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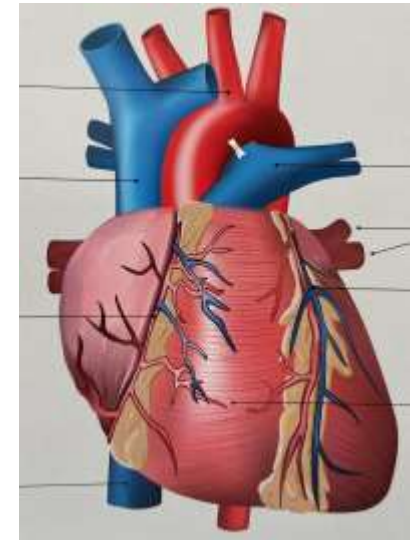
Treating Obesity to Promote Heart Health

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30 August 2023



2023 IFSO World Congress

Disclosures

I am currently or have recently been a paid consultant to the following companies and organizations:

Altimune

Amgen

Boehringer Ingelheim

Gelesis

Gilead Sciences

Eli Lilly & Company

Novo Nordisk

Pfizer

Rhythm Pharmaceuticals

Sidekick Health

The Obesity and Nutrition Institute

twenty30.health

Xeno Biosciences

Cardiac complications of obesity

- Atherosclerotic cardiovascular disease
- Heart failure with **reduced** ejection fraction (HFrEF)
- Atrial fibrillation
- Right heart failure
- Heart failure with **preserved** ejection fraction (HFpEF)

Does **obesity treatment improve** any or all of these complications?

Does **obesity treatment prevent** any or all of these complications?

Does any beneficial obesity treatment **depend on the weight loss**?

Metabolic surgery associated with reduced major cardiovascular events

Retrospective case-control study

Patients with obesity and type 2 diabetes

Primary endpoint:

3-point Major Adverse

Cardiovascular Events (MACE):

Non-fatal myocardial infarction **OR**

Non-fatal stroke **OR**

Cardiovascular death

Secondary endpoint:

6-point MACE:

Coronary artery events

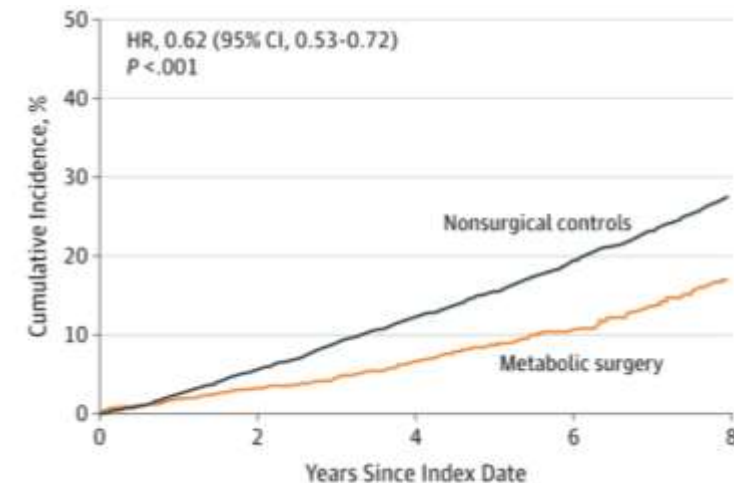
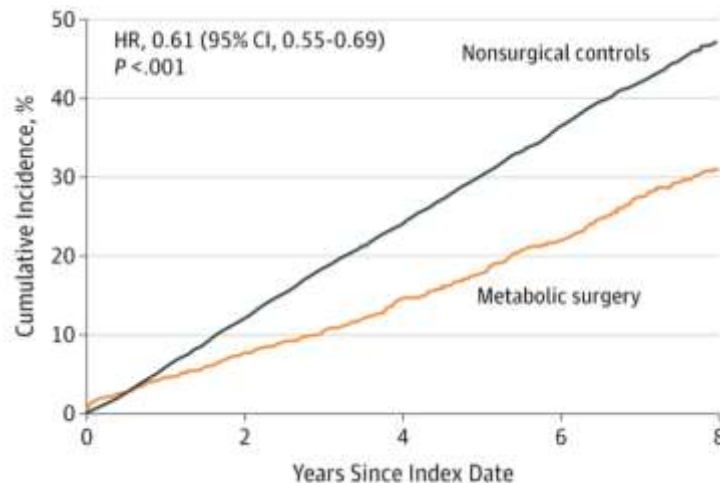
Cerebrovascular events

All-cause mortality

Heart failure

Atrial fibrillation

Nephropathy

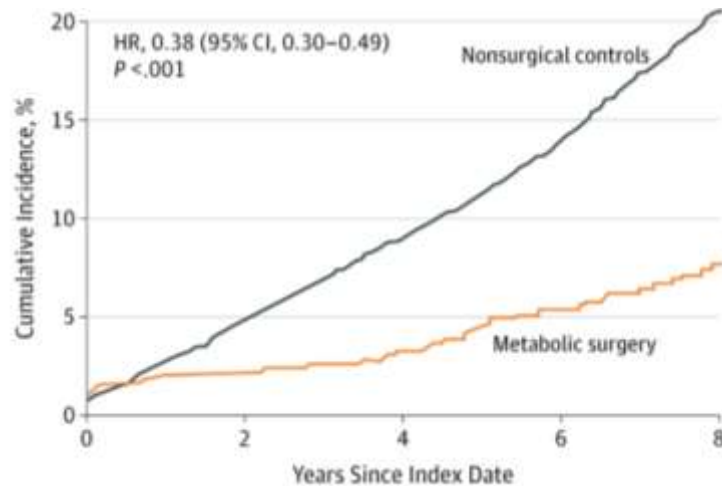


Metabolic surgery associated with reduced risk of heart failure and atrial fibrillation

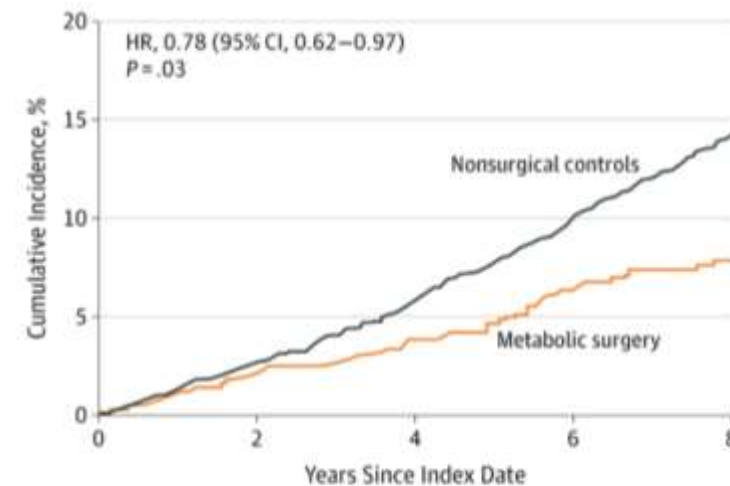
Retrospective case-control study

Patients with obesity and type 2 diabetes

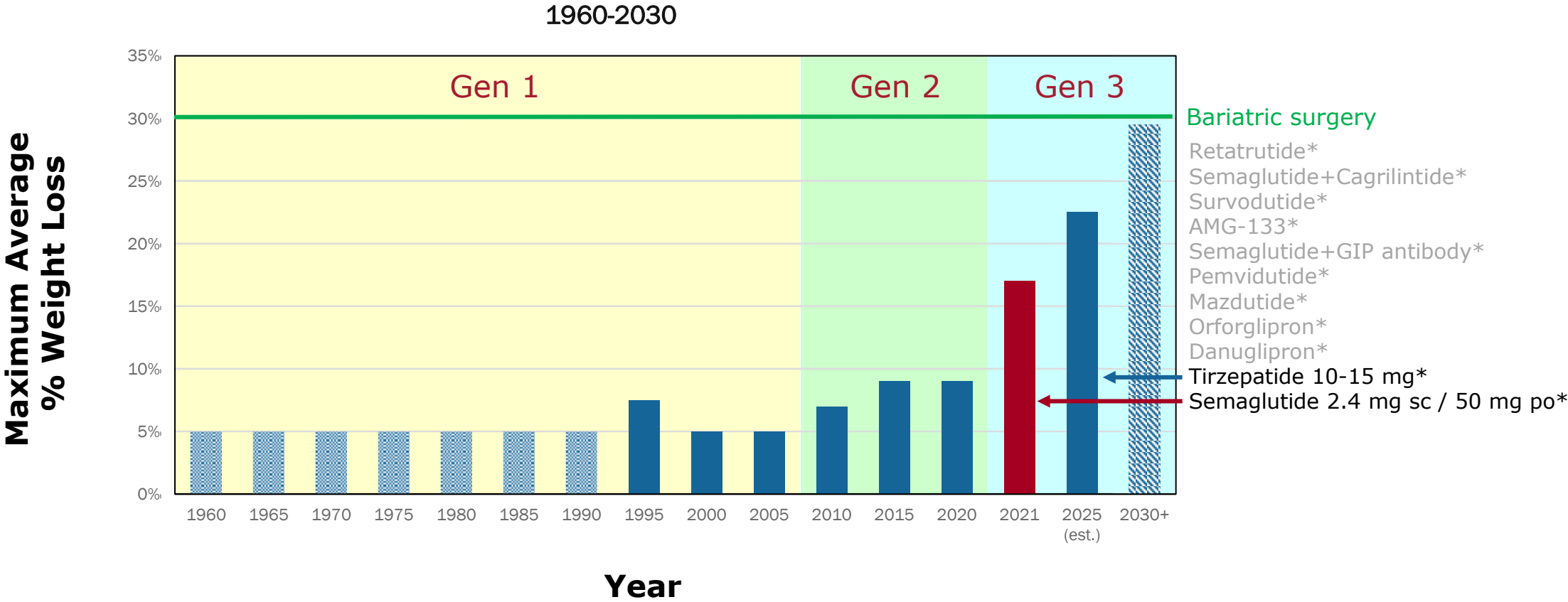
Heart failure (HF_rEF and HF_pEF)



Atrial fibrillation



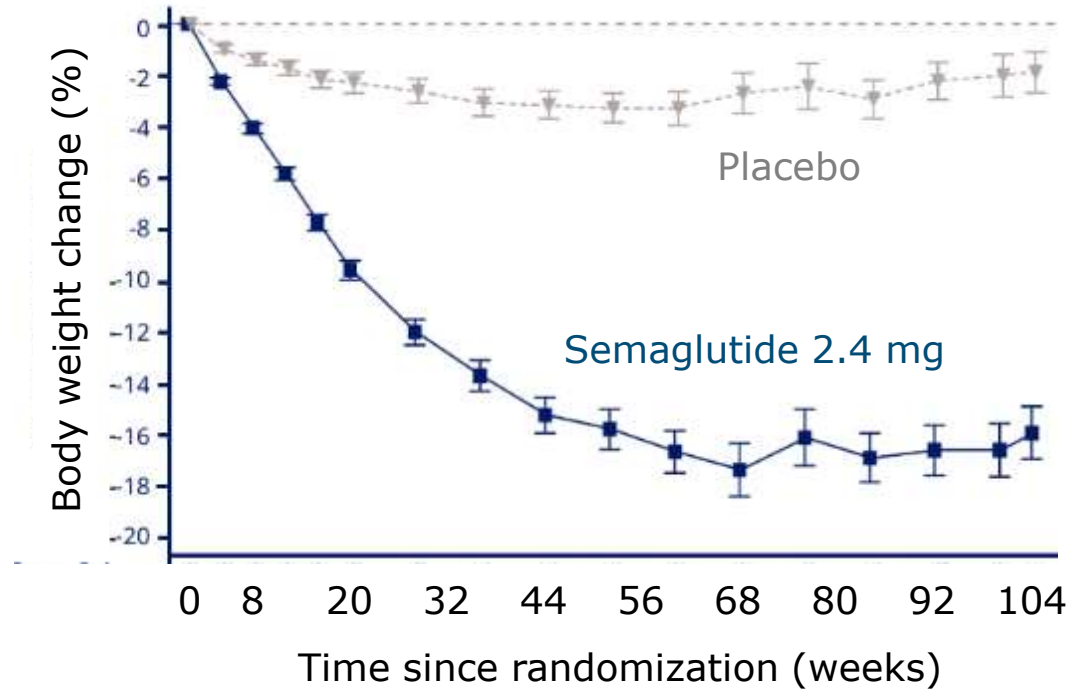
We have entered the 3rd generation of anti-obesity medications



*This medication is not approved for the treatment of obesity

Semaglutide induces sustained weight loss at 2 years

STEP 5 Trial Subjects without Diabetes



Semaglutide 2.4 mg reduces major cardiovascular events

SELECT Trial

Semaglutide 2.4 mg/week vs. placebo in people with obesity **without** diabetes

Participants \geq 45 years with established CVD
N=17,604



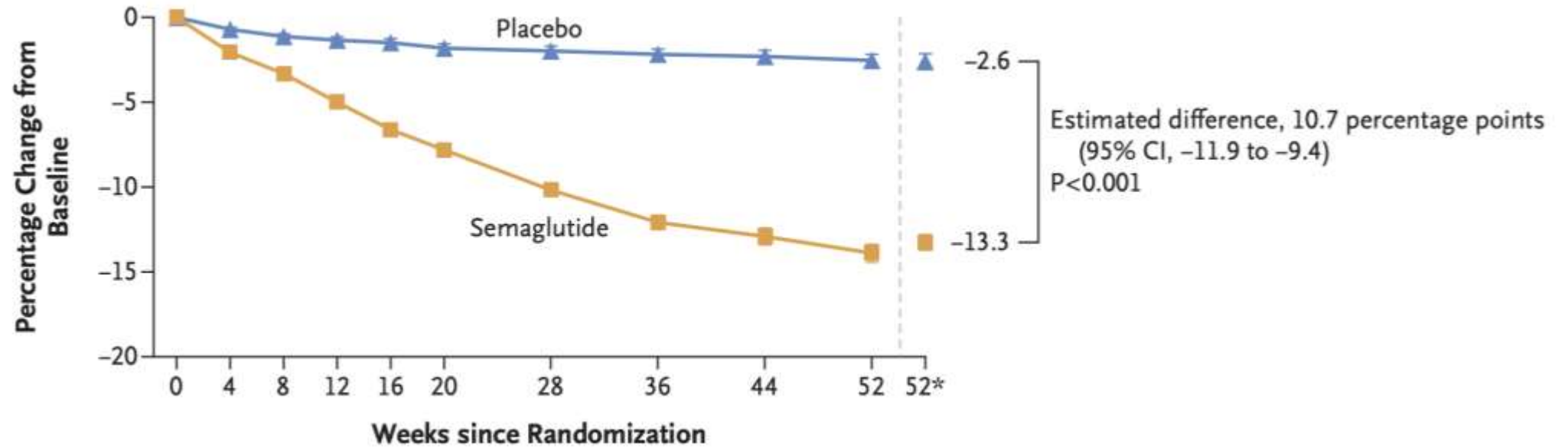
Primary endpoint: Time to first occurrence of **3-point MACE:**
Non-fatal myocardial infarction **OR** non-fatal stroke **OR** cardiovascular death

This is the first prospective randomized, controlled trial of any obesity therapy to demonstrate a reduction in major adverse cardiovascular events (MACE)

<https://www.globenewswire.com/news-release/2023/08/08/2720343/0/en/Novo-Nordisk-A-S-Semaglutide-2-4-mg-reduces-the-risk-of-major-adverse-cardiovascular-events-by-20-in-adults-with-overweight-or-obesity-in-the-SELECT-trial.html>

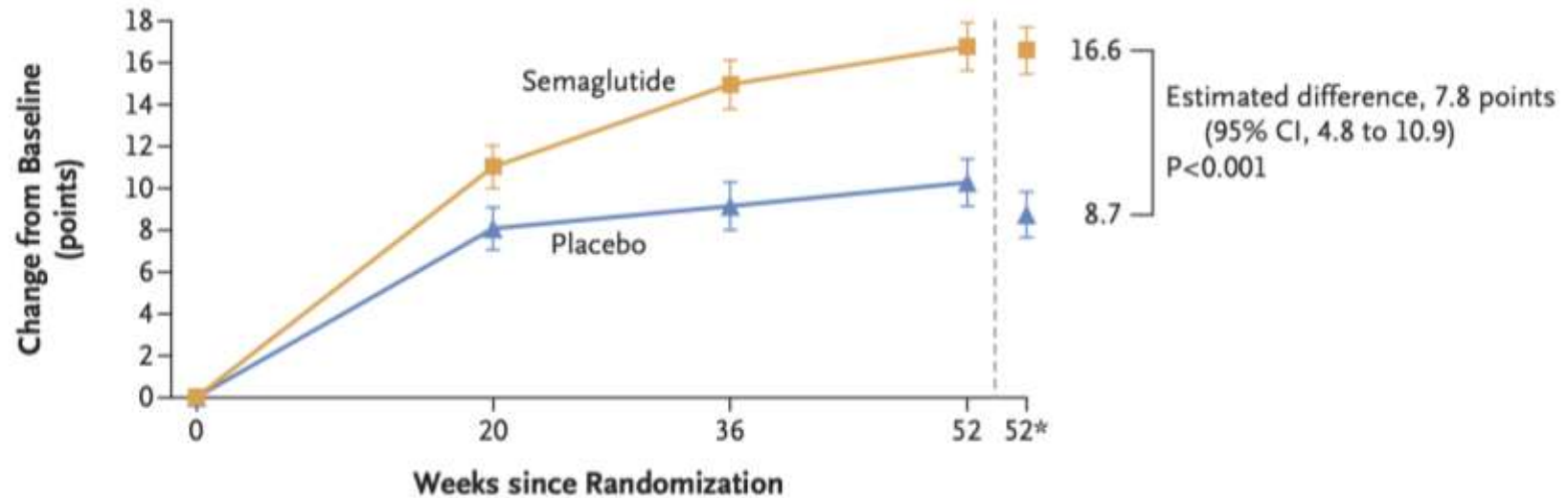
Semaglutide-induced weight loss in people with HFpEF

STEP-HFpEF Trial



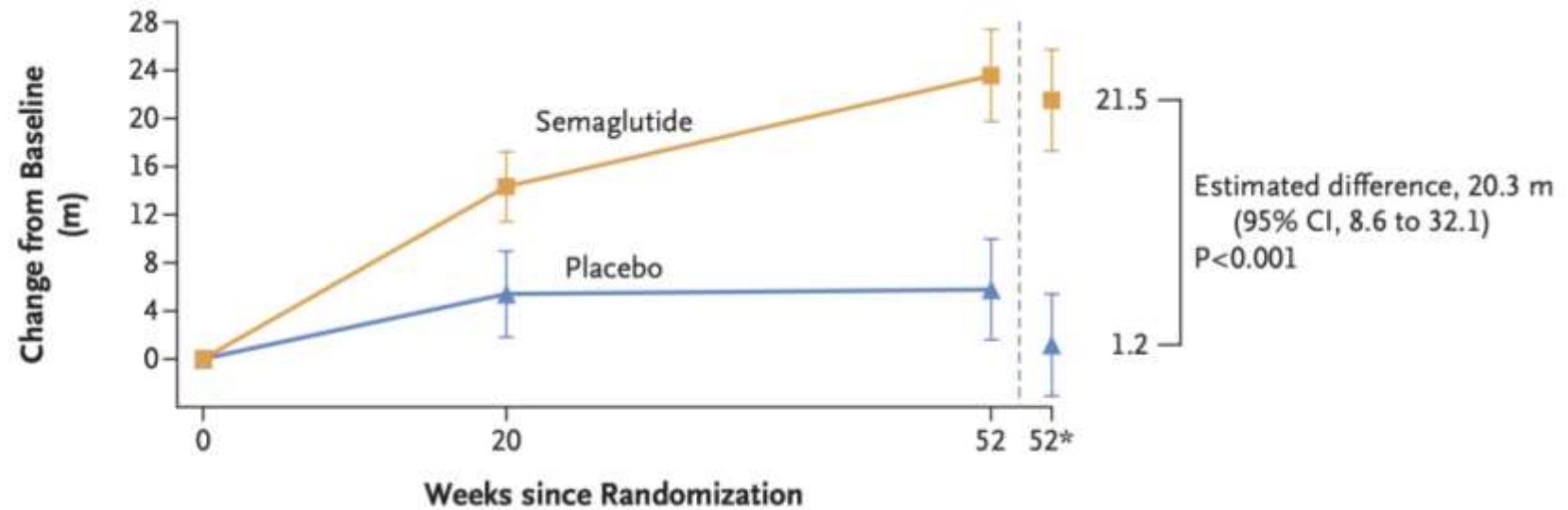
Semaglutide improves quality of life in people with HFpEF

Kansas City Cardiomyopathy Questionnaire Clinical Summary Score



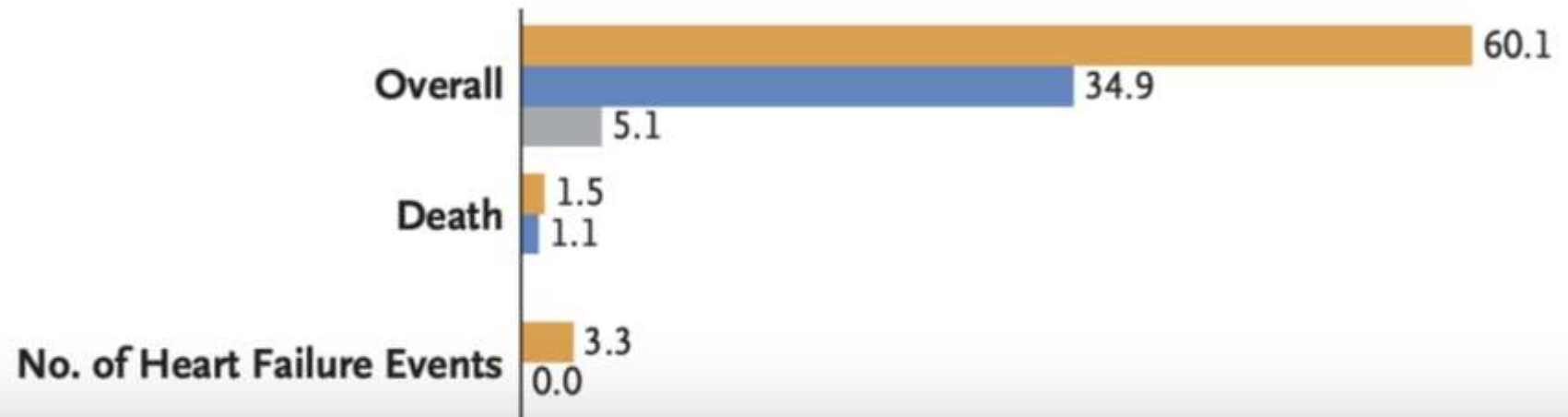
Semaglutide improves physical functioning in HFpEF patients

Distance during 6-minute walk test



Semaglutide improves cardiac outcomes and reduces major adverse cardiac events in patients with HFpEF

STEP-HFpEF Trial



Conclusions

- Both **metabolic surgery** and **generation 3 anti-obesity medications** have been shown to reduce **major adverse cardiovascular events (MACE)**
 - Surgery via **retrospective case-control studies** in patients with **obesity and diabetes**
 - Semaglutide via **RCTs** in patients with **obesity both with and without diabetes**
- Both **metabolic surgery** and **generation 3 anti-obesity medications** have been shown to reduce heart failure
 - **Surgery** in **all-cause heart failure** via case-control studies in patients with obesity and diabetes
 - **Semaglutide** in **HFpEF** via an RCT in patients with obesity
- **Metabolic surgery** has been shown to reduce **atrial fibrillation** via retrospective case-control studies
- **Treating obesity is an effective and valuable means of promoting heart health**



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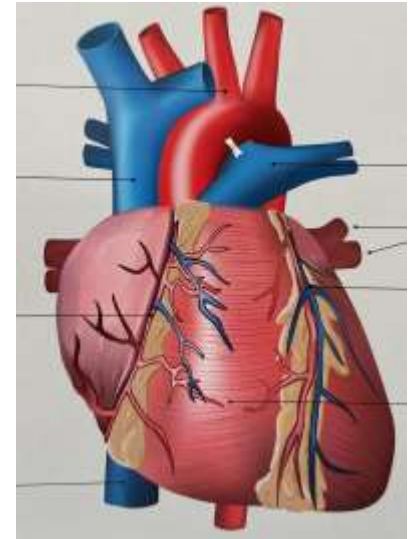
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