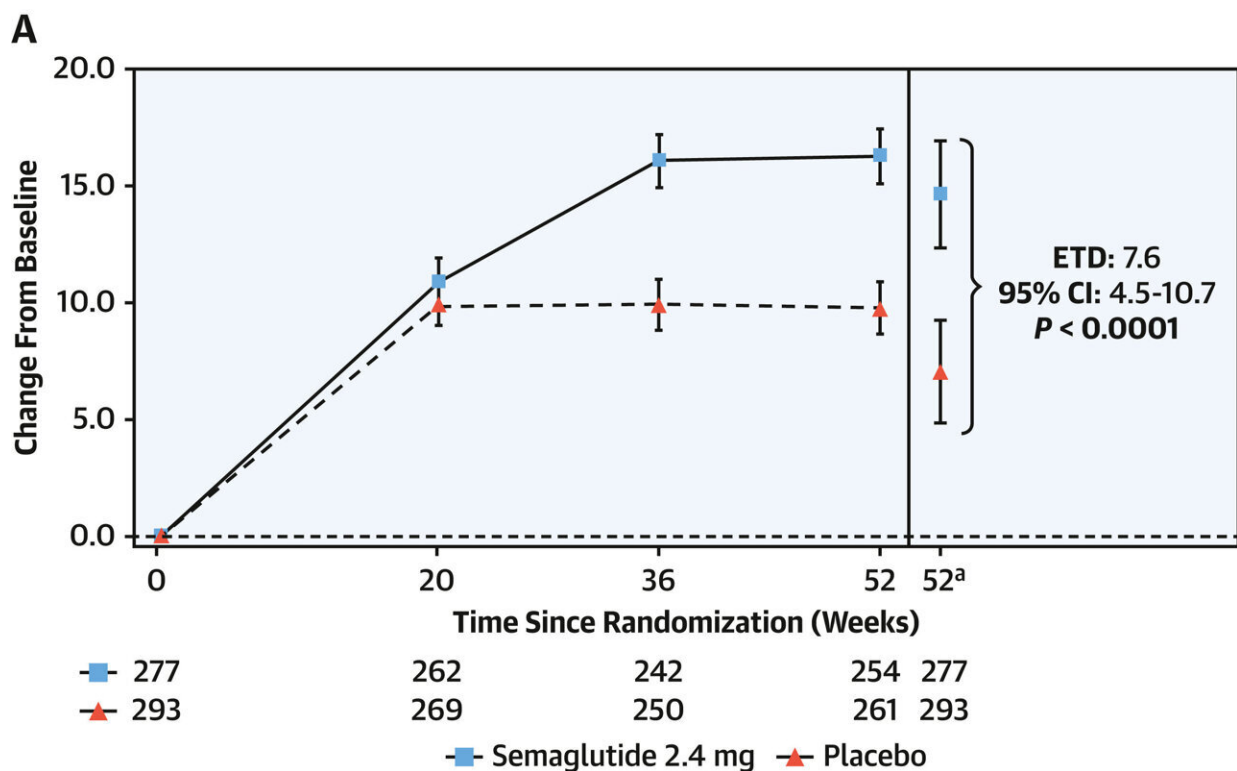


Semaglutide leads to greater weight loss in women than men with heart failure, improves symptoms

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Change in Kansas City Cardiomyopathy Questionnaire Clinical Summary Score in Women and Men. Credit: *Journal of the American College of Cardiology* (2024). DOI: 10.1016/j.jacc.2024.06.001

Semaglutide, a medication initially developed for type 2 diabetes and obesity, significantly improves symptoms in men and women with a common type of heart failure that has had few therapeutic options.

Women experienced greater weight loss and the same symptom benefits compared with men, according to research presented by Dr. Subodh Verma (St. Michael's Hospital, University of Toronto) at the American Diabetes Association's 2024 Scientific Sessions and [published](#) in the *Journal of the American College of Cardiology (JACC)*.

This secondary analysis of the STEP-HFpEF (Semaglutide Treatment Effect in People with Obesity and HFpEF) program reveals that semaglutide provides benefits for men and women that do not track directly with weight loss, suggesting the drug may also have weight-loss independent effects on the cardiovascular system.

The study (which included two trials) compared semaglutide with a placebo over 52 weeks in 1,145 participants, highlighting intriguing [sex differences](#).

The analysis sought to determine whether phenotypic features and treatment effects of semaglutide vary by sex in obesity-related heart failure (HF) with preserved ejection fraction (HFpEF). It evaluated the influence of sex on the disease's baseline characteristics and compared the effects of semaglutide versus placebo on key trial endpoints in the STEP-HFpEF program (comprised of STEP-HFpEF and STEP-HFpEF DM Trials).

"Understanding the sex differences in obesity-related HFpEF is of great importance. Obesity and visceral adiposity are key drivers of HFpEF development and progression, and this may be even more amplified in women, who represent the majority of people with the disease, and bear a heavier burden of symptoms and physical limitations due to HFpEF"

said Mikhail Kosiborod, MD, FACC, senior author of the study and a cardiologist at Saint Luke's Mid-America Heart Institute in Kansas City, Missouri.

"Our study sheds light on these differences and the consistent benefits of semaglutide for women and men."

Lead author, Dr. Subodh Verma commented that "women living with obesity and heart failure with a preserved ejection fraction were also found to have higher BMI's compared to men, and were much more symptomatic at baseline."

"Females had more systemic inflammation and compared to previous HfpEF studies, females with obesity-related HfpEF were also younger," Verma said.

The study analyzed the effects of semaglutide 2.4 mg administered to participants once weekly vs. placebo on the STEP-HFpEF program's dual primary and confirmatory secondary, and exploratory outcomes by sex. A total of 1,145 participants with obesity-related HFpEF were evaluated over 52 weeks, of which 570 were females.

Semaglutide, compared with placebo, similarly improved HF-related symptoms, physical limitations, exercise function, and reduced inflammation and natriuretic peptides regardless of sex.

Semaglutide-mediated improvements in HF-related symptoms and physical limitations were consistent in both male and [female participants](#) across key subgroups including age and BMI. It also lowered their systolic blood pressure and waist circumference.

However, there were sex differences in the treatment effects in terms of the reduction in body weight with semaglutide. Female participants

experienced [greater weight loss](#) than males, with a mean difference of -9.6% vs. -7.2%. Even though there was a significant reduction in [body weight](#) in both sexes, it was greater in females (a statistically significant interaction).

At baseline, females had higher left ventricular ejection fraction, presented with worse symptoms and physical limitations, and had higher levels of inflammation at baseline, but similar rates of hypertension and diuretic use and less [atrial fibrillation](#) compared with males, despite their higher BMI.

Researchers note that this may indicate that more female participants had a typical obesity phenotype of HFpEF compared with males who may also have left atrial myopathy HFpEF complicated by an increase in BMI.

In an accompanying [editorial](#), Anuradha Lala, MD, a cardiologist at the Mount Sinai School of Medicine and Director of Heart Failure Research for the NHLBI Cardiothoracic Surgery Network, said there is a need for further studies to illuminate the mechanism by which this drug provides benefits and continued attention to sex-specific differences in treatment responses.

More information: Efficacy of Semaglutide by Sex in Obesity-Related Heart Failure With Preserved Ejection Fraction: STEP-HFpEF Trials, *Journal of the American College of Cardiology* (2024). [DOI: 10.1016/j.jacc.2024.06.001](#)

John W. Ostrominski et al, Incretin-Based Therapies in Women With Obesity-Related HFpEF: Time to STEP into A Paradigm of Integrated Care, *Journal of the American College of Cardiology* (2024). [DOI: 10.1016/j.jacc.2024.06.006](#)

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