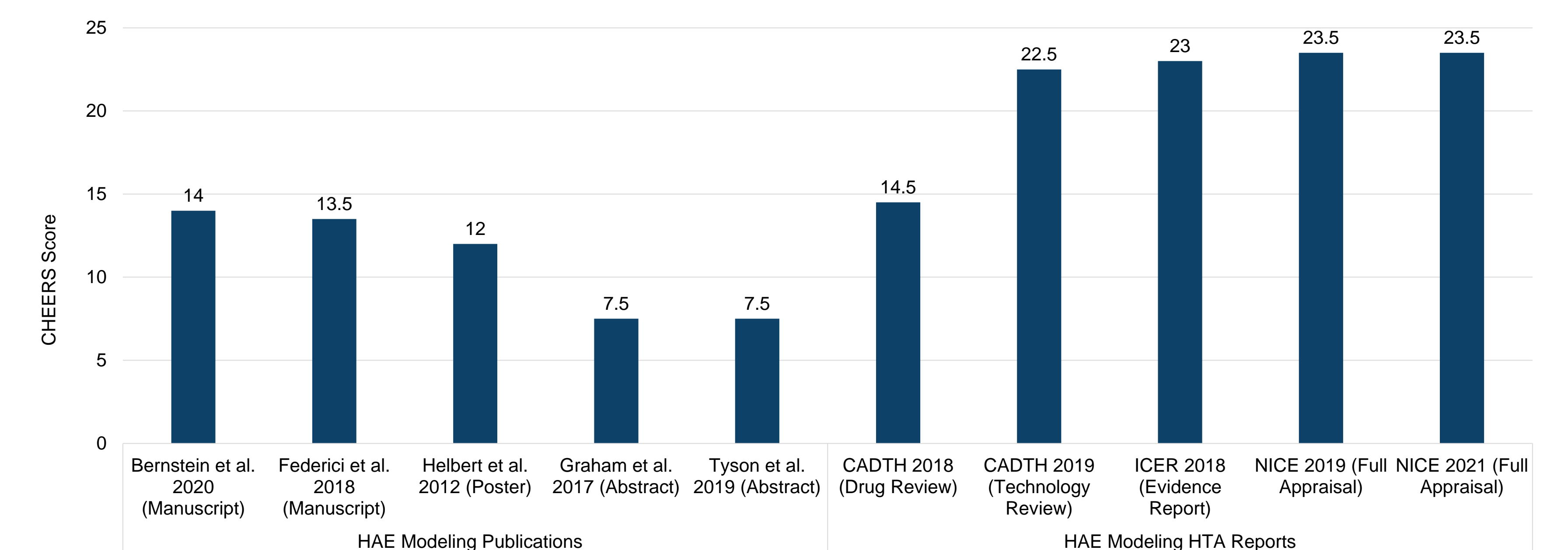
- All models simulated direct costs, with drug costs, drug administration costs, and hospitalization costs most frequently included (Figure 1); 3 models simulated indirect costs—all in scenario or exploratory analyses

Figure 1. Categories of Direct Costs Included in Models



- Attack characteristic simulation varied across models: attack location and severity were each simulated in half of reviewed models, while duration was simulated in nearly all (n=9), with varying operational definitions used
- Two reviewed models simulated disease-related mortality
- Economic outcomes were measured using different metrics across reviewed models: Health Utility (Quality-Adjusted Life Years, QALY) (n=5); Health Utility (QALY) and Life Years (n=2); HAE Attacks Avoided (n=1); Time to Onset of Symptom Relief (n=1); and Time to Complete Resolution of Attack Symptoms (n=1)
- Quality of reporting was higher in HTA reports compared to peer-reviewed publications (average CHEERS score of 21.4 versus 10.9, respectively) (Figure 2)

Figure 2. Quality of Reporting as Assessed by CHEERS II



Conclusions

- We found that existing HAE disease models do not fully capture relevant variables required to evaluate emerging HAE therapy options, including all attack characteristics and both direct costs and indirect economic impact
- The development of a new HAE disease model that incorporates a societal perspective is important to capture the true burden of disease and support health economic evaluations for future HAE therapies

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