



Mission Slimpossible: Semaglutide for weight loss

CLINICAL QUESTION

Is semaglutide effective for weight loss?

BOTTOM LINE

Used with lifestyle changes, 2.4mg weekly subcutaneous semaglutide resulted in an average 10-15% loss in weight (10-15kg) over 68 weeks versus 2-3% (3-4kg) with placebo. Most (70-80%) semaglutide participants lost 5% or more of their body weight. About $\frac{3}{4}$ of patients experienced gastrointestinal side effects, but few stop. Weight regain occurs once the medication is stopped.

EVIDENCE

- Four industry-funded, randomized, placebo-controlled trials (RCTs) of subcutaneous semaglutide 2.4mg/week for weight loss, plus lifestyle interventions (counseling, diet, and physical activity).¹⁻⁴ Baseline weight ~96-105kg.
 - 1961 non-diabetics.¹ After 68 weeks:
 - Mean weight loss: 15% of weight (15kg) versus 2% (3kg, placebo).

- Proportion who lost $\geq 5\%$ weight: 86% versus 32% (placebo), number need to treat (NNT)=2.
 - Lost $\geq 10\%$: 69% versus 12%, NNT=2.
 - Weight loss plateaued ~week 60.
- Adverse effects:
 - Gastrointestinal: 74% versus 48% (placebo), number needed to harm (NNH)=3.
 - Withdrawal due to adverse effects: 7% versus 3%, NNH=25.
- RCT of semaglutide with more intensive lifestyle intervention found similar [weight loss 16% (17kg) versus 6% (6kg, placebo)].²
- Dose-finding RCT, 1210 diabetics. Given semaglutide 2.4mg/week, 1.0mg/week or placebo.³ After 68 weeks:
 - Mean weight loss: 10% (2.4mg), 7% (1mg) and 3% (placebo)
 - Proportion who lost $\geq 5\%$ weight: 69% (2.4mg) versus 57% (1mg) versus 29% (placebo), 2.4mg versus 1mg: NNT=9.
 - Adverse effects similar between doses.
- Weight maintenance RCT. 803 non-diabetics given semaglutide 2.4mg/week for 20 weeks then randomized to continue semaglutide or switch to placebo. After 48 weeks:⁴
 - Continued semaglutide lost 8% versus 7% gain (placebo).

CONTEXT

- Weight loss with oral semaglutide studied as secondary outcome in cardiovascular disease and glucose-lowering trials. Participants weight loss was 4.6% (4.2kg) versus 0.9% (0.8kg, placebo) at 15.9 months in largest RCT.⁵
- High-dose semaglutide (0.4mg daily) superior to liraglutide (3mg daily) in semaglutide-sponsored RCT:
 - Weight loss: 14% semaglutide (17kg) versus 8% liraglutide (8kg).
 - Weight loss similar between 0.1mg daily semaglutide and liraglutide.⁶
- Semaglutide titration in RCTs: Every 4 weeks as tolerated.
- Semaglutide 2.4mg not currently available (Canada), but lower doses are.⁷
 - 1mg weekly costs ~\$200/month.⁸

REFERENCES

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