Assessing the Cost-effectiveness of Semaglutide 2.4 mg Injection for Chronic Weight Management in Portugal

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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, a glucagon-like peptide-1 (GLP-1) analogue, was granted marketing authorization for the treatment of adults with obesity or overweight. It is administered via weekly subcutaneous injection at a dose of 2.4 mg.

- This study assessed whether up to two-years treatment with semaglutide 2.4 mg, in combination with diet and exercise (D&E), is cost-effective compared to D&E alone, in adults with body mass index (BMI) ≥ 30 kg/m^2 and one or more weight-related comorbidity, taking a healthcare payer perspective, and assuming a lifetime horizon. A 4% discount rate was applied to both costs and outcomes. In scenario analyses, 3- and 6-years treatment durations were also considered.

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].

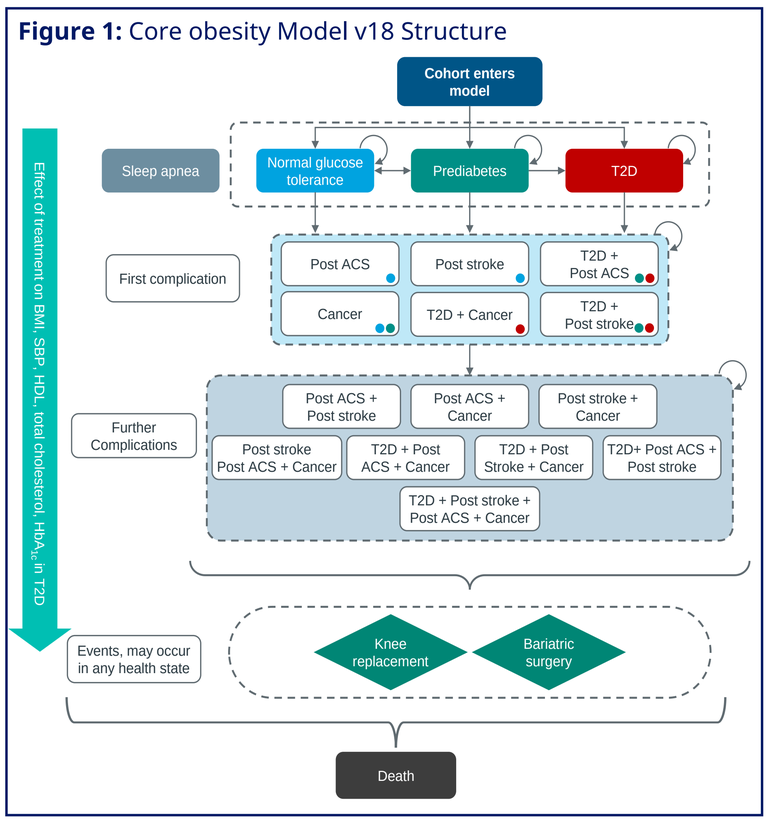
The following complications were considered: type 2 diabetes (T2D), acute coronary syndrome (ACS), stroke including transient ischemic attacks (TIA), obstructive sleep apnoea (OSA), cancer, knee replacement and mortality.

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 2.8% has a previous history of cardiovascular events.

Figure 1: Core obesity Model v18 Structure



- **Mortality:** Sex and age specific all-cause mortality for the general population was sourced from Portuguese life tables [8]. These were adjusted by considering HR dependent on BMI [9], to account for the increased mortality associated with obesity [10].

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: 366 € T2D microvascular complications: 734 €	-0.029
Post ACS	1,523 €	-0.037
OSA	599 €	-0.013
Cancer	1st year: Colon cancer treatment: 11.867 € Breast cancer treatment: 10.318 € Endometrial cancer treatment: 12.624 € Following years: 4.453 €	-0.073
Pots-stroke	1.072 €	-0.035
Acute event inputs	**Cost per event**	**Disutility**
Bariatric Surgery	Non-fatal: 3.850 €; fatal: 11.549 €	-0.184
ACS	MI: non-fatal: 3.359 €; fatal: 11.323 € Angina: Non-fatal: 1.311 €; fatal: 9.071 €	-0.129
Musculoskeletal (knee replacement)	Non-fatal: 3.839 €; fatal: 8.584 €	-0.023
Stroke	Non-fatal: 3.168 € Fatal: 8.364 €	-0.181
TIA	1.008 €	-0.033
Severe GI Events	95 €	-0.001
Severe Hypoglycaemia	160 €	-0.015
Non-severe Hypoglycaemia	0 €	-0.0062

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 in BMI (Figure 2).

Figure 2: BMI trajectory over time, base case analysis.

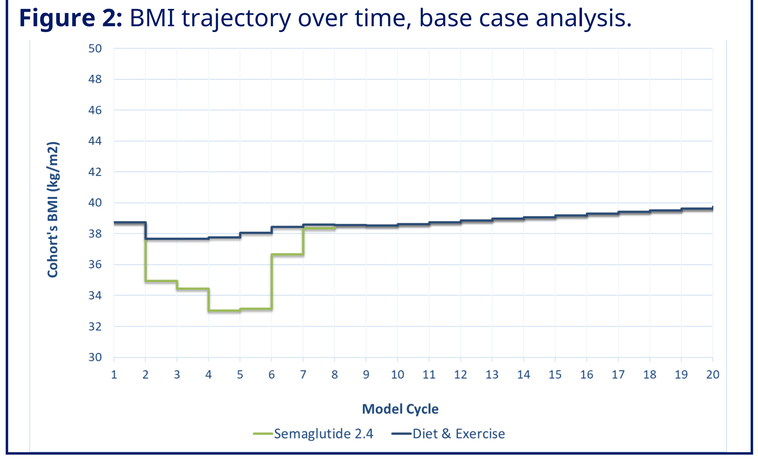


Table 3: Breakdown of Clinical Results Semaglutide 2.4 mg vs D&E.

Event Rate per 100 Patient-years	Semaglutide	D&E	Inc.
CV-events	2.08	2.10	-0.02
Bariatric surgery	0.33	0.33	0
Knee replacement	2.25	2.25	-0.01
Patient-years in Health State (Undiscounted)	**Semaglutide**	**D&E**	**Inc.**
No comorbidity + prediabetes reversal	10.51	9.79	0.72
Sleep apnea	11.04	11.25	-0.20
Pre-T2D	7.12	7.38	-0.25
T2D	7.00	7.36	-0.36
Post-ACS	2.38	2.38	0.01
Cancer	1.98	2.02	-0.04
Post-stroke	0.89	0.89	0

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

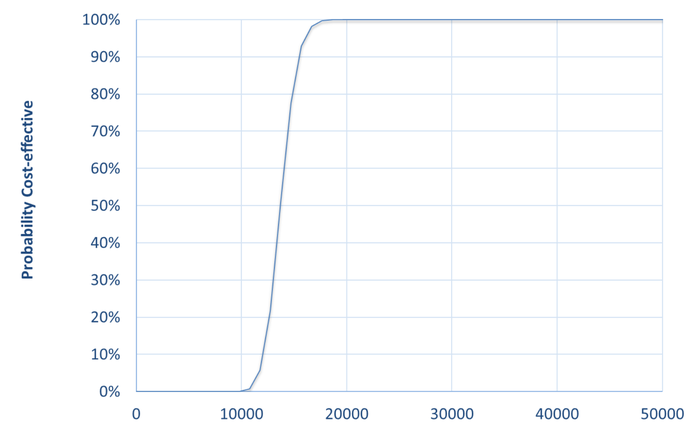
CEA RESULTS:	Semaglutide	D&E	Inc.
TOTAL COSTS	22,957 €	21,631 €	1,325 €
Obesity pharmacy & monitoring costs	6,008 €	4,138 €	1,870 €
T2D and BP pharmacy & monitoring costs	1,560 €	1,649 €	-88 €
Event costs	2,248 €	2,257 €	-8 €
Health state costs	13,140 €	13,587 €	-448 €
TOTAL QALYs	14.29	14.19	0.098
TOTAL LYs	16.23	16.15	0.078
ICUR (Cost/QALY)		**13,459 €**	
ICER (Cost/LY)		**17,027 €**	

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 (+0.078), QALY gains (+0.098) and cost savings of -545€ per patient (most savings regarding T2D microvascular complications), compensating additional obesity pharmacotherapy & monitoring costs of +1,870€.

Sensitivity Analysis

- The ICER remained robust across all scenario analysis, ranging between 10,797 € and 16,006 €, thus remaining below 20,000 €. From the scenarios conducted, the ICUR was the highest considering a longer treatment duration (6 years). Semaglutide 2.4 mg depicts a 100% probability of cost effectiveness against D&E alone at the set of 20,000 € willingness to pay threshold (Figure 3).

Figure 3: *CE Acceptability Curve Semaglutide 2.4 mg 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.

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