

## ORIGINAL ARTICLE

## Clinical Trials and Investigations

# Liraglutide versus semaglutide for weight reduction—a cost needed to treat analysis

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## Abstract

**Objective:** Higher doses of the glucagon-like peptide-1 agonists liraglutide and, more recently, semaglutide have demonstrated a significant reduction in body weight. However, their comparative value for money for this indication is unclear.

**Methods:** The cost needed to treat to achieve a 1% reduction in body weight using semaglutide or liraglutide was calculated. The body weight reductions were extracted from the published STEP 1 trial and the SCALE trial results, respectively. A scenario analysis was performed to mitigate the primary differences between the two studies' populations. Drug costs were based on US GoodRx prices as of October 2022.

**Results:** Liraglutide in STEP 1 resulted in a weight loss of 5.4% (95% CI: 5%-5.8%). Semaglutide in SCALE resulted in a weight loss of 12.4% (95% CI: 11.5%-13.4%). The total cost of therapy with liraglutide during the trial was estimated at \$17,585 compared with \$22,878 with semaglutide. Accordingly, the cost needed to treat per 1% of body weight reduction with liraglutide is estimated at \$3256 (95% CI: \$3032-\$3517) compared with \$1845 (95% CI: \$1707-\$1989) with semaglutide.

**Conclusions:** Semaglutide provides significantly better value for money than liraglutide for weight reduction.

## INTRODUCTION

A key global public health challenge is obesity, which carries a significant disease burden, including hypertension, type 2 diabetes mellitus, nonalcoholic fatty liver disease, malignancies, and cardiovascular disease [1-4]. Significant weight reduction has been shown to improve health outcomes and quality of life [5-7]. The traditional mainstay of management is lifestyle modifications, but long-term outcomes for sustained weight loss are poor [1, 2, 8, 9]. In recent years, clinical guidelines have

recommended pharmacological treatment as an adjunct therapy for weight reduction [1-3]. High doses of glucagon-like peptide-1 (GLP-1) agonists semaglutide and liraglutide have significantly reduced weight in the Semaglutide Treatment Effect in People with Obesity (STEP) 1 trial and the Satiety and Clinical Adiposity—Liraglutide Evidence in Nondiabetic and Diabetic Individuals (SCALE) trial, respectively [10, 11]. Although obesity-associated costs are expected to drop with these drugs, their costs may be a significant burden on health care systems [12].

Therefore, our objective is to provide an economic measure for comparing the cost per outcome of using liraglutide versus semaglutide for enabling weight loss in patients.

Joseph Azuri and Ariel Hammerman contributed equally to the manuscript.

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## METHODS

### Data sources for drug efficacy

Outcome data for both drugs were extracted from the published results of the STEP 1 and SCALE trials for semaglutide up to 2.4 mg per week and liraglutide titrated to 3 mg daily, respectively. Both trials' analyses were based on the maximum doses. These studies demonstrated measured weight change as a percentage of the original measured weight. All patients from STEP 1 and SCALE trials were included in our analysis.

### Primary outcome measures

The primary outcome of this study was the cost needed to treat (CNT) to achieve a 1% reduction in body weight using semaglutide or liraglutide. The analysis was performed from the US health care perspective.

### CNT analysis

The CNT was calculated by multiplying the annual drug costs by the follow-up time (in years) and then dividing by the mean percent weight reduction for each drug compared with placebo. Drug costs were based on US GoodRx prices as of October 2022 as a transparent approach to assessing outpatient drug costs for use in US economic evaluations.

### Scenario analysis

To evaluate the robustness of CNT results and mitigate differences between the randomized controlled trial (RCT) populations' baseline risks, we performed a scenario analysis that simulated each drug's effect while using the event rate in the other drug trial's control arm.

### Sensitivity analysis—for 5% weight reduction

The CNT per patient to reach 5% weight loss and above was calculated using the total treatment cost for the entire cohort divided by the number of patients who reached >5%.

## RESULTS

### Patient populations

The participants included in STEP 1 and SCALE trials were similar in baseline characteristics (Table 1). Most of the patients included in both trials were female. In addition, the average age, body weight, and body mass index (BMI) were all similar.

### Study Importance

#### What is already known?

- Semaglutide and liraglutide have proven effective in achieving significant weight loss.

#### What does this study add?

- Our findings show that semaglutide has a significantly lower cost needed to treat than liraglutide.

#### How might these results change the direction of research or the focus of clinical practice?

- Our results have immediate ramifications supporting semaglutide as a more cost-efficient weight loss agent.

### CNT

The step-by-step calculations are detailed in Table 2. Using liraglutide in STEP 1 resulted in a weight loss of 5.4% (95% CI: 5%-5.8%). Semaglutide in SCALE resulted in a weight loss of 12.4% (95% CI: 11.5%-13.4%). The total cost of therapy with liraglutide during the study period was estimated at \$17,585 compared with \$22,878 with semaglutide. Accordingly, the CNT per 1% of body weight reduction with liraglutide was estimated at \$3256 (95% CI: \$3032-\$3517) compared with \$1845 (95% CI: \$1707-\$1989) with semaglutide.

### Scenario analysis

The results of the scenario analysis are found in Table 3. The difference between the costs increased by nearly 25% in favor of semaglutide.

**TABLE 1** Baseline characteristics

Trial	STEP 1	SCALE
Intervention	Semaglutide	Liraglutide
Dosage (mg)	2.4 weekly	3 daily
Number of participants in the intervention arm	1306	2487
Age (y) (median)	46 ± 13	45.2 ± 12.1
Female sex (%)	955 (73.1)	1957 (78.7)
White (%)	973 (74.5)	2107 (84.7)
Body weight (kg)	105.4 ± 21.5	106.2 ± 21.2
BMI	37.8 ± 6.7	38.3 ± 6.4
Follow-up (wk)	68	56

**TABLE 2** Step-by-step CNT calculations

Parameter	Semaglutide	Liraglutide
Patients in the intervention arm	1306	2487
Follow-up (wk)	68	56
Annual drug cost (\$)	17,543.07	16,373.54
Weekly drug cost (\$)	336.44	314.01
Cost of therapy (weekly cost multiplied by the number of weeks followed up) (\$)	$336.44 * 68 = 22,878.09$	$314.01 * 56 = 17,584.73$
Average weight loss (%)	12.4	5.4
CNT for 1% weight loss (\$) (95% CI)	$22,878.09 / 12.4 = 1845.01$	$17,584.73 / 5.4 = 3256.43$

Abbreviation: CNT, cost needed to treat.

**TABLE 3** Scenario analysis

	SOC, % body weight reduction	Therapy group, % body weight reduction (95% CI)	CNT per % body weight (95% CI)
Semaglutide in STEP 1	2.41%	14.85% (13.95%-15.85%)	\$1845.01
Simulated semaglutide in SCALE	2.6%	16.02% (15.12%-17.02%) (simulated)	\$1404.35 (\$1306.94-\$1505.34)
Liraglutide in SCALE	2.6%	8% (7.6%-8.4%)	\$3256.43
Simulated liraglutide in STEP 1	2.41%	7.40% (7.0%-7.8%) (simulated)	\$4449.72 (\$4107.35-\$4854.36)

Abbreviations: CNT, cost needed to treat; SOC, standard of care.

## Sensitivity analysis

In the STEP 1 trial, the number of patients who reached >5% weight reduction in the treatment group over the control group was 922. Likewise, in the SCALE trial, 2437 patients received liraglutide, and the number of patients who reached >5% weight reduction in the treatment group over the control group was 1208. Therefore, the calculated CNT for patients who reached >5% weight reduction for semaglutide was \$32,406 compared with \$35,475 for liraglutide.

## DISCUSSION

In recent years, several pharmacological agents have been approved as adjuncts in enabling weight loss, such as orlistat and naltrexone/bupropion combination [13, 14]. GLP-1 agonists have proven very effective with relatively few side effects [3]. Moreover, weight reduction has resulted in cardiovascular risk reduction [15].

The two large-scale RCTs that investigated the weight loss properties of semaglutide and liraglutide demonstrated a significant weight reduction exceeding that of placebo. The STEP 1 trial demonstrated that the weight reduction achieved with once-weekly 2.4 mg semaglutide was greater than that reported in the SCALE trial with once-daily 3.0 mg liraglutide. It should be noted that the doses used in the two trials were the maximum doses indicated for weight reduction. A recent study attempted to indirectly calculate quality-adjusted life years for GLP-1 agonists based on existing data and found that semaglutide was the most cost-effective of the drugs tested. However, this study evaluated only submaximal doses [16]. Moreover, the CNT for each drug has not previously been evaluated. Our analysis demonstrates that the CNT for semaglutide (\$1845) is significantly lower

than liraglutide (\$3256) for 1% weight loss as adjunct pharmacotherapy. The difference was further increased in the scenario analysis simulation, with a cost reduction of \$441 for the simulated semaglutide CNT in the SCALE study and a cost increase of \$1193 for the simulated liraglutide CNT in the STEP 1 study. This further emphasizes the CNT gap between the two medications. Furthermore, when considering treatment success as a >5% weight reduction, the CNT gap in favor of semaglutide was maintained.

Treatment regimens for weight reduction always aim to achieve the maximum possible dose, as was used in both trials. Nevertheless, although the participants in the SCALE study who completed the study were receiving the maximum dose, in the STEP 1 trial (with semaglutide), nearly 10% of patients received reduced doses because of side effects. With the intention-to-treat analysis of the trials, the CNT gap in favor of semaglutide might only increase.

Other factors beyond cost influence physicians and patients when choosing the appropriate drug. These include frequency of administration, long-term weight loss, safety profile, and side effects. In this analysis, we focused only on CNT. However, the more convenient administration of semaglutide, once-weekly versus once-daily injection, further favors semaglutide.

Recent real-world data studies have replicated the findings of the SCALE and STEP 1 trials, with significant weight loss achieved, and the weight loss was similar across different doses [17, 18]. This reinforces the importance of GLP-1 agonists as an effective treatment. Our study demonstrates a strong economic impact of choosing semaglutide over liraglutide, which may have immediate practical implications for decision-makers.

Our analysis has several limitations. The first is that the drugs were not tested in a head-to-head trial. However, the baseline age, weight, and BMI characteristics in STEP 1 and SCALE studies were very similar, with

even a slightly higher BMI in the SCALE trial, enhancing the finding of the superiority of semaglutide.


Second, the CNT per 1% weight reduction was calculated by the total cost divided by the total weight reduction, which assumes a linear correlation. However, this reflects the average cost per weight reduction unit. Furthermore, the CNT calculations were based on published data for both drugs, showing weight reduction during 56 to 68 weeks of treatment. This analysis does not consider future costs to maintain the weight reduction (>5% reduction or less) by continuing the treatment. This issue should be addressed in future follow-up studies for both drugs.

Third, our analysis cannot replace a comprehensive cost-effectiveness evaluation regarding achieved quality-adjusted life years and cost savings from reduced morbidity. However, a direct complete economic comparison of these interventions is unavailable at this time. Nevertheless, we suggest using the CNT analysis as a preliminary comparative measure that should be used cautiously. CNT measures have previously correlated with later published cost-effectiveness analysis results [19].

Another limitation is that the proportion of patients who completed the trial for liraglutide was comparatively low, which further demonstrates the disparity between the two medications.

Finally, our results are based on the published results of only two RCTs. Therefore, more data are required to confirm the findings. Nevertheless, the professional societies' guidelines and statements stem from the same data.

## CONCLUSION

Semaglutide provides significantly better value for money in weight reduction than liraglutide in the United States. However, regarding other health care settings, the CNT results should be validated according to local drug tariffs, as the relative annual price of the two drugs significantly impacts the comparative CNT. Our economic results support the use of semaglutide as a pharmacological adjunct to weight loss. A formal comparative cost-effectiveness analysis is warranted to confirm our findings. 

## CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

## DATA AVAILABILITY STATEMENT

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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