Cost-Effectiveness of Semaglutide 2.4 mg and Tirzepatide for Treatment of Obesity in Portugal: An Updated Health Economic Analysis

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Background & objectives

- Obesity is defined as abnormal or excessive fat accumulation that may impair health and increase the risk of long-term complications [1]. Its prevention and management are an emerging public health priority [2]. In Portugal, the prevalence of obesity ranges from 22 to 29% [3,4]. However, reimbursement for effective obesity pharmacotherapy is generally lacking in Portugal. Semaglutide and Tirzepatide, glucagon-like peptide-1 (GLP-1) analogues, were granted marketing authorization for the treatment of adults with obesity or overweight. Semaglutide is administered via weekly subcutaneous injection at a dose of 2.4 mg, while tirzepatide has a maximum maintenance dose of 15.0 mg, administered through subcutaneous injection
- This study assessed whether up to two-years treatment with semaglutide 2.4 mg or tirzepatide 15 mg, both in combination with diet and exercise (D&E), are cost-effective compared to D&E alone, in adults with body mass index (BMI) ≥ 30 kg/m2 and one or more weight-related comorbidity, taking a Portuguese healthcare payer perspective, and assuming a lifetime time horizon. Costs and health outcomes were discounted at an annual rate of 4%

Methods

Model: The cost-utility analysis was performed using the Core Obesity Model, a Markov model designed to evaluate costs and health outcomes of developing obesity complications as a function of risk factors, using clinical efficacy data from the Semaglutide Treatment Effect in People with obesity (STEP) 1 trial [5-7]. Efficacy and safety data for tirzepatide was sourced from the SURMOUNT-1 trial [8,9]

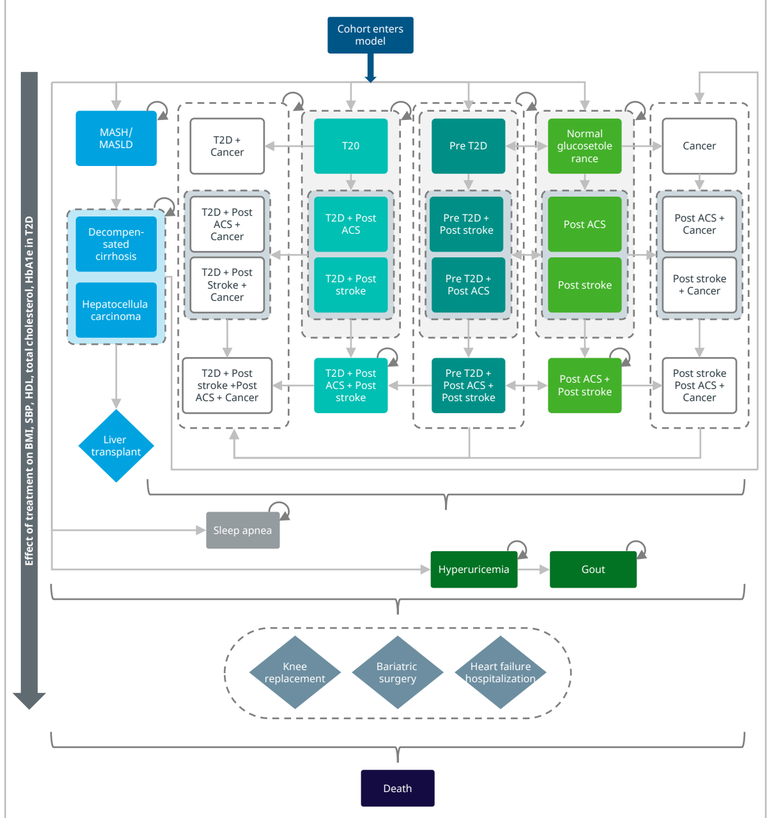
The following complications were considered: type 2 diabetes (T2D), acute coronary syndrome (ACS), stroke, transient ischemic attacks (TIA), obstructive sleep apnoea (OSA), cancer, knee replacement; as well as mortality

The cycle length of the model was 3-months long in the first year, and annual thereafter. Half cycle corrections were applied from the second year onwards

Treatment effects: The development of obesity complications (Figure 1) is predicted via risk equations using treatment-modifiable risk factors (such as weight change and glycaemic change) to predict the incidence of obesity complications, and differences between treatment arms in these

Baseline cohort: The baseline cohort is mainly female (72.9%), with a starting age of 48 years and BMI of 38.7 kg/m2. More than half of the cohort (52.4%) has prediabetes, 1.8% has T2D and 3.8% has a previous history of cardiovascular events

Figure 1: Core obesity Model v26 Structure



ACS – acute coronary syndrome; T2D - Type 2 diabetes; MASH – Metabolic dysfuction-associated steatohepatitis; MAFLD - Metabolic dysfunction-associated steatotic liver disease; BMI – Body mass index; HbA1c – Haemoglobin A1c; HDL – High-density lipoprotein

Mortality: Sex and age specific all-cause mortality for the general population was sourced from Portuguese life tables [10]. These were adjusted by considering HR dependent on BMI [11], to account for the increased mortality associated with obesity [12]

Utilities: A baseline utility, dependent on the cohort's BMI, was sourced from short form-36 (SF-36), as reported in STEP 1. These were mapped to SF-6D utilities using the Sheffield algorithm with Portuguese preferences. Baseline, age-adjusted, disease-free utility was estimated to be 0.897. Correlations between the SF-6D index and baseline BMI were investigated using multiple linear regression analyses. Disease-specific disutilities, sourced from literature, were applied to each health state, additive to BMI and age-specific utilities (Table 1)

Costs: Portuguese specific resource use was sourced from multiple sources including primary health care and specialized care microdata, as well as published literature. Resources were valued according to publicly available national unit cost data - national legislation (Portaria nº 207/2017) and official national drug cost databases (Infomed) (Table 1)

Table 1. Costs and disutilities per health state and acute event

Health state inputs	Annual Cost	Disutility
T2D	T2D pharmacotherapy: 287 € T2D microvascular complications: 816 €	-0.029
Post ACS	1,523 €	-0.037
OSA	599 €	-0.013
Cancer	1st year: Colon cancer treatment: 12,342 € Breast cancer treatment: 10,731 € Endometrial cancer treatment: 13,129€ Following years: 4,599 €	-0.073
Post-stroke	860 €	-0.035
Acute event inputs	**Cost per event**	**Disutility**
Bariatric Surgery	Non-fatal: 3,867 €; Fatal: 15,769 €	-0.184
ACS	MI: Non-fatal: 3,997 €; Fatal: 13,824 € Angina: Non-fatal: 1,761 €; Fatal: 6,040 €	-0.129
Musculoskeletal (knee replacement)	Non-fatal: 5,241 €; Fatal: 11,720 €	-0.023
Stroke	Non-fatal: 4,326 €; Fatal: 11,421 €	-0.181
TIA	1,358 €	-0.033
Severe GI Events	96 €	-0.001
Severe Hypoglycaemia	160 €	-0.015
Non-severe Hypoglycaemia	0 €	-0.006

Table 2: Monitoring costs for obesity & costs with D&E

Monitoring annual costs	Cost
Monitoring cost for obesity, annual	254 €
D&E, annual	0 €

ACS – acute coronary syndrome; BP – blood pressure; D&E – diet & exercise; GI – gastrointestinal; MI – myocardial infarction; OSA – obstructive sleep apnoea; TIA – transient ischemic attacks; T2D - Type 2 diabetes

Results

The predicted change in BMI over time exhibits the positive treatment effect of semaglutide 2.4 mg and tirzepatide 15mg in BMI (Figure 2)

Figure 2 BMI trajectory over time, base case analysis

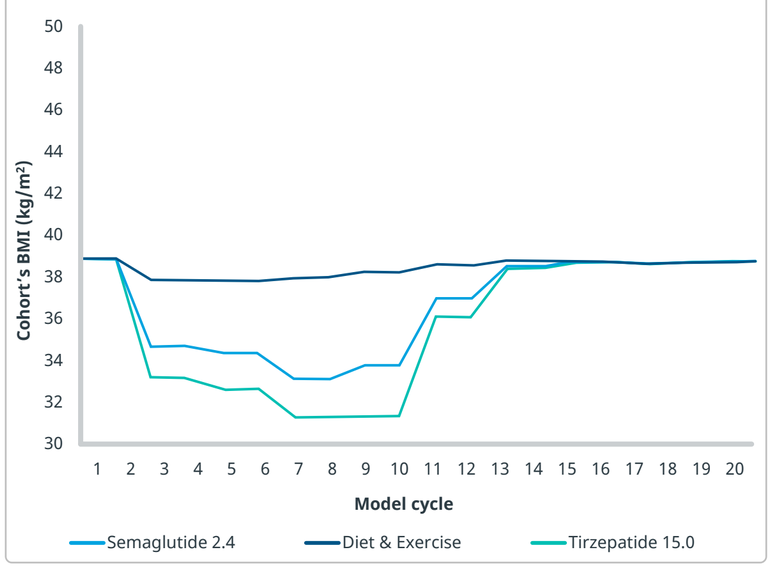


Table 3: Breakdown of Clinical Results Semaglutide 2.4 mg and Tirzepatide 15mg vs D&E

Event Rate per 100 Patient-years	Semaglutide	D&E	Tirzepatide	Semaglutide Inc.	Tirzepatide Inc.
CV-events	49.02	49.31	49.04	-0.30	-0.27
Bariatric surgery	8.79	8.75	8.81	0.04	0.06
Knee replacement	46.83	46.73	46.84	0.10	0.11

Table 3: Breakdown of Clinical Results Semaglutide 2.4 mg and Tirzepatide 15mg vs D&E

Patient-years in Health States (Undiscounted)	Semaglutide	D&E	Tirzepatide	Semaglutide Inc.	Tirzepatide Inc.
No comorbidity + prediabetes reversal	9.69	8.92	9.62	0.78	0.70
Sleep apnea	10.44	10.66	10.37	-0.22	-0.29
Pre-T2D	7.32	7.65	7.46	-0.34	-0.19
T2D	5.83	6.21	5.82	-0.39	-0.39
Post-ACS	2.45	2.47	2.46	-0.01	-0.01
Cancer	2.62	2.64	2.61	-0.02	-0.03
Post-stroke	0.87	0.88	0.87	-0.01	-0.01

Table 4. Cost-effectiveness Results for Semaglutide 2.4 mg and Tirzepatide 15mg vs D&E

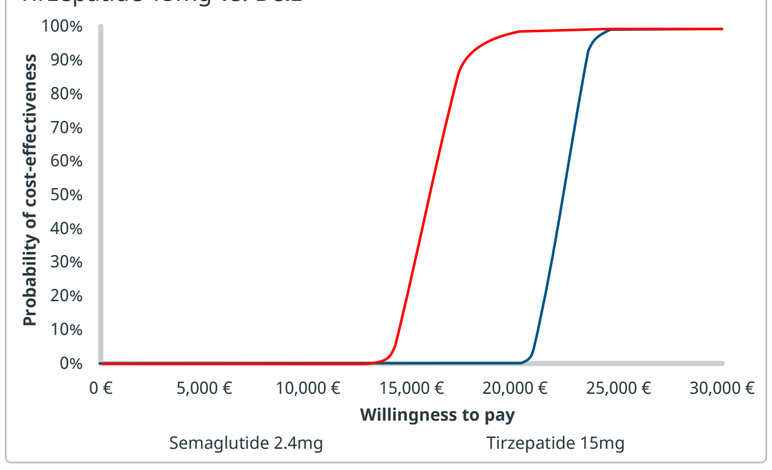
CEA results	Semaglutide	D&E	Tirzepatide	Semaglutide Inc.	Tirzepatide Inc.
Total costs	23,417	21,985	24,864	1,432	2,879
Obesity pharmacy & monitoring costs	5,950	4,000	7,481	1,950	3,481
T2D and BP pharmacy & monitoring costs	1,011	1,081	1,009	-70	-72
Health state costs	14,253	14,688	14,172	-435	-516
Event costs	2,204	2,217	2,201	-12	-16
Total QALYs	13.68	13.58	13.72	0.10	0.14
Total LYs	15.67	15.60	15.70	0.08	0.10
ICUR Cost/QALY)				14,088	21,039
ICER (Cost/LY)				18,626	28,396

Trial-observed differences in risk factors were projected and resulted in reductions of the occurrence of further obesity complications and associated costs, translating into LY gains (+0.08 and +0.10 for semaglutide and tirzepatide respectively), QALY gains (+0.10 and +0.14) and cost offsets of -517€ and -603€ per patient (most savings regarding T2D microvascular complications), compensating additional obesity pharmacotherapy & monitoring costs of +1,950€ and +3,481€, respectively, for semaglutide 2.4mg and tirzepatide 15mg

Sensitivity analysis

Semaglutide's ICUR remained robust across different populations, ranging between 14,088 € and 19,396 €, thus remaining below the 20,000 € willingness to pay (WTP) threshold; depicting a nearly 100% probability of cost effectiveness against D&E alone at that WTP (Figure 3). Tirzepatide 15mg required a higher WTP threshold to achieve a 100% probability of cost effectiveness, as well as cost effectiveness across different populations

Figure 3: CE Acceptability Curves Semaglutide 2.4 mg and Tirzepatide 15mg vs. D&E



Conclusion

The analyses conducted demonstrate that semaglutide 2.4 mg is a cost-effective treatment option, as it can delay the occurrence of complications and associated costs, when compared to D&E alone in Portugal. Cost-effectiveness for tirzepatide 15mg was sensitive to the assumed WTP threshold versus D&E alone, while it achieved delays in the occurrence of complications and associated costs

Acknowledgments

The research was funded by Novo Nordisk, Portugal. We would like to thank Administração Central do Sistema de Saúde, I.P., for their access to Portuguese hospital morbidity database (Base de dados de morbilidade hospitalar)

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33rd European Congress on Obesity. 12-15 May 2026. Istanbul, Türkiye Acceptance code: 0304