

## INTRODUCTION

- Obesity is one of the most prevalent chronic conditions in the United States.<sup>1,2</sup>
- Prevalence of obesity surpassed 40% of US adults in 2018.<sup>3</sup>
- Total estimated direct healthcare cost attributed to obesity is \$260 billion in the US in 2016.<sup>4</sup>
- Chronic obesity management includes diet/exercise interventions, behavioral therapy, surgical procedures, and medication therapies.<sup>5,6</sup>

## OBJECTIVE

To estimate the cost effectiveness of semaglutide (SEM), liraglutide (LIR), phentermine/topiramate (P/T), and bupropion/naltrexone (B/N) plus lifestyle modification (LSM) compared to standard LSM alone, and to each other, for life-long weight management in the treatment of overweight and obesity.

## METHOD

- We developed a decision model followed by Markov chains with lifetime time horizon, from a healthcare sector perspective, with a cycle length of one year.
- The study outcomes were direct health care costs in 2022 US dollars, quality adjusted life years (QALYs), life years, and equal-value life years (eVLYs). All the outcomes were discounted at an annual rate of 3%.

### Model Structure and population

- The model population includes adults with average BMI of 38 kg/m<sup>2</sup> and average age of 45 years.
- Patients without diabetes and without major adverse cardiovascular event at baseline could transition to states with diabetes, myocardial infarction (MI), stroke, other cardiovascular comorbidity (i.e., angina, transient ischemic attack, or peripheral vascular disease), and heart failure. [Figure 1]

### Model Inputs

- Drug-related weight-lowering effects were identified from a review and network meta-analysis of clinical trial results. [Table 1]
- Annual incidence of type 2 diabetes mellitus was calculated using exponential equation on BMI and HbA1C data.<sup>7-9</sup>
- Annual risk of developing cardiovascular conditions was calculated using the 2013 American College of Cardiology/ American Heart Association (ACC/AHA) guideline risk equation.<sup>10</sup>
- All other model inputs were sourced from peer-reviewed literature and publicly available data.

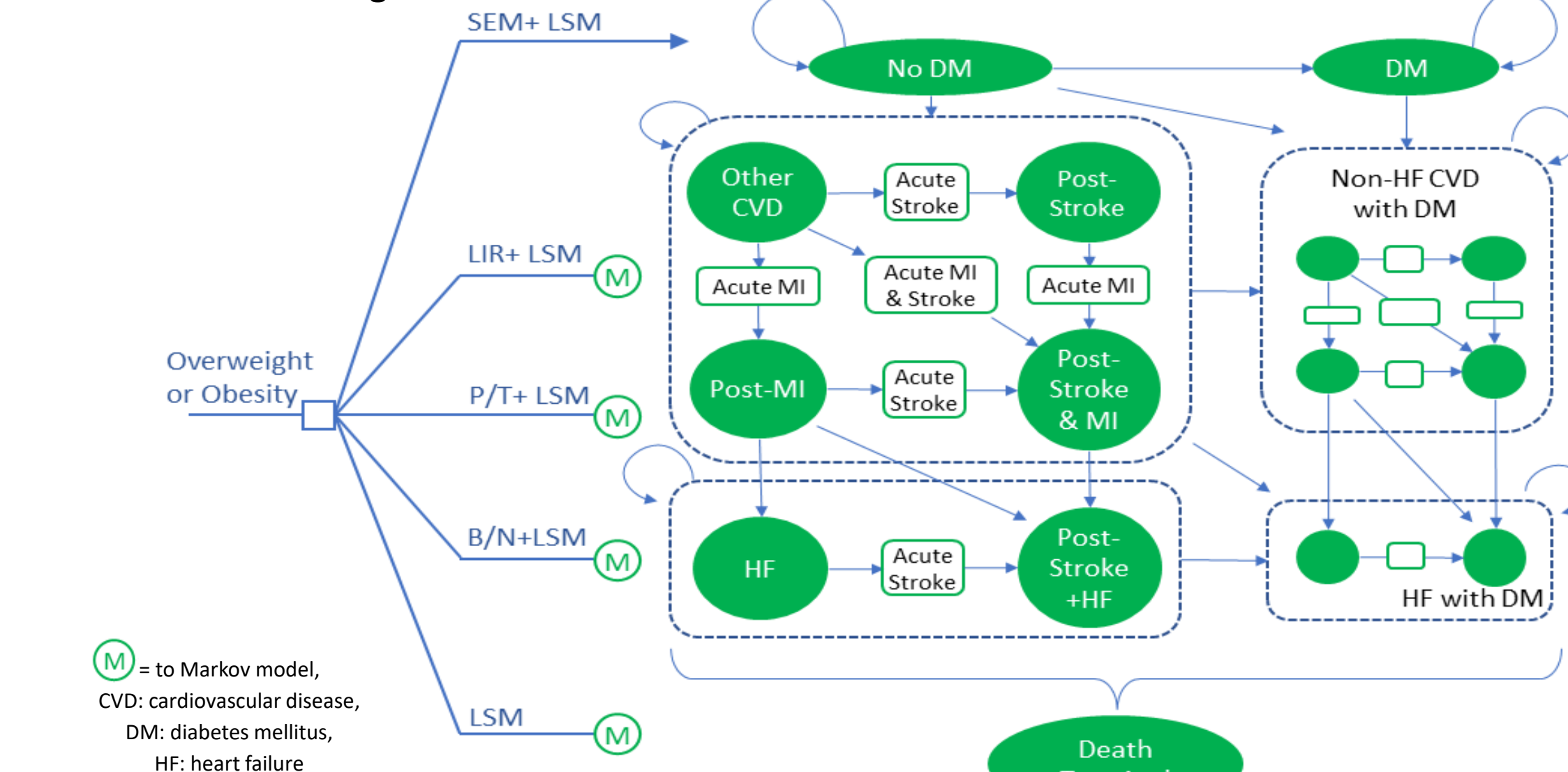
Table 1: Key Model Inputs

Value	Percentage
<b>Absolute Difference in % Weight Change</b>	
Semaglutide v. Lifestyle Modification	-13.7%
Liraglutide v. Lifestyle Modification	-5.0%
Phentermine/Topiramate v. Lifestyle Modification	-9.1%
Bupropion/Naltrexone v. Lifestyle Modification	-4.6%
<b>Absolute Difference in HbA1C Change (% points)</b>	
Semaglutide v. Lifestyle Modification	-0.30
Liraglutide v. Lifestyle Modification	-0.20
Phentermine/Topiramate v. Lifestyle Modification	0.00
Bupropion/Naltrexone v. Lifestyle Modification	0.00
<b>Probabilities of CV Conditions<sup>11</sup></b>	
Probability of MI from CV Risk	0.22
Probability of Stroke from CV Risk	0.23
Probability of Other CV Disease from CV Risk	0.55
<b>Cost Inputs (Annual)</b>	
Semaglutide	\$13,618
Liraglutide	\$11,760
Phentermine/Topiramate	\$1,465
Bupropion/Naltrexone	\$2,095
<b>Quality of Life Input</b>	
Disutility per BMI Unit Increase	-0.0033

### Additional Analyses

- Sensitivity Analysis: probabilistic and one-way sensitivity analyses of key inputs to examine uncertainty.
- Threshold Analysis: examine drug prices required to achieve cost-effectiveness thresholds ranging from \$50-200k per QALY and eVLY gained.

FIGURE 1: Model Diagram



## RESULTS: Base Case

- Lifetime cost, life years, QALY, and eVLYs estimates are presented in Table 2.
- Compared to LSM, the estimated incremental cost-effectiveness ratio (ICER) for SEM, LIR, P/T, and B/N were \$237k, \$483k, \$8k, and \$123k per QALY gained, respectively [Table 3]
- The cost-effectiveness plane [Figure 2] portrays the estimated cost and effectiveness in the base-case result for a particular therapy option added to lifestyle modification

Table 2: Discounted Base-Case Results

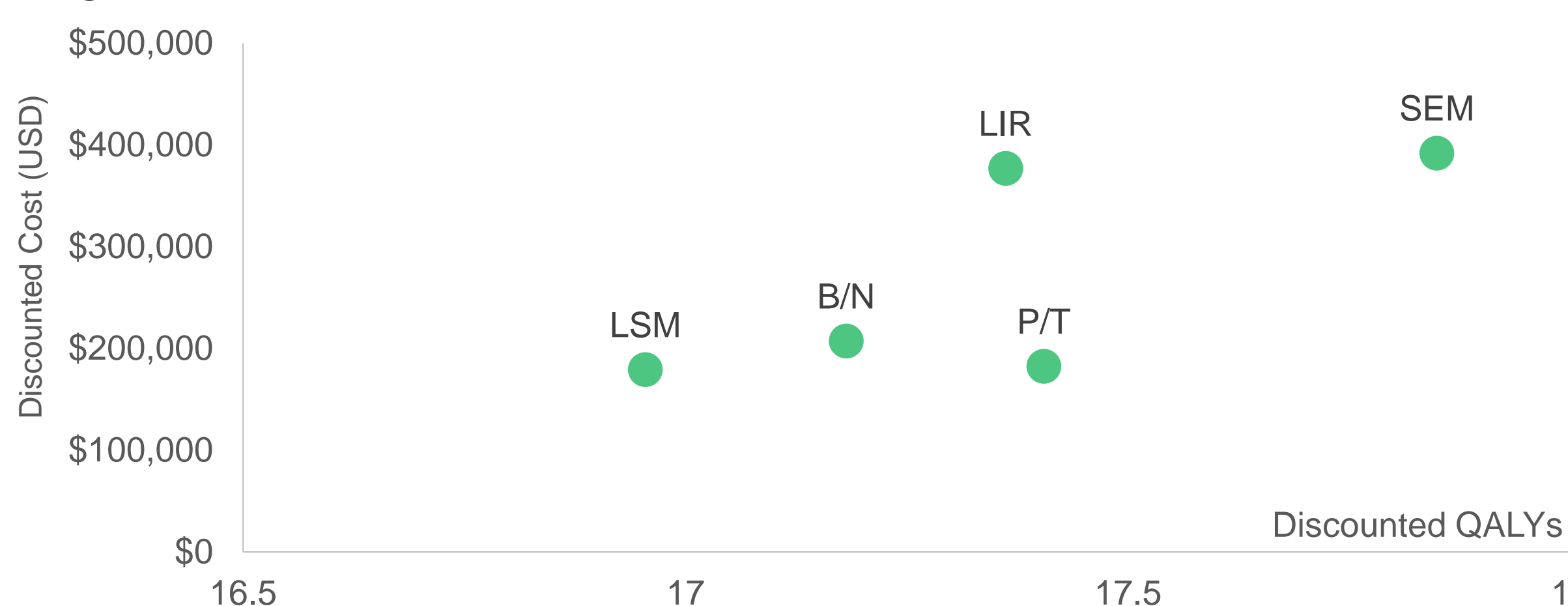
Treatment	Drug Cost	Non-Drug Cost	Total Cost	Life Years	QALYs	eVLYs
Semaglutide	\$285,800	\$106,200	\$392,100	21.04	17.83	17.84
Liraglutide	\$241,800	\$135,200	\$377,000	20.86	17.34	17.35
Phentermine/Topiramate	\$39,700	\$142,800	\$182,600	20.85	17.38	17.39
Bupropion/Naltrexone	\$52,200	\$155,100	\$207,300	20.78	17.16	17.16
Lifestyle Modification*	\$11,400	\$167,800	\$179,200	20.70	16.93	16.93

\*Reference for eVLY calculation for all active treatments.

Table 3: Incremental Cost-Effectiveness Ratios for the Base Case

Treatment	Comparator	Cost per Life Year Gained	Cost per QALY Gained	Cost per eVLY Gained
Semaglutide	Lifestyle modification	\$624,000	\$237,000	\$234,000
Liraglutide	Lifestyle modification	\$1,210,000	\$483,000	\$473,000
Phentermine/Topiramate	Lifestyle modification	\$22,000	\$8,000	\$7,000
Bupropion/Naltrexone	Lifestyle modification	\$360,000	\$123,000	\$121,000
Semaglutide	Liraglutide	\$85,000	\$31,000	\$31,000
	Phentermine/Topiramate	\$1,128,000	\$469,000	\$465,000
	Bupropion/Naltrexone	\$703,000	\$275,000	\$272,000

Figure 2: Cost-Effectiveness Plane



## RESULTS: Probabilistic Sensitivity Analysis

- Incremental cost-effectiveness scatterplots show results for 1,000 Monte-Carlo simulations [Figures 3a-d].
- Acceptability curves depict the proportion of cost-effective simulations at varying cost-effectiveness thresholds [Figures 4a-d].

Incremental Cost-Effectiveness Scatterplot

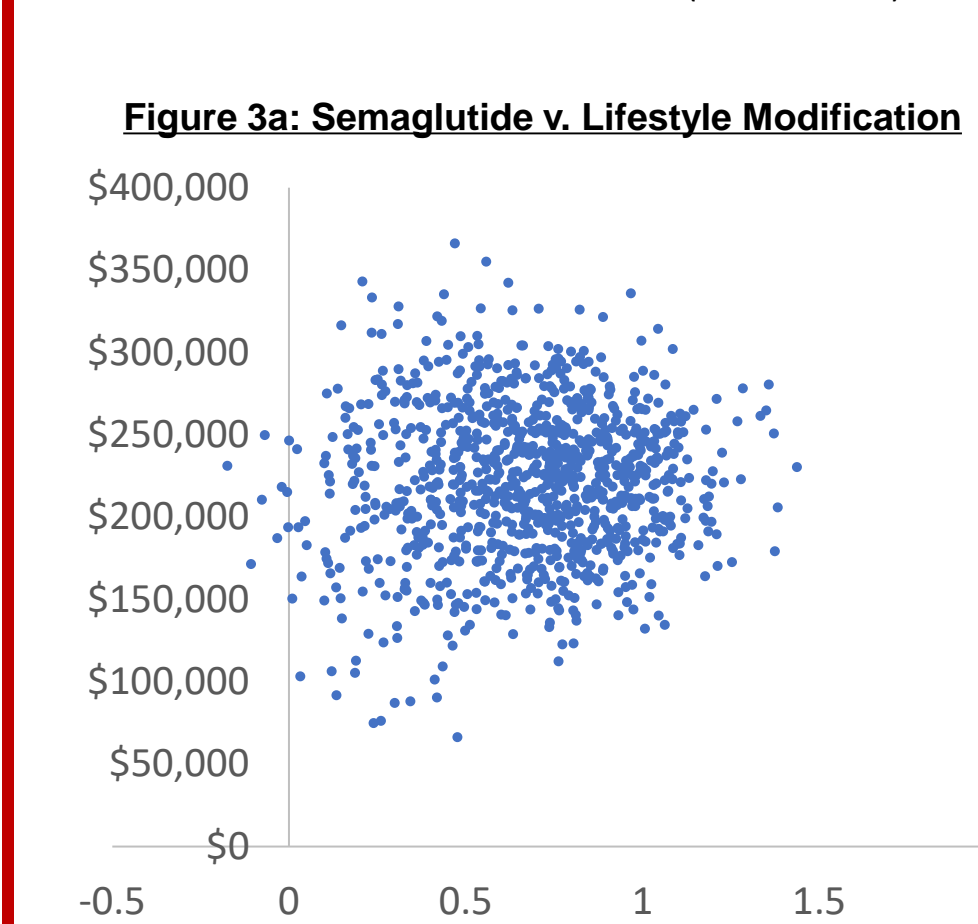


Figure 3b: Liraglutide v. Lifestyle Modification

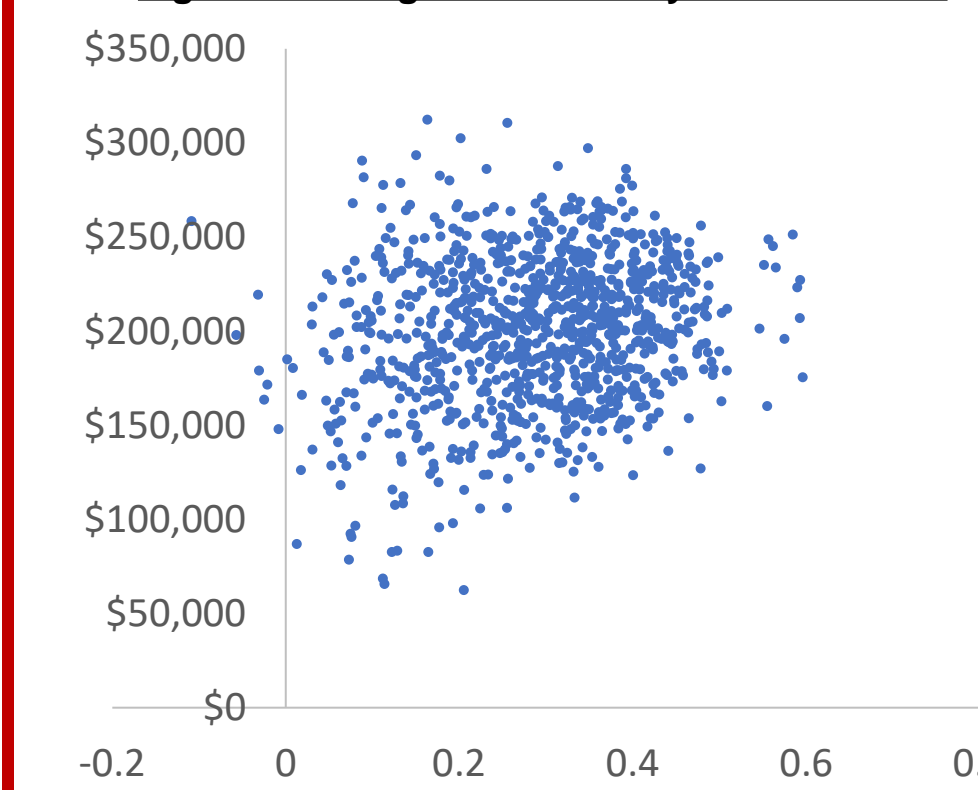
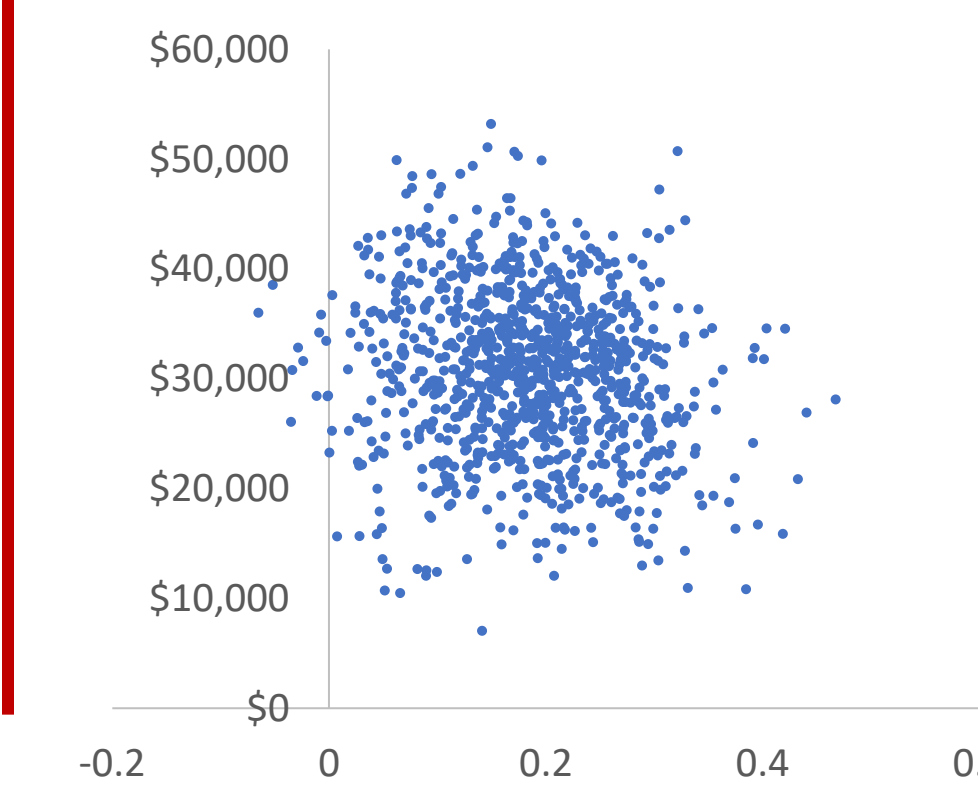


Figure 3c: Phentermine/Topiramate v. Lifestyle Modification



Figure 3d: Bupropion/Naltrexone v. Lifestyle Modification



Acceptability Curve

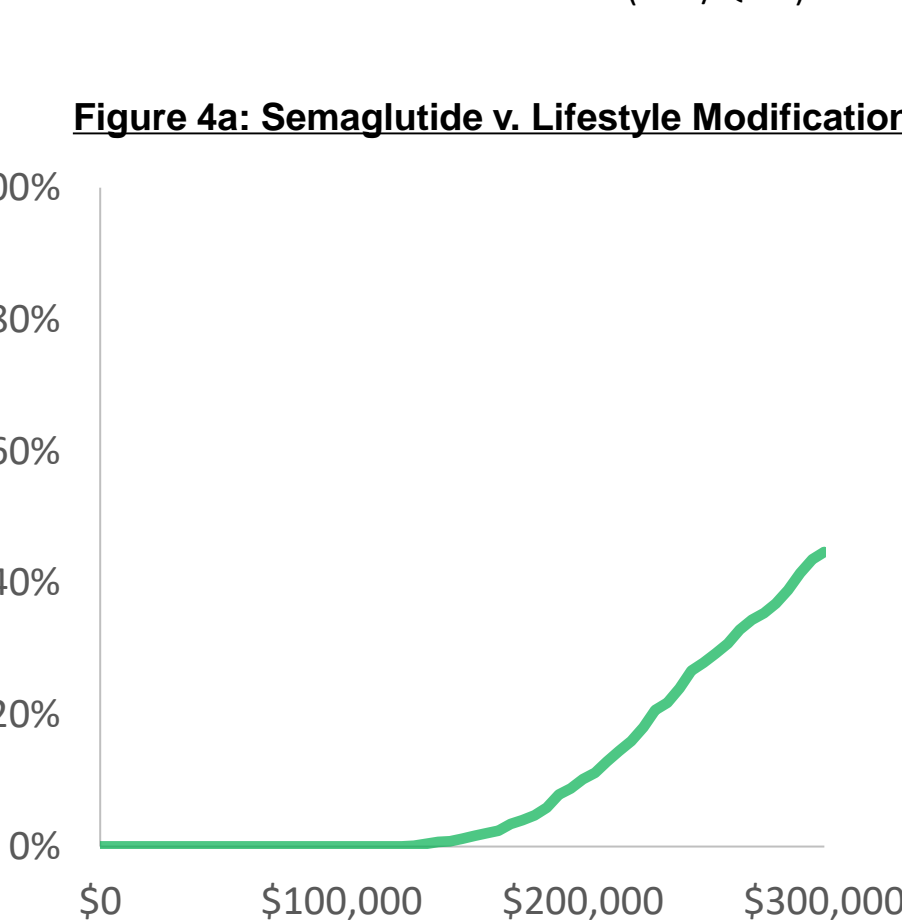


Figure 4b: Liraglutide v. Lifestyle Modification

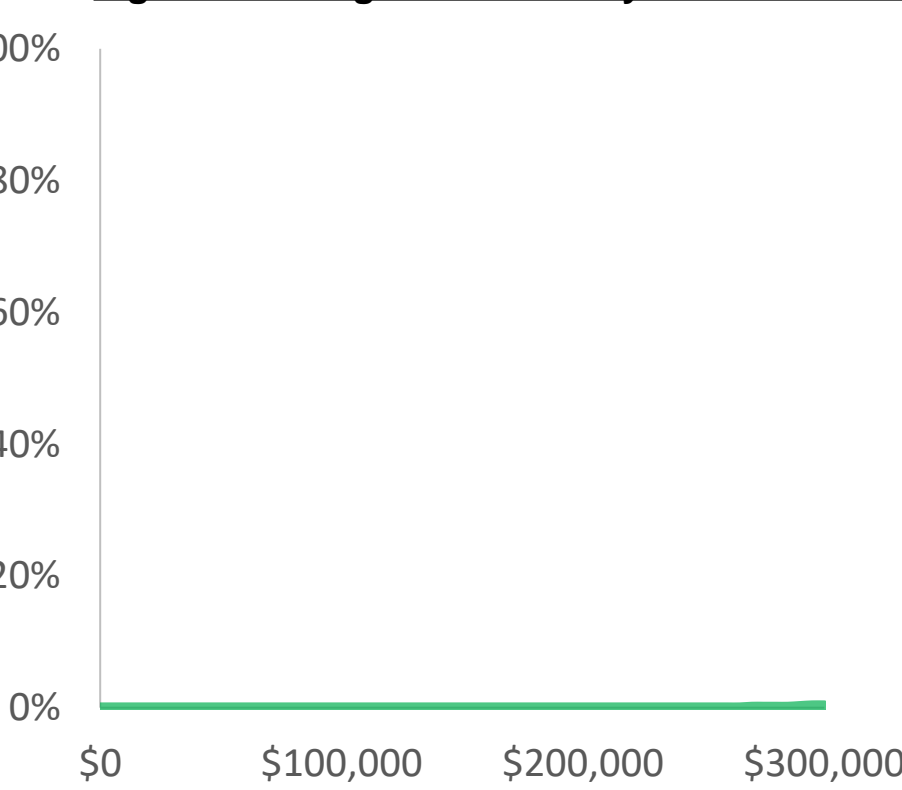


Figure 4c: Phentermine/Topiramate v. Lifestyle Modification

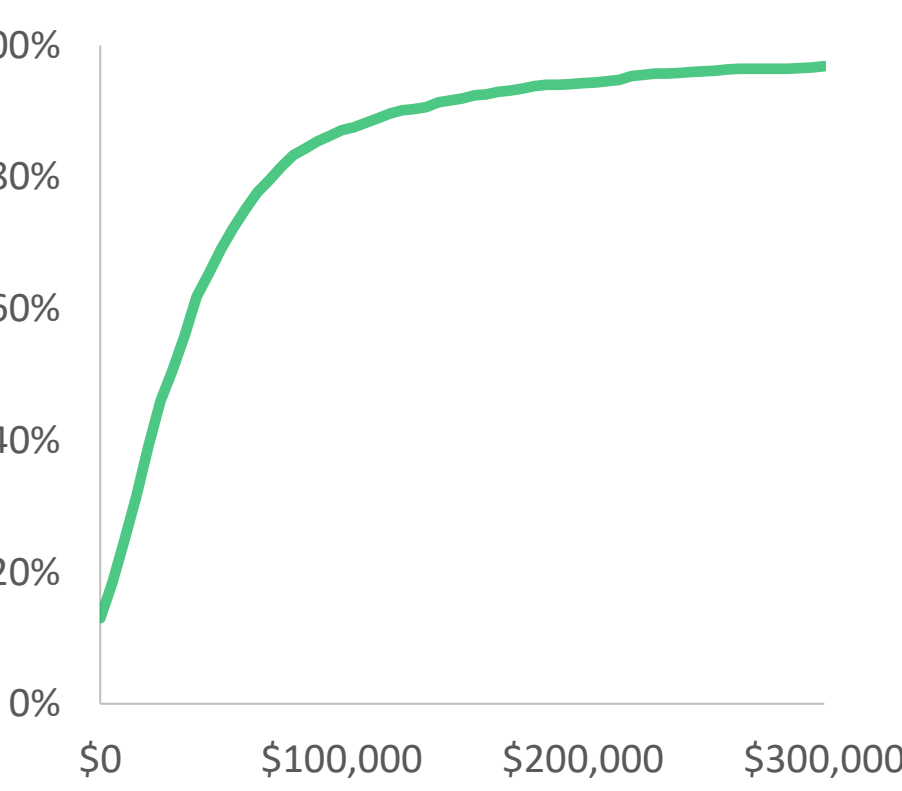
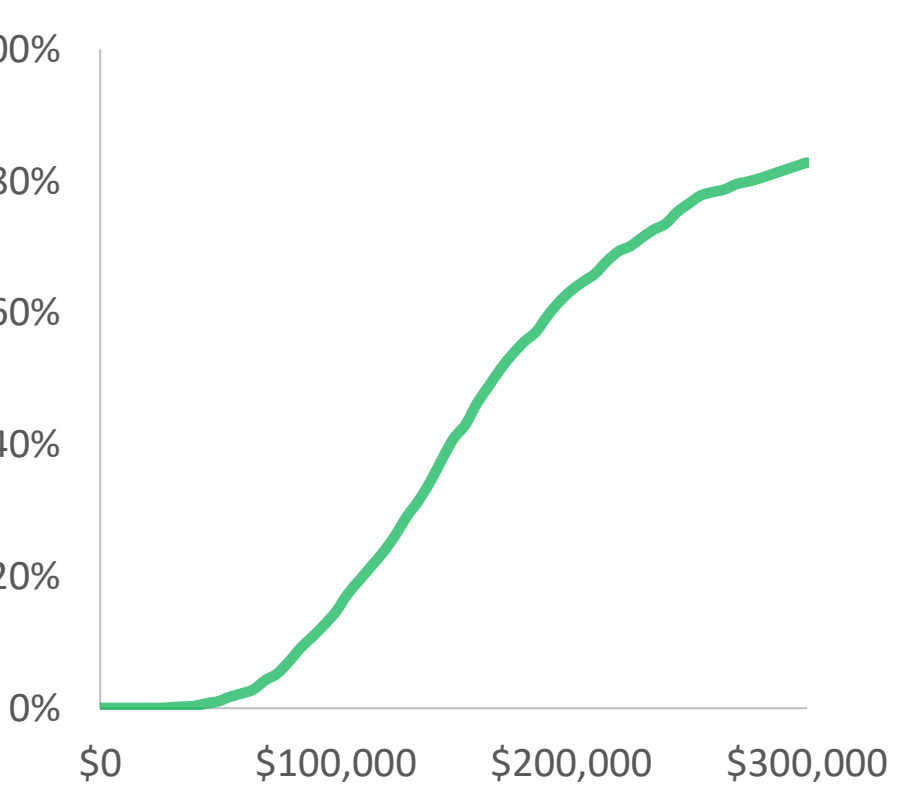


Figure 4d: Bupropion/Naltrexone v. Lifestyle Modification



## RESULTS: One-Way Sensitivity Analysis

- The model was sensitive to disutility per BMI change, effectiveness of each drug in achieving weight loss and/or HbA1c, baseline HbA1C, and cost of diabetes care. [Figure 5a-d]

Figure 5a: Semaglutide

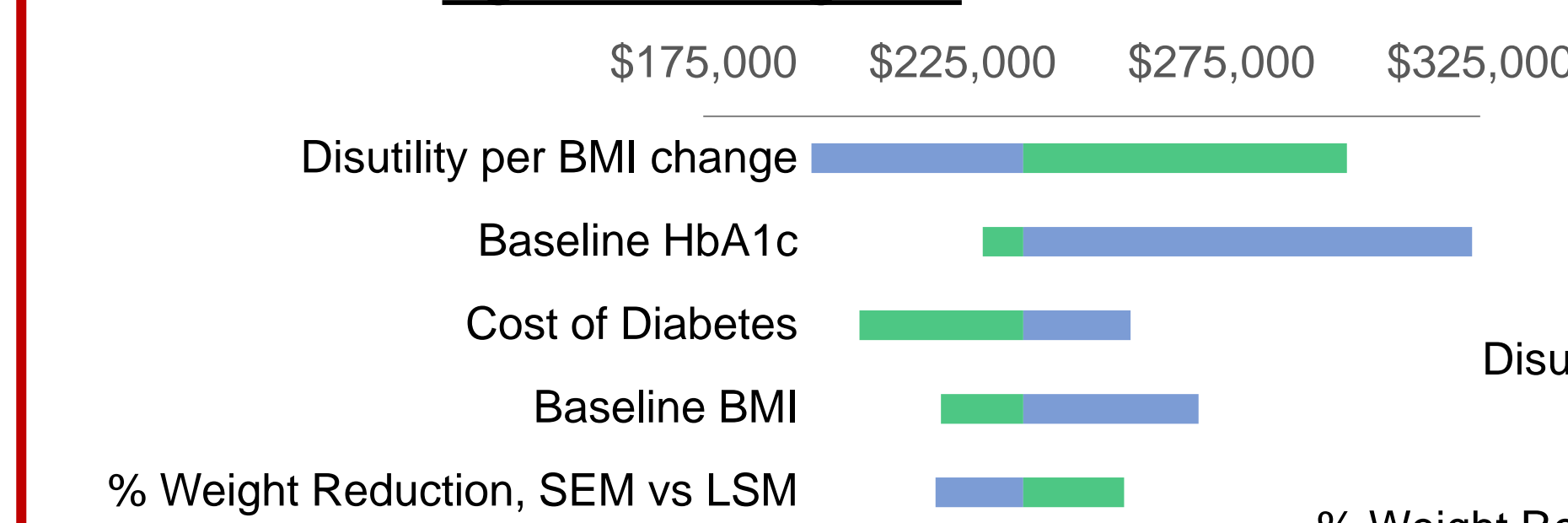


Figure 5b: Liraglutide

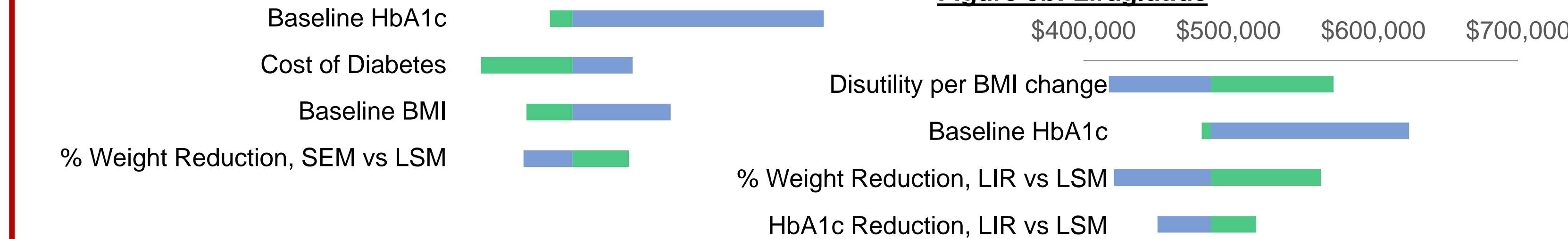


Figure 5c: Phentermine/Topiramate

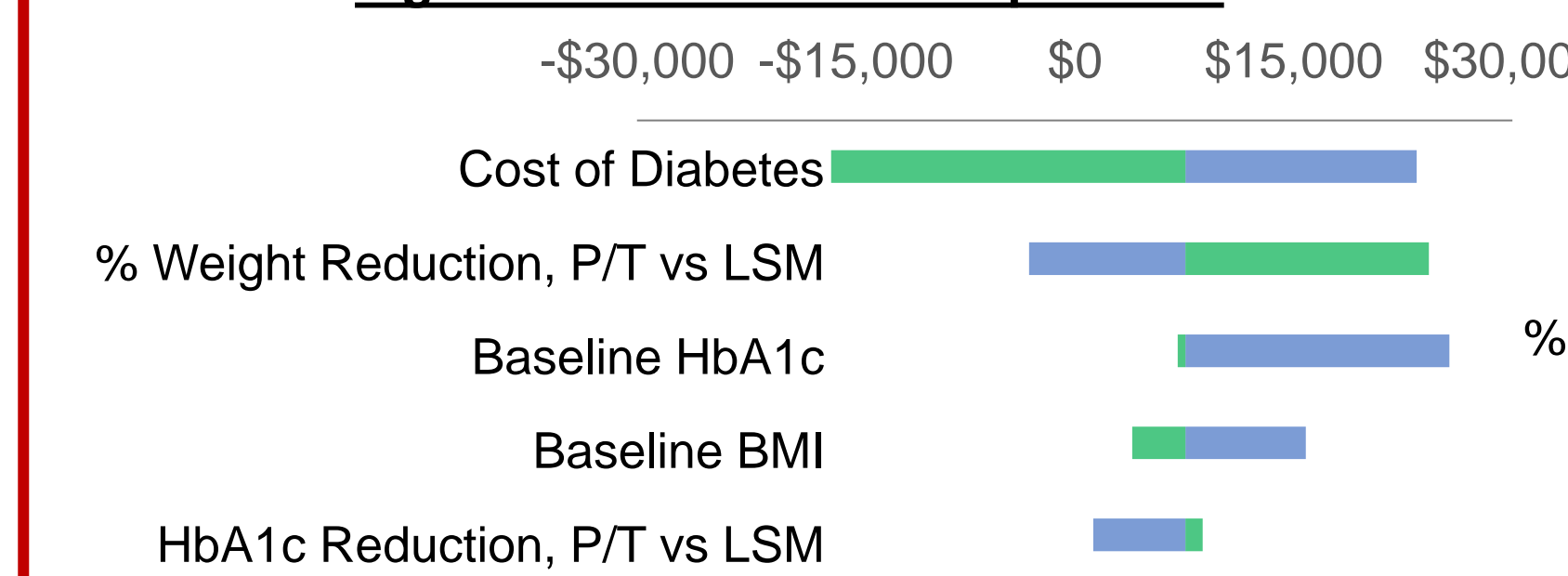
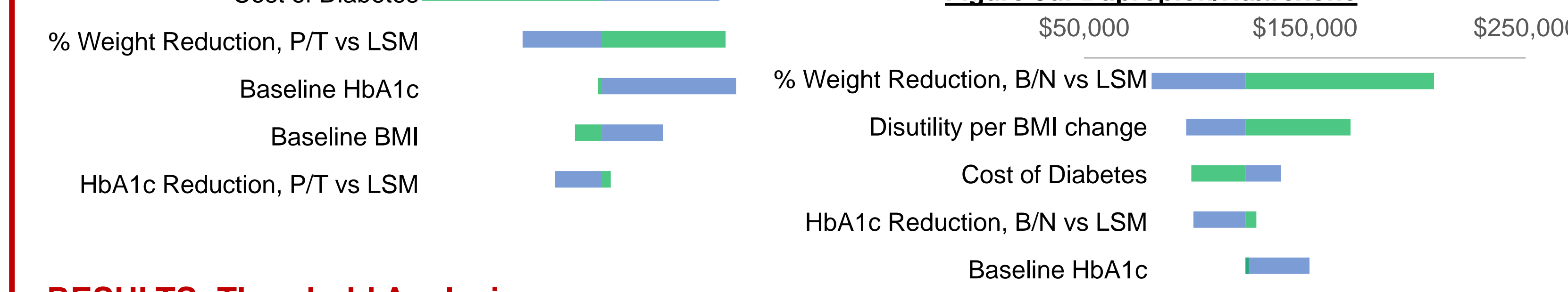


Figure 5d: Bupropion/Naltrexone



## RESULTS: Threshold Analysis

- Annualized prices required to achieve thresholds of \$50,000 to \$200,000 per QALY and eVLY gained are presented in Tables 4 and 5.

Table 4: QALY-Based Threshold Analysis Results

	Annual Net Price	Annualized Price to Achieve \$50,000 per QALY Gained	Annualized Price to Achieve \$100,000 per QALY Gained	Annualized Price to Achieve \$150,000 per QALY Gained	Annualized Price to Achieve \$200,000 per QALY Gained
Semaglutide	\$13,618	\$5,300	\$7,500	\$9,700	\$12,000
Liraglutide	\$11,760	\$2,700	\$3,800	\$4,800	\$5,900
Phentermine/Topiramate	\$1,465	\$2,500	\$3,600	\$4,800	\$5,900
Bupropion/Naltrexone	\$2,094	\$1,200	\$1,800	\$2,400	\$3,000
Lifestyle Modification		Reference			

Table 5: eVLY-Based Threshold Analysis Results

	Annual Net Price	Annualized Price to Achieve \$50,000 per eVLY Gained	Annualized Price to Achieve \$100,000 per eVLY Gained	Annualized Price to Achieve \$150,000 per eVLY Gained	Annualized Price to Achieve \$200,000 per eVLY Gained
Semaglutide	\$13,618	\$5,300	\$7,600	\$9,800	\$12,000
Liraglutide	\$11,760	\$2,700	\$3,800	\$4,900	\$5,900
Phentermine/Topiramate	\$1,465	\$2,500	\$3,600	\$4,800	\$6,000
Bupropion/Naltrexone	\$2,094	\$1,300	\$1,900	\$2,400	\$3,000
Lifestyle Modification		Reference			

## CONCLUSION

Long-term medication therapy to manage obesity may provide individuals with opportunities for sustained weight loss; however, semaglutide and liraglutide would generally require discounted prices to become a cost-effective life-long obesity management strategy.

## REFERENCES

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