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STEP 9:
Efficacy and Safety of Once-Weekly Semaglutide 2.4 mg in People with Obesity and Knee Osteoarthritis

A Novo Nordisk-developed overview of Bliddal H. et al. N Engl J Med. 2024. doi: 10.1056/NEJMoa2403664.

This presentation was developed by Novo Nordisk Inc.

Access the approved PI

Click the URL

https://www.novo-pi.com/wegovy.pdf

OR

Scan the QR code

Semaglutide 2.4 mg OW: approved indications

PI, prescribing information; OW, once-weekly; QR, quick response; URL, uniform resource locator.

Semaglutide 2.4 mg has not been approved by the FDA for treatment of knee osteoarthritis in people with obesity, and the safety and efficacy of semaglutide 2.4 mg for the treatment of knee osteoarthritis has not been established

FDA, Food and Drug Administration.

Box Warning

WARNING: RISK OF THYROID C-CELL TUMORS

- **In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined *[see Warnings and Precautions (5.1), Nonclinical Toxicology (13.1)]*.**
- **WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) *[see Contraindications (4)]*. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY *[see Contraindications (4), Warnings and Precautions (5.1)]*.**

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Indications and Usage

Section 1

Indication

WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in:
  - Adults and pediatric patients aged 12 years and older with obesity.
  - Adults with overweight in the presence of at least one weight-related comorbid condition.
- For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stage F2-F3 fibrosis). This indication is approved under accelerated approval based on improvement of MASH and fibrosis [see Clinical Studies (14.4)]. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in confirmatory trials.

WEGOVY tablets are indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.

Abbreviations: F, fibrosis; MASH, metabolic dysfunction-associated steatohepatitis.

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Indications and Usage

Section 1

Limitations of use

Concomitant use of WEGOVY (semaglutide) tablets or WEGOVY (semaglutide) injection with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended.

Abbreviations: GLP-1, glucagon-like peptide-1.

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Contraindications

Section 4

Contraindications

WEGOVY is contraindicated in the following conditions:

- A personal or family history of MTC or in patients with MEN 2 [see Warnings and Precautions (5.1)].
- Known hypersensitivity to semaglutide or any of the excipients in WEGOVY® tablets or WEGOVY® injection [see Warnings and Precautions (5.7)].

MEN 2, multiple endocrine neoplasia syndrome type 2; MTC, medullary thyroid carcinoma.
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Warnings and Precautions

Section 5.1

Risk of Thyroid C-Cell Tumors

In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures [see Nonclinical Toxicology (13.1)]. It is unknown whether WEGOVY causes thyroid C-cell tumors, including MTC, in humans, as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

GLP-1, glucagon-like peptide-1; MTC, medullary thyroid carcinoma.
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Warnings and Precautions

Section 5.1

Risk of Thyroid C-Cell Tumors

WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY. Such monitoring may increase the risk of unnecessary procedures, due to the low-test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values greater than 50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

Abbreviations: MEN 2, Multiple Endocrine Neoplasia syndrome type 2; MTC , medullary thyroid carcinoma..
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Warnings and Precautions

Section 5.2

Acute Pancreatitis

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including WEGOVY [see Adverse Reactions (6)]. After initiation of WEGOVY, observe patients carefully for signs and symptoms of acute pancreatitis, which may include persistent or severe abdominal pain, (sometimes radiating to the back), and which may or may not be accompanied by nausea or vomiting. If acute pancreatitis is suspected, discontinue WEGOVY and initiate appropriate management.

Abbreviations: GLP-1, glucagon-like peptide-1.
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Warnings and Precautions

Section 5.3

Acute Gallbladder Disease

Treatment with WEGOVY is associated with an increased occurrence of cholelithiasis and cholecystitis. The incidence of cholelithiasis and cholecystitis was higher in WEGOVY injection-treated pediatric patients aged 12 years and older than in WEGOVY injection-treated adults. In randomized clinical trials in adults for weight reduction, cholelithiasis was reported by 1.6% of WEGOVY injection-treated patients and 0.7% of placebo injection-treated patients. Cholecystitis was reported by 0.6% of WEGOVY injection-treated adult patients and 0.2% of placebo injection-treated patients. In a clinical trial in pediatric patients aged 12 years and older for weight reduction, cholelithiasis was reported by 3.8% of WEGOVY injection-treated patients and 0% placebo injection-treated patients. Cholecystitis was reported by 0.8% of WEGOVY injection-treated pediatric patients and 0% placebo injection-treated patients [see Adverse Reactions (6.1)].

Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder disease was greater in WEGOVY-treated patients than in placebo-treated patients, even after accounting for the degree of weight loss. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

Warnings and Precautions

Section 5.4

Hypoglycemia

WEGOVY lowers blood glucose and can cause hypoglycemia.

In a trial of WEGOVY injection in adult patients with type 2 diabetes and body mass index (BMI) greater than or equal to 27 kg/m^2 for weight reduction (Study 3), hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in more patients treated with WEGOVY versus placebo. One episode of severe hypoglycemia (requiring the assistance of another person) was reported in one WEGOVY-treated patient versus no placebo-treated patients [see Clinical Studies (14.2)].

In glycemic control clinical trials, the risk of hypoglycemia was increased when semaglutide injection or tablet was used concomitantly with insulin or an insulin secretagogue (e.g., sulfonylurea). Patients with diabetes mellitus taking WEGOVY in combination with insulin or an insulin secretagogue may have an increased risk of hypoglycemia, including severe hypoglycemia. The use of WEGOVY in patients with type 1 diabetes mellitus or in combination with insulin has not been evaluated.

Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes, monitor blood glucose prior to starting WEGOVY and during WEGOVY treatment. When initiating WEGOVY, consider reducing the dose of concomitantly administered insulin or insulin secretagogue (such as sulfonylureas) to reduce the risk of hypoglycemia [see Drug Interactions (7.1)].

Abbreviations: BMI, body mass index.

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Warnings and Precautions

Section 5.5 and 5.6

Acute Kidney Injury Due to Volume Depletion

There have been postmarketing reports of acute kidney injury, in some cases required hemodialysis, in patients treated with semaglutide [see Adverse Reactions (6)]. The majority of the reported events occurred in patients who experienced gastrointestinal reactions leading to dehydration such as nausea, vomiting, or diarrhea [see Adverse Reactions (6)].

Monitor renal function in patients reporting adverse reactions to WEGOVY that could lead to volume depletion, especially during dosage initiation and escalation of WEGOVY.

Severe Gastrointestinal Adverse Reactions

Use of WEGOVY has been associated with gastrointestinal adverse reactions, sometimes severe [see Adverse Reactions (6.1)]. In clinical trials for adults for weight reduction, severe gastrointestinal adverse reactions were reported more frequently among patients receiving WEGOVY than placebo. Severe gastrointestinal adverse reactions were reported in 4.1% and 0.9% of WEGOVY-injection and placebo-treated patients, respectively, and in 2% of WEGOVY tablet-treated and 0% of placebo-treated patients, respectively. Severe gastrointestinal adverse reactions have also been reported postmarketing with GLP-1 receptor agonists.
WEGOVY is not recommended in patients with severe gastroparesis.

Wegovy® [package insert]. Novo Nordisk Inc.

Warnings and Precautions

Section 5.7

Hypersensitivity Reactions

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with WEGOVY. If hypersensitivity reactions occur, discontinue use of WEGOVY, treat promptly per standard of care, and monitor until signs and symptoms resolve. WEGOVY is contraindicated in patients with a prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY [see Adverse Reactions (6.2)].

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with WEGOVY.

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide-1.
Wegovy® [package insert]. Novo Nordisk Inc.

Warnings and Precautions

Section 5.8

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in adult patients with type 2 diabetes and high CV risk, diabetic retinopathy complications (which was a 4-component adjudicated endpoint) occurred in patients treated with semaglutide injection (3%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (semaglutide injection 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%).

In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m^2 for weight reduction (Study 3), diabetic retinopathy was reported by 4% of WEGOVY injection-treated patients and 2.7% placebo-treated patients [see Clinical Studies (14.2)].

In a glycemic control trial evaluating a dose comparable to the 9 mg dose and the 25 mg semaglutide tablet dose in patients with type 2 diabetes, a similar proportion of patients in each dose group reported diabetic retinopathy related adverse reactions during the trial; 1.3% and 1.9% of patients in the 9 mg and 25 mg semaglutide group, respectively, reported moderate-severe non-proliferative diabetic retinopathy events, and 0% and 0.4% reported proliferative retinopathy events, respectively.

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

Abbreviations: BMI, body mass index; CV, cardiovascular.
Wegovy® [package insert]. Novo Nordisk Inc.

Warnings and Precautions

Section 5.9

Heart Rate Increase

Treatment with WEGOVY was associated with increases in resting heart rate. Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in WEGOVY injection-treated adult patients compared to placebo in clinical trials for weight reduction. More adult patients treated with WEGOVY injection compared with placebo had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively). In a clinical trial in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with WEGOVY injection compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%) [see Adverse Reactions (6.1)]. Findings were similar in a trial with the WEGOVY tablets.

Monitor heart rate at regular intervals consistent with usual clinical practice. Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY treatment. If patients experience a sustained increase in resting heart rate, discontinue WEGOVY.

Bpm, beats per minute; Wegovy® [package insert]. Novo Nordisk Inc.

Warnings and Precautions

Section 5.10

Pulmonary Aspiration During General Anesthesia or Deep Sedation

WEGOVY delays gastric emptying [see Clinical Pharmacology (12.2)]. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations.

Available data are insufficient to inform recommendations to mitigate the risk of pulmonary aspiration during general anesthesia or deep sedation in patients taking WEGOVY, including whether modifying preoperative fasting recommendations or temporarily discontinuing WEGOVY could reduce the incidence of retained gastric contents. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking WEGOVY.

Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide-1.
Wegovy® [package insert]. Novo Nordisk Inc.

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** Bliddal H. et al. N Engl J Med. 2024. doi: 10.1056/NEJMoa2403664.*

This presentation was developed by Novo Nordisk Inc.

Trial design and methodology

Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

STEP 9: knee osteoarthritis trial design

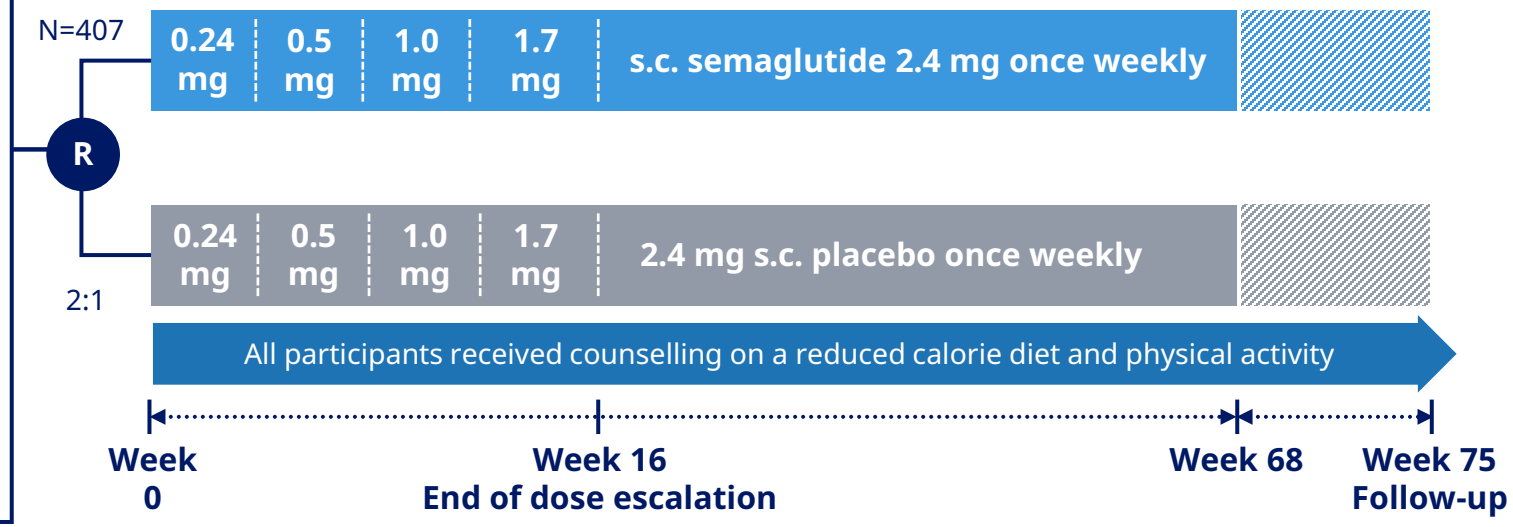
NCT05064735

Key inclusion criteria

- Aged ≥18 years
- BMI ≥30 kg/m^2
- Clinical diagnosis of Knee OA as per ACR criteria* with moderate radiographic changes (Kellgren-Lawrence grade 2 or 3) in the target knee
- Pain due to KOA (WOMAC pain ≥40 out of 100 at randomization)

Key exclusion criteria

- Joint replacement, arthroscopy or injections, or other joint disease in target knee
- Chronic, wide-spread pain, including neuropathic pain and hip osteoarthritis
- HbA_{1c} ≥48 mmol/mol (6.5%) or history of T1D or T2D
- Treatment with any glucagon-like peptide-1 receptor agonist in the 90 days before screening
- MI, stroke, hospitalization for unstable angina, TIA, HF†



Trial information

- Dual primary end points: Percentage change in bodyweight and change in WOMAC pain score
- 68-week, randomized, double-blind, placebo-controlled trial conducted at 61 sites in 11 countries

**Defined as knee pain plus at least three of: >50 years old, stiffness <30 minutes, crepitus,, bony tenderness, bony enlargement, and no palpable warmth. †Classified by New York Heart Association Class IV.*
AE, adverse event; ACR, American College of Rheumatology; BMI, body mass index; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, glycated hemoglobin; HF, heart failure; KOA, knee osteoarthritis; MI, myocardial infarction; SAE, serious adverse event; s.c., subcutaneous; T1D, type 1 diabetes; T2D, type 2 diabetes; TIA, transient ischemic attack; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Bliddal H. et al. N Engl J Med 2024;391:1573-83.

Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

Key study endpoints

Primary	Confirmatory secondary endpoints	Supportive secondary endpoints
• Change in WOMAC® pain score • Change in bodyweight	• Proportion of participants with a bodyweight reduction ≥5% or ≥10% • Change in WOMAC physical function score • Change in SF-36v2 physical functioning score	• Changes in: ○ Waist circumference ○ WOMAC stiffness score ○ WOMAC total score ○ Pain intensity (measured using an 11-point NRS) ○ Use of pain medication

All endpoints measured from baseline to week 68

NRS, numeric rating scale; SF-36v2, Short Form-36v2 Health Survey acute version; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Bliddal H. et al. N Engl J Med 2024;391:1573-83

The Western Ontario and McMaster Universities Arthritis Index (WOMAC®)

Evaluation of hip and knee osteoarthritis

WOMAC®

- A tri-dimensional, patient reported outcome (PRO) consisting of 24 questions on pain, stiffness, and physical function
- All items are scored on an 11-item (0–10) numerical rating scale
- All scores are normalized and analyzed on a scale from **0–100** with **higher** scores corresponding to a **worse** outcome

Domains covered by the questionnaire:

Pain
(5 items)

Stiffness
(2 items)

Physical function
(17 items)

A total score is generated

Illustrative example

WOMAC® Osteoarthritis Index NRS 3.1
Section A

PAIN

Think about the pain you felt in your study joint caused by the arthritis during the last 24 hours
(Please give your answers by selecting one of the boxes for each question.)

QUESTION: How much pain have you had...

1. when walking on a flat surface?

No Pain	1	2	3	4	5	6	7	8	9	10	Extreme Pain

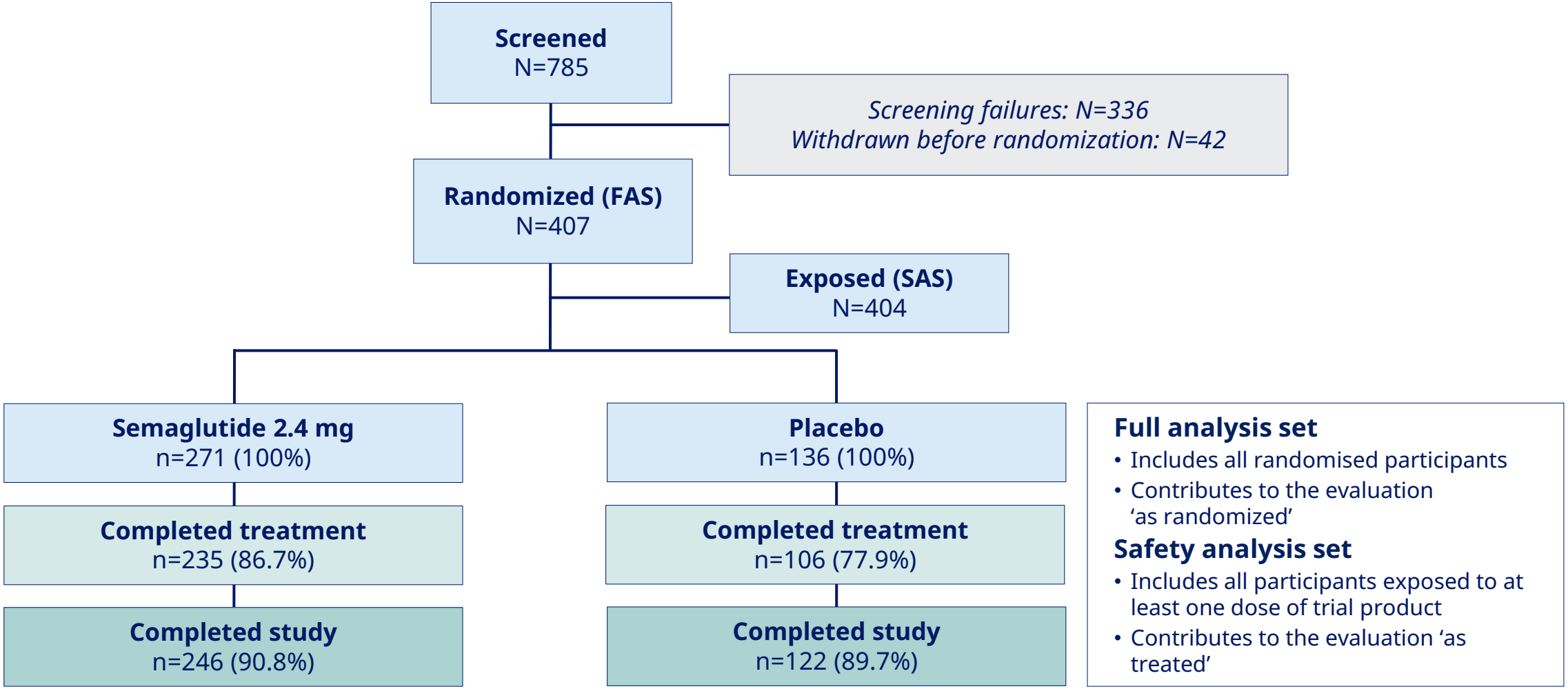
2. when going up or down stairs?

No Pain	1	2	3	4	5	6	7	8	9	10	Extreme Pain

1. **Bliddal H. et al.** *N Engl J Med 2024;391:1573-83 ; 2. https://clinicaltrials.gov/study/NCT05064735#study-plan.*

Participant disposition and baseline characteristics

Participant disposition



Full analysis set

- Includes all randomised participants
- Contributes to the evaluation 'as randomized'

Safety analysis set

- Includes all participants exposed to at least one dose of trial product
- Contributes to the evaluation 'as treated'

FAS, full analysis set; SAS, safety analysis set.

Bliddal H. et al. N Engl J Med 2024;391:1573-83

Demographics and baseline characteristics

Full analysis set (N=407)

Male/Female

18.4%/81.6%

Mean age

56 years

Race: White/
Native American*/Black/Other†

60.9%/11.8%/7.6%/19.7%

Mean bodyweight

108.6 kg

Mean BMI

40.3 kg/m²

Mean waist circumference

118.7 cm

WOMAC pain score

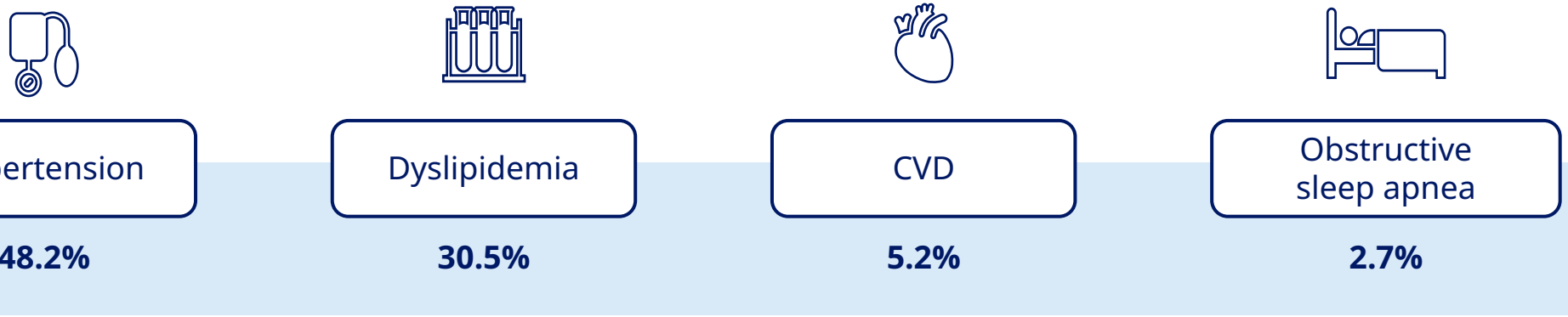
70.9‡

**Native American refers to American Indian or Alaska Native; †Other refers to Asian or Other or Not reported; ‡Presented on a scale of 0–100, with higher scores indicating more pain.*
%, proportion of participants in full analysis set; BMI, body mass index; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
Bliddal H. et al. N Engl J Med 2024;391:1573-83

Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

Major comorbidities at screening

Full analysis set (N=407)



68% of participants had ≥1 of these comorbidities at screening

%, proportion of participants in full analysis set; CVD, cardiovascular disease.

Bliddal H. et al. N Engl J Med 2024;391:1573-83, Novo Nordisk data on file

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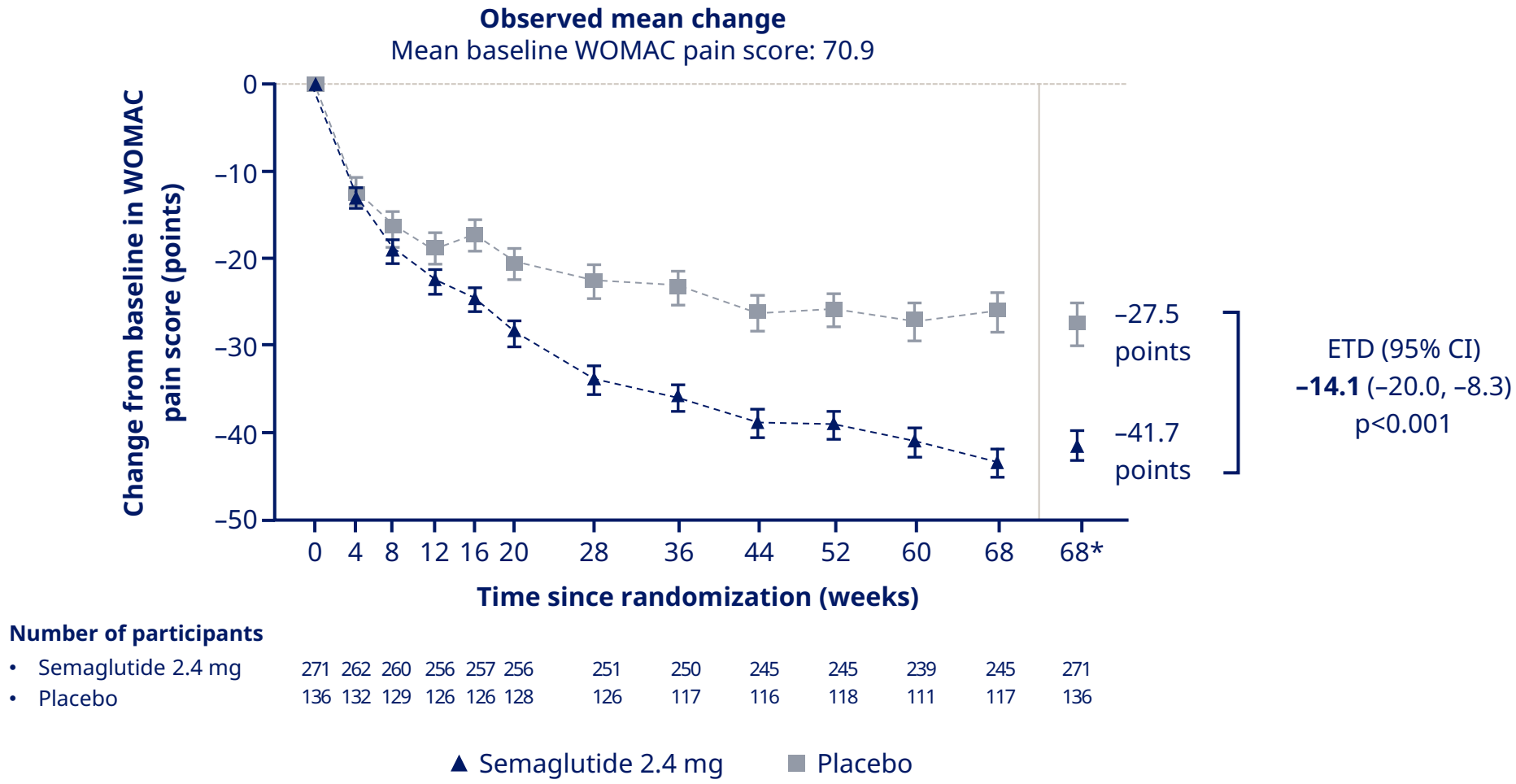
Efficacy

Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

Change in WOMAC pain score



Data are observed values from the in-trial period. Error bars are ± SEM. Numbers below the graph show the number of participants contributing to each mean.
**Estimated mean change at week 68 using the treatment policy estimand strategy. ETDs were calculated by analysis of covariance according to the treatment policy strategy.*
CI, confidence interval; ETD, estimated treatment difference; SEM, standard error of the mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index
Bliddal H. et al. N Engl J Med 2024;391:1573-83

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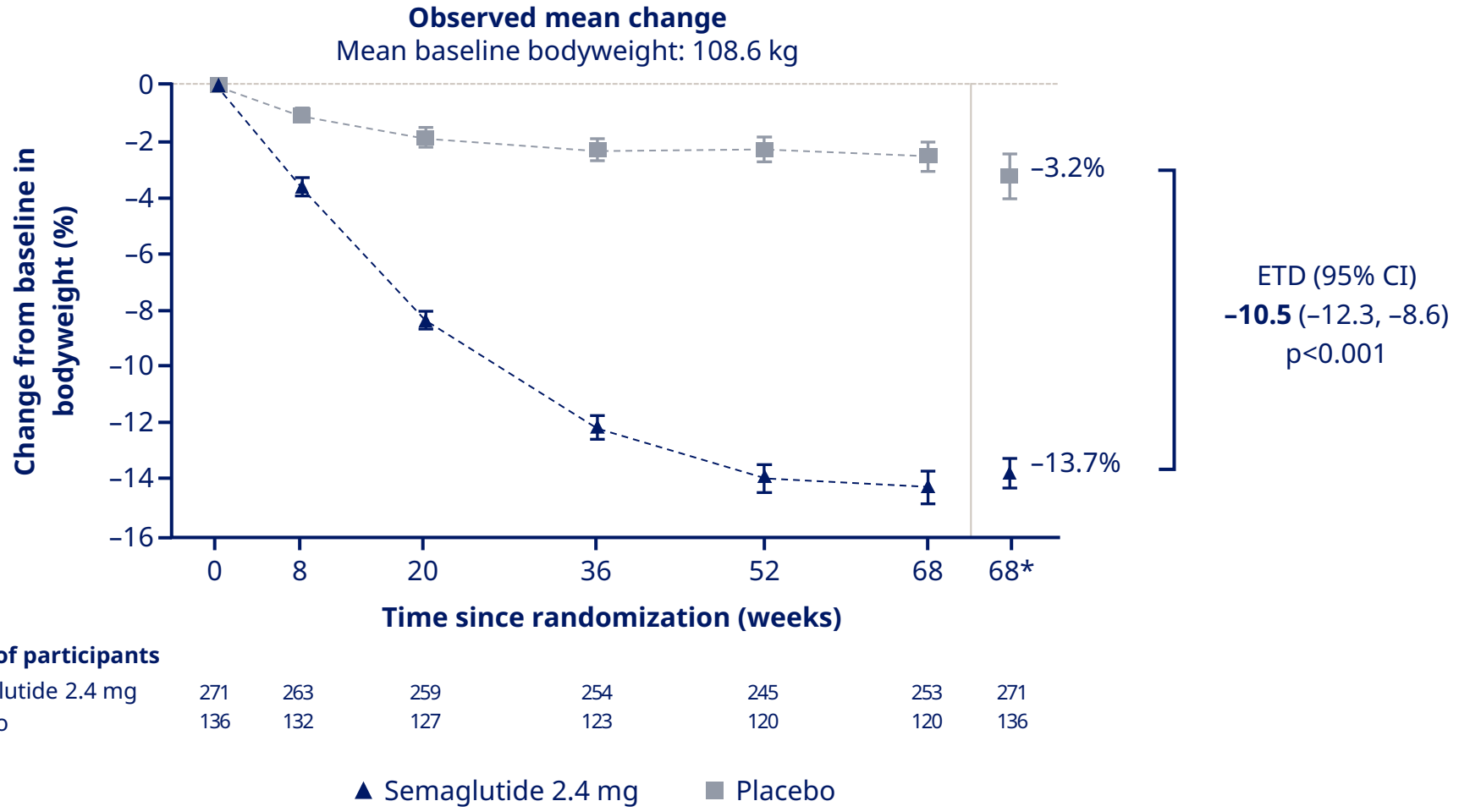
Change in bodyweight



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**Estimated mean change at week 68 using the treatment policy estimand strategy. ETDs were calculated by analysis of covariance according to the treatment policy strategy.*
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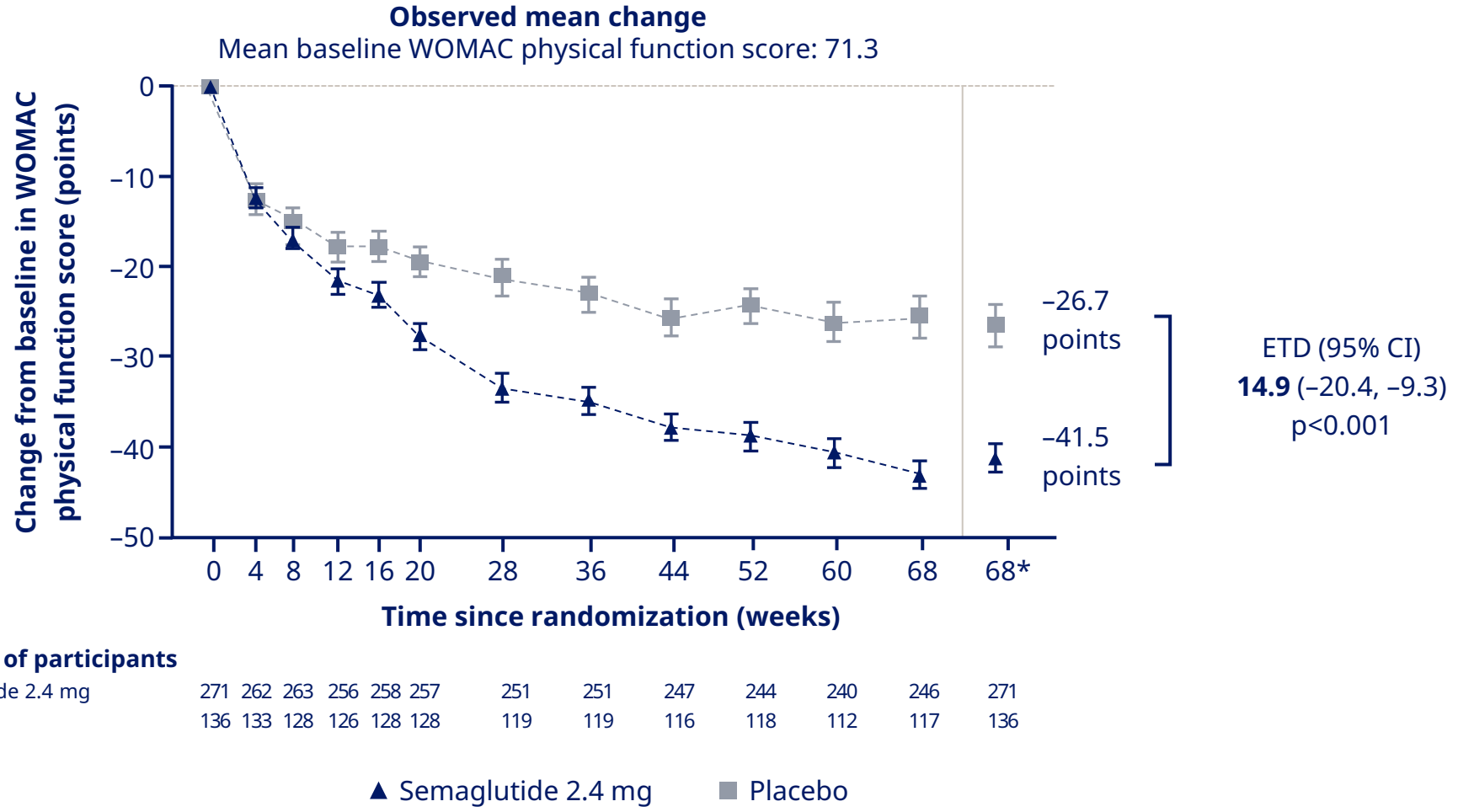
Change in WOMAC physical function score



Data are observed values from the in-trial period. Error bars are ± SEM. Numbers below the graph show the number of participants contributing to each mean.
**Estimated mean change at week 68 using the treatment policy estimand strategy. ETDs were calculated by analysis of covariance according to the treatment policy strategy.*
CI, confidence interval; ETD, estimated treatment difference; SEM, standard error of the mean; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
Bliddal H. et al. N Engl J Med 2024;391:1573-83; Novo Nordisk data on file.

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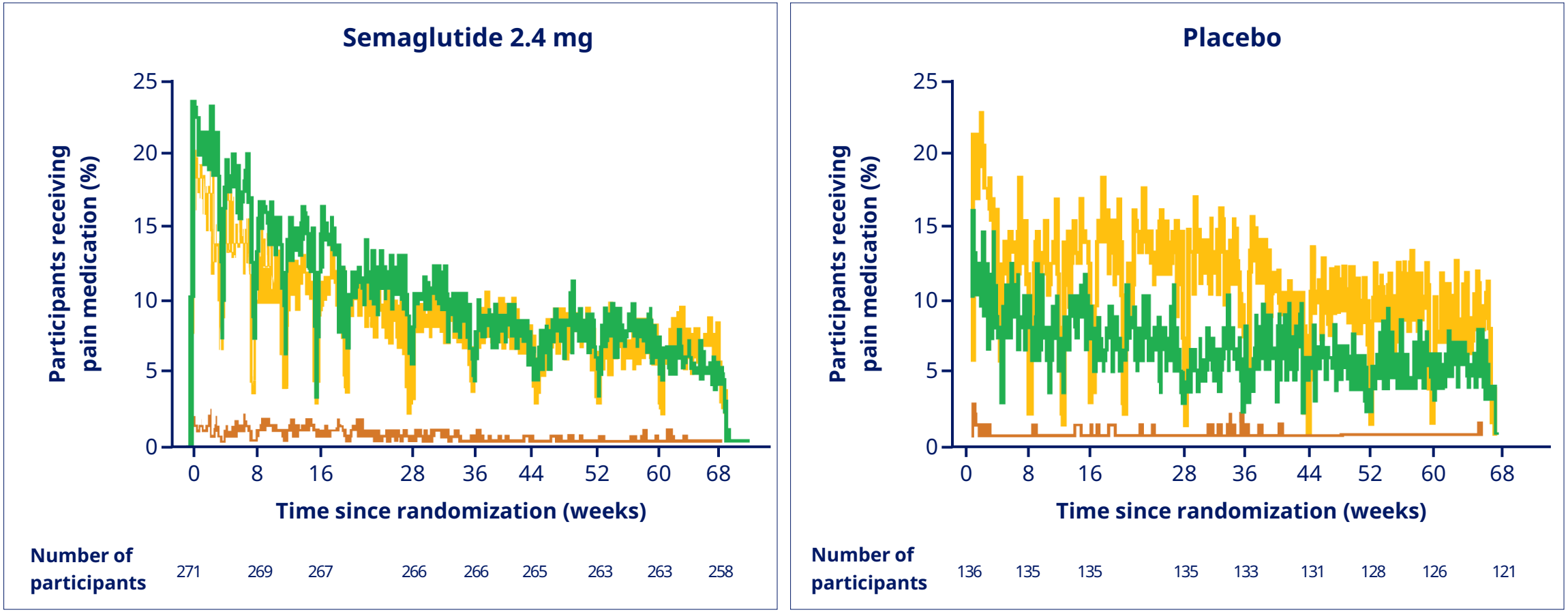
Usage of pain medication

Observed data by pain medication category over time



Data are observed data from the in-trial period. Numbers below the graphs show the number of participants contributing to the analysis at each time point. Current opioid use was an exclusion criterion at randomization; three cases of ongoing use of opioids at randomization (protocol deviations) were identified.
NSAID, non-steroidal anti-inflammatory drug
Bliddal H. et al. N Engl J Med 2024;391:1573-83

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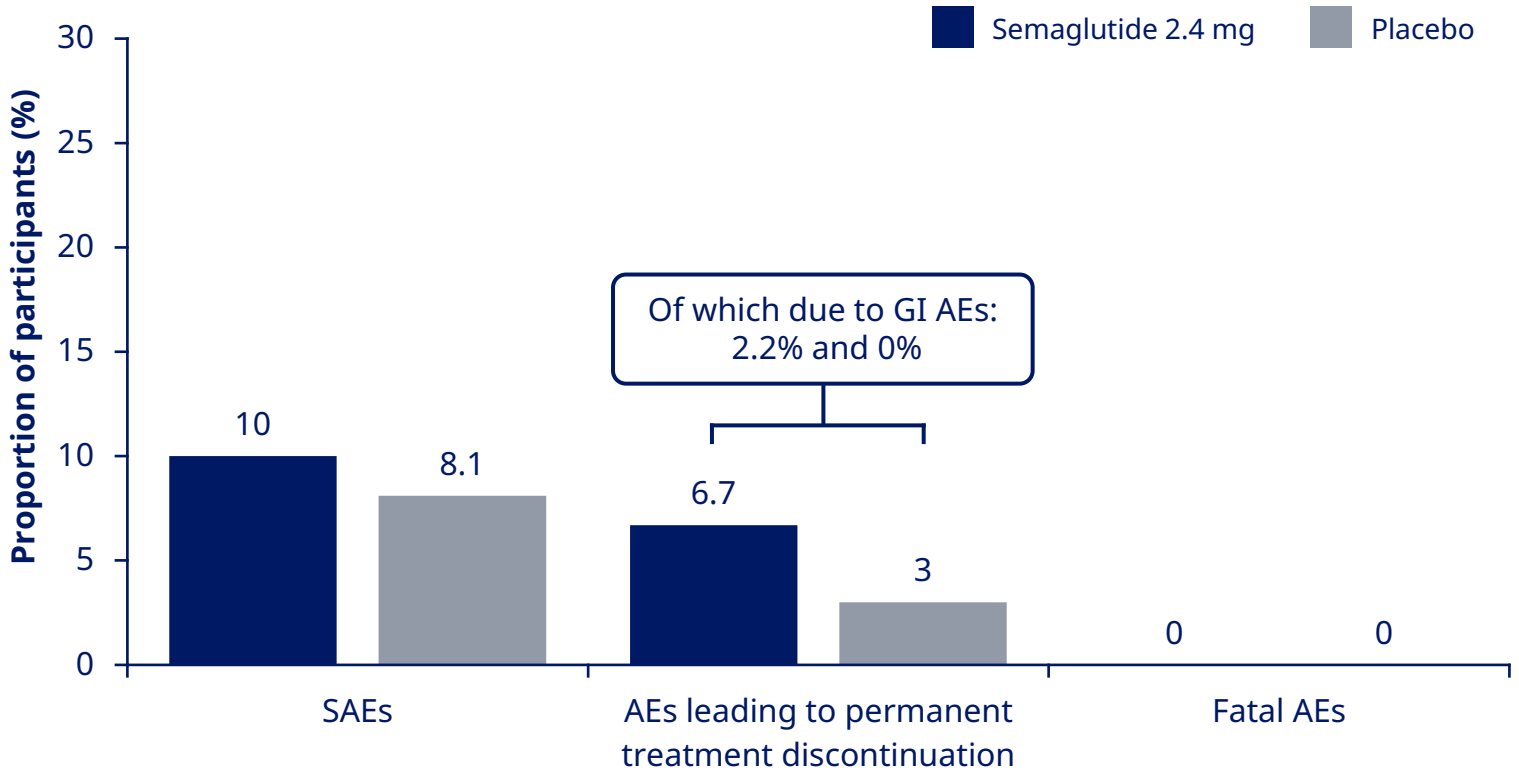
Safety

Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

Adverse events overview

On-treatment observation period



As the incidence of mild/moderate AEs has been characterised in previous trials of semaglutide 2.4 mg, AE reporting in STEP 9 was **selective**, with the following reported:

- SAEs
- AEs leading to treatment discontinuation
- AEs requiring invasive knee procedures
- Medication error
- Acute pancreatitis
- COVID-19
- Pregnancy or pregnancy-related AEs

The on-treatment period is defined as the interval from first trial product administration to last trial product administration plus a 2-week ascertainment window (excluding any off-treatment time intervals) – used for safety assessments.
AE, adverse event; GI, gastrointestinal; SAE, serious adverse event.
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Semaglutide 2.4 mg has not been approved by FDA for treatment of knee osteoarthritis in people with obesity. Safety and efficacy of semaglutide 2.4 mg for knee osteoarthritis in people with obesity has not been established. There is no guarantee that semaglutide 2.4 mg will become commercially available for this use under clinical investigation.

Adverse events overview

Safety focus areas

AEs within safety focus area	Semaglutide 2.4 mg (n=269) n (%)	Placebo (n=135) n (%)
COVID-19	51 (19.0)	32 (23.7)
Neoplasms*†	10 (3.7)	6 (4.4)
Malignant neoplasms*†	8 (3.0)	2 (1.5)
Gastrointestinal AEs*†	4 (1.5)	1 (0.7)
Acute gallbladder disease*†	3 (1.1)	1 (0.7)
Cardiovascular disorders*†	3 (1.1)	2 (1.5)
Medication errors#	2 (0.7)	4 (3.0)
Acute renal failure*†	0	1 (0.7)
Psychiatric disorders*†	0	1 (0.7)

**In-trial period; †Only serious adverse events were considered; #Medication error was defined as an unintended failure with the investigational product, including administration of the wrong drug, incorrect route of administration, missed doses, or drug misuse or abuse by the participant (e.g., drug overdose to maximize the effect or with the intention to cause harm).*
%, proportion of participants with event(s); AE, adverse event

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Conclusions

Semaglutide 2.4 mg showed greater improvements compared to placebo with respect to changes in bodyweight and knee OA–related pain

Improvements were also seen in physical function with semaglutide 2.4 mg versus placebo, without an increase in the use of analgesics

Safety and tolerability with semaglutide 2.4 mg were consistent with the global STEP programme and the GLP-1RA class in general

GLP-1RA, glucagon-like peptide-1 receptor agonist; OA, osteoarthritis; STEP, Semaglutide Treatment Effect in People with obesity.

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