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Synopsis of the original article ***'Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss'***

Wharton S, et al. Diabetes, Obesity and Metabolism 2021;1–12. doi: 10.1111/dom.14551

Synopsis created and reviewed by Novo Nordisk

Introduction

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Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) with FDA approval for weight management in individuals with obesity or overweight with ≥1 weight-related comorbidity

In the Semaglutide Treatment Effect in People with obesity (STEP) trials, once-weekly semaglutide 2.4 mg produced clinically meaningful weight loss~~es~~

Gastrointestinal (GI) adverse events (AEs) are frequently reported by people taking medicines belonging to the GLP-1RA class

We evaluated GI AEs in participants taking semaglutide 2.4 mg in the STEP 1–4 trials, and examined whether these AEs contributed to the observed weight loss

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Methods

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STUDY POPULATIONS

Pooled analysis of STEP 1–3:
Participants randomized to 68 weeks' semaglutide 2.4 mg (**N = 2117**) or placebo (**N = 1262**)

Analysis of STEP 4:
Participants tolerating 20-weeks' semaglutide run-in (**N = 803**)

QUESTIONS

- How much weight loss was mediated by GI AEs?
- Did patients with more GI AEs lose more weight?
- How much weight loss was unrelated to GI AEs?
- What was the GI tolerability in those on semaglutide maintenance therapy vs those stopping treatment after dose escalation?

AE, adverse event; GI, gastrointestinal.

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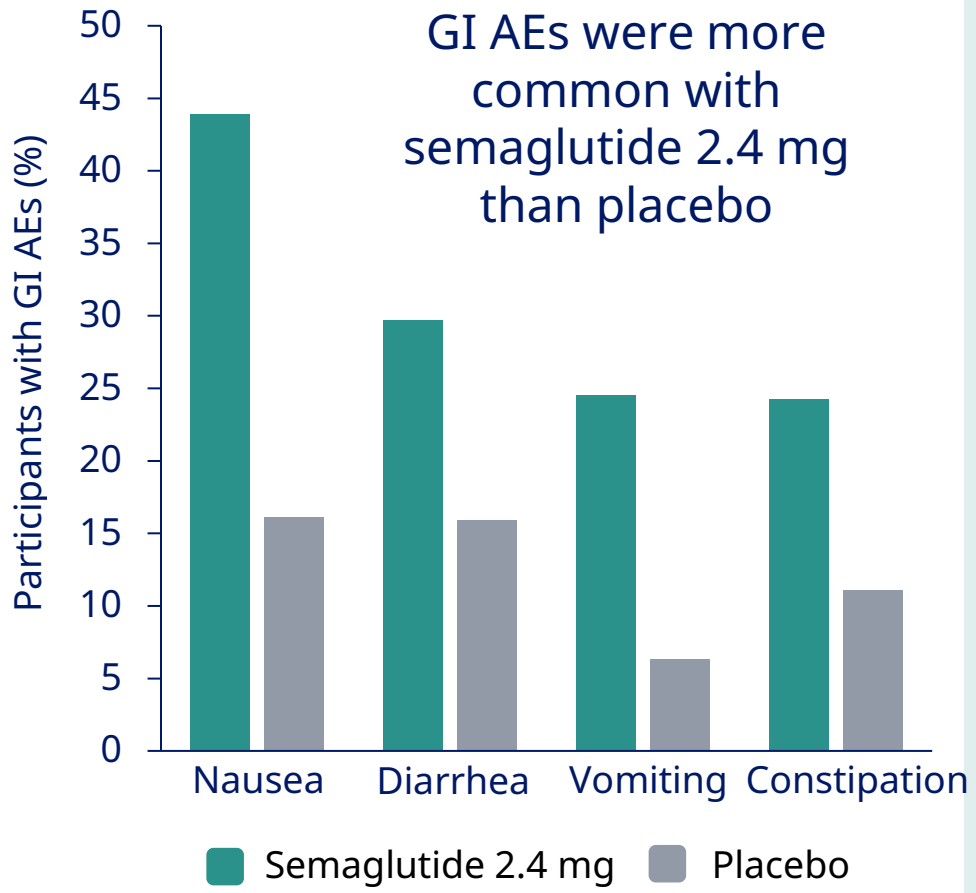
Results



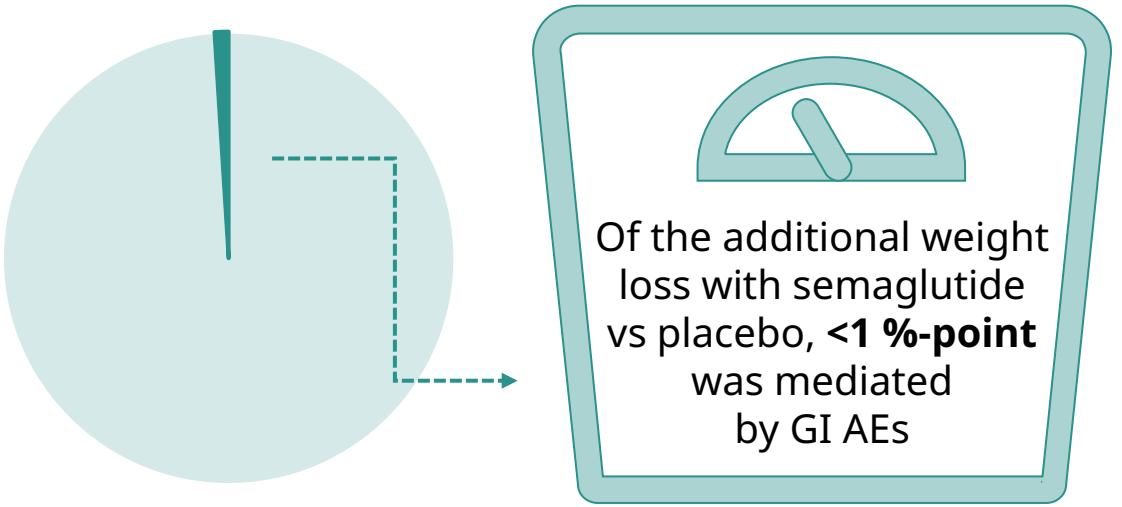
However, most GI AEs with semaglutide were…

Non-serious (99.5%)	Mild-to-moderate (98.1%)	Transient (occurred during/shortly after dose escalation)

Mean weight loss in STEP 1–3 was similar in participants with and without GI AEs

With AEs **11.4%–17.7%**

Without AEs **9.6%–17.1%**



AE, adverse event; GI, gastrointestinal; STEP, Semaglutide Treatment Effect in People with obesity.

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Conclusions

GI AEs were more common with semaglutide 2.4 mg than placebo, but were typically mild-to-moderate and transient

Semaglutide-induced weight loss was largely independent of GI AEs

AE, adverse event; GI, gastrointestinal.

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