Economic evaluation of weight loss medications compared to lifestyle therapy alone in weight loss management among postpartum women

Abstract

Objective: To evaluate the cost-effectiveness of weight loss medications (semaglutide, liraglutide, phentermine/topiramate, and bupropion/naltrexone) plus lifestyle therapy compared to lifestyle therapy alone in weight loss management among postpartum women.

Method: With a health care sector perspective, we developed a stochastic microsimulation model and projected outcomes of hypertension (HTN), cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) development at two timepoints of interest: 2-year postpartum and over the lifetime. Variations in model parameters were incorporated in one-way sensitivity analysis and probabilistic sensitivity analyses. All costs were inflation adjusted to 2021 U.S. dollars. Future costs and QALYs were discounted at 3% annually.

Main outcomes: Estimated T2DM, HTN, and CVD cases, estimated life expectancy, costs, QALYs-gained, and incremental cost-effectiveness ratio.

Results: Among a starting cohort of 10,000 postpartum women in the U.S., the mean age was 29 and mean BMI was 37.92 kg/m^2 (SD, 5.76). Over the lifetime, Semaglutide would avert 1440 HTN cases, 910 CVD cases. Phentermine/Topiramate would avert the highest number of T2DM cases (250) and second highest number of HTN cases (1160). Semaglutide produced the largest potential improvement in QALYs with a population-level increase of 3881.78 QALYs, followed by Phentermine/Topiramate with a population-level increase of 2251 incremental QALYs. Despite their positive impact on health outcomes, Semaglutide and Phentermine/Topiramate had incremental cost-effectiveness ratios of $1,854,987 per QALY and $113,035 per QALY, respectively. Neither were cost effective under the willingness-to-pay threshold of $100,000/QALY for the US. Bupropion/Naltrexone and Liraglutide were strongly dominated. Probability of Phentermine/Topiramate being cost-effective increased as WTP threshold and parameter varied in uncertainty analyses.

Limitations: This model carries limitations in its assumptions that medication will be taken over the lifetime without accounting for discontinuation. Additionally, the model is limited in its incorporation of pregnancy-related risks. Model parameters need to be refined to better represent the cohort of interest.

Conclusions: This economic evaluation found that while all 4 medication strategies offered substantial health benefits, none were cost-effective. As weight loss medications continue to increase in popularity and as more medications are approved, policy makers should place emphasis on reductions in medication costs to ensure equitable access to treatments.

Introduction

Obesity is an important public health issue in the United States. For two decades, from 1999 through 2018, prevalence of obesity (body mass index BMI 30kg/m^2 or higher) in the US increased from 30.5% to 42.4%, while the prevalence of severe obesity increased from 4.7% to 9.2%.[1] Obesity severely increases the risk of chronic diseases and conditions such as hypertension, type 2 diabetes mellitus (T2DM), coronary heart disease, stroke, and some cancers, making it a major driver of rising health care costs.[2] Obesity and its comorbidities also disproportionally affect women. Between 2021 and 2023, 41.3% of women aged 20 and older were obese.[3] Comorbidities like T2DM and hypertension have shown to demonstrate sex-specific pathways and are more strongly associated with obesity among women compared to men.[4]

Pregnancy and postpartum periods are particularly vulnerable times in a woman's life, involving substantial physiological and lifestyle changes. Increased BMI places women at higher risk for a host of perinatal outcomes such as gestational diabetes, hypertension, and preeclampsia, and complications during childbirth and recovery postpartum.[5] Additionally, pregnancy is a risk factor for women becoming overweight or obese as many women do not lose the weight they gain during pregnancy. In a study assessing postpartum weight retention and obesity at 1 year postpartum, researchers found that 75% of women in the study sample were heavier at 1 year postpartum compared to pre-pregnancy and 30% of women who were normal weight pre-pregnancy were overweight or obese at 1 year postpartum.[6] High postpartum weight retention places women at heightened risk for subsequent overweight and obesity in ensuing pregnancies and over the lifetime, as well as increased risk for chronic diseases.

Medication for the treatment of overweight and obesity has increased in popularity. Originally approved for diabetes treatment, semaglutide was the top drug in 2023 by expenditure.[7] The market for medical weight loss has risen exponentially in the past 5 years.[8] However, few existing studies on weight loss drugs have looked at postpartum women. In this study, we aim to evaluate the cost-effectiveness of weight loss medications (semaglutide, liraglutide, phentermine/topiramate, and bupropion/naltrexone) plus lifestyle therapy compared to lifestyle therapy alone in weight loss management among postpartum women.

Methods

Cohort

Our target population were postpartum women eligible for medical treatment of weight loss, i.e. adult postpartum women aged 18-40 with BMI⩾30kg/m2 and have not achieved a 5% weight loss despite 6 months of comprehensive lifestyle intervention. We simulated individuals from 6 months postpartum until death, with an additional timepoint of interest at 2 years postpartum. Through this model we aim to capture the health and economic effects of weight loss medications during postpartum and over a lifetime horizon.

Simulation model

We developed a stochastic microsimulation model to project hypertension (HTN), cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) development. The model is organized into

two dimensions: 1) cardiovascular states and 2) T2DM states. Figure 1 shows the health states and transitions between health states for each dimension. At any point in time, an individual resides in one health state in each dimension and moves between health states based on calculated annual transition probabilities that account for BMI. Treatment strategies have differential effects on percent weight change, which thereby affects the risk of HTN, CVD, and T2DM. Weight loss medications were assumed to be taken over the lifetime. We made a conservative assumption that weight loss occurs in the first cycle and maintains for the rest of lifetime. Patients with hypertension were assumed to be optimally controlled with antihypertensive medication. Since weight change is measured in absolute difference in percent weight change relative to LST only, effect of LST on weight and its annual cost were assumed to be zero. The study cohort is assumed to have no T2DM cases at cycle zero and no parental history of T2DM.

Comparison strategies

We compared four medication strategies (semaglutide, liraglutide, phentermine/topiramate, and bupropion/naltrexone) plus lifestyle therapy to lifestyle therapy alone. Appendix table 1 shows the tradeoffs between the medication strategies. Semaglutide and Liraglutide are administered subcutaneously using injection pens, while Burpropion/Naltrexone and Phentermine/Topiramate are oral pills. Frequency of administration varies between treatment strategies, as well as cost, effect on weight loss, and side effects.

Outcomes

We used QALYs as primary health outcome and total lifetime cost as primary cost outcome. Costs were assessed from the health care sector perspective and inflation adjusted to 2021 U.S. dollars. Future health and cost outcomes were discounted at 3% per year.[9] We evaluated the cost-effectiveness of each treatment strategy by estimating its ICER and assumed a $100,000 per QALY as the base-case cost-effectiveness threshold. Strategies with an ICER below this threshold were considered cost-effective. Secondary health outcomes included life expectancy and incremental HTN, CVD, and T2DM cases per 100,000 people.

Sensitivity Analyses

We conducted sensitivity analysis on the treatment strategy that showed highest likelihood of being cost-effective. We conducted a one-way sensitivity analysis to assess how ICER changes when varying effectiveness of treatment strategy on percent weight loss, disutility of HTN, cost of HTN, and cost of CVD. We additionally ran a probabilistic sensitivity analysis on cohort size of 1000 with 100 iterations using the distributions in our parameters.

Results

Our model cohort began with a mean age of 29 and mean BMI of 37.92 kg/m^2 (SD, 5.76). Table 2 and 3 shows estimated lifetime costs, QALYs, ICERs and health outcomes of the treatment strategies. In terms of incremental QALYs, Semaglutide produced the largest potential improvement with a population-level increase of 3881.78 QALYs. This is followed by Phentermine/Topiramate, which had a population-level increase of 2251 incremental QALYs relative to lifestyle therapy alone. Semaglutide had the largest potential improvement in HTN

and CVD outcomes and was estimated to avert 1440 HTN cases and 910 CVD cases. Phentermine/Topiramate had the highest number of T2DM (250) cases averted and the second highest number of HTN (1160) cases averted, while liraglutide had the second largest number of CVD cases (810) averted.

Compared to lifestyle therapy alone, treatment strategies produced positive health effects. However, ICER of Phentermine/Topiramate ($113,035 per QALY) and Semaglutide ($1,854,987 per QALY) exceeded the assumed WTP threshold of $100,000. Bupropion/Naltrexone and Liraglutide were strongly dominated as they had higher costs and lower effectiveness compared to Phentermine/Topiramate. Appendix table 2 and 3 shows results for the same outcomes at 2 years postpartum rather than lifetime. We draw similar conclusions in terms of costs, QALYs, and cost-effectiveness with the 2-year postpartum results. However, we observe greater variation in incremental cases averted.

Phentermine/Topiramate was the strategy with ICER closest to our cost effectiveness threshold. We, therefore, limited our sensitivity analyses to this strategy to assess how parameter uncertainty affects its cost effectiveness. Figure 3 shows one-way sensitivity analysis results where we selected 4 parameters to vary. We see that Phentermine/Topiramate cost-effectiveness was most sensitive to uncertainty in effectiveness of medication on BMI change, followed by disutility of HTN, cost of HTN, and cost of CVD. On the lower bound of effectiveness of Phentermine/Topiramate on change in BMI (i.e. a bigger drop in BMI), ICER is $84,500 per QALY, which is under our WTP threshold.

Figure 4 compares our comparison strategies and their proportion of cost-effectiveness by WTP. Below around $80,000 per QALY, lifestyle therapy has highest likelihood of being the optimal strategy. As the WTP threshold increases, likelihood of Phentermine/Topiramate being the optimal strategy rises and that of lifestyle therapy drops. As WTP increases above $80,000 per QALY, Phentermine/Topiramate becomes more likely than lifestyle therapy to be cost effective.

Discussion

In this study, we assessed the health, benefits, costs, and cost-effectiveness of weight loss medications among postpartum women at 2-year postpartum and over the lifetime. We found that treatment strategies produced positive clinical effects, however, they exceed the willingness-to-pay threshold at the base case. In additional sensitivity analyses, we find that Phentermine/Topiramate was likely to be cost-effective given variations in parameters and WTP threshold.

This analysis carried limitations. First, while the starting cohort age distribution is modelled to represent postpartum women in the US in 2021, the model did not incorporate pregnancy-related risk factors such as gestational diabetes and hypertension. This contributed to the 2-year postpartum results having little variation compared to results over the lifetime for costs, QALY and cost-effectiveness, as well as the wide variation in clinical outcomes. Additionally, the model does not account for discontinuation rates over the lifetime and disutility from medication side effects. Finally, the current model assumes a starting cohort with no T2DM and assumes no parental history of T2DM. This along with parameter sources need to be refined.

This is the first study to assess cost effectiveness of weight loss medication among women postpartum, a particularly vulnerable time involving substantial physical, psychological, and lifestyle changes. Comparing our results to published CEAs with focus on general population in the U.S.[10,11,12], our results were consistent on findings related to clinical effectiveness, specifically all treatment strategies produced positive estimated effects on health outcomes and QALYs. Lee et al. 2024 and Lim et al. 2023 both identified Phentermine/Topiramate as the cost-effective pharmacologic weight-loss strategy[12,11]. Hwang et al. 2025 identified Bupropion/Naltrexone as cost-saving among their compared strategies[10]. These published studies all identified Semaglutide as most clinically effective in reducing BMI but was too costly to be considered cost-effective in the US context.

Conclusions

This economic evaluation found that while all 4 medication strategies offered substantial health benefits, none were cost-effective. As weight loss medications continue to increase in popularity and as more medications are approved, policy makers should place emphasis on reductions in medication costs to ensure equitable access to treatments.

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Figure 1. Model Schematic

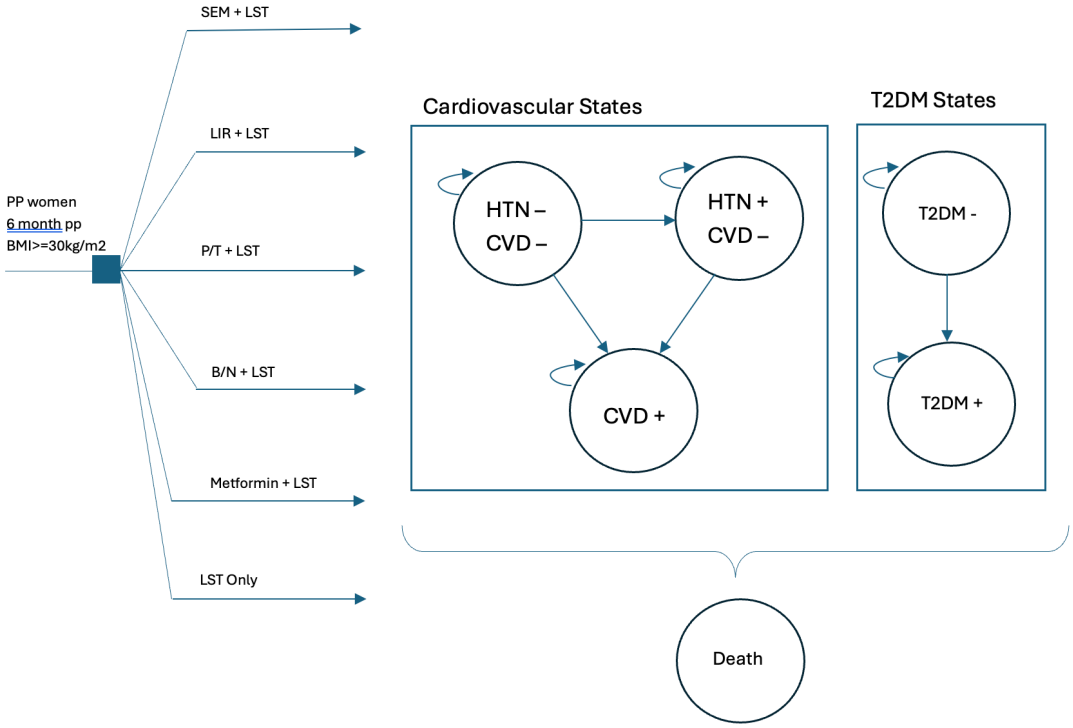


Table 1. Model variables with base-case values and ranges used in one-way sensitivity analysis

Parameter	Input	Source
Mean Age	29	2021 birth rate, National population by age distribution
Mean BMI (SD)	37.92 kg/m^2 (5.76)	CONQUER[1], EQUIP[2], COR-I[3], SCALE[4], STEP 1[5], STEP 8[6],
Mean systolic BP (SD)	124.11mmHg (12.71)	
Diagnosis of T2DM	0%	Assumption
Prevalence of Smoking 3m pp	0.07	Allen et al. 2025[7]
Starting Prevalence		
probability of starting healthy	1-p_htn-p_cvd	
Age-adjusted prevalence of HTN among women in US in 2017-2020 (4year)	0.467	Martin et al. 2025[8]
Prevalence of CVD excluding HTN overall, 2017-2020 NHANES (4year)	0.099	
Disease Attributable Mortality Rate		
Age-adjusted mortality rate attributable to CVD (include htn),	183.1 (182.6–183.7)	Martin et al. 2025[8]

female, 2022 (per 100,000)		
Age-adjusted mortality rate attributable primarily to HBP, female, 2022 (per 100,000)	27.6 (27.4–27.8)	
Age-adjusted mortality rate attributable to diabetes, female, 2022 (per 100,000)	18.8 (18.6–18.9)	
Absolute difference in % weight change		
Mean (95% CI) diff in kg weight change LST	0	Assumption
Absolute diff in % weight change SEM vs. LST	-0.137	ICER REPORT 2022[9]
Absolute diff in % weight change LIR vs. LST	-0.05	
Absolute diff in % weight change P/T vs. LST	-0.091	
Absolute diff in % weight change B/N vs. LST	-0.046	
Absolute diff in % weight change Met vs. LST		
Transition Probability		
4yr Risk of HTN	1-exp(-exp((log(4)-(22.9495-0.1564*(age_initial+t)-0.2029*1-0.0593*SBP-0.1285*DBP-0.1907*smoke-0.1661*0-0.0339*BMI+0.0016*(age_initial+t)*DBP))/0.8769))	Framingham Heart Study: Parikh et al. 2008[10]
10yr Risk of CVD	1-0.94833^exp((2.72107*log(age_initial+1)+0.51125*BMI+2.88267*log(SBP)+0.61868*smoke+0.77763*n_t2dm)-29.4016)	Framingham Heart Study: D'Agostino et al. 2008[11]
7year Risk of diabetes	1/(1+exp(-(-5.517-0.018*if((age_initial+t>=50) & (age_initial+t<=64),1,0)-0.081*if(age_initial+t>=65,1,0)+0.301*if((BMI>=25) & (BMI<=29.9),1,0)+0.92*if(BMI>=30,1,0)+0.498*if(SBP>130,1,0)+0.944*if(hdlc<50,1,0)+0.575*if(triglyceride>=150,1,0)+1.98*if((fglucose>=100) & (fglucose<=126),1,0))))	Framingham Heart Study: Wilson et al. 2007 [12]
Utility Input		
Utility Normal BMI	0.9442- 0.0007×Age	ICER Report[9]

Disutility per BMI increase	0.0033	
multiplicative proportion of Other CVD	0.55	
multiplicative proportion of MI	0.22	
multiplicative proportion of Stroke	0.23	
Disutility of Other CVD (Heart Disease), additive beta (SD)	-0.014 (0.0001)	Sullivan et al. 2005[13]
Disutility of MI, additive beta (SD)	-0.012 (0.0002)	
Disutility of Stroke, additive beta (SD)	-0.04 (0.0002)	
Disutility of HTN, additive beta (SD)	-0.02 (0.0001)	
Disutility of T2DM, additive beta (SD)	-0.024 (0.0001)	
Cost Input		
Average annual per capita cost of Coronary Heart Disease, 2021 dollars	12143.29 (681.89)	Kazi et al. 2024[14]
Average annual medical expenditure attributable to patients with T2DM, 2021 dollars	$11,230	Parker et al. 2024[15]
unadjusted mean annual medical expenditure attributable to patients with HTN, 2021 dollars	10200.69 (9988.58, 10412.81)	Kirkland et al. 2018[16]
Cost of Life Style Therapy	0	Assumption
Cost of Semaglutide	13618	ICER report[9]
Cost of Liraglutide	11309	
Cost of Phentermine/Topiramate	1355	
Cost of Bupropion/Naltrexone	2034	

Table 2. Estimated lifetime Costs ($), quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios ($/QALY) of weight loss medications for base-case analysis

Strategy	Cost	QALE	ICER	Notes
Lifestyle Therapy (LST)	$ 1,777,367,450.01	210198.3868	---	Baseline
Phentermine/Topiramate + LST	$ 2,031,767,246.58	212449.003	113035.6185	
Bupropion/Naltrexone + LST	$ 2,254,721,580.14	211182.3747	---	Strongly Dominated
Liraglutide + LST	$ 4,552,268,936.26	211159.4478	---	Strongly Dominated
Semaglutide + LST	$ 5,057,530,379.98	214080.153	1854987.659	

Table 3. Estimated lifetime health outcomes

Strategy	Life Expectancy (mean (SD))	#HTN cases per 100,000 people	Incremental HTN cases	#CVD cases per 100,000 people	Incremental CVD cases	#T2DM cases per 100,000 people	Incremental T2DM cases
Lifestyle Therapy	51.56 (14.1)	77570	Ref	9640	Ref	14120	Ref
Phentermine/Topiramate	51.27 (14.25)	76410	-1160	9230	-410	13870	-250
Bupropion/Naltrexone	51.35 (14.17)	77270	-300	9560	-80	14230	110
Liraglutide	51.23 (14.1)	76780	-790	8830	-810	14160	40
Semaglutide	51.35 (14.25)	76130	-1440	8730	-910	13980	-140

Figure 2. Cost-effectiveness plane

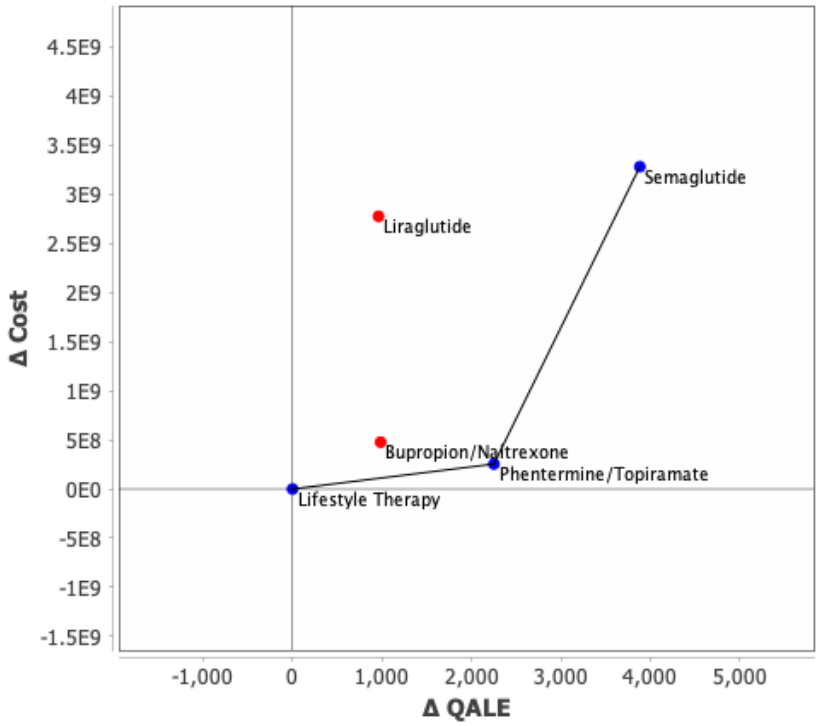


Figure 3. Tornado Diagram of one-way sensitivity analysis by Incremental Cost Effectiveness Ratio for Phentermine/Topiramate

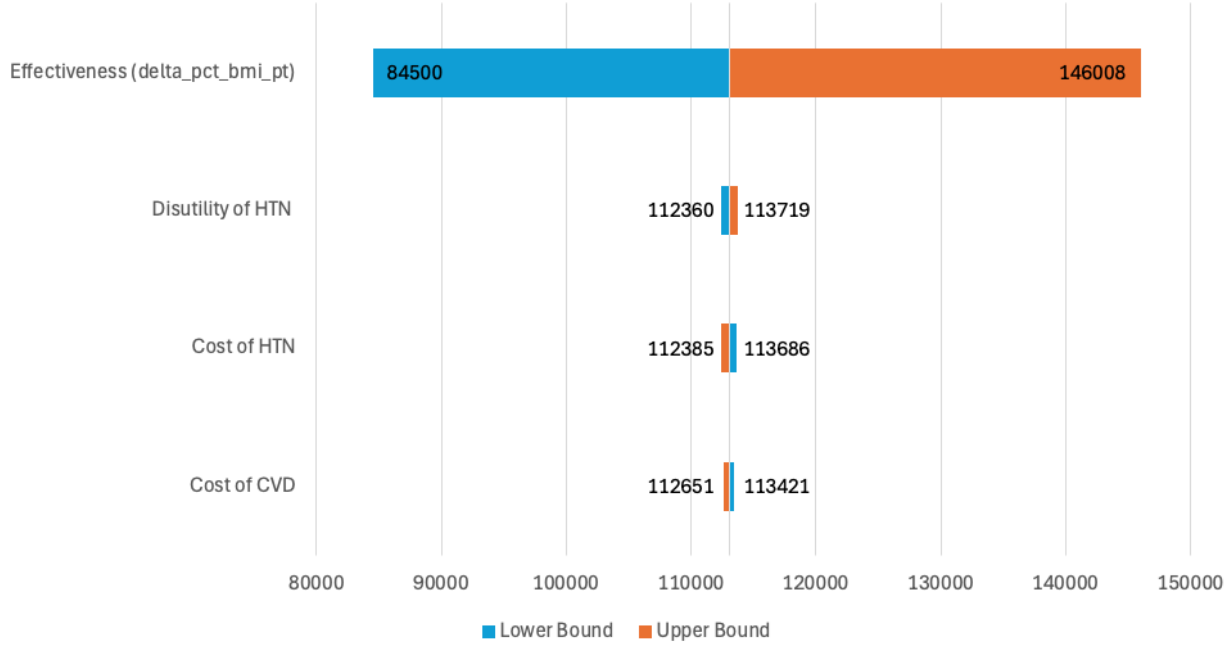
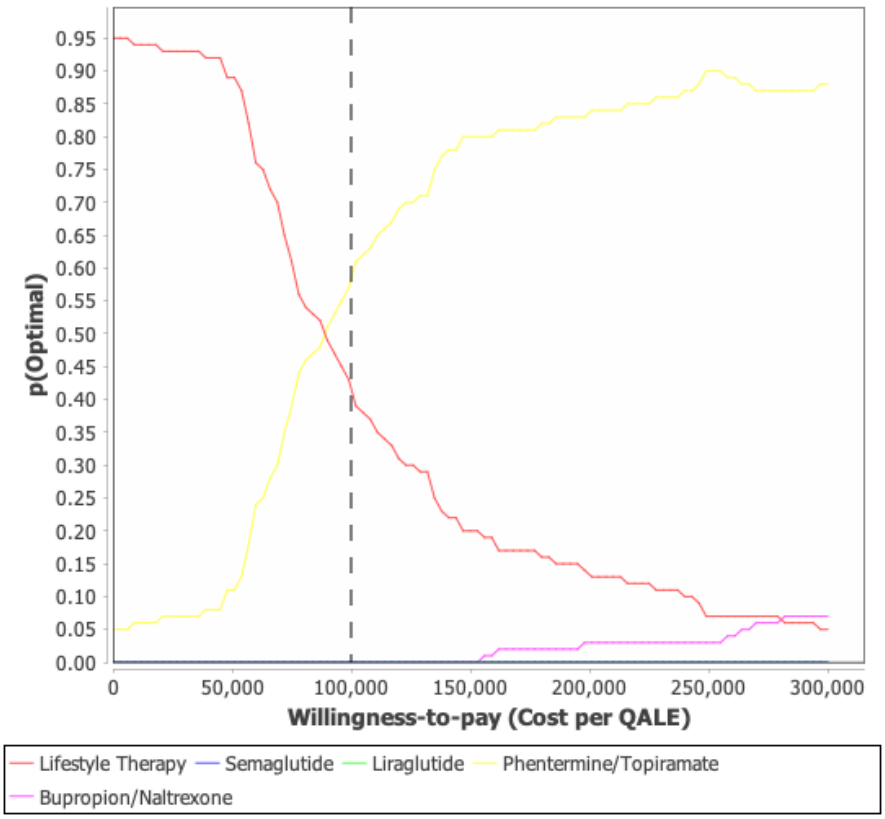


Figure 4. Probabilistic Sensitivity Analysis Cost-effectiveness acceptability curve with second-order uncertainty, n=1000, 100 PSA's



Appendix Table 1. Strategy comparisons and trade-offs

Strategy	Mechanism of Action	Route	Frequency	Annual Cost (net price, ICER report, US FSS database)	Difference in % weight loss at 1 yr compared to placebo *	Common side-effects
Semaglutide	GLP-1 receptor agonist	Subcutaneous	Weekly	$13,618	-13.7 (-12.6 to -15.1)	GI side effects: Nausea, vomiting, diarrhea, constipation, abdominal pain, headache, fatigue, GERD
Liraglutide	GLP-1 receptor agonist	Subcutaneous	Daily	$11,309	-5.0 (-3.9 to -6.1)	GI side effects similar to Semaglutide
Bupropion/Naltrexone	Combination opioid antagonist/aminoketone antidepressant	Oral	Daily	$2,034	-4.6 (-3.0 to -6.0)	Blurred vision, discouragement, dizziness, fear or nervousness, feeling sad or empty, headache, irritability, loss of interest or pleasure, insomnia, trouble concentrating, fatigue
Phentermine/Topiramate	Central Nervous System stimulant/carbonic anhydrase inhibitor and glutamate receptors antagonist	Oral	Daily	$1,355	-9.1 (-7.1 to -11)	Dysgeusia (taste disorder), insomnia, constipation, dry mouth, Paresthesia (tingling), dizziness,

**among participants with obesity alone; source: ICER report 2022.*

Appendix Table 2. Estimated 2-year postpartum Costs ($), quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios ($/QALY) of weight loss medications for base-case analysis

Strategy	Cost	QALE	ICER	Notes
Lifestyle Therapy	$ 39,498,875.32	16313.5622	---	Baseline
Phentermine/Topiramate	$ 64,286,838.08	16526.6785	116311.9118	
Bupropion/Naltrexone	$ 77,433,040.90	16419.5467	---	Strongly Dominated
Liraglutide	$ 252,018,805.69	16428.8194	---	Strongly Dominated
Semaglutide	$ 295,102,917.61	16633.3992	2162804.474	

Appendix Table 3. Estimated 2-year postpartum Health Outcomes

Strategy	#HTN cases per 100,000 people	Incremental HTN cases	#CVD cases per 100,000 people	Incremental CVD cases	#T2DM cases per 100,000 people	Incremental T2DM cases
Lifestyle Therapy	9070	Ref	460	Ref	1050	Ref
Phentermine/Topiramate	7940	-1130	480	20	930	-120
Bupropion/Naltrexone	8810	-260	500	40	1020	-30
Liraglutide	8480	-590	460	0	1080	30
Semaglutide	7650	-1420	480	20	980	-70

Reference (Tables, exhibits, and appendix)

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CHEERS 2022 Checklist

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Page 1, before abstract
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Page1
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	under Introduction
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Methods, simulation model
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methods, cohort
Setting and location	6	Provide relevant contextual information that may influence findings.	Methods, cohort
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methods, comparison strategies
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Methods, outcomes
Time horizon	9	State the time horizon for the study and why appropriate.	Methods, simulation model
Discount rate	10	Report the discount rate(s) and reason chosen.	Methods, outcomes

Topic	No.	Item	Location where item is reported
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methods, outcomes
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Methods, outcomes
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Methods, outcomes
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Methods, outcomes
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methods, outcomes
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Methods, simulation model
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methods, simulation model
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Not Applicable
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Not Applicable
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Methods, Sensitivity Analyses
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Not Applicable
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Tables and exhibits; Table 1

Topic	No.	Item	Location where item is reported
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Results, paragraph 1-2
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Results, paragraph 3-4
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Not Applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Discussion
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Not Applicable
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Not Applicable

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