Cost-Effectiveness Analysis of Orforglipron and Semaglutide for the Treatment of Adults with Obesity in the United States

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BACKGROUND

- Obesity increases the risk of type 2 diabetes, hypertension, and cardiovascular events.[1]
- Glucagon-like peptide-1 (GLP-1) receptor agonists have become central to obesity management.
- The FDA approved orforglipron, an oral GLP-1 receptor agonist on April 1, 2026.
- Oral semaglutide was first approved by the FDA in September 2019 to improve blood sugar control in adults with type 2 diabetes. Later, in December 2025, the FDA approved an oral formulation of semaglutide for chronic weight management.
- However, the cost-effectiveness of oral GLP-1 formulations has not been investigated.

OBJECTIVE

- To conduct a cost-effectiveness analysis comparing oral semaglutide and orforglipron as adjuncts to lifestyle modification (LSM) versus LSM alone from a healthcare sector perspective in the US adult population with obesity.

METHODS

Study Design:

- Model: Cohort state-transition Markov model developed in Microsoft Excel
- Clinical events modeled: Myocardial infarction, stroke, heart failure, diabetes progression, and cardiovascular death.
- Time horizon: 10 years
- Cycle length: 3-months
- Discounting: 3% annually for costs and outcomes

Data Sources:

- Treatment efficacy: Obtained from ATTAIN-1 and OASIS-4 clinical trials.[2,3]
- Mean body weight reduction: semaglutide 13.6%; orforglipron 11.2%.[2,3]
- Transition probabilities: Cardiovascular event risks were estimated using office-based Framingham risk equations incorporating age, sex, systolic blood pressure, BMI, smoking status, hypertension treatment, and diabetes.[4]
- Costs and utilities: Obtained from published U.S. literature; all costs were inflated to 2024 U.S. dollars
- We assumed price parity for semaglutide and orforglipron
- Base-case annual treatment costs: oral semaglutide/orforglipron $6,829; lifestyle modification $605.

Analysis:

- Base-case analysis: 1-year weight-loss phase followed by a weight-maintenance phase with continued therapy and sustained weight reduction
- Sensitivity analyses: One-way and probabilistic sensitivity analyses (PSA) varying costs of acute and chronic events, utilities, discontinuation, and drug pricing assumptions.

Outcomes:

- Quality-adjusted life-years (QALYs), cardiometabolic disease-free life-years (DFLYs), costs, and ICERs
- Cost-effectiveness was assessed using the ACC/AHA willingness-to-pay (WTP) threshold of $120,000 per QALY gained.[5]

RESULTS

TABLE 1: 10-year time horizon costs and health outcomes

	Total			Incremental			ICER
Treatment	**Costs, $**	**QALY**	**DFLY**	**DFLY**	**Costs, $**	**QALYs**	**ICER ($/QALY)**
Semaglutide + LSM	61,986	7.48	7.40	0.95	40,213	0.28	141,143
Orforglipron + LSM	58,892	7.43	7.32	0.87	37,119	0.23	161,466
LSM only	21,773	7.20	6.45	-	-	-	-

Note: All incremental outcomes are calculated relative to lifestyle modification (LSM) alone. We modeled sustained weight maintenance over 10-years. Patients continued to incur maintenance-phase treatment costs beyond year 1. Abbreviation: LSM – lifestyle modification, QALY -quality-adjusted life-years, DFLY – disease-free life-years, ICER – incremental cost-effectiveness ratio.

KEY FINDINGS

31%
Probability of semaglutide being cost-effective at a WTP threshold of $120,000 per QALY gained

76%
Probability of semaglutide being cost-effective at a WTP threshold of $200,000 per QALY gained

$141,143
Semaglutide: ICER

23%
Probability of orforglipron being cost-effective at a WTP threshold of 120,000 per QALY gained

67%
Probability of orforglipron being cost-effective at a WTP threshold of 200,000 per QALY gained

$161,466
Orforglipron: ICER

Note: Probabilities derived from PSA.

DISCUSSION/IMPLICATIONS

- Orforglipron and semaglutide extend the duration of cardiometabolic health (improvements in cardiometabolic disease-free life-years) compared to LSM alone, but oral semaglutide provides a slightly greater benefit than orforglipron.
- To be cost-effective at $120,000/QALY, the annual treatment cost for semaglutide plus LSM and orforglipron plus LSM may not exceed $6,572 and $5,968, respectively.
- Compared to LSM alone, semaglutide plus LSM and orforglipron plus LSM were not cost-effective at $6,829, and a WTP threshold of $120,000 per QALY gained. Both drugs may offer greater value in groups with a higher baseline risk; hence, policymakers and payers may consider risk-targeted coverage or value-based pricing to improve affordability.

FIGURE 1: one-way sensitivity analyses for semaglutide

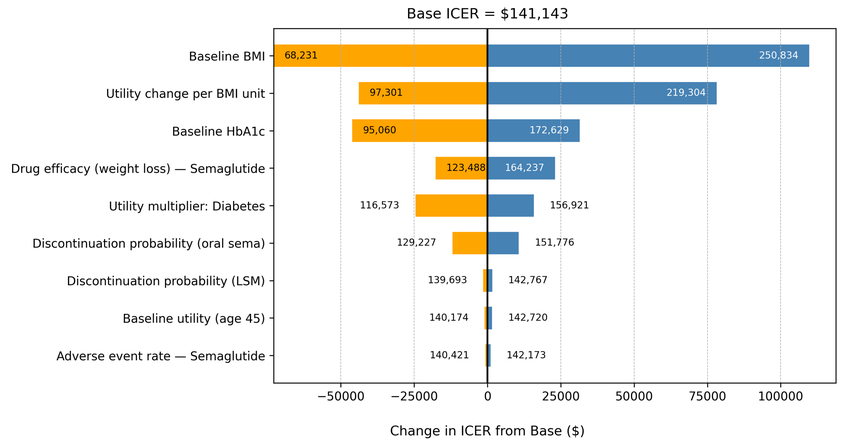
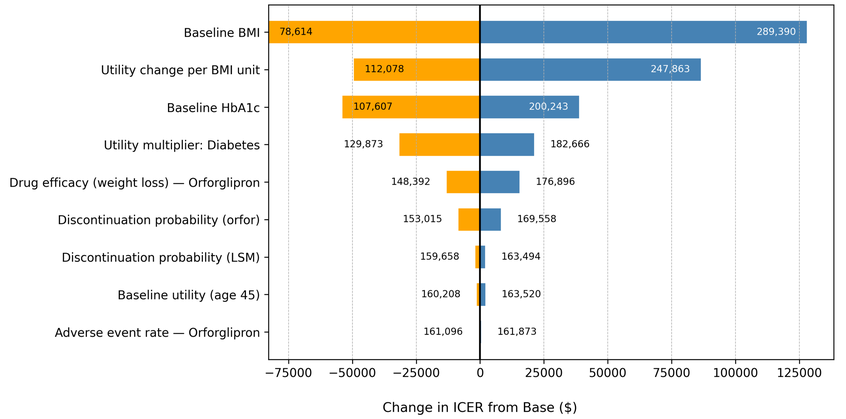


FIGURE 2: One-way sensitivity analyses for orforglipron



LIMITATIONS

- Our analyses focused on outcomes related to cardiovascular disease and diabetes.

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