

# Semaglutide for weight loss.

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## Clinical question

Is semaglutide (SGT) effective for weight loss?

## Bottom line

Used with lifestyle changes, 2.4 mg of subcutaneous SGT weekly resulted in a mean 10% to 15% weight loss (10 to 15 kg) over 68 weeks versus 2% to 3% (3 to 4 kg) with placebo (PC). Most (70% to 80%) lost 5% or more of their body weight. About 75% had gastrointestinal side effects, but few discontinued treatment. Weight was regained on medication discontinuation.

## Evidence

Differences were statistically significant unless noted.

- In 4 RCTs, patients (baseline weight 96 to 105 kg) were treated for weight loss with 2.4 mg of subcutaneous SGT weekly and lifestyle interventions (counseling, diet, and physical activity).<sup>1-4</sup>
  - An RCT of nondiabetic patients (N = 1961)<sup>1</sup>: After 68 weeks, mean weight loss was 15% (15 kg) versus 2% (3 kg) PC. The proportion of those who lost weight ( $\geq 5\%$ ) was 86% versus 32% (PC), with a number needed to treat (NNT) = 2, while the proportion who lost more weight ( $\geq 10\%$ ) was 69% versus 12% (PC), NNT = 2. Weight loss plateaued around week 60.
  - Gastrointestinal adverse effects (AEs): 74% versus 48% (PC), number needed to harm (NNH) = 3. Withdrawals due to AEs were 7% versus 3% (PC), NNH = 25.
  - Similar results in an RCT (N = 611) of SGT with intensive lifestyle interventions: 16% (17 kg) versus 6% (6 kg) PC.<sup>2</sup>
  - Dose-finding RCT<sup>3</sup> of diabetic patients (N = 1210) given either 2.4 mg of SGT weekly, 1.0 mg of SGT weekly, or PC: After 68 weeks, mean weight loss was 10% (2.4 mg), 7% (1.0 mg), and 3% (PC). Proportion who lost weight ( $\geq 5\%$ ) was 69% (2.4 mg) versus 57% (1.0 mg) versus 29% (PC). For 2.4 mg versus 1.0 mg, NNT = 9.
  - The AEs were similar between doses.
  - Weight-maintenance RCT (N = 803)<sup>4</sup>: Nondiabetic participants were given 2.4 mg of SGT weekly for 20 weeks and then randomized to either continued SGT or PC. After 48 weeks, the continued SGT group lost 8% body weight compared with a 7% weight gain in the PC group.

## Context

- Weight loss with oral SGT studied as a secondary outcome in cardiovascular disease and glucose-lowering trials found that weight loss was 4.6% (4.2 kg) versus 0.9% (0.8 kg) with PC at 15.9 months.<sup>5</sup>
- In an SGT-sponsored RCT, high-dose SGT (0.4 mg/day) was superior to liraglutide (3 mg/day). Weight loss was 14% (17 kg) SGT versus 8% (8 kg) liraglutide. Weight loss was similar between 0.1 mg of SGT daily and liraglutide.<sup>6</sup>
- Semaglutide (2.4 mg) is not available now in Canada, but lower doses are<sup>7</sup> (1 mg/week costs about \$200/month<sup>8</sup>).

## Implementation

Besides weight loss, SGT increased quality of life for 40% to 50% of participants compared with about 30% taking PC.<sup>1</sup> Semaglutide is usually started at 0.25 mg weekly and is increased by 0.25 mg every 4 weeks until the target dose is reached (as tolerated).<sup>9</sup> Nausea and gastrointestinal upset are reported AEs, particularly during dose escalation.<sup>1,9</sup> Adherence to weekly subcutaneous injections may be better than for daily injections.<sup>10</sup> Other glucagon-like peptide 1 agonists and SGT should likely be avoided in patients with history of medullary thyroid carcinoma, pancreatitis, or tachyarrhythmias.<sup>9</sup>

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