Real-World Comparative Effectiveness of Semaglutide 2.4 mg Versus Other Commercially Available Medications for Chronic Weight Management in Adults With Obesity in the United States: A Pragmatic Clinical Study

Results from POSEY (Pragmatic Obesity Semaglutide Trial in EmploYer Setting)

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Presenter disclosure

Lauren Wilson reports the following:

- Employee of Novo Nordisk, Inc.

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Introduction

In the US, the prevalence of obesity is increasing. In addition to increased health risks and reduced quality of life, employees with obesity are more likely to experience increased absenteeism, premature disability and reduced productivity[1]

In the phase 3a STEP 1 study, once-weekly subcutaneous semaglutide 2.4 mg provided clinically relevant weight loss in adults with overweight or obesity,[2] leading to its FDA approval for weight management in June 2021

This post-approval pragmatic study evaluated the real-world comparative effectiveness of once-weekly subcutaneous semaglutide 2.4 mg versus other commercially available AOMs on body weight reduction in adults with obesity in a multiple-employer US setting

AOM, anti-obesity medication; FDA, US Food and Drug Administration.

1. Yaborough CM, et al. J Occup Environ Med. *2018;60(1):97-107. 2. Wilding JPH, et al.* N Engl J Med. *2021;384:989-1002.*

Peters W, et al. Presented at ISPOR 2026, May 17-20, 2026; Philadelphia, PA, USA.

Study design

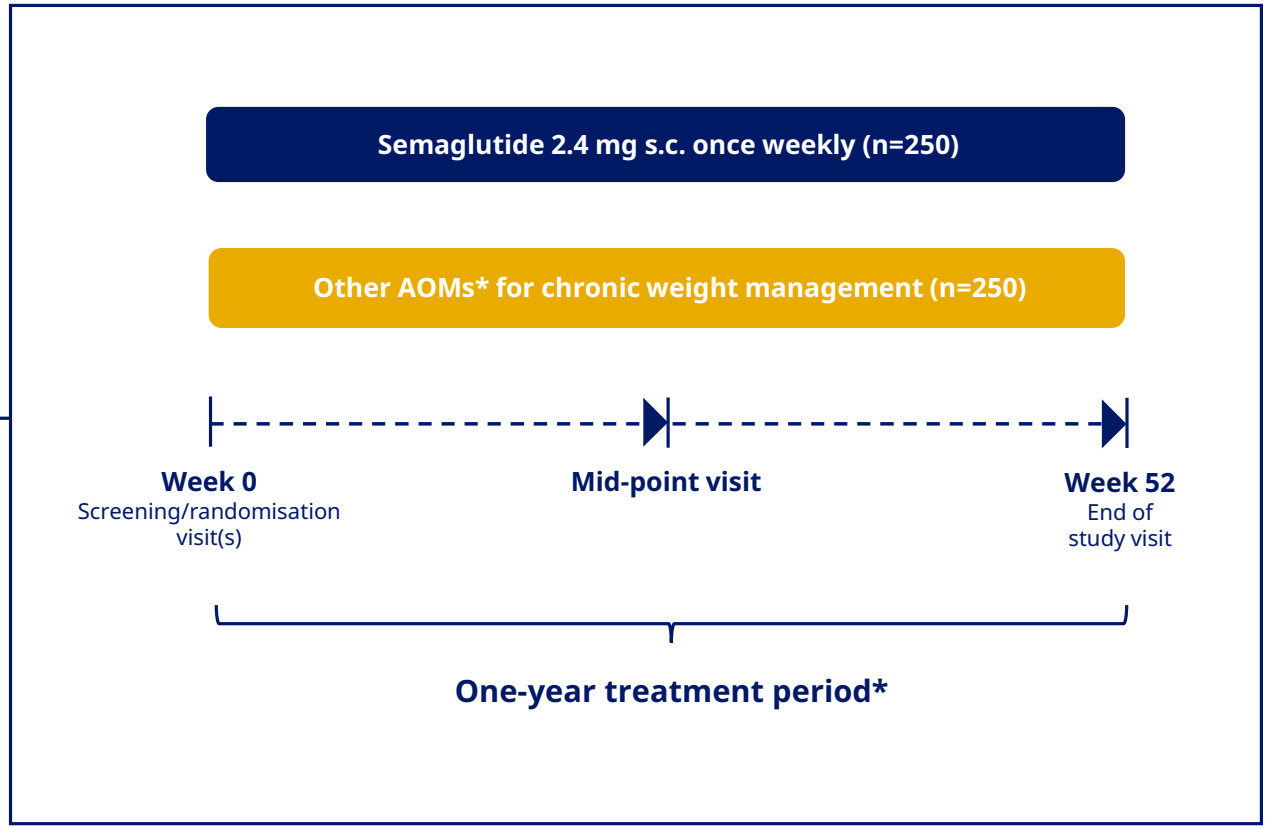
Key inclusion criteria

- Age ≥18 years
- BMI: ≥30 kg/m^2
- Employed at randomisation
- No history of type 1 or type 2 diabetes mellitus

Trial information

Interventional, 1:1 randomised, open-label, parallel-group, active comparator–controlled, 2-armed pragmatic study in a multiple employer setting in the US

- Loma Linda University
- Inland Empire Health Plan



*Intermediate visits occurred according to local clinical practice.
AOM, anti-obesity medication; BMI, body mass index; s.c., subcutaneous.

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Study interventions

Semaglutide 2.4 mg (Wegovy®)

Other AOMs

Chosen at investigator discretion:

- Orlistat (Xenical®)
- Phentermine/topiramate ER (Qsymia®)
- Naltrexone/bupropion ER (Contrave®)
- Liraglutide 3.0 mg (Saxenda®)

Treatment switching

- Semaglutide group – switching to other AOM was not allowed
- Other AOM group – switching between other AOMs was allowed at investigator discretion

Randomised treatments

- Dispensed by a pharmacy **(drug was not provided)**
- Partial reimbursement (copay assistance) was provided for out-of-pocket costs

AOM, anti-obesity medication.

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Study endpoints

Change at Week 52

Primary

- Achieving body weight reduction ≥10.0%

Confirmatory secondary

- Body weight (%)
- IWQOL-Lite-CT physical function domain score

Select Supportive secondary

- Achieving body weight reduction ≥15.0%, ≥20.0%
- Achieving IWQOL-Lite-CT physical function domain score change ≥14.6
- Covered by study product ≥80% of days

Exploratory

- Treatment satisfaction assessed by TSQM-9 Global Satisfaction total score

IWQOL-Lite-CT, Impact of Weight on Quality of Life – Lite for Clinical Trials; TSQM-9, Treatment Satisfaction Questionnaire for Medication.

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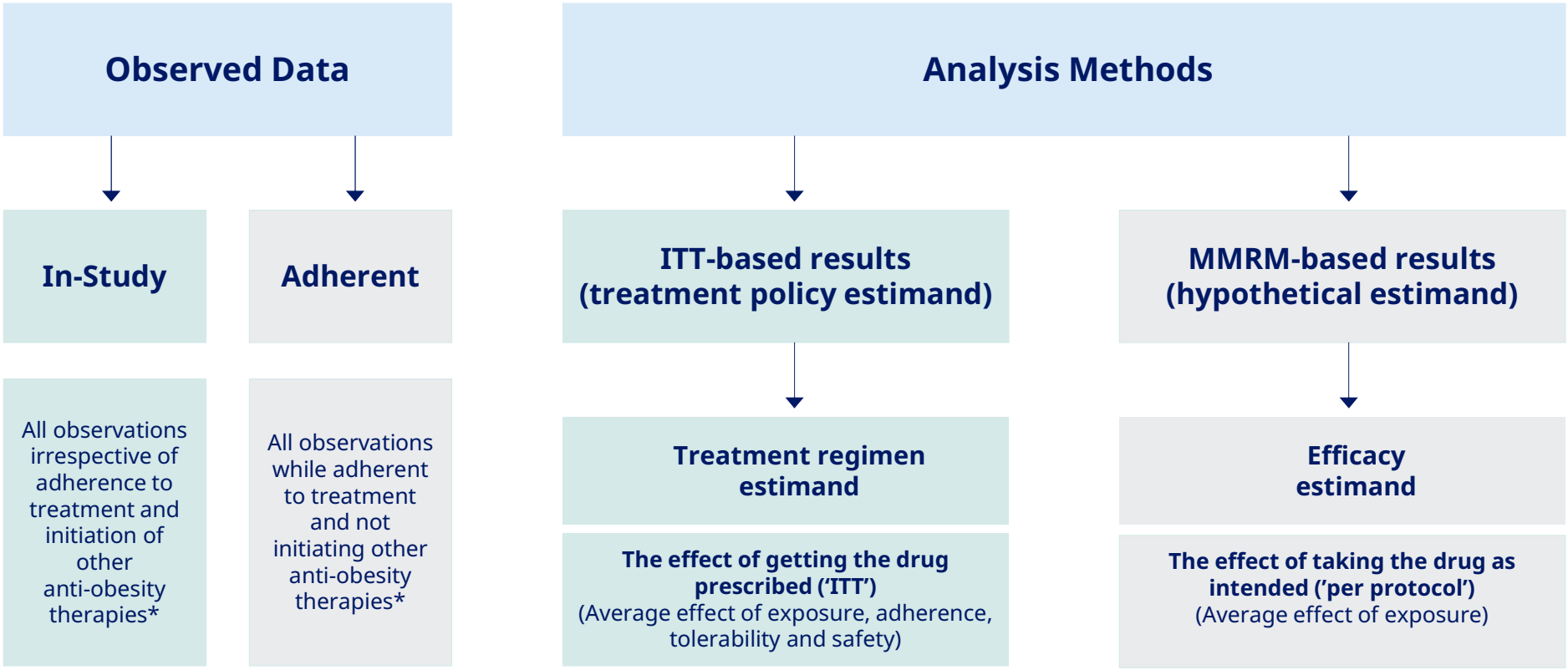
Statistical analysis strategies



**Weight management drugs or bariatric surgery.*
ITT, intent to treat; MMRM, mixed model for repeated measures.

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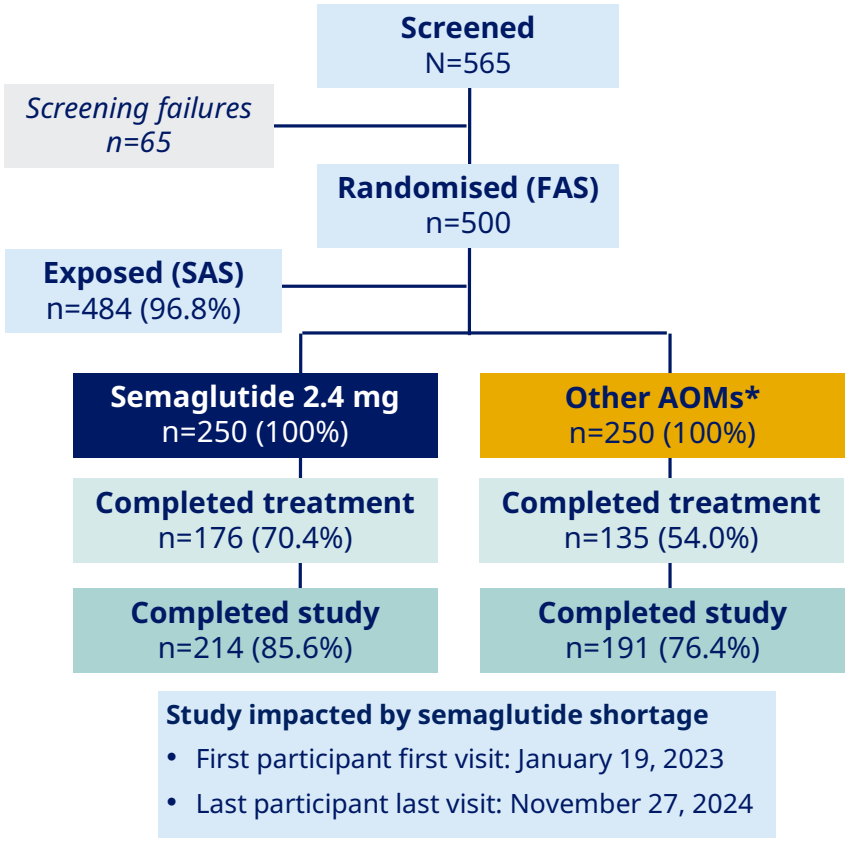
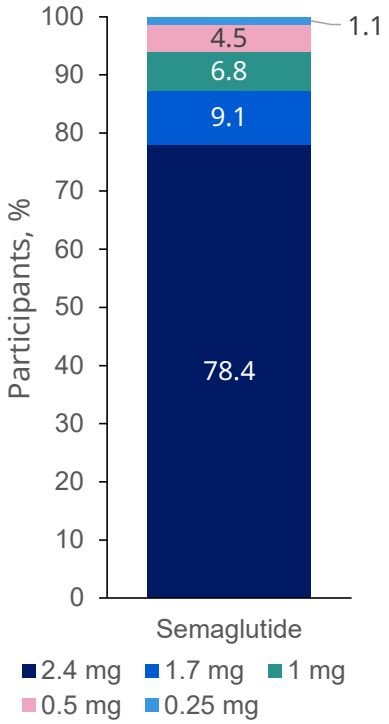
Participant disposition and treatments



Last dose for treatment completers – Semaglutide

Observed data – In-Study



Other AOMs

Observed data – In-Study

Other AOMs	N (%)
Number of participants	242
AOM prescribed at randomisation	
Liraglutide	141 (58.3)
Phentermine/topiramate	96 (39.7)
Naltrexone/bupropion	5 (2.1)
Switched to ≥1 other AOM	65 (26.9)

**Orlistat (Xenical®); phentermine/topiramate ER (Qsymia®); naltrexone/bupropion ER (Contrave®); liraglutide 3.0 mg (Saxenda®).*
%, proportion of participants from full analysis set; AOM, anti-obesity medication; FAS, full analysis set; SAS, safety analysis set.

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Demographics and baseline characteristics

Female | Male

89.6/10.4%

Mean age

41.3 years

White | Black | Asian | Other*

79.0/10.0/4.8/6.2%

Mean body weight

101.6 kg/ 224.0 lb

Mean BMI

37.4 kg/m^2

Overweight/ OC I/OC II/OC III

0.6/42.2/33.6/23.6%

**Other refers to American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander and multiple.*
The baseline characteristics at randomisation are reported. The obesity categories are defined as follows: normal weight: 18.5–24.9, overweight: 25.0–29.9, obesity class I: 30.0–34.9, obesity class II: 35.0–39.9, ≥40, obesity class III.
BMI, body mass index; OC, obesity class.

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Comorbidities at screening





Hypertension	Dyslipidaemia	Asthma	GERD	CVD*
17.0%	13.2%	10.6%	9.8%	7.6%

Number of participants with none to 5 or more comorbidities at screening†:

None	1	2	3	4	≥5
55.2%	27.0%	10.6%	4.8%	2.2%	0.2%

**CVD included the medical history terms coronary heart disease, stable angina pectoris, angina pectoris unstable, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, stroke, transient ischemic attack, carotid artery stenosis (≥50% stenosis), peripheral arterial disease (atherosclerotic disease) and peripheral revascularisation or the medical history system organ class of cardiovascular disease within cardiac disorders. †Comorbidities evaluated included hypertension, dyslipidaemia, asthma, GERD, CVD, obstructive sleep apnoea, polycystic ovarian syndrome, liver disease, knee osteoarthritis, gout, chronic obstructive pulmonary disease, infertility, kidney disease and psoriasis.*
%, proportion of participants; CVD, cardiovascular disease; GERD, gastroesophageal reflux disease.

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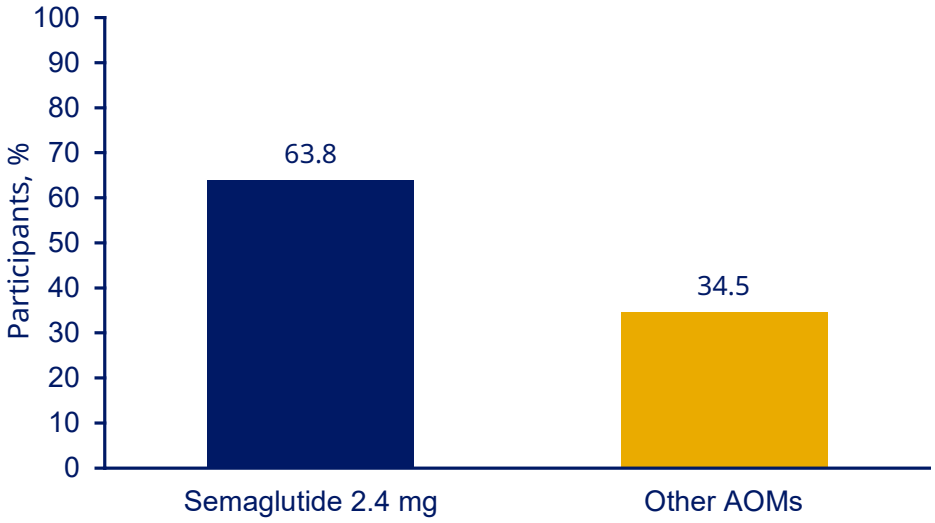
Primary endpoint: Body weight reduction ≥10.0%

After 52 weeks of treatment

In-Study

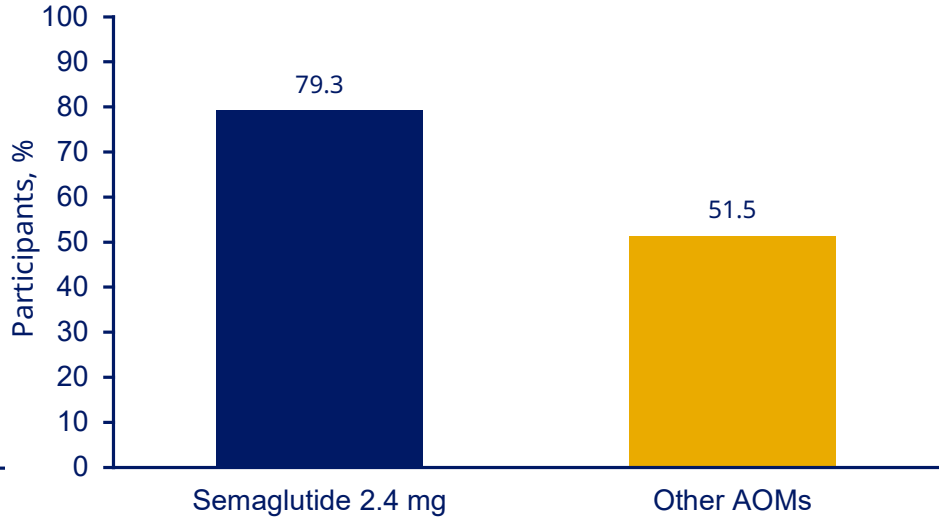
Mean baseline body weight: 101.6 kg



Analysis at week 52	OR	95% CI	*P*-value
Semaglutide 2.4 mg vs other AOMs	3.18	2.12, 4.78	<0.0001

Adherent*

Mean baseline body weight: 101.6 kg



Analysis at week 52	OR	95% CI	*P*-value
Semaglutide 2.4 mg vs other AOMs	9.20	6.11, 13.83	<0.0001

**All observations while adherent to treatment and not initiating other anti-obesity therapies.*
AOM, anti-obesity medication; CI, confidence interval; OR, odds ratio.

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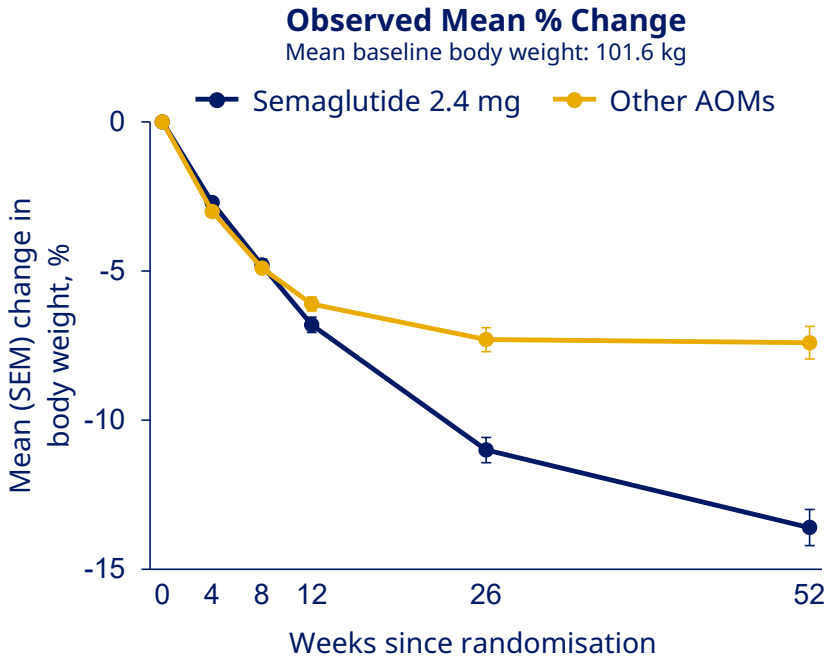
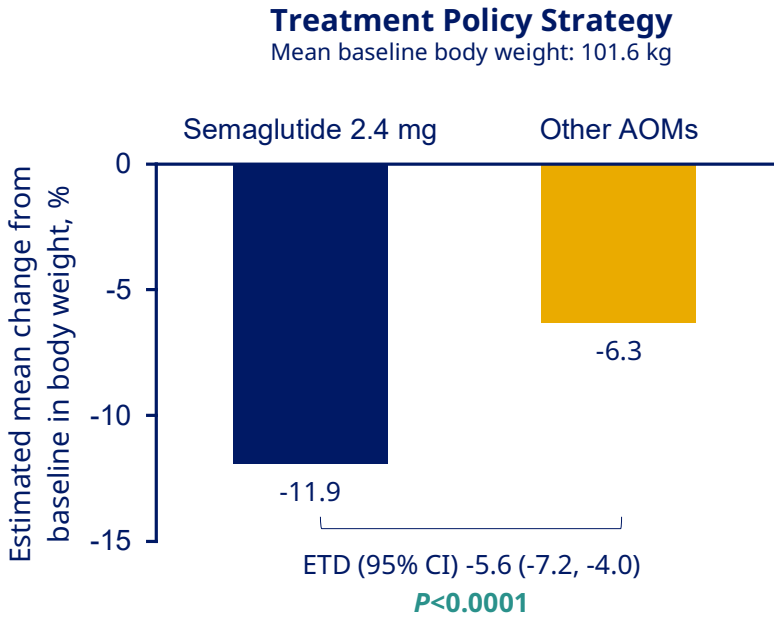
Secondary endpoint: Change in body weight (%)

Observed and estimated means – Treatment Policy Strategy after 52 weeks of treatment





Numbers shown in the lower panel of the figure (left) are numbers of participants contributing to the mean.
AOM, anti-obesity medication; CI, confidence interval; ETD, estimated treatment difference; SEM, standard error of the mean.

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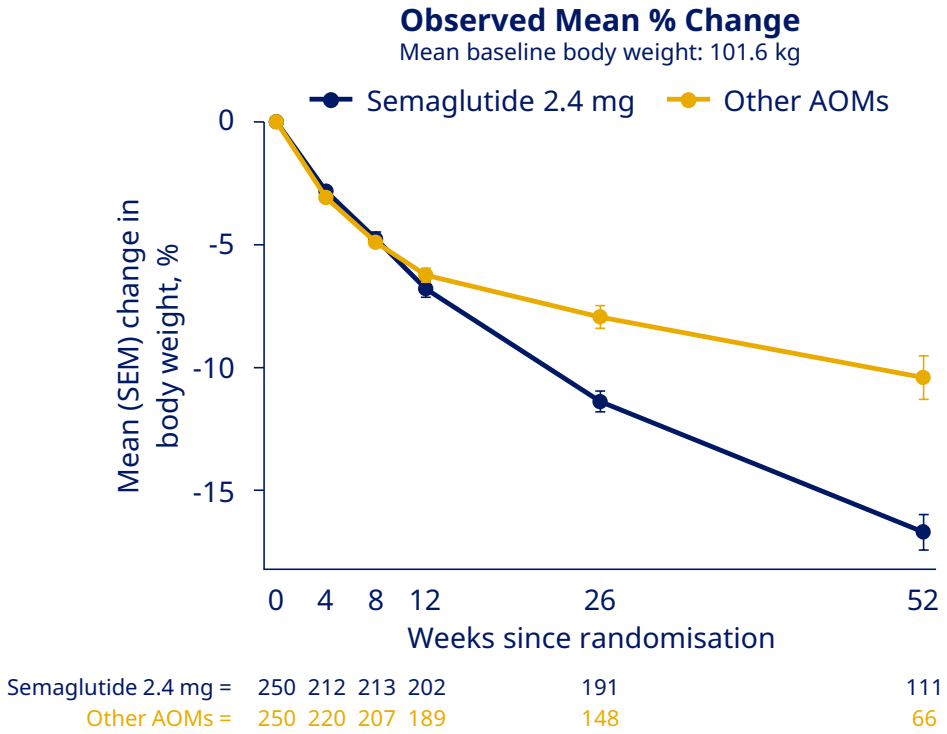
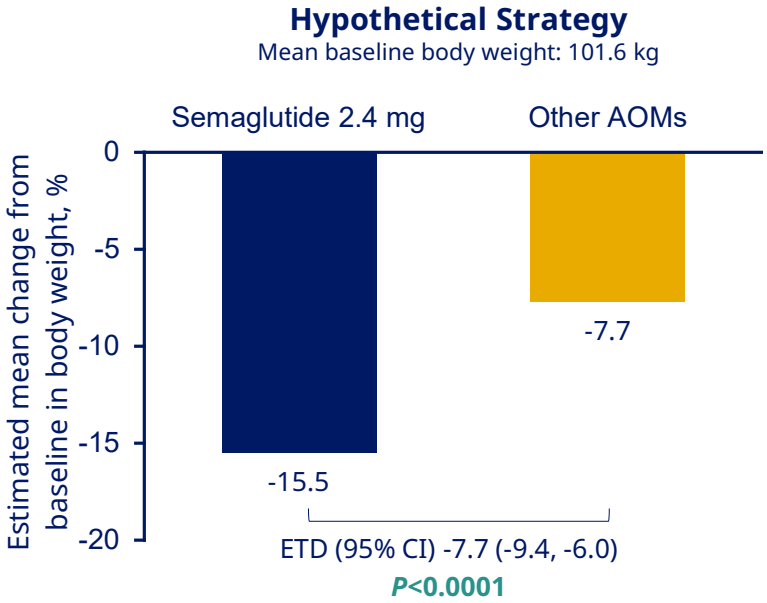
Secondary endpoint: Change in body weight (%)

Observed and estimated means – Hypothetical Strategy after 52 weeks of treatment





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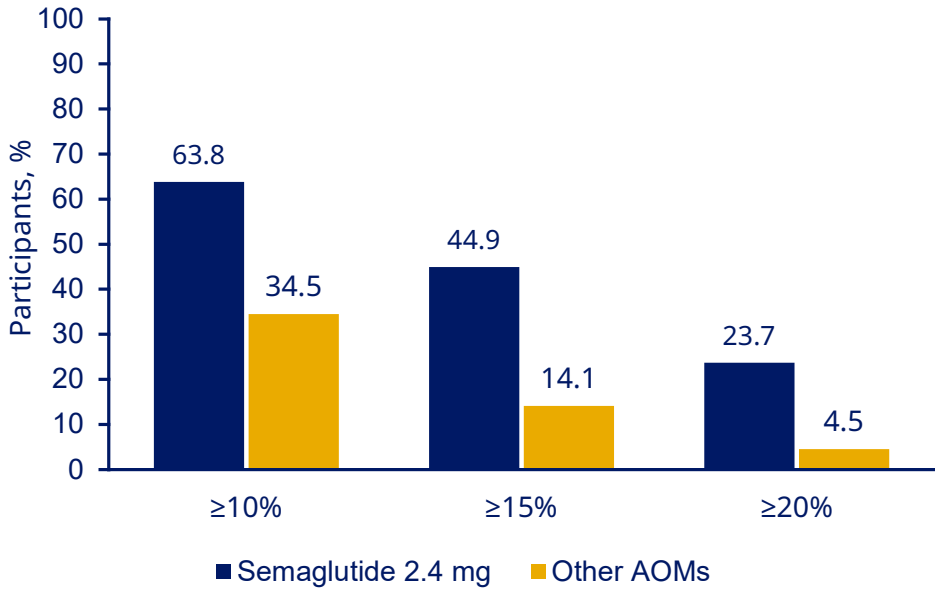
Supportive secondary endpoints – Categorical weight loss

Observed proportions after 52 weeks of treatment

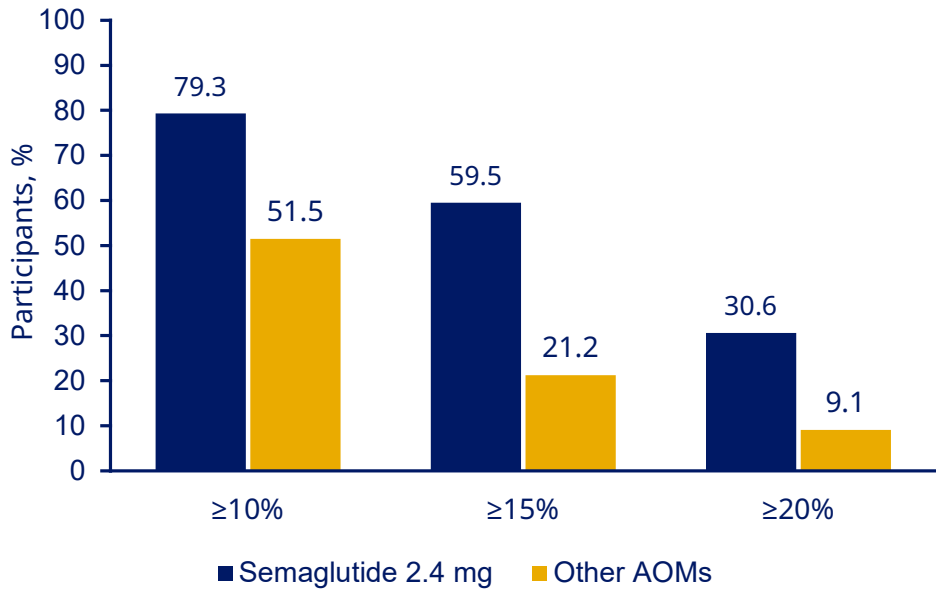
In-Study

Weight loss ≥10%, ≥15% and ≥20% at week 52



Adherent

Weight loss ≥10%, ≥15% and ≥20% at week 52



AOM, anti-obesity medication.

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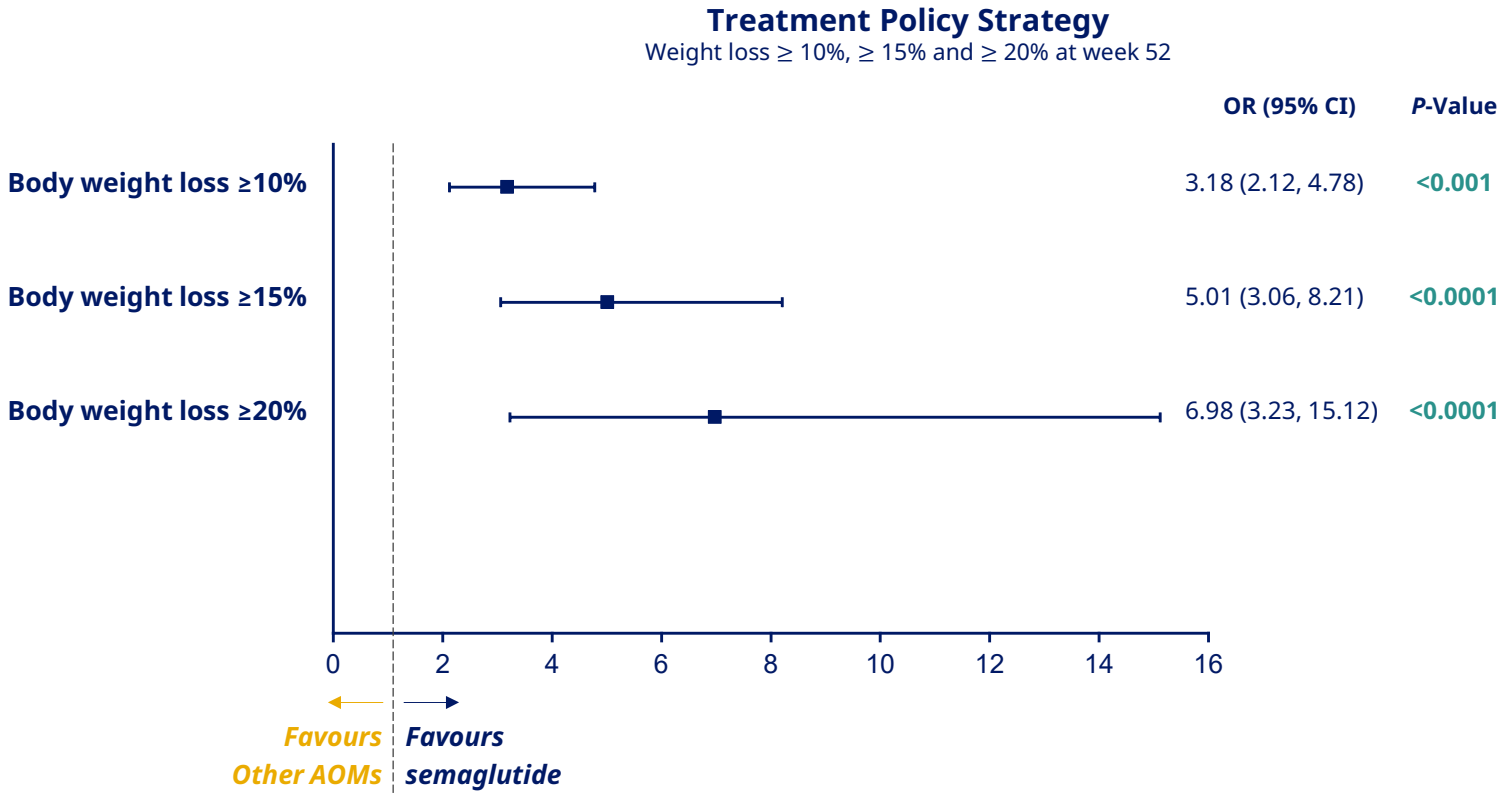
Supportive secondary endpoints – Categorical weight loss

Estimated odds ratio after 52 weeks of treatment



Observed data.
AOM, anti-obesity medication; CI, confidence interval; OR, odds ratio.

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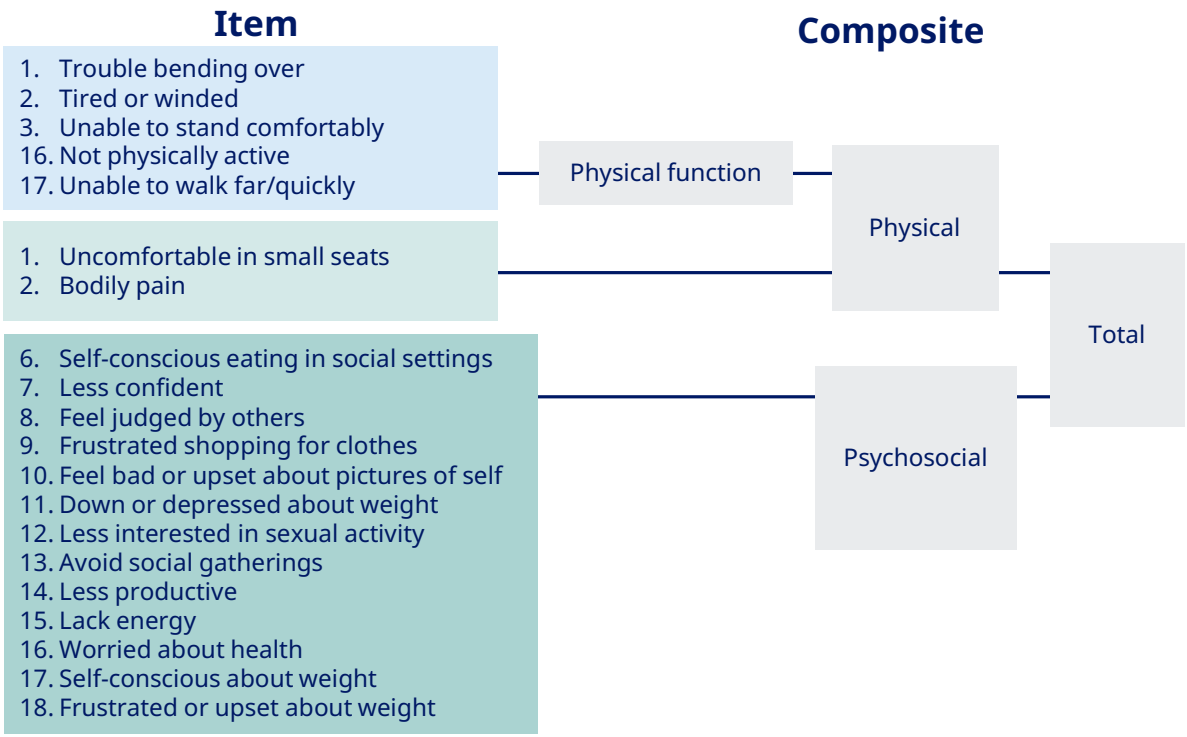
IWQOL-Lite-CT

Impact of Weight on Quality of Life-Lite for Clinical Trials Version[1,2]



Scoring[2]:

- 1 = never; not true at all
- 2 = rarely; a little true
- 3 = sometimes; moderately true
- 4 = usually; mostly true
- 5 = always; completely true
  - Larger values reflect *worse* outcomes

Composite scores range from 0 to 100, with higher scores reflecting *better* outcomes

IWQOL-Lite-CT, Impact of Weight on Quality of Life – Lite for Clinical Trials.

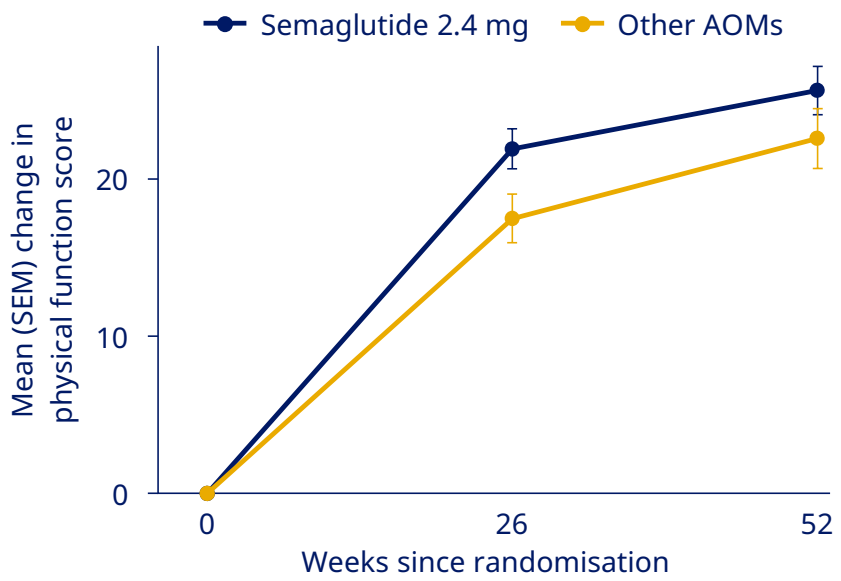
1. Kolotkin RL, et al. Clin Obes. *2017;7(5):290-9. 2. Kolotkin RL, et al.* Clin Obes. *2019;9(3):e12310.*
Peters W, et al. Presented at ISPOR 2026, May 17-20, 2026; Philadelphia, PA, USA.

Secondary endpoint: Change in IWQOL-Lite-CT physical function score

Observed and estimated means – Treatment Policy Strategy after 52 weeks of treatment

Observed Mean Change

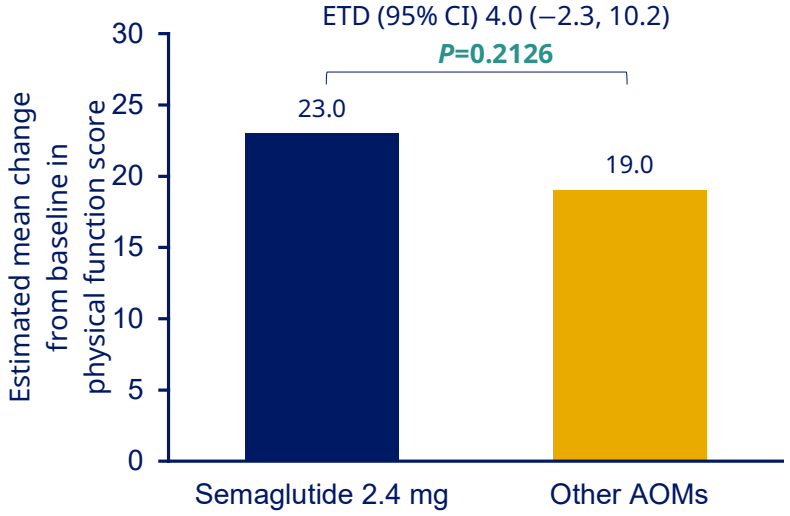
Mean baseline IWQOL-Lite-CT physical function score: 45.2



Semaglutide 2.4 mg =	250	207	189
Other AOMs =	250	185	163

Treatment Policy Strategy

Mean baseline IWQOL-Lite-CT physical function score: 45.2



**Estimated means. Error bars are ± standard error of the mean. Numbers shown in the lower panel of the figure (left) are numbers of participants contributing to the mean.*
AOM, anti-obesity medication; CI, confidence interval; ETD, estimated treatment difference; IWQOL-Lite-CT, Impact of Weight on Quality of Life – Lite for Clinical Trials; SEM, standard error of the mean.

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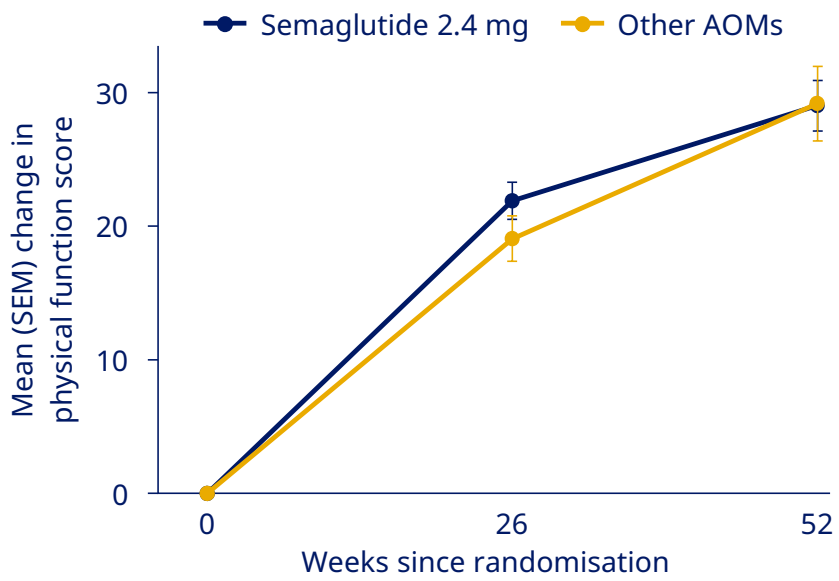
Secondary endpoint: Change in IWQOL-Lite-CT physical function score

Observed and estimated means – Hypothetical Strategy after 52 weeks of treatment

Observed Mean Change

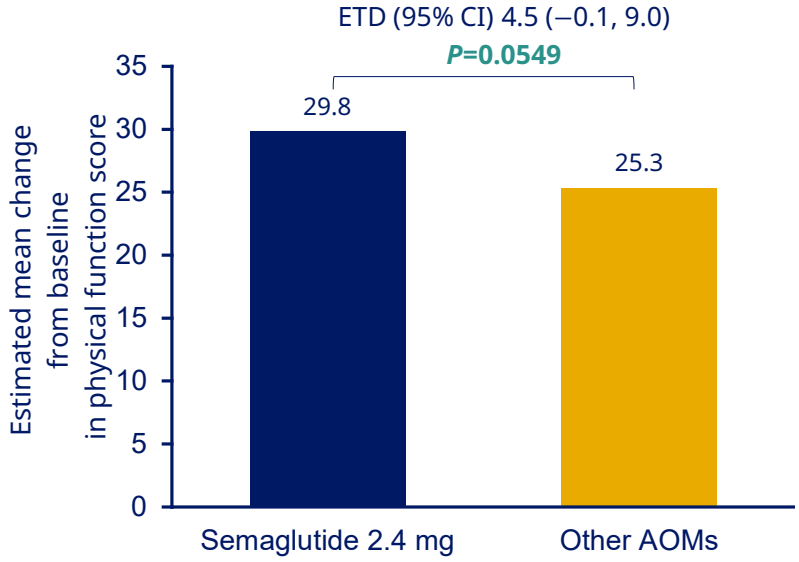
Mean baseline IWQOL-Lite-CT physical function score: 45.2



Semaglutide 2.4 mg =	250	188	110
Other AOMs =	250	146	63

Hypothetical Strategy

Mean baseline IWQOL-Lite-CT physical function score: 45.2



**Estimated means. Error bars are ± standard error of the mean. Numbers shown in the lower panel of the figure (left) are numbers of participants contributing to the mean.*
AOM, anti-obesity medication; CI, confidence interval; ETD, estimated treatment difference; IWQOL-Lite-CT, Impact of Weight on Quality of Life – Lite for Clinical Trials; SEM, standard error of the mean.

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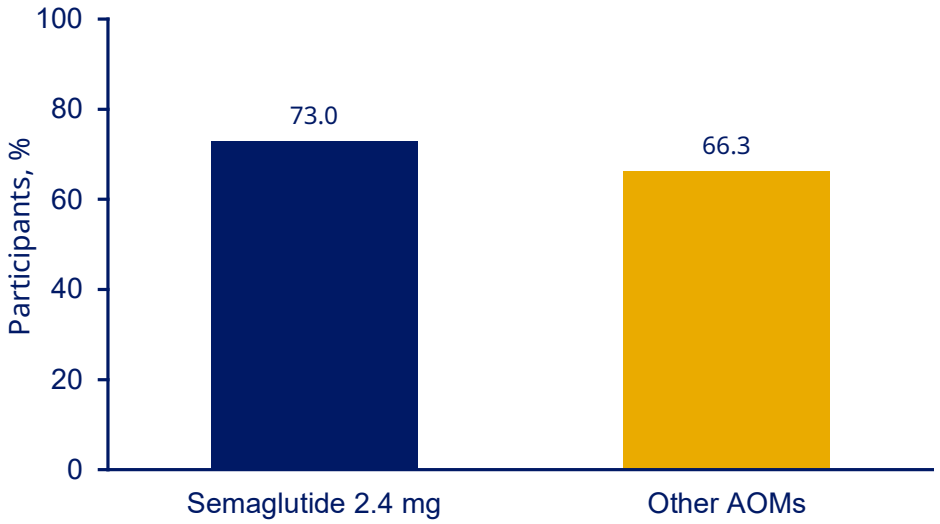
Secondary endpoint: Change in IWQOL-Lite-CT physical function score ≥14.6

Observed proportions – Treatment Policy Strategy after 52 weeks of treatment

Treatment Policy Strategy

Mean baseline IWQOL-Lite-CT physical function score: 45.2



Statistical Analysis at Week 52 – Treatment Policy Strategy

Analysis at week 52	OR	95% CI	P-value
Semaglutide 2.4 mg vs other AOMs	1.47	0.91, 2.38	0.1163

AOM, anti-obesity medication; CI, confidence interval; IWQOL-Lite-CT, Impact of Weight on Quality of Life – Lite for Clinical Trials; OR, odds ratio.

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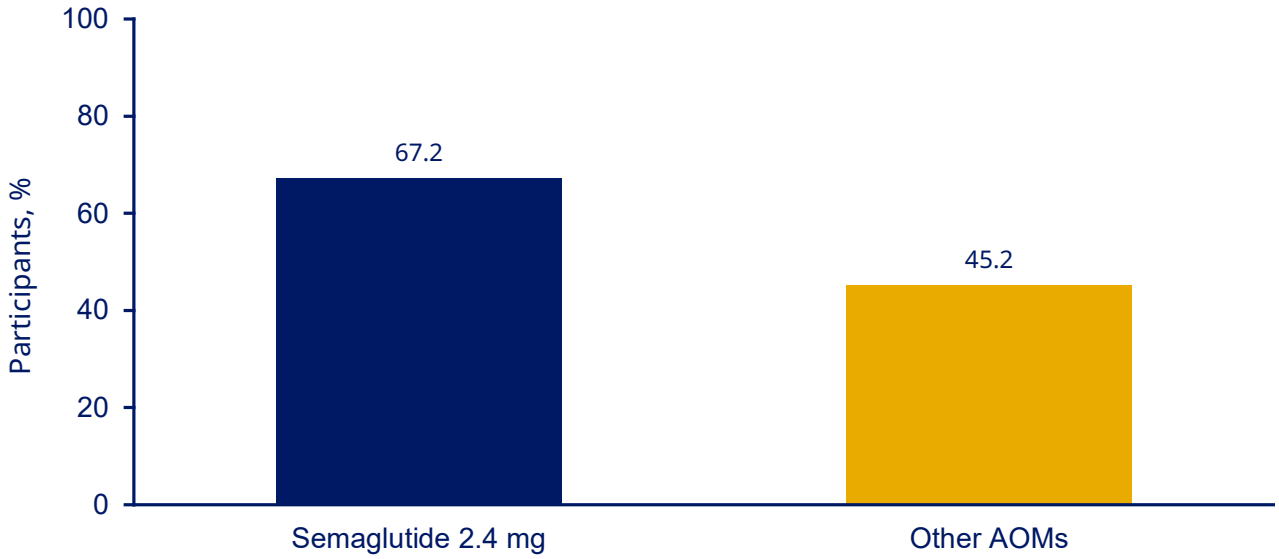
Secondary endpoint: Covered by study product ≥80% of days

Observed proportions – Treatment Policy Strategy after 52 weeks of treatment



AOM, anti-obesity medication.

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Exploratory endpoint: TSQM-9 Global Satisfaction total score

Observed proportions – Treatment Policy Strategy after 52 weeks of treatment

Treatment	N	Mean (SD)	Min, max
In-Study			
Semaglutide 2.4 mg	188	80.1 (24.4)	0, 100
Other AOMs	161	67.3 (30.6)	0, 100
Adherent			
Semaglutide 2.4 mg	110	87.7 (16.5)	14.3, 100
Other AOMs	62	77.6 (22.2)	28.6, 100

The TSQM-9 is a modified self-administered questionnaire that does not consider the role of side effects in satisfaction; scores range from 0 to 100, with higher scores indicating better treatment satisfaction. There are 3 key domains; effectiveness, convenience and global satisfaction.[1]

AOM, anti-obesity medication; N, number of participants with an observation at the visit; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

1. Bharmal M, et al. Health Qual Life Outcomes. *2009;7:36.*

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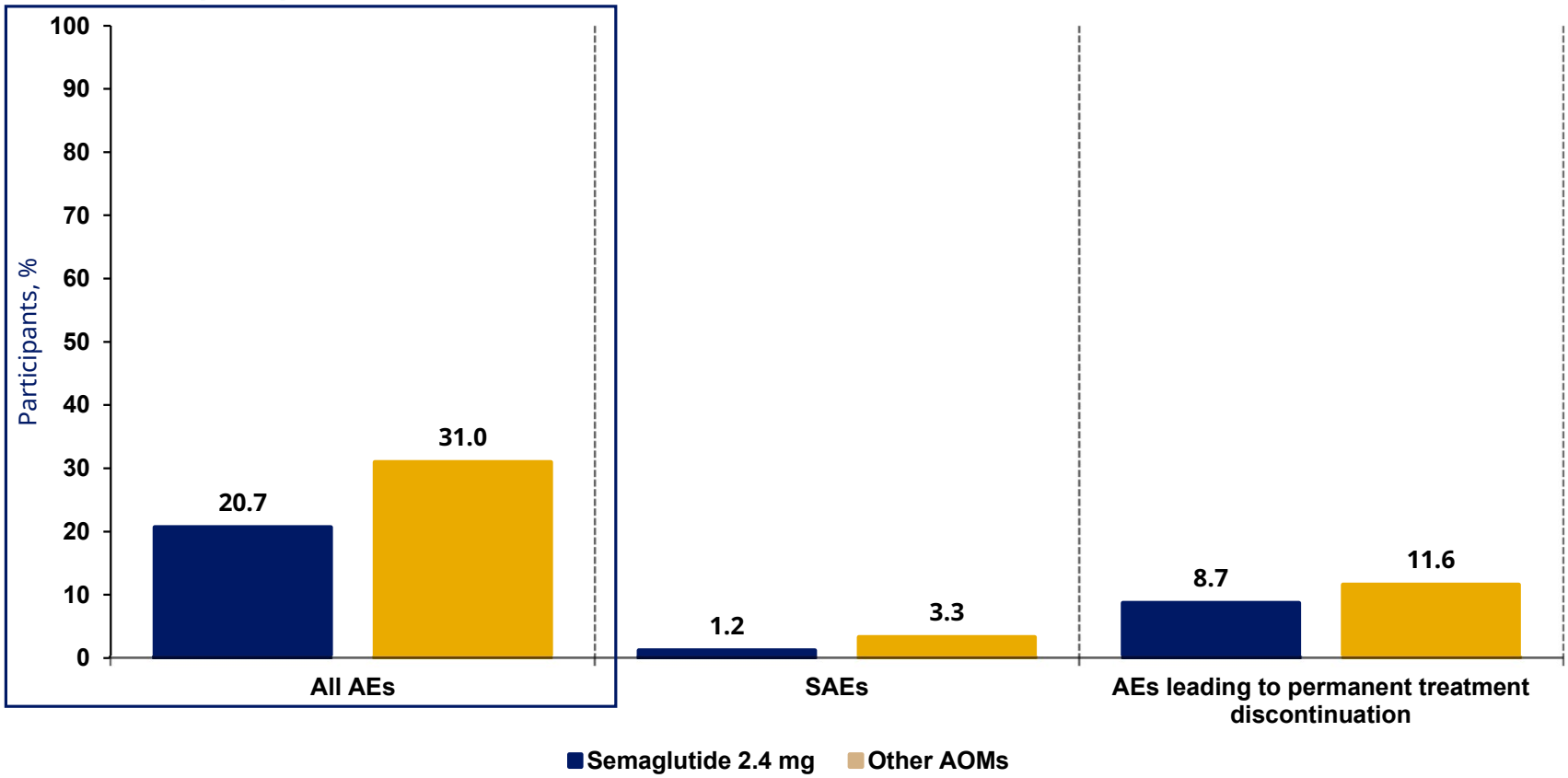
Safety

Observed proportions



AE, adverse event; AOM, anti-obesity medication; SAE, serious adverse event.

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POSEY, STEP 1 and STEP 8: Efficacy results

Indirect treatment comparison: Hypothetical Strategy*

	POSEY		STEP 1		STEP 8		
Investigational agent/comparator	**Semaglutide 2.4 mg**	**Other AOMs**	**Semaglutide 2.4 mg**	**Placebo**	**Semaglutide 2.4 mg**	**Liraglutide 3.0 mg**	**Placebo**
Change in BW (%)	−15.45	−7.74	−16.86	−2.44	−17.06	−6.59	−1.79
Participants achieving 10% weight loss (%)	79.3	51.5	74.8	11.8	73.6	28.3	15.9
Participants achieving 15% weight loss (%)	59.5	21.2	54.8	5	56.6	14.1	5.8
Participants achieving 20% weight loss (%)	30.6	9.1	34.8	2	40.6	6.5	2.9

**In STEP studies, Hypothetical Strategy refers to the hypothetical estimand and on-treatment data; in POSEY, Hypothetical Strategy refers to the additional estimand and adherent data.*
AOM, anti-obesity medication; BW, body weight.

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Conclusions

- Semaglutide 2.4 mg was superior to other AOMs with respect to participants achieving ≥10.0% body weight reduction and change in body weight (%)
- More participants treated with semaglutide 2.4 mg achieved ≥15% and ≥20% body weight reduction from baseline compared with other AOMs
- A trend towards greater improvement in IWQOL-Lite-CT physical function score was observed with semaglutide 2.4 mg compared with other AOMs, though this difference did not reach statistical significance
- Safety and tolerability were consistent with the overall well-established profile of semaglutide

These findings demonstrate real-world effectiveness of semaglutide 2.4 mg comparable to that observed in the phase 3a STEP trials

AOM, anti-obesity medication; IWQOL-Lite-CT , Impact of Weight on Quality of Life – Lite for Clinical Trials.

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