**GitHub**

For all materials related to this project, see <https://github.com/alepigna12/eeii_icer_project>.

**Objective**

The aim of this project is to evaluate the cost-effectiveness of FDA-approved medications for obesity management.

**Interventions**

The following medications are considered: Semaglutide (SEM), Lliraglutide (LIR), Phentermine/topiramate (P/T), Bupropion/naltrexone (B/N). Each intervention is associated with lifestyle modification and compared to lifestyle modification alone (LSM).

**Target Population**

The target population includes patients with BMI at the obesity level. The base-case population is 80% female, with a mean BMI of 38, a 35% prevalence of diagnosed hypertension and a 12.5% prevalence of smoking.

**Perspective**

This analysis is conducted from the Health Care sector perspective.

**Time Horizon**

A lifetime horizon is used, assuming no patients live beyond 119 years old.

**Discount Rate**

All costs and Quality-Adjusted Life Years (QALYs) are annually discounted. The base-case rate is 3%.

**Costing Year**

The costing year used is the same as the one used in the *Medications for Obesity Management: Effectiveness and Value* Final Evidence Report. It is not explicitly reported, but it appears to be 2022.

**Study Design**

The Markov state transition model used in the analysis is shown in Figure 4.1. The model cycle length was one year; transition probabilities are time-dependent and functions of BMI and Glycated hemoglobin percentage (HbA1C) among other variables. Only one CVD event (either MI, Stroke or HF) can occur in any given cycle – this is the main difference between this project and the original ICER report. Different interventions affect BMI and HbA1C, which in turn affect rates of CVD and Diabetes.

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**Data Sources**

The main data source is the [*Medications for Obesity Management: Effectiveness and Value* Final Evidence Report](https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Ficer.org%2Fwp-content%2Fuploads%2F2022%2F03%2FICER_Obesity_Final_Evidence_Report_and_Meeting_Summary_102022.pdf&data=05%7C02%7Capignat1%40jh.edu%7C892470f4f1ff401c442408dd12364560%7C9fa4f438b1e6473b803f86f8aedf0dec%7C0%7C0%7C638686746497896590%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C0%7C%7C%7C&sdata=rzWmyOu4dVKvOUH6Mir4sNyIpKjyv6b7qQQZAlGiAHM%3D&reserved=0)*.* References listed within the report are sometimes used to obtain more information about parameter ranges for sensitivity analysis. 2018 US Life Tables are used for all-cause mortality.

**Outcome Measures**

Utility is measured in QALYs, costs are measured in US dollars. Discounted ICER is the primary endpoint.

**Results of base-case analysis**

Table 4.6 shows the ICERs for pairwise treatment comparisons.

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Table Extra 1 shows the full incremental analysis: LSM is the preferred treatment at WTP < ~$34,000/QALY, P/T is the preferred treatment at WTPs between ~$34,000/QALY and ~$309,000/QALY, SEM is the preferred treatment at WTP > ~$309,000/QALY. At most widely-used WTP, P/T should be chosen.

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**Results of uncertainty analysis**

One-way sensitivity analysis is performed in Excel, and Tornado diagram are included there for each pairwise comparison with lifestyle modification alone. Generally, the disutilities associated with a one-point increase in BMI and one year increase in age respectively are the most influential parameters.

Probabilistic sensitivity analysis is performed in R by associating a statistical distribution to approximately 60 model parameters. Distributions are chosen to match 95% confidence intervals when those are readily available in the original Report and to have a standard deviation that is 10% of the mean when no data is easily available for the natural uncertainty/variation in the parameter.

1,000 draws are generated – Figures E4 display the results with scatterplots and acceptability curves. A graph of a blue dot

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**Limitations**

CVD rates are likely underestimated to some extent due to the assumption that only one CVD can happen during any given cycle.

Obesity is linked to conditions beyond CVDs and diabetes. This analysis likely underestimates the utility gain due to the interventions’ effects on rates for these other conditions (which are not accounted for by the model).

The Framingham Risk Calculation Equation is used to calculated CVD risk with the best estimates for the regression coefficient. These coefficients come with an associated uncertainty, which is ignored in this project.

**Conclusions**

Phentermine/topiramate (P/T) is highly cost effective for obesity management because it offers low QALY gains at a very low cost. SEM offers the highest QALY gain, however it was not cost-effective in the Base-case at the price used in the Report.

**Discussion**

This project’s model captures the essential elements of the original model. Results agree on a qualitative basis. Probabilistic Sensitivity Analysis results differ more due to a lack of information about the exact distributional assumptions and confidence intervals in the original model, hence a difficulty replicating the original model values. Figures E1 show the general agreement between the models in the base-case, which is an encouraging sign this may be a useful working model as a starting point for further analysis.

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