# Cost-Effectiveness of Olanzapine Compared to Standard of Care for Cancer Cachexia Management: A Markov Model

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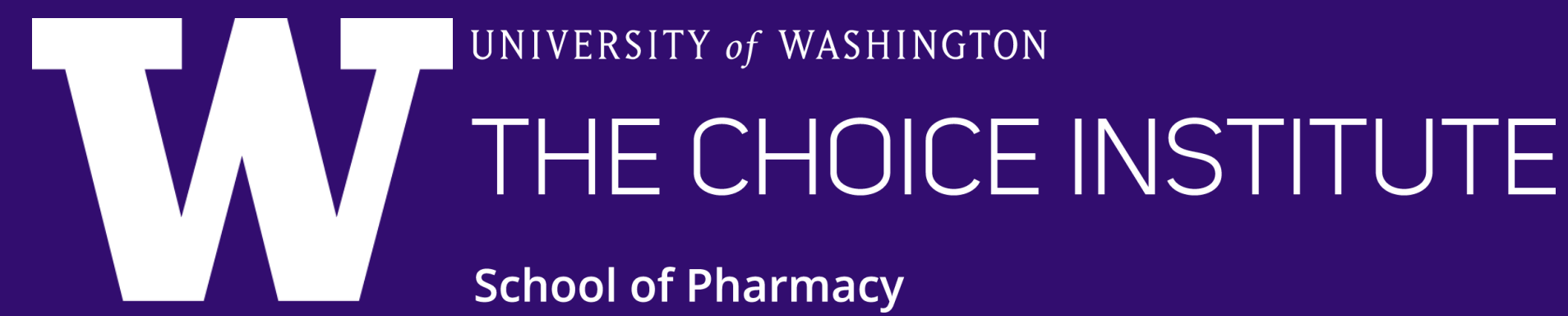
Background

- Cancer cachexia is a wasting disease characterized by inadequate food intake, loss of muscle mass, weight loss, and changes in metabolism.[1–3]
- It is estimated that cachexia affects 73% of pancreatic cancer patients, about 50% of lung and colorectal cancer, and 30% of breast cancer patients of all stages.[4]
- In response to data from Sandya et al. 2023, cancer care guidelines have updated their recommendations that physicians may offer patients low-dose olanzapine to improve weight gain and appetite. [5-7]

Study Objective: To assess the cost-effectiveness of olanzapine vs best supportive care for management of cancer cachexia in patients with advanced Non-Small Cell Lung Cancer (NSCLC).
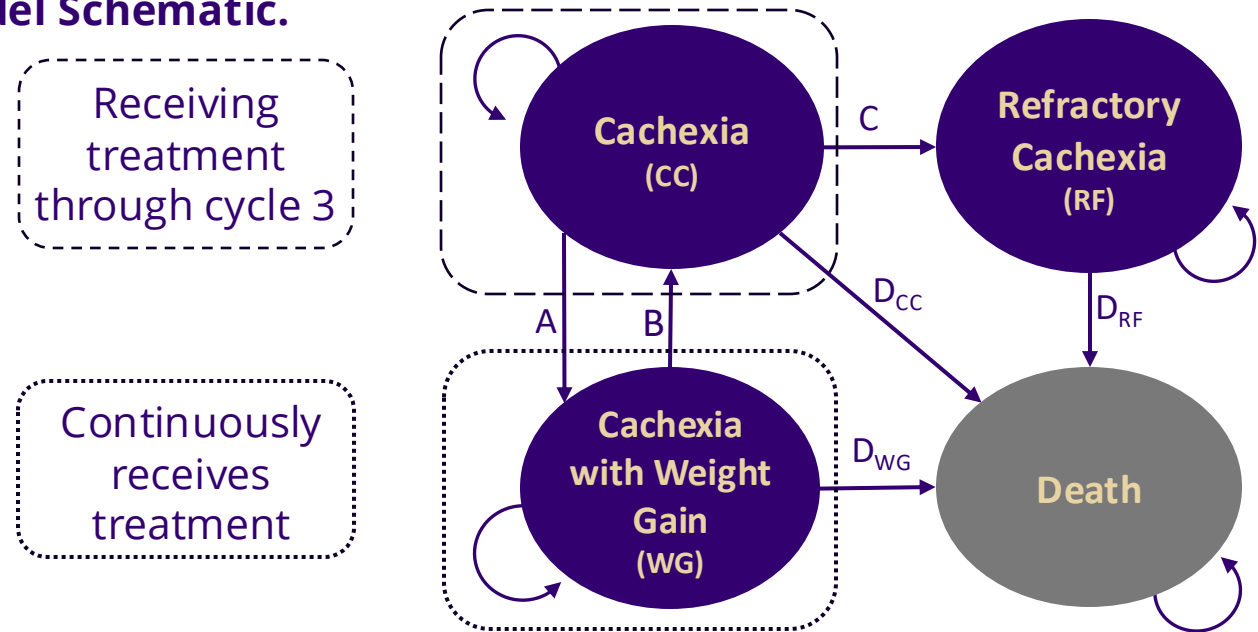
Methods

We created a Markov model in Microsoft Excel to assess the cost-effectiveness of olanzapine versus standard of care in advanced stage NSCLC patients with cachexia.

- **Population**: Stage III locally advanced or stage IV metastatic NSCLC
- **Treatment:** Olanzapine 2.5mg tablet once daily + Standard of Care (supportive care) vs Standard of Care alone (best supportive care)
- **Cycle length**: 1 month
- **Outcomes**: Lifetime costs, life-years, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratio (ICER)
- **Utility**: FAACT quality-of-life measures were mapped to EQ5D based utility values using an algorithm by Meregaglia et al.[8]
- **Perspective**: US healthcare payer perspective
- **Costs**: Olanzapine drug cost (wholesale acquisition cost), hospitalizations, emergency room visits, and disease related costs. Costs in 2024 US dollars.
- **Discount Rate**: Costs and QALYs were discounted at a 3% annual rate.

Transition probabilities:
A. Cachexia to cachexia with weight gain: based on proportion who achieved >5% weight gain in olanzapine and placebo treatment arms by the end of 12 weeks.[5] Transition probability becomes 0 after 12 weeks.
B. Cachexia with weight gain to cachexia: estimated from proportion of people in the placebo group who lost weight over 12-week period.
   o Proportions were converted to a monthly transition probability using methods described in Gidwani et al.[9]
C. Cachexia to refractory cachexia: monthly rate of lung cancer progression, derived from the progression free survival curve in Jo et al.[10], was a proxy for this probability.
D. Death (D_{WG}, D_{CC}, D_{RF}): Each health state's time-varying survival was modeled and fit to survival curves reported in Blum et al.[11] Cachexia with weight gain was modeled from pre-cachexia curve.

Figure 1. Model Schematic.

Receiving treatment through cycle 3

Continuously receives treatment

Key Model Assumptions

- The weight gain seen in Sandya et al. 2023, which included multiple cancers (35% lung cancer), was assumed to be applicable NSCLC.
- Costs of cancer care in each health state are assumed to be the same.

Methods (continued)

Table 1. Inputs Table.

Model Inputs	Deterministic Value	Low Value	High Value	References
Transition Probabilities				
Cachexia to Weight Gain	0.032	0.026	0.038	Sandhya et al. [5]
Cachexia to Weight Gain after 12 weeks	0.000	0.000	0.038	Assumption
Cachexia to Weight Gain, Olanzapine	0.265	0.212	0.318	Sandhya [5]
Cachexia to Weight Gain after 12 weeks, Olanzapine	0.000	0.000	0.318	Assumption
Cachexia to Refractory Cachexia	0.165	0.116	0.365	Jo et al. [10]
Weight Gain to Cachexia	0.257	0.180	0.334	Sandhya et al. [5]
Survival Curve, Weibull Inputs				Blum et al. [11]
Cachexia to Death, Intercept	6.091	6.052	6.131	Calculated
Cachexia to Death, Log-scale	-0.479	-0.535	-0.440	Calculated
Weight Gain to Death, Intercept	6.293	6.260	6.332	Calculated
Weight Gain to Death, Log-scale	-0.979	-1.053	-0.939	Calculated
Refractory Cachexia to Death, Intercept	5.740	5.646	5.779	Calculated
Refractory Cachexia to Death, Log-scale	-0.347	-0.467	-0.308	Calculated
Utilities				
Intercept	0.495	0.404	0.587	Meregaglia et al. [8]
FAACT Adjustment	0.003	2.52E-03	4.08E-03	Meregaglia et al. [8]
ECOG Adjustment	-0.174	-0.235	-0.113	Meregaglia et al. [8]
Proportion ECOG ≥2 for Weight Gain	0.197	0.099	0.295	Zhou et al.[12]
Proportion ECOG ≥2 for Cachexia	0.266	0.168	0.364	Sandhya et al. [5]
Proportion ECOG ≥2 for Refractory Cachexia	0.737	0.639	0.835	Zhou et al. [12]
FAACT Weight Gain (weighted) [b]	28	11	48	Sandhya et al. [5]
FAACT Cachexia	16	4	37	Sandhya et al. [5]
FAACT Refractory Cachexia	12	3	28	Calculated [a]
Costs				
Drug cost, Olanzapine 2.5mg per 30-day cycle	$24	$2.40	$401	Redbook [13]
Average Monthly Cost of Cancer Care				
Hospital Outpatient, Average Cost	$3,049	$1,525	$16,877	Dagenais et al.[14]
Office Visits, Average Cost	$1,305	$653	$10,229	Dagenais et al.[14]
Home Health / Telehealth, Average Cost	$212	$106	$1,243	Dagenais et al.[14]
Other Lung Cancer Care, Average Cost	$4,232	$2,116	$29,253	Dagenais et al.[14]
Monthly Hospitalization Rate - Lung Cancer	0.19	0.04	0.34	Korytowsky et al.[15]
Average Costs of Hospitalization Weight Gain	$3,064	$1,532	$24,818	Calculated
Average Costs of Hospitalization Cachexia	$4,079	$2,040	$31,243	Dagenais et al.[14]
Average Costs of Hospitalization Refractory	$4,487	$2,243	$34,367	Calculated
Emergency Room Visit Cost Lung Cancer	$984	$194	$1,549	Panattoni et al. [16]
Monthly ER Visit Rate Weight Gain [c]	0.13	0.06	0.19	Vigano et al. [17]
Monthly ER Visit Rate Cachexia	0.18	0.07	0.24	Vigano et al. [17]
Monthly ER Visit Rate Refractory Cachexia	0	0.00	0.06	Vigano et al. [17]

[a] Refractory cachexia FAACT estimated to be 25% less than cachexia FAACT based on Zhou 2018; [b] Weighted final FAACT score between treatment and placebo groups for the proportion who achieved weight gain; [c] Used pre-cachexia ER visit rates as a proxy for the weight gain rate. FAACT: Functional Assessment of Anorexia Cachexia Therapy; ECOG: Eastern Cooperative Oncology Group performance status scale ; ER: Emergency Room

Results

Deterministic Results

In our comparison of olanzapine to standard of care management of cancer cachexia, we estimated that patients receiving olanzapine would gain 0.061 life-years and 0.042 QALYs. Incremental costs were $7,160 more in the olanzapine group compared to standard of care. The resulting cost per QALY gained was $170,706.
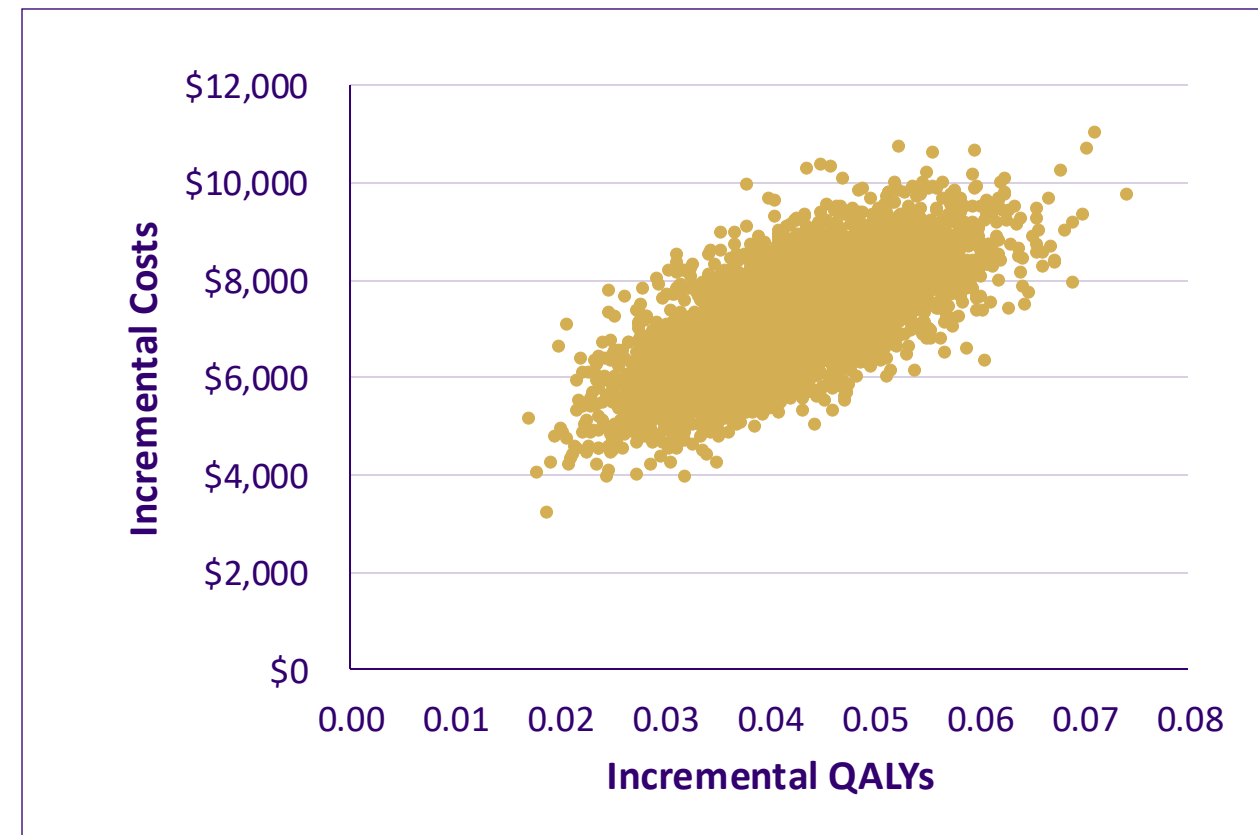
One-Way Sensitivity Analysis

Key model drivers identified in the one-way sensitivity analysis (OWSA) were costs associated with routine cancer care, inputs for calculating health state cachexia and cachexia with weight gain utility, and hospitalization costs.

Probabilistic Sensitivity Analysis

Results from the probabilistic sensitivity analysis showed olanzapine to have a 95% credible range of $5,151–$9,197 incremental costs and a 0.03–0.06 incremental QALYs gained. The resulting 95% credible range of the ICER was $132,944–$230,980.
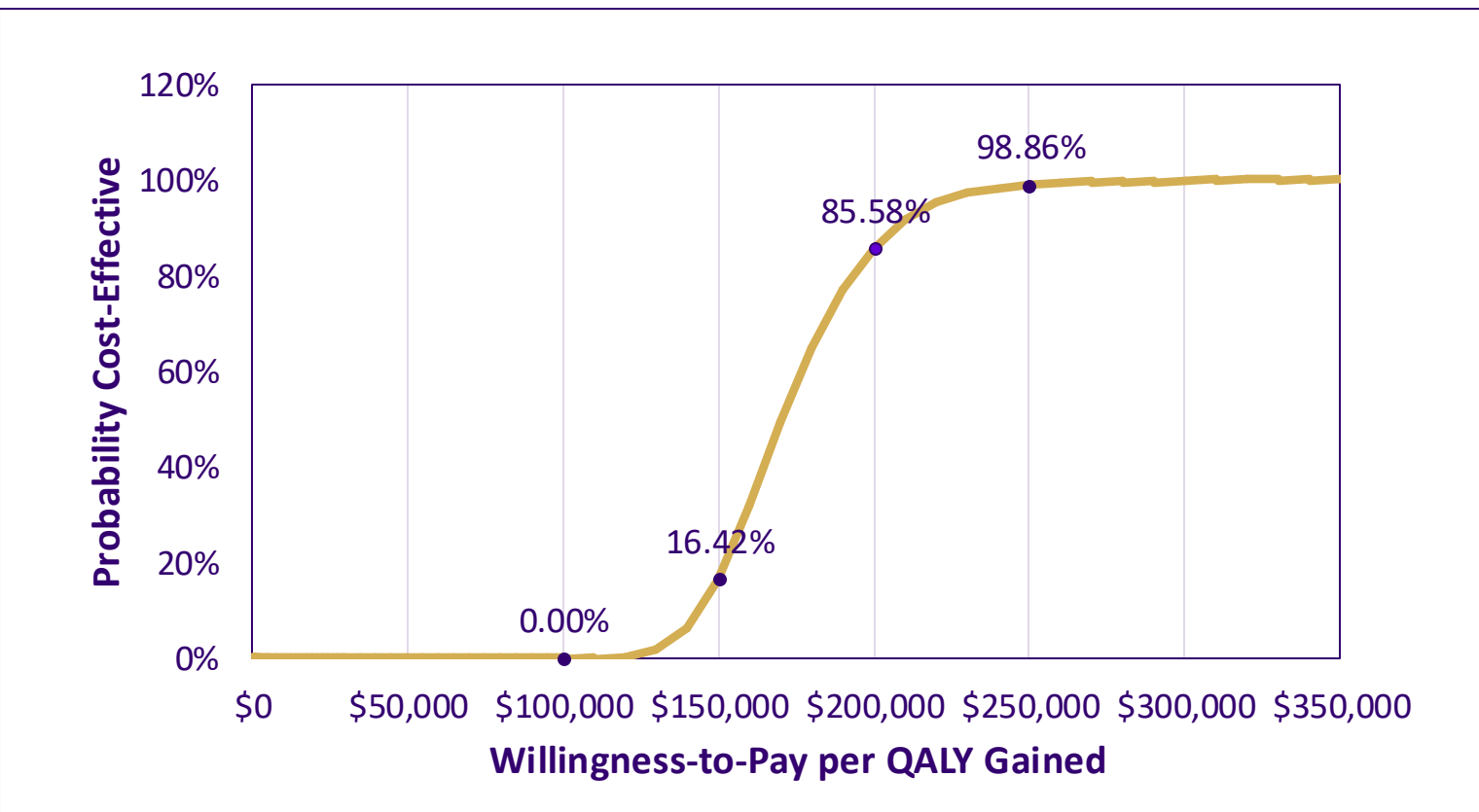
The probabilities of olanzapine being cost-effective compared to standard of care at willingness-to-pay thresholds from $100,000 - $250,000 are presented in Figure 4.

Table 2. Deterministic Model Results.

	Standard of Care	Olanzapine	Incremental Results
Costs	$104,243	$111,403	$7,160
Life-Years	0.886	0.947	0.061
QALYs	0.397	0.439	0.042
Cost per Life-Year Gained			**$117,328**
Cost per QALY Gained			**$170,706**

QALYs: Quality-Adjusted Life Years

Figure 2. One-Way Sensitivity Analysis.

FAACT: Functional Assessment of Anorexia Cachexia Therapy; EQ-5D: EuroQol-5 Dimensions

Figure 3. Cost-Effectiveness Scatter Plot.

QALYs: Quality-Adjusted Life Years

Figure 4. Cost-Effectiveness Acceptability Curve.

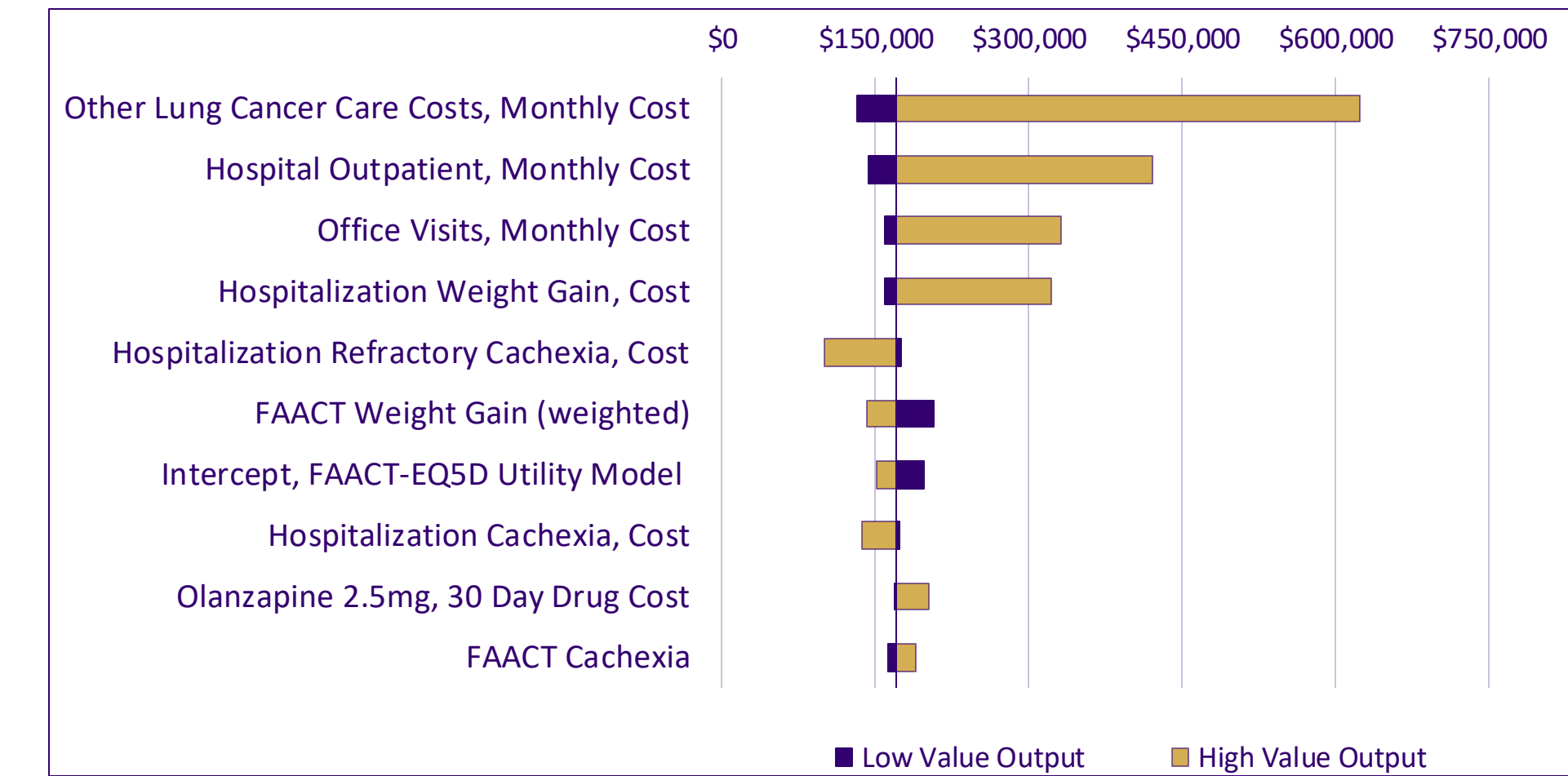
QALY: Quality-Adjusted Life Year

Conclusions

In this Markov model assessing the olanzapine versus standard of care in advanced NSCLC patients with cachexia, olanzapine was found unlikely to be cost-effective based on a typical willingness-to-pay threshold of $150,000 per QALY gained.[18] Cost of cancer care and health state utility are two big drivers highlighted by the OWSA that impact these model results.

Future research is needed to better understand cachexia progression in relation to cancer progression. More work is also needed to understand how the treatment and cost of cancer care changes as cachexia progresses.

Limitations

- Data from general cancers is assumed to be applicable to NSCLC.
- This model does not directly account for use of appetite-stimulating treatments like progesterone analogs or corticosteroids used for cachexia symptom management. Though, olanzapine does not preclude the use of these medications.
- Costs of olanzapine adverse reactions (ADR) were not included in this model as there were no significant difference in ADR profiles between treatment groups in Sandhya et al. Low ADRs likely attributable to low-dose olanzapine. In models with higher doses, ADR costs will likely need to be incorporated.

References

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