Weight Change With Semaglutide

Team A: Dave Little, MD, Joe Deckert, PhD
Team B: Kersten Bartelt, RN, Manisha Ganesh, Ted Stamp
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Key Findings:

- 60 weeks after starting semaglutide, diabetics lost 8% and non-diabetics lost 11% of their body weight at the highest recommended dose (2.4 mg).
- Even at lower doses, semaglutide resulted in weight loss in most diabetic and non-diabetic patients.
- However, 25% of patients on the lowest doses gained weight in the same timeframe.

Semaglutide injections, also known as Ozempic and Wegovy, were originally only approved for treating diabetic patients. Recently, they were additionally approved for the treatment of obesity. The U.S. Food and Drug Administration (FDA) recommends patients prescribed semaglutide for weight loss start at a 0.25 mg dose and increase gradually to 2.4 mg over 16 to 20 weeks. Previous randomized control trials of semaglutide in diabetic and non-diabetic populations have suggested that non-diabetic patients lose more weight than diabetic patients when prescribed semaglutide, but those studies do not represent real-world data and did not evaluate doses lower than 2.4 mg. 4

Semaglutide is considered a long-term medication as some clinical trials showed that discontinuing use may cause weight gain.^{5,6} We did not evaluate the impact of discontinuing semaglutide or the potential side effects reported in previous trials, which include an elevated risk of developing thyroid cancer, gallbladder-related disorders, or gastrointestinal disorders.^{3,7,8,9} This study is not a recommendation for a particular treatment but rather an observational analysis of available data for patients prescribed semaglutide.

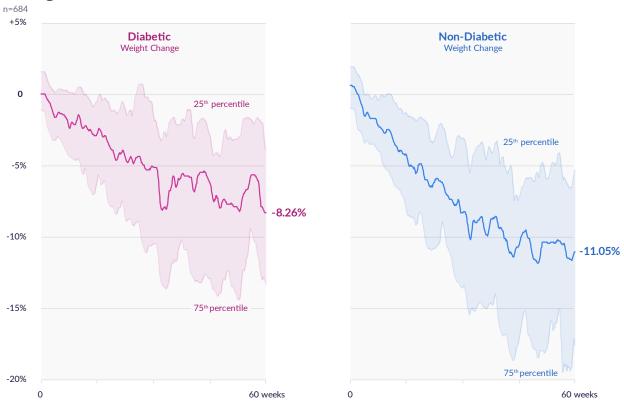
We studied 14,814 patients—half with type 2 diabetes and the other half without diabetes. The populations were matched by sex, height, weight, race, ethnicity, social vulnerability index (SVI), and age. We then calculated percentage weight change across 60 weeks after starting semaglutide. We stratified patients by the maximum dose of semaglutide the patient was prescribed within the first year.

Figure 1 shows weight loss for patients on 2.4 mg of semaglutide, the FDA-approved dose for chronic weight management. ³ Figure 2 shows weight loss for patients on a medium dose (1-2 mg) of semaglutide and Figure 3 shows results from patients on the lowest dose (0.25-0.5 mg). In each figure, week zero represents the percentage difference between a patient's average weight from the year prior to starting semaglutide and their weight when starting semaglutide.

Overall, regardless of dose, diabetics and non-diabetics lost weight. At the 1-2mg and 2.4 mg doses, non-diabetics lost more than diabetics. At the 0.25-0.5mg dose, while most diabetics and non-diabetics lost weight, 25% of patients gained weight. These findings align with the previous randomized control trials for semaglutide at 2.4 mg and provide additional insight into median weight loss for diabetic and non-diabetic patients at lower doses. 4.7



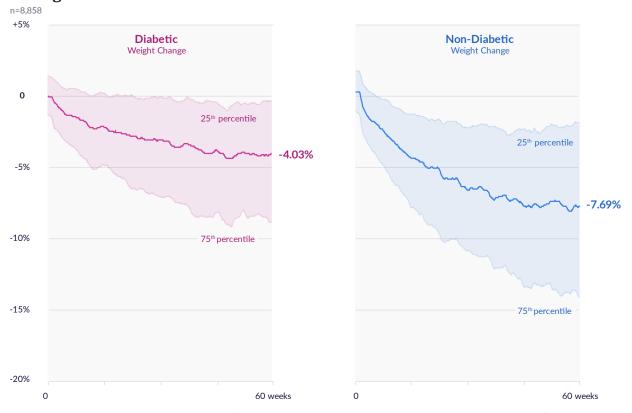
Median Weight Loss for Diabetic & Non-Diabetic Patients on 2.4 mg Semaglutide



"Median Weight Loss for Diabetic & Non-Diabetic Patients on 2.4 mg Semaglutide," 2023. EpicResearch.org

Figure 1. Five-day rolling average of median weight change percentage among diabetic and non-diabetic patients on 2.4 mg of semaglutide.

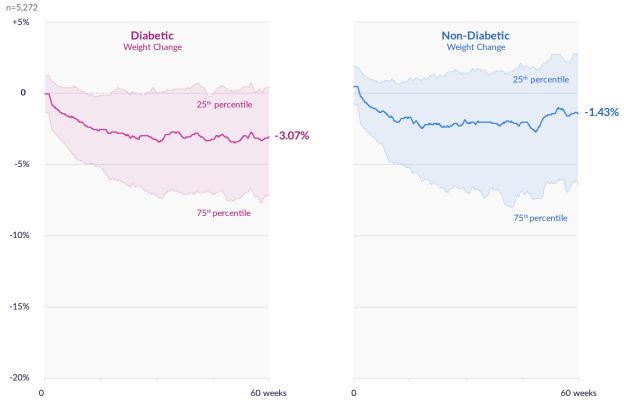
Median Weight Loss for Diabetic & Non-Diabetic Patients on 1, 1.7, or 2 mg Semaglutide



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Figure 2. Five-day rolling average of median weight change percentage among diabetic and non-diabetic patients on 1, 1.7, or 2 mg of semaglutide.

Median Weight Loss for Diabetic & Non-Diabetic Patients on 0.25 or 0.5 mg Semaglutide



"Median Weight Loss for Diabetic & Non-Diabetic Patients on 0.25 or 0.5 mg Semaglutide," 2023. EpicResearch.org

Figure 3. Five-day rolling average of median weight change percentage among diabetic and non-diabetic patients on 0.25 or 0.5 mg of semaglutide.

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 184 million patients from 199 Epic organizations including 1,141 hospitals and more than 24,900 clinics, serving patients in all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions.

References

- 1. Hinnen, Deborah. "Glucagon-Like Peptide 1 Receptor Agonists for Type 2 Diabetes." Diabetes Spectrum, vol. 30, no. 3, American Diabetes Association, Aug. 2017, pp. 202–10. https://doi.org/10.2337/ds16-0026.
- Research Center for Drug Evaluation. "FDA approves weight management drug for patients aged 12 and older." U.S. Food And Drug Administration, September 30, 2021, https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-weight-management-drug-patients-aged-12-and-older.
- 3. Office of the Commissioner. "FDA Approves New Drug Treatment for Chronic Weight Management, First Since 2014." *U.S. Food And Drug Administration*, June 15, 2021, weight-management-first-2014.



- 4. Jensterle, Mojca, et al. "Efficacy of GLP-1 RA Approved for Weight Management in Patients With or Without Diabetes: A Narrative Review." Advances in Therapy, vol. 39, no. 6, Springer Science+Business Media, May 2022, pp. 2452–67. https://doi.org/10.1007/s12325-022-02153-x.
- 5. Wilding, John P..H., et al. "Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension." Diabetes, Obesity, and Metabolism, vol. 24, no. 8, Pharmacology and Therapeutics, August 2022, pp. 1553-1564. https://doi.org/10.1111/dom.14725.
- 6. Rubino, Domenica, et al. "Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults with Overweight or Obesity." *JAMA*. 2021;325(14):1414-1425. doi:10.1001/jama.2021.3224. https://jamanetwork.com/journals/jama/article-abstract/2777886.
- 7. Wilding, John P. H., et al. "Once-Weekly Semaglutide in Adults With Overweight or Obesity." The New England Journal of Medicine, vol. 384, no. 11, Massachusetts Medical Society, Feb. 2021, pp. 989–1002. https://doi.org/10.1056/nejmoa2032183.
- 8. WEGOVY (semaglutide) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215256s000lbl.pdf.
- 9. Ozempic (semaglutide) [package insert]. U.S. Food and Drug Administration website. https://www.accessdata.fda.gov/drugsatfda docs/label/2020/209637s003lbl.pdf.

Data Definitions

Term	Definition
Study period	10/7/2016 - 3/12/2023
Study population	 Patients that met the following criteria: Over age 18 Not pregnant while taking semaglutide Not an amputee (ICD-10-CM S[0-9]8.*) At least three vitals measurements in the year before their semaglutide prescription where their weight did not fluctuate more than 10% over that period and weight remained between 60 and 1,000 pounds Active semaglutide prescription for at least a year
Diabetic patient	Patients that have a type 2 diabetes diagnosis (SNOMED code 44054006) or have both an A1C level > 6.5 and medication order for one of the following medication classes: • Alpha-glucosidase inhibitors • Amylin analogs • Antidiabetic agents • Antidiabetic combinations • Insulin • Meglitinides • Sulfonylureas • Thiazolidinediones The above diabetic criteria were met before semaglutide prescription.
Non-diabetic patient	Patients who are not classified as a diabetic patient.



Semaglutide prescription	Active prescription of semaglutide and pharmaceutical subclass of GLP-1 Receptor Antagonist with a route of subcutaneous.
Starting weight	The patient's average weight from the year prior to their semaglutide prescription, including weight taken on day of their prescription if available.
Median weight change	A 21-day rolling median percent change from the starting weight for each day studied.

Full data available upon request.

