

LONG-TERM COST EFFECTIVENESS OF MAVACAMTEN FOR TREATMENT OF HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY (HOCM)

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BACKGROUND

- Hypertrophic cardiomyopathy (HCM) is a genetic disorder involving sarcomeres in heart muscle.
- For patients with hypertrophic obstructive cardiomyopathy (HOCM), a specific subtype of HCM, obstruction of the left ventricular outflow tract (LVOT) can cause exertional symptoms.
- For HOCM patients with shortness of breath related to LVOT obstruction, beta blockers and calcium channel blockers can improve symptoms.
- When these first-line therapies are insufficient or not well tolerated, second-line treatment options include adding disopyramide or performing septal reduction procedures (myectomy or septal ablation).
- Mavacamten is a first-in-class cardiac myosin modulator for HOCM.

OBJECTIVE

- This study assessed the cost effectiveness of mavacamten in addition to standard of care (SoC) compared with SoC alone, as well as disopyramide, myectomy, and septal ablation each in addition to SoC.

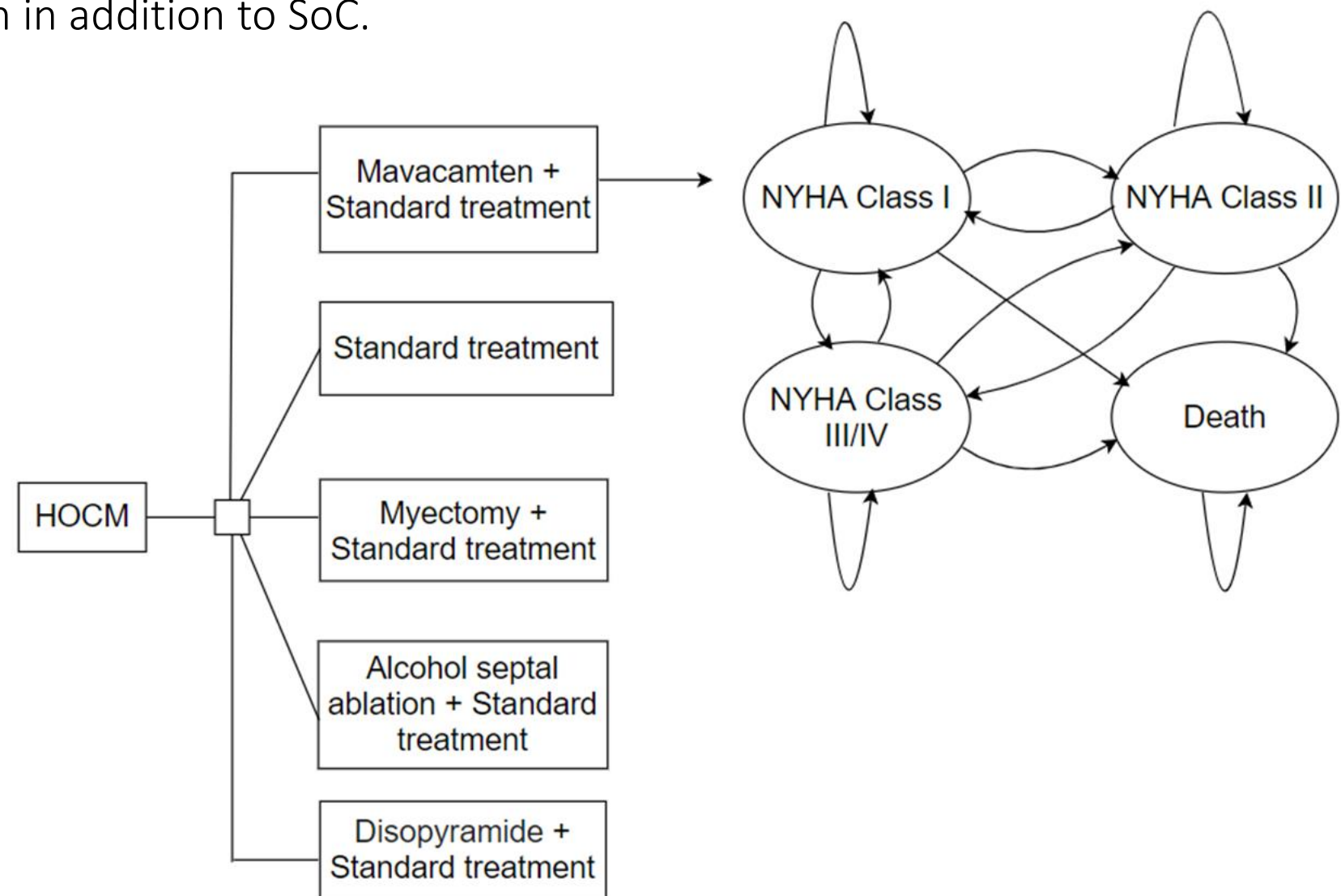


FIGURE I: Model Schematic

METHOD

- A semi-Markov model was used over a lifetime time horizon from a healthcare sector perspective and the cycle length was 4 weeks.
- Patient utilities were estimated via New York Heart Association functional classes (NYHA) but assuming mortality was the same across all classes.
- Evidence from clinical trials, related literature and expert experience were the basis for model inputs.
- A placeholder price for Mavacamten (\$75,000/year) was used in the cost estimates.
- Both costs and outcomes were discounted at a rate of 3%.
- Cost per quality adjusted life year (QALY) gained, cost per life year (LY) gained, cost per equal value LY gained (evLYG), and cost per additional year in NYHA class I were the outcomes of interest.
- Sensitivity and scenario analyses were conducted to test the robustness of the model.

MODEL INPUTS

TABLE I: Treatment effect of Mavacamten¹

	NYHA I	NYHA II	NYHA III	NYHA IV	Missing
Baseline	0%	71.5%	28.5%	0%	0%
Week 14	31.7%	55.3%	3.3%	0%	9.8%
Week 30	49.6%	42.3%	6.5%	0%	1.6%

TABLE II: Treatment effect of SoC¹

	NYHA I	NYHA II	NYHA III	NYHA IV	Missing
Baseline	0%	74.2%	25.8%	0%	0%
Week 14	16.4%	64.1%	14.8%	0%	4.7%
Week 30	21.1%	57.8%	19.5%	0%	1.6%

TABLE III: Quality of Life (QOL) Parameters for Mavacamten and standard of care²

QOL	Utility for Mavacamten	Utility for standard of care
NYHA Class I	0.950	0.952
NYHA Class II	0.866	0.850
NYHA Class III/IV	0.708	0.704

RESULTS

- In comparison to SoC alone and disopyramide (with SoC), the cost/QALY gained by mavacamten was \$1.2 and \$1.5 million, respectively.
- Compared with myectomy and septal ablation, mavacamten resulted in fewer QALYs, slightly more LYs gained, and incremental costs of \$5.6 and \$7 million per LY respectively.
- Mavacamten produced additional NYHA I years compared to SoC and disopyramide at costs over \$200,000/NYHA I year.
- Sensitivity and scenario analyses results supported the robustness of the findings.

TABLE IV: Base case results

Treatment	Total Drug Cost	Total Cost	QALYs	Life Years	NYHA I Years	evLY
Mavacamten	\$1,258,000	\$1,568,000	14.75	16.58	8.50	14.75#
Standard of care	\$12,600	\$434,000	13.78	16.58	3.33	13.78
Disopyramide	\$116,000	\$509,000	14.06	16.58	4.69	14.06
Septal Ablation	\$67,800	\$297,000	14.97	16.40	12.49	14.97
Myectomy	\$135,000	\$364,000	14.97	16.37	12.47	14.97

TABLE V: Incremental cost-effectiveness ratios

Treatment	Comparator	Cost per QALY Gained	Cost per Life Year Gained	Cost per evLY Gained	Cost per Additional NYHA I Year
Mavacamten*	Standard of care	\$1,200,000	Undefined	\$1,200,000	\$219,000
	Disopyramide	\$1,500,000	Undefined	\$1,500,000	\$278,000
	Myectomy	Dominated	\$5,600,000	N/A	Dominated
	Septal ablation	Dominated	\$7,000,000	N/A	Dominated

SENSITIVITY ANALYSIS

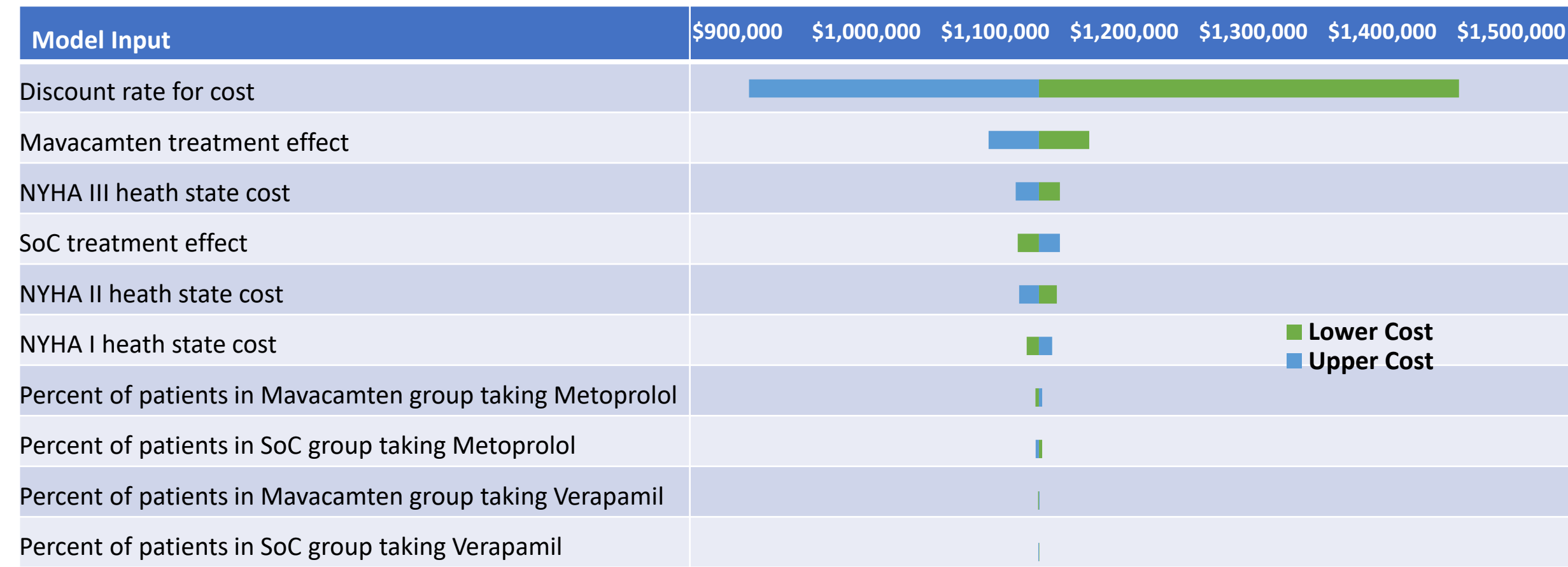


FIGURE II: Mavacamten vs SoC cost: one way sensitivity analysis

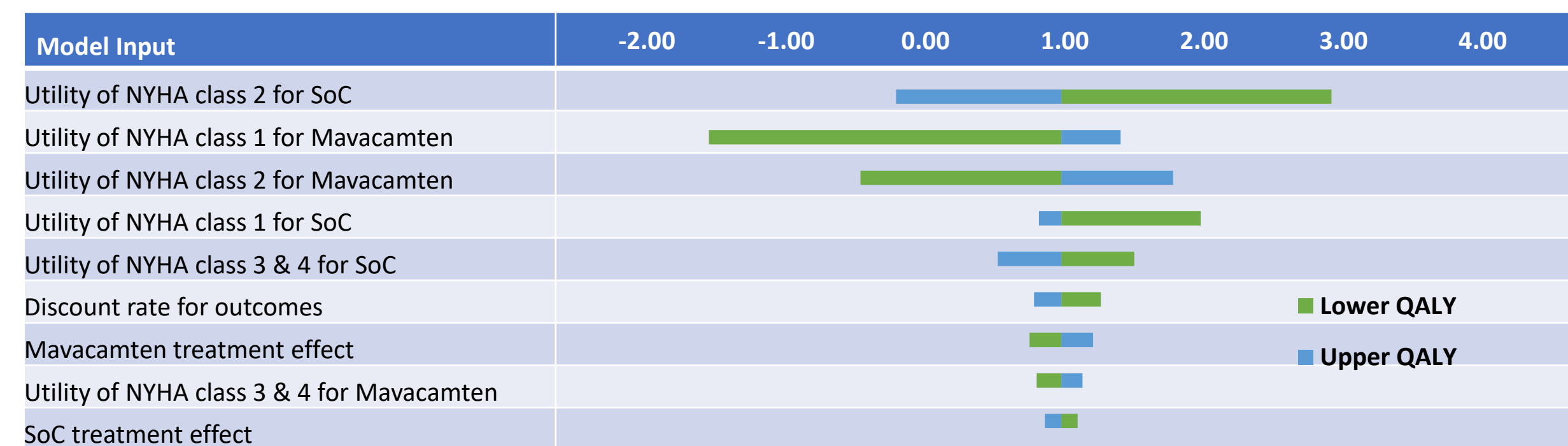


FIGURE III: Mavacamten vs SoC QALY: one way sensitivity analysis

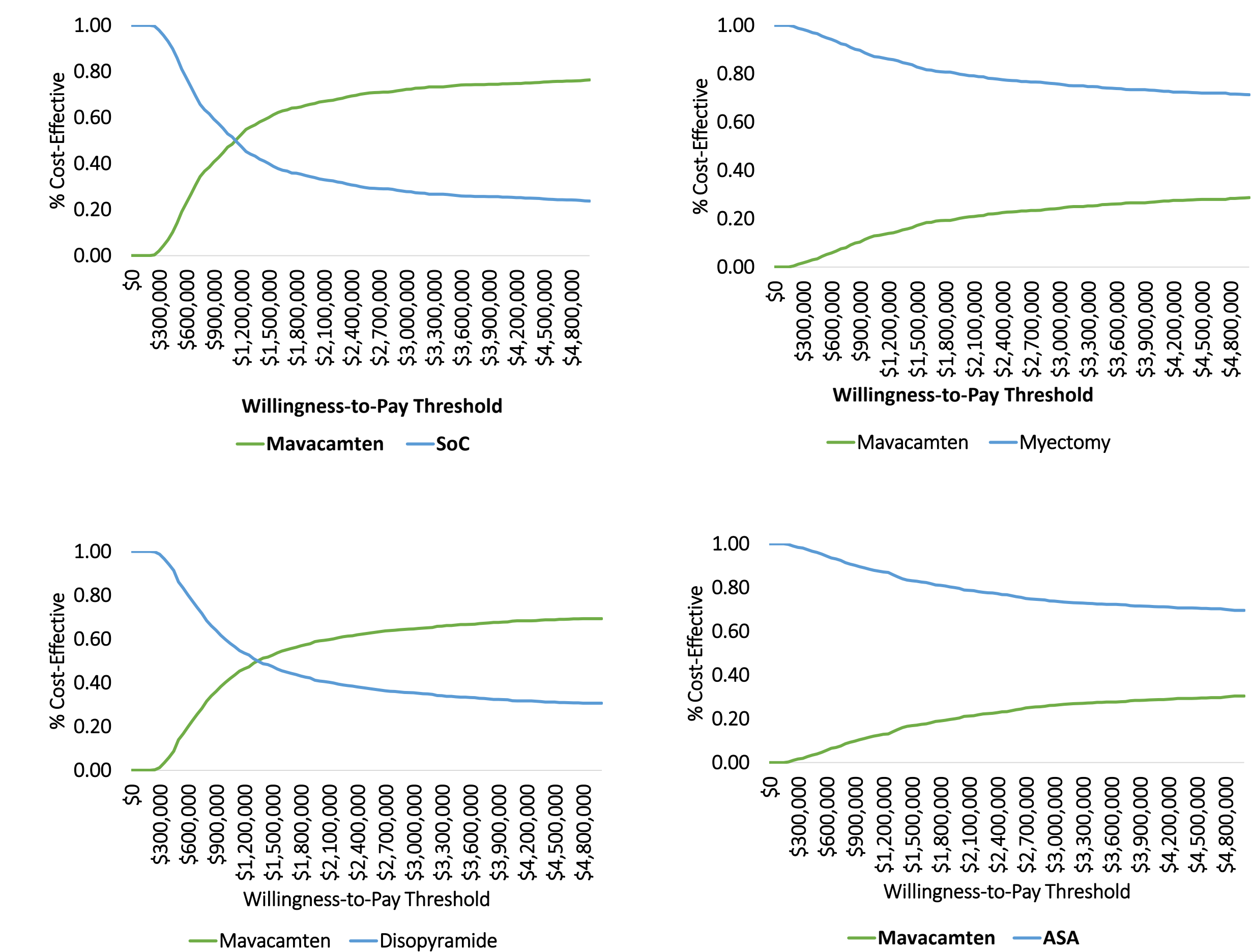


FIGURE IV: Cost-effectiveness Acceptability Curves: Mavacamten vs Comparators

SCENARIO ANALYSIS

TABLE VI: Incremental cost-effectiveness ratios for Mavacamten in scenario with higher mortality for NYHA class III/IV

Comparator	Cost/QALY Gained	Cost /Life Year Gained	Cost/evLY Gained	Cost/NYHA I Year Gained
Standard treatment	\$893,000	\$2,600,000	\$693,000	\$219,000
Disopyramide	\$1,100,000	\$3,100,000	\$874,000	\$279,000
Myectomy	Dominated	\$15,800,000	N/A*	Dominated
Septal ablation	Dominated	\$29,900,000	N/A*	Dominated

TABLE VII: Societal perspective related scenario analysis

Scenario	Cost/QALY Gained	Cost/ evLY Gained	Cost/ NYHA I Year Gained
Full employment for NYHA I and not for class II and III/IV (both mavacamten and standard treatment group)	\$876,000	\$876,000	\$165,000
Full employment for all patients in mavacamten group	\$242,000	\$242,000	\$46,000

LIMITATIONS

- There were only 30 weeks of data available for mavacamten in the clinical trial on which to base projected treatment effects by NYHA class.
- The clinical trial data may not generalize to other patient populations.
- There was a lack of evidence from direct comparison with myectomy, septal ablation and disopyramide.
- The evidence for myectomy, septal ablation, and disopyramide comes from observational studies.
- Due to absence of actual societal cost data, the scenario analysis from societal perspective was conducted using hypothetical data.
- The model is based on placeholder price for mavacamten.
- Heterogeneity in HOCM patients is not addressed in the model.

CONCLUSION

- Actual cost-effectiveness of mavacamten will depend on its price.
- At the placeholder price, the incremental cost effectiveness ratios of mavacamten over SoC and disopyramide are well beyond standard threshold levels.
- Also, mavacamten is dominated by septal reduction procedures in terms of QALYs.

REFERENCES

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- Xie J, Wang Y, Xu Y, Fine JT, Lam J, Garrison LP. Assessing health-related quality-of-life in patients with symptomatic obstructive hypertrophic cardiomyopathy: EQ-5D-based utilities in the EXPLORER-HCM trial. *J Med Econ*. 2022;25(1):51-58.

