European Review for Medical and Pharmacological Sciences 2024; 28: 3365-3374

Cost-effectiveness analysis of once-weekly semaglutide *vs.* once-daily liraglutide administered subcutaneously in patients with overweight and obesity: a decision analysis

M. ALSHAHAWEY[1], M. GHAZY[2], M. EL MORSHEDY[2], N.O. EL SAID[3]

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt
[2]Department of Internal Medicine and Endocrinology, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[3]Department of Pharmacy Practice and Clinical Pharmacy, Faculty of Pharmacy, Future University in Egypt, Cairo, Egypt

Abstract. – OBJECTIVE: Obesity presents an enduring and multifaceted dilemma that impacts individuals, society, economies, and healthcare systems alike. Glucagon-like peptide-1 (GLP-1) receptor agonists, including liraglutide and semaglutide, have received FDA approval for obesity treatment. This study aims to present a cost-effectiveness analysis to compare the cost and clinical outcomes of semaglutide vs. liraglutide on weight loss in people with overweight and obesity.

MATERIALS AND METHODS: A cost-effectiveness analysis was conducted to compare the cost and the clinical outcomes of adding weekly 2.4 mg SC semaglutide vs. daily 3.0 mg SC liraglutide or placebo to physical activity and diet control in overweight and obese patients. A clinical outcome of achieving ≥15% weight loss was chosen. A simple decision analysis model from a third-payer perspective was applied. Drug costs were based on the retail price of the USA market. One-way sensitivity analyses were performed.

RESULTS: Results showed that 2.4 mg weekly semaglutide, when added to physical activity and diet control, was the most cost-effective choice in terms of ≥15% weight loss (ICER: $ 7,056/patient/68 weeks). The model was robust against the 50% increase in the unit cost of semaglutide and the 50% decrease in the unit cost of liraglutide, as well as the changes in probabilities by the corresponding 95% confidence intervals across the model.

CONCLUSIONS: This cost-effectiveness analysis suggests that employing once-weekly 2.4 mg semaglutide emerges as a remarkably cost-effective option when contrasted with once-daily 3.0 mg liraglutide in patients with overweight and obesity when added to physical activity and diet control.

Key Words:
Cost-effectiveness, Obesity, Semaglutide, Liraglutide, Decision analysis.

Introduction

Obesity is described as an enduring and recurring health condition that imposes a significant burden not only on individuals but also on society, the economy, and healthcare systems[1]. Attaining and sustaining weight loss over an extended duration poses difficulties attributed to metabolic adaptation[2] and the intricate nature of adhering to lifestyle modifications[3].

Indeed, an elevated body mass index (BMI) >25 kg/m² is associated with an increased risk of mortality and cardiometabolic diseases[4]. This well-established correlation has been consistently supported since the 1970s, drawing upon numerous studies[5] that utilize actuarial data from life insurance companies and observational investigations involving diverse populations.

According to the American Association of Clinical Endocrinologists[6] and the European Guidelines for Obesity Management in Adults[7], it is recommended to achieve a sustained weight reduction within the range of 5% to 15%, with the use of pharmacological assistance, in order to improve diverse health conditions associated with overweight/obesity. As per American Family Physician guidelines, obesity was defined as a BMI of 30 kg per m^2 or greater and overweight as a BMI of 27 kg per m^2 or greater in the presence of one weight-related comorbidity[8]. The battle

Corresponding Author: Nouran Omar El Said, Ph.D; e-mail: nomar@fue.edu.eg

against obesity involves more than just changing lifestyles. It also includes using medications along with behavior changes, diet adjustments, and increased physical activity. From 2005 onward, the clinical availability of glucagon-like peptide 1 (GLP-1) receptor agonists has brought about a noteworthy transformation in diabetes care, impacting both weight management and the regulation of glucose levels.

GLP-1 is a hormone that regulates food intake and glucose homeostasis. Therefore, it is a promising target for the treatment of obesity, as it increases feelings of fullness and decreases hunger[9]. Also, extended-release versions of the naturally existing incretin and those adapted to engage with receptors for glucose-dependent insulinotropic polypeptide (GIP) have demonstrated substantial effectiveness as well. Notably, the unimolecular dual agonist Tirzepatide, engaging both GLP-1R and GIP-R receptors, and the triple incretin receptor agonist Retatrutide have demonstrated exceptional effectiveness in lowering both glucose and weight. However, these agents are still under controlled trial phases[10,11].

Glucagon-like peptide-1 receptor agonists, such as liraglutide and semaglutide, are medications that mimic the effects of GLP-1. Both are approved by the U.S. Food and Drug Administration (FDA) for the treatment of obesity[12]. However, there are some differences between the two medications.

Semaglutide (2.4 mg) is administered as a once-weekly subcutaneous injection, while liraglutide (3.0 mg) is a once-daily subcutaneous injection. Additionally, semaglutide (2.4 mg) has been approved by the FDA for the treatment of obesity, while liraglutide (3.0 mg) is approved for the treatment and management of both obesity and type 2 diabetes. Both medications were proven[12] to be effective in weight loss in overweight and obese patients.

In one clinical trial, patients who received semaglutide 2.4 mg once weekly lost an average of 15.3 pounds over 68 weeks, while those who received a placebo lost an average of 3.7 pounds over the same period[13]. Moreover, a recent study by Xiang et al[14] on a group of 53 obese patients who underwent a 24-week intervention involving lifestyle modifications alongside semaglutide treatment has found that 6 months of treatment had led to a significant reduction in the patient's weight and 93% of these patients achieved a weight loss ≥5%, while 54% of these patients achieved ≥10% weight loss. The treatment also led to decreases in fasting blood glucose, fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index, blood uric acid, and blood lipid levels.

Using once daily 3.0 mg liraglutide, on the other hand, made a weight loss of an average of 8.4 pounds over 56 weeks, while those who received a placebo lost an average of 2.2 pounds over the same period[15]. Another clinical trial[16] has found that patients who received liraglutide 3.0 mg once daily lost an average of 9.2 pounds over 68 weeks, while those who received placebo lost an average of 1.5 pounds over the same period. A recommendation by Singh et al[9] to perform a cost-effective analysis in order to help clinicians decide whether semaglutide is a good option for patients compared with other weight loss drugs has been considered. This study aims to present a cost-effectiveness analysis to compare the impact of once-weekly subcutaneous semaglutide, 2.4 mg, *vs*. once-daily subcutaneous liraglutide, 3.0 mg (both with diet control and physical activity) on weight loss, in patients with overweight or obesity.

Materials and Methods

Study Design

A simple decision analysis framework was used to assess 68 weeks' costs and clinical outcomes of using two types of GLP-1 agents (2.4 mg SC semaglutide, 3.0 mg SC liraglutide) *vs*. placebo in overweight and obese patients (Figure 1).

Data Sources

This cost-effectiveness analysis was based on the data published in the randomized clinical trial by Rubino et al[17] in 2022. We have presented our data in accordance with the updated 2022 CHEERS reporting checklist[18].

Population

The targeted study population included adults (≥18 years old) who had experienced at least one unsuccessful attempt at dietary weight loss. Patients should have had a BMI of ≥ 30 or a BMI of ≥ 27 with one or more weight-related comorbidities (such as hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease). Exclusion criteria involved individuals with diabetes, a hemoglobin A1C level of 6.5% (48 mmol/mol) or higher, and those who reported significant body weight changes (more than 5 kg) within 90 days prior to screening.

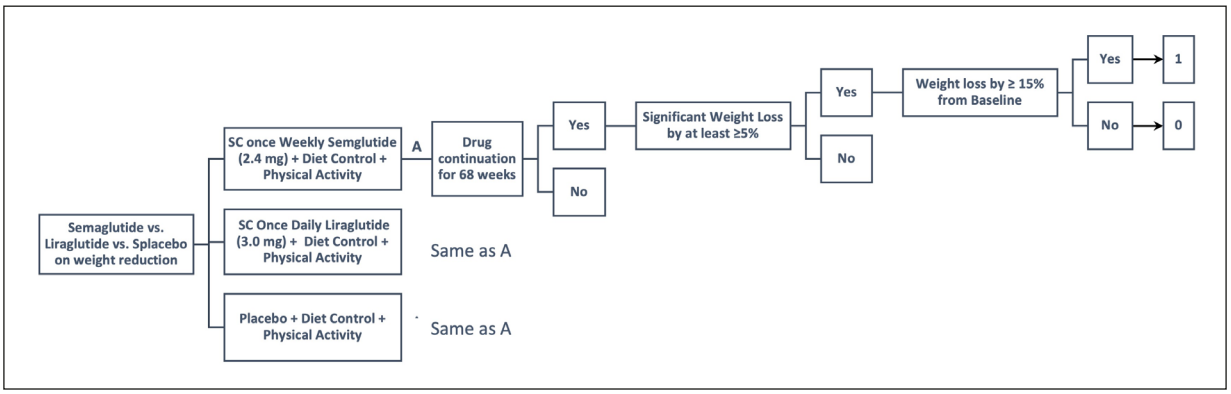

Figure 1. Cost-effectiveness decision analysis model.

All study interventions were provided alongside lifestyle interventions, which involved regular counseling sessions led by a dietician or similarly qualified healthcare professional. These counseling sessions occurred every 4 to 6 weeks, either through in-person visits or *via* phone contact. The counseling focused on dietary adjustments, aiming for a 500-kcal deficit per day based on the estimated total daily energy expenditure, and encouraged engaging in a minimum of 150 minutes of physical activity per week.

Main Outcomes and Time Horizon

The primary outcome was the achievement of 15% or more of weight loss from baseline, during a time horizon of 68 weeks (17 months) period.

Costs

The estimated cost of semaglutide was around $ 1,304.68, which is 24% off the average retail price of $ 1,718.50, and the estimated cost for liraglutide $ 1,304.68, which is 18% off the average retail price of $ 1,608.12. This was the estimated lowest GoodRx price for one month of treatment. The actual cost will vary by region and with insurance. Information was obtained at https://www.goodrx.com (accessed on February 5th, 2023; zip code: 23219). Study outcomes included direct health care costs in 2023 United States dollars (USD) from a third-party payer's perspective (Medicare/Medicaid, Commercial) in the United States. The liraglutide drug package did not include needles, so the cost of daily needles was added for the whole 68-week study period. Semaglutide was administered initially with a multi-dose pen injector during the study period of week 1 to week 44, so we assumed a cost of extra 44 needles. After this period, all patients were shifted to regular single-dose pen injectors with the needles already inserted (week 45 to week 68), so no extra costs were added. All the costs were inflated and adjusted to 2023 US dollars ($ USD). We have assumed 2 consecutive initial visits for participant selection and enrollment purposes (CPT code 99203: New patient office visit, duration: 30-44 minutes; $ 113/visit), while study follow-up visits for health professionals every 4-6 weeks were estimated to be (CPT code 99202: $ 73/physical follow-up visit, 15-30-minute session), and $ 15/follow up phone call (CPT code 98966) (Table I).

Model Assumptions

1. We assumed that each participant had two initial visits for the purpose of enrollment and selection, while patients had 8 follow-up physical visits and 9 follow-up phone calls during the 68-week study period.
2. For the placebo group, we have assumed that either a multi-dose injector pen or a single-dose injector pen (for the matched semaglutide group from week 44 and forward) were prescribed to the patients on a weekly basis (1 pen/week). The multi-dose pen was used in the initial 44 weeks period of the matched semaglutide group, which incurred a total of 44 needles, while for the matched Liraglutide placebo group, 68 multi-dose pens were prescribed, with a total of 467 needles for the daily use of the 68-weeks study period.
3. Based on supplement 3 and Figure 4, provided by the clinical trial[17], we have noticed that almost 99.1% of the patients have completed 44 weeks of the treatment period in the semaglutide group, while 98.3% of the patients have completed 24 weeks of the treatment period in Liraglutide group. So, we assumed that patients who discontinued the treatment in the Sema-

Table I. Costs and probabilities in the study.

Variable	Unit Price ($ US)¶	68 weeks price ($ US)¶	Source
I-Costs			
Drug: SC semaglutide 2.4 mg/month	1,305	22,185	https://www.goodrx.com/
Drug: SC liraglutide 3.0 mg/month	1,305	22,185	https://www.goodrx.com/
Multidose/single dose pen injector	30	2,040	Assumed
Fine needle costs	0.7	333	https://www.goodrx.com/
Initial 2 visits for enrollment and selection (CPT code 99203)	113	226	https://www.cms.gov/medicare-coverage-database/
Follow-up clinic visit cost (CPT code 99202)	73	584	https://www.cms.gov/medicare-coverage-database/
Follow-up phone call cost (CPT code 98966)	15	135	https://www.cms.gov/medicare-coverage-database/
II-Probabilities	**Probability**	**(95% confidence interval)**	**Source**
Probability for treatment continuation on SC semaglutide 2.4 mg/week	0.865	0.799-0.905	[16]
Probability for treatment continuation on SC liraglutide 3.0 mg/day	0.724	0.661-0.781	[16]
Probability for treatment continuation on placebo	0.824	0.756-0.880	[16]
Probability of treatment success on SC semaglutide 2.4 mg/week	0.906	0.857-0.944	[16]
Probability of treatment success on SC liraglutide 3.0 mg/day	0.620	0.528-0.707	[16]
Probability of treatment success on placebo	0.295	0.208-0.392	[16]
Probability of achievement ≥15% weight loss from baseline on SC semaglutide 2.4 mg/week	0.556	0.482-0.628	[16]
Probability of achievement ≥15% weight loss from baseline on SC liraglutide 3.0 mg/day	0.120	0.071-0.172	[16]
Probability of achievement ≥15% weight loss from baseline on placebo	0.064	0.027-0.121	[16]

$ US: United States Dollar, ¶: average wholesale price for unit price.

glutide group incurred all the treatment costs for 44 weeks, while the patients who discontinued the treatment in the Liraglutide group incurred all the treatment costs for 24 weeks only. By week 44, the patients in the semaglutide group had incurred semaglutide drug cost for 44 weeks, 44 fine needles, 5 physical follow-up visits, and 6 follow-up phone calls, while for the Liraglutide group, drug discontinuation occurred at week 24, by which the patients had incurred the liraglutide drug cost for 24 weeks, 168 fine needles, 3 follow-up physical costs, 3 follow-up phone calls. For placebo groups, we assumed a pooled placebo discontinuation to have occurred by week 36. Pooled costs of pens and fine needles were considered. The cost of 4 follow-up physical visits and 5 follow-up phone calls were considered as well.

4. This cost-effectiveness model has not considered adverse events, as there was no statistically significant difference between the three study groups. Adverse events were reported by 95.2%, 96.1%, and 95.3% of patients in semaglutide, liraglutide, and placebo, respectively ($p > 0.05$).

Decision Analysis Model

A decision analysis framework was built using Microsoft Excel 2021 (Microsoft, Redmond, WA, USA) to assess 68 weeks' costs and clinical outcomes of using two types of GLP-1 agents *vs.* placebo in overweight and obese patients. Out of a total of 338 patients, 92.3% (n=312) underwent a body weight assessment in week 68. Data were missing for 9 patients in the semaglutide group, 10 in the Liraglutide group, and 7 in the placebo group. This has left 117, 117, and 75 patients

in the semaglutide group, Liraglutide group, and placebo group, respectively, to assess an outcome of achieving a ≥15% weight loss at week 68. The model started with the question, "Which is the more cost-effective option to be added to physical activity and diet control in achieving 15% or more of weight loss from baseline for 68 weeks period?". The model then presents the probability of patients' discontinuation of treatment for any reason. Afterward, the model considers the probability of achieving ≥ 5% weight loss as a cut-off value for "treatment success". The model then illustrates the clinical effectiveness of each intervention (semaglutide, liraglutide *vs.* placebo) added to physical activity and diet control to achieve an outcome of 15% or more of weight loss from baseline. Effectiveness evaluation was based on a binary outcome, with the value (1) indicating a favorable outcome ("Yes"), and the value (0) indicating an unfavorable outcome ("No").

Sensitivity Analysis

In accordance with the revised guidelines outlined in the 2022 release of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS): ISPOR Task Force report by Husereau et al[18], a one-way sensitivity analysis was carried out. This analysis was designed to gauge the model's robustness and ability to adapt to changes in variables by investigating different ranges of probabilities and acquisition costs. More precisely, the one-way sensitivity analysis utilized the upper and lower limits of the 95% confidence interval to scrutinize all probabilities within the model as follows:

- Probability of treatment continuation;
- Probability of treatment success;
- Probability ≥15% of weight loss from baseline;

Also, a one-way sensitivity analysis to test the model's robustness against a change in average retail unit cost was performed as follows: the semaglutide unit cost increased by +50%, and the liraglutide unit cost decreased by -50%.

Results

The results of this cost-effectiveness analysis suggest that weekly 2.4 mg SC semaglutide is more cost-effective than daily 3.0 mg SC liraglutide in terms of achieving a clinical outcome ≥15% of weight loss from baseline in a 68-week study period (Table II). According to this model, the effectiveness provided by the semaglutide regimen (0.436) is higher than the effectiveness provided by the liraglutide regimen (0.054), as illustrated in Table II. The average retail unit cost of both medications is apparently the same ($ 1,305); however, by applying the current model, semaglutide seems to have a higher estimated overall cost ($ 21,940) compared to $ 19,246 for liraglutide. These costs have yielded an ICER of $ 7,056/patient/68 weeks) (Table II).

The model was robust against the 50% increase in the retail unit cost of semaglutide and the 50% decrease in liraglutide retail unit cost (Table III).

Upper and lower bounds of the 95% confidence interval were used to test the sensitivity of the model to the changes in the probabilities. The model was conservative regarding the changes in the probabilities of treatment continuation, treatment success, and the probability of achieving 15% or more weight loss from baseline (Table IV).

Discussion

This cost-effectiveness analysis showed that SC 2.4 mg weekly semaglutide, when added to

Table II. Cost-effectiveness analysis of SC semaglutide 2.4 mg/week or SC liraglutide 3.0 mg/day for physical activity and diet control *vs.* placebo.

Base case effectiveness	Cost ($ US)	Marginal cost ($ US)	Effectiveness	Marginal effectiveness	C:E Ratio	ICER
Semaglutide	21,940		0.436		50,353	
Liraglutide	19,246	2,694	0.054	0.382	357,297	7,056
Semaglutide	21,940		0.436		50,353	
Placebo	2,799	19,141	0.016	0.420	179,948	45,555
Liraglutide	19,246		0.054		357,297	
Placebo	2,799	16,447	0.016	0.038	179,948	429,318

$ US: United States Dollar, C:E: Cost Effectiveness per patient, ICER: Incremental Cost-Effectiveness Ratio/patient/year.

Table III. One-way sensitivity analysis of cost acquisitions.

Base case effectiveness	Cost ($ US)	Marginal cost ($ US)	Effectiveness	Marginal effectiveness	C:E Ratio	Marginal C:E
Sensitivity analysis with 50% increase in semaglutide unit cost						
Semaglutide	43,068		0.436		98,841	
Liraglutide	19,246	23,822	0.054	0.382	357,297	62,384
Sensitivity analysis with 50% decrease in liraglutide unit cost						
Semaglutide	21,940		0.436		50,353	
Liraglutide	10,134	11,806	0.054	0.382	188,144	30,916

$ US: United States Dollar; C:E: Cost-effectiveness per patient.

Table IV. One-way sensitivity analysis of probabilities across the model.

Base case (confidence interval 95%)	Semaglutide *vs.* liraglutide ICER=7,056*	Semaglutide *vs.* placebo ICER=45,555*	Liraglutide *vs.* placebo ICER=429,318*
Probability for treatment continuation on SC semaglutide 2.4 mg/week			
0.799	3,370	45,541	429,318
0.905	8,993	45,562	429,318
Probability of treatment success on SC semaglutide 2.4 mg/week			
0.857	7,520	48,262	429,318
0.944	6,734	43,656	429,318
Probability of achievement ≥15% weight loss from baseline on SC semaglutide 2.4 mg/week			
0.482	8,319	52,849	429,318
0.628	6,148	40,161	429,318
Probability for treatment continuation on SC liraglutide 3.0 mg/day			
0.661	10,772	45,555	445,457
0.781	3,614	45,555	417,780
Probability of treatment success on SC liraglutide 3.0 mg/day			
0.528	6,911	45,555	542,512
0.707	7,198	45,555	358,570
Probability of achievement ≥15% weight loss from baseline on SC Liraglutide 3.0 mg/day			
0.071	6,672	45,555	1,008,163
0.172	7,515	45,555	266,771
Probability for treatment continuation on placebo			
0.756	7,056	45,905	420,604
0.880	7,056	45,265	436,945
Probability of treatment success on Placebo			
0.208	7,056	45,063	383,400
0.392	7,056	46,116	495,480
Probability of achievement ≥15% weight loss from baseline on placebo			
0.027	7,056	44,600	347,689
0.121	7,056	47,108	672,579
50% increase in semaglutide unit cost:	62,384	95,838	429,318
50% decrease in liraglutide unit cost:	30,916	45,555	191,472

*ICER: Incremental Cost-Effectiveness Ratio/patient/68 weeks.

physical activity and diet control, was the most cost-effective regimen in terms of 15% or more weight loss (ICER: $ 7,056/patient/68 weeks). The C:E ratio is markedly in favor of the semaglutide group (US $ 50,353), compared to $ 357,297 in Liraglutide group, or $ 179,948 in the placebo group (Table II). In other words, it cost only an extra $ 7,056/patient to achieve ≥15% weight loss from baseline when adding SC weekly 2.4 mg semaglutide to physical activity and diet control for a duration of 68 weeks. An ICER of $ 7,056/patient/68 weeks or $ 4,891/patient/year to achieve ≥15% weight loss falls within the acceptable range of willingness to pay threshold (WTP) in the United States ($ 150,000-$ 195,000/quality-adjusted life year[19,20]".

It is worth saying that previous studies[21] have focused on presenting the cost-effectiveness of GLP-1 agents from a glycemic control point of view in patients with diabetes. However, the current study focuses on the economic analysis of the weight loss properties of both semaglutide and liraglutide in overweight and obese patients. The current model considers attaining ≥15% weight loss from baseline as the clinical outcome. This model also considers the rate of patients' discontinuation and the rate of treatment success, as defined as the achievement of at least ≥5% weight loss.

The rate of patients' discontinuation was higher in the liraglutide group (27.5%) *vs.* semaglutide group (13.5%), and according to the primary results of the clinical trial, this was mainly attributed to the fact that Liraglutide possesses a shorter half-life (13-15 hours) compared to semaglutide (165 hours), and this could potentially result in a more rapid and perceptible resurgence of hunger in liraglutide group. Also, liraglutide necessitates more frequent SC injections compared to semaglutide[17].

Generally, a 5% weight loss from baseline is accepted as a "clinically meaningful" amount[22,23]. In our model, we used a value ≥5% of weight loss from baseline as a cut-off value for "treatment success". Patients in the semaglutide group had a higher probability of treatment success (90.6%) *vs.* 62% in the Liraglutide group. This is also supported by Deng et al[24] in their 2022 recent systematic review, comparing the clinical efficacy of both liraglutide and semaglutide on individuals with obesity and overweight without diabetes. The results of this systematic review illustrated a pooled median probability of 86.6% in the semaglutide group *vs.* 65.3% in the Liraglutide group as a probability of achieving at least 5% weight loss from baseline. Also, a head-to-head study performed by O'Neil et al[25] in 2018 compared the efficacy and safety of semaglutide 7 mg once weekly with liraglutide 3.0 mg once daily and placebo for weight loss in patients with obesity. The study was a randomized, double-blind, placebo-controlled, dose-ranging phase 2 trial that involved 957 patients. The results showed that semaglutide 7 mg once weekly was significantly more effective in reducing body weight compared to liraglutide and placebo. The mean weight loss for the once-weekly semaglutide 7 mg was 8.4 kg, compared to 5.5 kg for liraglutide and 2.3 kg for placebo, after 68 weeks of treatment. In addition, semaglutide was also associated with significant reductions in waist circumference, total body fat, and hip circumference, compared to both liraglutide and placebo. The safety profile of semaglutide was similar to that of liraglutide, with both medications being well tolerated by the majority of patients. Overall, the results of this study suggest that semaglutide 7 mg once weekly is a promising treatment option for weight loss in patients with obesity, providing greater weight loss benefits compared to liraglutide and placebo. Also, in 2022, Rubino et al[17] compared semaglutide to liraglutide and placebo and found it to be superior, resulting in significantly more weight loss after 68 weeks (mean weight reduction = -15.8% *vs.* -6.4%). We used the data published in the latter study to perform our cost-effectiveness analysis. The primary outcome was the percentage change in weight after 68 weeks of the study period, while the secondary outcomes of the study were attaining a weight loss of ≥ 10%, ≥ 15%, and ≥ 20%.

In our model, the clinical outcome of attaining a modest weight loss of 15% or more is selected based on the existing literature, driven by its substantial advantages. Better glycemic improvement, greater triglyceride reduction rates, higher levels of high-density lipoproteins[26,27], lower hepatic steatosis rates[28], and finally, higher scores for quality of life[29] were all associated with 15% or more weight loss.

The current model has illustrated that semaglutide had a higher probability of achieving the clinical outcome (55.6%), followed by liraglutide (12%) and placebo (6.4%). As the cost of both semaglutide and liraglutide are somehow comparable, greater efficacy and higher probability of achieving the outcome shown in the semaglutide group has markedly affected the cost-effective-

ness model's conclusion. Using one-way sensitivity analysis, the model was shown to be robust against the changes in retail costs (±50% change in unit cost) and all probabilities across the model.

Limitations

The discontinuation rate in the Liraglutide group was higher than that in the semaglutide group, so the attainable weight loss through liraglutide might have been influenced, given that patients may have adhered to the treatment for a shorter duration, resulting in reduced benefits. This scenario could introduce potential bias into the treatment comparisons. Additionally, the costs linked to adverse drug reactions were not included in this analysis due to the non-significant differences between the three groups. Patient satisfaction and patient adherence' rates were not considered in the current cost-effectiveness analysis; however, they were not considered in the primary clinical trial either.

Conclusions

In conclusion, this cost-effectiveness analysis underscores the remarkable cost-effectiveness of incorporating SC 2.4 mg weekly semaglutide into a regimen of physical activity and diet control in the context of achieving a 15% or more weight loss from baseline. The incremental cost of $ 7,056/patient translates into a noteworthy achievement of ≥15% of weight loss from baseline in overweight and obese patients. Nonetheless, it is essential to acknowledge that the expenses associated with these medications are relatively high. As a result, prudent considerations should be given to the inclusion of these treatments under governmental insurance coverage. Striking a balance between the promising benefits and financial feasibility is pivotal to ensuring equitable access to these therapeutic options for the benefit of the target patient population. The findings of this study suggested that future weight loss medications could exert a substantial influence on regional budgets, underscoring the need for additional budget impact analysis. These considerations are essential for optimizing resource allocation and providing access to effective treatments while maintaining fiscal responsibility within the healthcare system.

Conflict of Interest

The authors declare no conflicts of interest.

Ethics Approval

As it is a cost-effective analysis that is based on already published and readily publicly available data, the Research Ethics Committee at the Faculty of Pharmacy, Future University in Egypt, has waived the ethical approval for the study protocol.

Informed Consent

Not applicable, since this is a non-human subjects research based on economic evaluation of publicly available data.

Funding

There is no source of funding or sponsorship associated with this study.

Authors' Contributions

All authors contributed to the study's conception and design. Material preparation, data collection and analysis were performed by Mona Alshahawey, Nouran Elsaid, Mohamed El Morshedy and Manar Ghazy. The first draft of the manuscript was written by Mona Alshahawey, and all authors read and approved the final manuscript.

ORCID ID

Mona Alshahawey: 0000-0001-7424-279
Nouran Omar El Said: 0000-0001-5663-4924

Availability of Data and Materials

The underlying data that substantiates the conclusions of this study can be obtained upon request from the corresponding author.

References

1) Frühbeck G, Busetto L, Dicker D, Yumuk V, Goossens GH, Hebebrand J, Halford JG, Farpour-Lambert NJ, Blaak EE, Woodward E. The ABCD of obesity: an EASO position statement on a diagnostic term with clinical and scientific implications. Obesity Facts 2019; 12: 131-136.
2) Leibel RL, Seeley RJ, Darsow T, Berg EG, Smith SR, Ratner R. Biologic Responses to Weight Loss and Weight Regain: Report From an American Diabetes Association Research Symposium. Diabetes 2015; 64: 2299-2309.
3) Lemstra M, Bird Y, Nwankwo C, Rogers M, Moraros J. Weight loss intervention adherence and factors promoting adherence: a meta-analysis. Patient Prefer Adherence 2016; 10: 1547-1559.
4) Klenk J, Nagel G, Ulmer H, Strasak A, Concin H, Diem G, Rapp K, Vhm, Group PPS. Body mass index and mortality: results of a cohort of 184,697 adults in Austria. Eur J Epidemiol 2009; 24: 83-91.

5) Ryan D, Yockey S. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. Curr Obes Rep 2017; 6: 187-194.

6) Garvey W, Mechanick J, Brett E, Garber A, Hurley D, Jastreboff A, Nadolsky K, Pessah-Pollack R, Plodkowski R. Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract 2016; 22: 1-203.

7) Yumuk V, Tsigos C, Fried M, Schindler K, Busetto L, Micic D, Toplak H, Obesity Management Task Force of the European Association for the Study of O. European Guidelines for Obesity Management in Adults. Obes Facts 2015; 8: 402-424.

8) Bald E, Raber H. Semaglutide (Wegovy) for the Treatment of Obesity. Am Fam Physician 2023; 107: 90-91.

9) Singh G, Krauthamer M, Bjalme-Evans M. Wegovy (semaglutide): a new weight loss drug for chronic weight management. J Investig Med 2022; 70: 5-13.

10) Rosenstock J, Frias J, Jastreboff AM, Du Y, Lou J, Gurbuz S, Thomas MK, Hartman ML, Haupt A, Milicevic Z, Coskun T. Retatrutide, a GIP, GLP-1 and glucagon receptor agonist, for people with type 2 diabetes: a randomised, double-blind, placebo and active-controlled, parallel-group, phase 2 trial conducted in the USA. Lancet 2023; 402: 529-544.

11) Tsukamoto S, Tanaka S, Yamada T, Uneda K, Azushima K, Kinguchi S, Wakui H, Tamura K. Effect of tirzepatide on glycaemic control and weight loss compared with other glucagon-like peptide-1 receptor agonists in Japanese patients with type 2 diabetes mellitus. Diabetes Obes Metab 2024; 26: 262-274.

12) Patel D, Smith A. Patient initiation and maintenance of GLP-1 RAs for treatment of obesity. Expert Rev Clin Pharmacol 2021; 14: 1193-1204.

13) Colin IM, Gérard KM. Once-weekly 2.4 mg Semaglutide for Weight Management in Obesity: A Game Changer? touchREV Endocrinol 2022; 18: 35-42.

14) Xiang J, Ding XY, Zhang W, Zhang J, Zhang YS, Li ZM, Xia N, Liang YZ. Clinical effectiveness of semaglutide on weight loss, body composition, and muscle strength in Chinese adults. Eur Rev Med Pharmacol Sci 2023; 27: 9908-9915.

15) Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, Lau DC, le Roux CW, Violante Ortiz R, Jensen CB, Wilding JP; SCALE Obesity and Prediabetes NN8022-1839 Study Group. A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. N Engl J Med 2015; 373: 11-22.

16) Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, McGowan BM, Rosenstock J, Tran MTD, Wadden TA, Wharton S, Yokote K, Zeuthen N, Kushner RF; STEP 1 Study Group. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med 2021; 384: 989-1002.

17) Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, Wadden TA, Wizert A, Garvey WT, Arauz-Pacheco C. Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: the STEP 8 randomized clinical trial. JAMA 2022; 327: 138-150.

18) Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, Caulley L, Chaiyakunapruk N, Greenberg D, Loder E, Mauskopf J, Mullins CD, Petrou S, Pwu RF, Staniszewska S. Correction to: Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Appl Health Econ Health Policy 2022; 20: 781-782.

19) Kim N, Wang J, Burudpakdee C, Song Y, Ramasamy A, Xie Y, Sun R, Kumar N, Wu EQ, Sullivan SD. Cost-effectiveness analysis of semaglutide 2.4 mg for the treatment of adult patients with overweight and obesity in the United States. J Manag Care Spec Pharm 2022; 28: 740-752.

20) Hu Y, Zheng SL, Ye XL, Shi JN, Zheng XW, Pan HS, Zhang YW, Yang XL, Huang P. Cost-effectiveness analysis of 4 GLP-1RAs in the treatment of obesity in a US setting. Ann Transl Med 2022; 10: 152.

21) Htike ZZ, Zaccardi F, Papamargaritis D, Webb DR, Khunti K, Davies MJ. Efficacy and safety of glucagon-like peptide-1 receptor agonists in type 2 diabetes: A systematic review and mixed-treatment comparison analysis. Diabetes Obes Metab 2017; 19: 524-536.

22) Williamson DA, Bray GA, Ryan DH. Is 5% weight loss a satisfactory criterion to define clinically significant weight loss? Obesity 2015; 23: 2319.

23) Schetz M, De Jong A, Deane AM, Druml W, Hemelaar P, Pelosi P, Pickkers P, Reintam-Blaser A, Roberts J, Sakr Y, Jaber S. Obesity in the critically ill: a narrative review. Intensive Care Med 2019; 45: 757-769.

24) Deng Y, Park A, Zhu L, Xie W, Pan CQ. Effect of semaglutide and liraglutide in individuals with obesity or overweight without diabetes: a systematic review. Ther Adv Chronic Dis 2022; 13: 20406223221108064.

25) O'Neil PM, Birkenfeld AL, McGowan B, Mosenzon O, Pedersen SD, Wharton S, Carson CG, Jepsen CH, Kabisch M, Wilding JPH. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet 2018; 392: 637-649.

26) Wing RR, Lang W, Wadden TA, Safford M, Knowler WC, Bertoni AG, Hill JO, Brancati FL,

Peters A, Wagenknecht L, Look ARG. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. Diabetes Care 2011; 34: 1481-1486.

27) Unick JL, Beavers D, Jakicic JM, Kitabchi AE, Knowler WC, Wadden TA, Wing RR, Look ARG. Effectiveness of lifestyle interventions for individuals with severe obesity and type 2 diabetes: results from the Look AHEAD trial. Diabetes Care 2011; 34: 2152-2157.

28) Lazo M, Solga SF, Horska A, Bonekamp S, Diehl AM, Brancati FL, Wagenknecht LE, Pi-Sunyer FX, Kahn SE, Clark JM, Fatty Liver Subgroup of the Look ARG. Effect of a 12-month intensive lifestyle intervention on hepatic steatosis in adults with type 2 diabetes. Diabetes Care 2010; 33: 2156-2163.

29) Kolotkin RL, Crosby RD, Williams GR, Hartley GG, Nicol S. The relationship between health-related quality of life and weight loss. Obes Res 2001; 9: 564-571.