
Semaglutide/
Cyanocobalamin (GLP-1)
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# Obesity- from the 2020 National Diabetes Statistics Report

- 43% of Americans are overweight
- Childhood obesity has tripled in the last 30 years
- Approximately 88 million Americans have pre diabetes
- 1/3 Americans have pre diabetes


. https://www.cdc.gov/obesity/data/adult.html

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# Question

**Which hormone is associated with Pre Diabetes, Alzheimer, Hypertension, Heart disease, Stroke, Impotence, Infertility, Obesity Autoimmune disease and Cancer?**

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# Answer

## High Insulin Levels!!!

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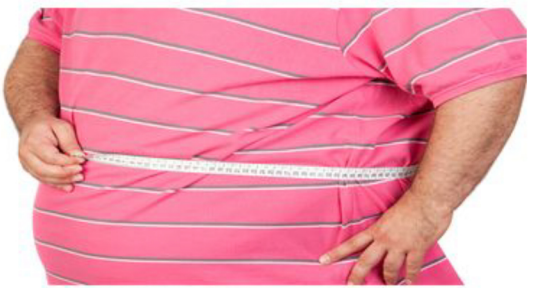
# Insulin Resistance



- Precursor of Diabetes
- Elevated Insulin levels
- Fat, Muscle and Liver become resistant to insulin
- The pancreas thus produces more insulin since the demand is higher.

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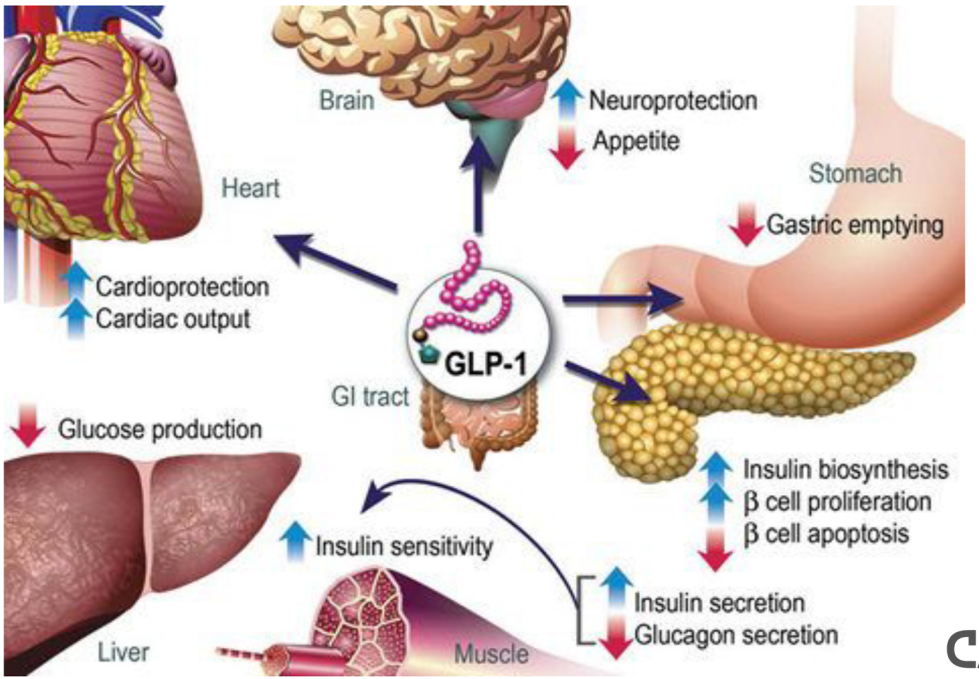
# GLP-1 (Glucagon-Like Peptide 1)

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# Glucagon Like Peptides

- GLP-1 is a hormone produced in the small intestine that stimulates insulin secretion and inhibits glucagon secretion, thereby lowering blood sugar.
- Shorter-acting agonists of the GLP-1 receptor are particularly effective at lowering post-meal glucose spikes, whereas longer-acting GLP-1 agonists have more balanced effects on lowering post-meal and fasting glucose levels.

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# Semaglutide

## What Is Semaglutide?

- **Semaglutide** acts as a GLP-1 receptor agonist.
- It increases intracellular cyclic AMP (cAMP) leading to insulin release in the presence of elevated glucose concentrations. This insulin secretion subsides as blood glucose concentrations decrease and approach euglycemia.
- Semaglutide also decreases glucagon secretion in a glucose-dependent manner. The mechanism of blood glucose lowering also involves a delay in gastric emptying and improves beta cell function in the pancreas.

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# Semaglutide: HbA1c

**Semaglutide** reduces **HbA1c** across baseline **HbA1c** subgroups across SUSTAIN 1–5 Clinical Trials. **Semaglutide**, a GLP-1 analog for once-weekly subcutaneous treatment of T2D, demonstrated superior reductions in **HbA1c** and body weight across SUSTAIN 1–5 clinical trials. (Tsoukas)

Mean HbA1c decreased by 0.7 (2.5%) with semaglutide 0.5mg and 0.9 (2.8%) with semaglutide 1.0mg, vs 1.8% to an increase of 0.6% with comparators (Tsoukas)

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## June 4, 2021 The FDA approves Semaglutide for weight loss

Today, the U.S. Food and Drug Administration approved Wegovy (semaglutide) injection (2.4 mg once weekly) for chronic weight management in adults with obesity or overweight with at least one weight-related condition (such as high blood pressure, type 2 diabetes, or high cholesterol), for use in addition to a reduced calorie diet and increased physical activity. This under-the-skin injection is the first approved drug for chronic weight management in adults with general obesity or overweight since 2014. The drug is indicated for chronic weight management in patients with a body mass index (BMI) of 27 kg/m2 or greater who have at least one weight-related ailment or in patients with a BMI of 30 kg/m2 or greater.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Once-Weekly Semaglutide in Adults with Overweight or Obesity

John P.H. Wilding, D.M., Rachel L. Batterham, M.B., B.S., Ph.D., Salvatore Calanna, Ph.D., Melanie Davies, M.D., Luc F. Van Gaal, M.D., Ph.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Barbara M. McGowan, M.D., Ph.D., Julio Rosenstock, M.D., Marie T.D. Tran, M.D., Ph.D., Thomas A. Wadden, Ph.D., Sean Wharton, M.D., Pharm.D., Koutaro Yokote, M.D., Ph.D., Niels Zeuthen, M.Sc., and Robert F. Kushner, M.D., for the STEP 1 Study Group*

ABSTRACT

# Semaglutide: Weight Loss

- Double-blind trial, 1961 adults with a BMI of 30 or greater, who did not have diabetes.
- 68 weeks of treatment with once-weekly subcutaneous semaglutide (at a **dose of 2.4 mg**) or placebo, plus lifestyle intervention.
- Mean change in body weight from baseline to week 68 was **−14.9%** in the semaglutide group as compared with −2.4% with placebo
- Change in body weight from baseline to week 68 was **−15.3 kg (33.7 pounds)** in the semaglutide group as compared with −2.6 kg in the placebo group 86% of participants attaining at least 5% weight loss.
- Participants who received semaglutide had a greater improvement with respect to cardiometabolic risk factors and a greater increase in participant-reported physical functioning from baseline.

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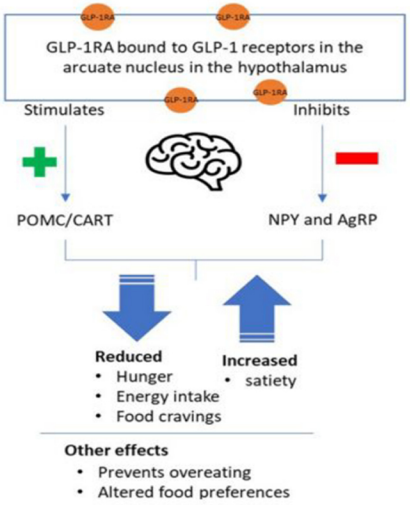
# Weight Loss




**A** In the central nervous system, GLP-1 receptors are located in the hypothalamus, which is involved in regulating food intake

**B** The reduced feelings of hunger were associated with an increase in functional connectivity of the nucleus tract with the hypothalamus

**C** GLP-1 directly stimulates POMC/CART neurons and indirectly inhibits neuropeptide Y (NPY) and agouti-related peptide (AgRP) to increase measures of satiety and decrease hunger

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# Weight Loss

- Increased postprandial insulin secretion
- Decreased food cravings
- Delays gastric emptying
- Associated with decreased appetite, by potentially increasing leptin sensitivity
- Increased satiety

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GLP-1 and B12

•A major side effect with GLP-1 agonists is nausea and/or malaise.



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# A Vitamin B12 Conjugate of Exendin-4 Improves Glucose Tolerance Without Associated Nausea or Hypophagia in Rodents

Elizabeth G. Mietlicki-Baase,[1,*] Claudia G. Liberini,[1,*] Jayme L. Workinger,[2,*] Ron L. Bonaccorso,[2] Tito Borner,[3] David J. Reiner,[1] Kieran Koch-Laskowski,[1] Lauren E. McGrath,[1] Rinzin Lhamo,[1] Lauren M. Stein,[1] Bart C. De Jonghe,[3] George G. Holz,[4] Christian L. Roth,[5] Robert P. Doyle,[2,4,&#] and Matthew R. Hayes[1,3,&#]

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# GLP-1 and B12

- A study between March 2014 and April 2015, included 304 non-diabetic obese patients discovered a high prevalence of vitamin B12 (13.5%) deficiency (O. Cigerli 2016)
- In a large nationally representative sample of U.S. adults (9,075 participants), higher serum vitamin B12 levels were inversely associated with obesity (Yangbo Sun 2019)
- Clinical and biochemical vitamin B12 deficiency is highly prevalent among patients with both type 1 and type 2 DM
    - This prevalence of deficiency is significantly higher for those patients being treated with metformin

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