Supplementary Online Content 1

Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. *JAMA.* Published online February 24, 2021. doi:10.1001/jama.2021.1831

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. List of Investigators in the Semaglutide Treatment Effect in People with obesity (STEP) 3 Trial

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eAppendix 2. Participant Enrollment and Exclusions by Study Site

Site	Participants enrolled		Withdrew prior to randomization (n)
	Semaglutide group (n)	Placebo group (n)	
201	7	6	0
202	14	7	0
203	9	4	0
204	9	7	0
205	10	5	0
206	7	9	0
207	17	6	0
208	10	4	0
209	12	5	0
210	5	9	1
211	9	5	0
212	11	3	0
214	17	3	0
215	13	3	0
216	15	5	0
217	14	2	0
218	11	7	0
219	10	4	0
220	11	9	0
221	6	4	0
222	8	7	0
223	8	6	0
224	10	3	0
225	8	5	0
226	11	3	0
227	8	8	0
228	10	4	0
229	12	1	0
230	4	8	0
231	10	4	0
232	8	4	1
233	13	4	0
234	9	1	0
235	13	5	0
237	6	4	0
238	6	4	0
239	6	2	0
240	12	5	0
241	9	7	0
242	6	6	0
243	13	6	0
Total	**407**	**204**	**2**

eAppendix 3. Inclusion and Exclusion Criteria

Inclusion Criteria

Participants were eligible to be included in the trial only if all of the following criteria applied:

- Informed consent obtained before any trial-related activities. Trial-related activities are any procedures that were carried out as part of the trial, including activities to determine suitability for the trial
- Male or female, age ≥18 years at the time of signing informed consent
- Body mass index (BMI) ≥30.0 kg/m^2 or ≥27.0 kg/m^2 with the presence of at least one of the following weight-related comorbidities (treated or untreated): hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease
- History of at least one self-reported unsuccessful dietary effort to lose body weight

Exclusion Criteria

Participants were excluded from the trial if any of the following criteria applied:

Glycemia-Related:

- Glycated hemoglobin (HbA_{1c}) ≥48 mmol/mol (6.5%), as measured by the central laboratory at screening
- History of type 1 or type 2 diabetes mellitus
- Treatment with glucose-lowering agent(s) within 90 days before screening

Obesity-Related:

- A self-reported change in body weight >5 kg (11 lbs) within 90 days before screening irrespective of medical records
- Treatment with any medication for the indication of obesity within the past 90 days before screening
- Previous or planned (during the trial period) obesity treatment with surgery or a weight loss device. However, the following are allowed: (1) liposuction and/or abdominoplasty, if performed >1 year before screening; (2) lap banding, if the band has been removed >1 year before screening; (3) intragastric balloon, if the balloon has been removed >1 year before screening; or (4) duodenal-jejunal bypass sleeve, if the sleeve has been removed >1 year before screening
- Uncontrolled thyroid disease, defined as thyroid stimulating hormone (TSH) >6.0 mIU/L or <0.4 mIU/L as measured by the central laboratory at screening

Mental Health:

- History of major depressive disorder within 2 years before screening
- Diagnosis of other severe psychiatric disorder (eg, schizophrenia, bipolar disorder)
- A Patient Health Questionnaire-9 (PHQ-9) score of ≥15 at screening
- A lifetime history of a suicidal attempt
- Suicidal behavior within 30 days before screening
- Suicidal ideation corresponding to type 4 or 5 on the Columbia-Suicide Severity Rating Scale (C-SSRS) within the past 30 days before screening

General Safety:

- Participant was unable to adhere to low-calorie diet as judged by the investigator
- Physical activity was considered to be unsafe as judged by the investigator
- Presence of acute pancreatitis within the past 180 days prior to the day of screening

- History or presence of chronic pancreatitis
- Calcitonin ≥100 ng/L as measured by the central laboratory at screening
- Personal or first-degree relative(s) history of multiple endocrine neoplasia type 2 or medullary thyroid carcinoma
- Renal impairment measured as estimated glomerular filtration rate (eGFR) value of eGFR <15 mL/min/1.73 m^2 as defined by KDIGO 2012[1] by the central laboratory at screening
- History of malignant neoplasms within the past 5 years prior to screening. Basal and squamous cell skin cancer and any carcinoma in-situ were allowed
- Any of the following: myocardial infarction, stroke, hospitalization for unstable angina, or transient ischemic attack within the past 60 days prior to screening
- Participant classified as being in New York Heart Association (NYHA) Class IV
- Surgery scheduled for the duration of the trial, except for minor surgical procedures, in the opinion of the investigator
- Known or suspected abuse of alcohol or recreational drugs
- Known or suspected hypersensitivity to trial product(s) or related products
- Previous participation in this trial. Participation is defined as signed informed consent
- Participation in another clinical trial within 90 days before screening
- Other participant(s) from the same household participating in any semaglutide trial
- Female who was pregnant, breast-feeding or intended to become pregnant or was of child-bearing potential and not using a highly effective contraceptive method
- Any disorder, unwillingness or inability, not covered by any of the other exclusion criteria which, in the investigator’s opinion, might have jeopardized the participant’s safety or compliance with the protocol

eAppendix 4. Intensive Behavioral Therapy Methodology

During the STEP 3 trial, participants in both the semaglutide and placebo groups were prescribed a low-calorie meal-replacement diet for the first 8 weeks, and intensive behavioral therapy (IBT; decreased energy intake, increased physical activity, and counseling sessions) for the trial duration.

Dietary intervention started after randomization. The first 8 weeks consisted of a 1000–1200 kcal/day low-calorie diet (LCD), provided as meal replacements (eg, liquid shakes and solid bars) and heat-and-serve, pre-prepared meals. These foods were manufactured by Nutrisystem and supplied to participants free of charge by Novo Nordisk. After 8 weeks on LCD, participants were gradually transferred to a less strict hypo-caloric diet comprised of conventional foods. From week 8 to the end of treatment, the daily caloric target was calculated based on body weight at randomization (Visit 2) according to the algorithm below:

- Participants weighing less than 200 lbs (91 kg) were prescribed a diet of 1200 kcal/day
- Participants weighing between 200 lbs (91 kg) and 300 lbs (136 kg) were prescribed a diet calculated as: *Daily caloric target (kcal) = body weight (lb) * 6 (kcal/lb)*
- Participants weighing more than 300 lbs (136 kg) were prescribed 1800 kcal/day

This caloric target was kept for the remainder of the trial. If a participant achieved a BMI ≤22.5 kg/m^2, the recommended energy intake was re-calculated with no caloric deficit for the remainder of the trial.

Physical activity was initiated from randomization and was prescribed with a target of 100 minutes physical activity/week. Participants were counseled to be physically active in bouts of >10 minutes in duration with moderate intensity (such as brisk walking), and the physical activity was spread equally across 4–5 days each week. The physical activity target progressed gradually by 25 minutes every 4 weeks and up to 200 minutes/week, consistent with targets required for maintenance of lost weight.

Each IBT counseling session covered a specific topic, for example, advice on modifying diet or physical activity as well as behavioral strategies to facilitate these changes (eg, monitoring food intake, challenging negative thoughts, obtaining social support). From the randomization visit through week 12, participants received weekly IBT counseling from a dietitian (or a similarly qualified healthcare professional) who discussed participants' progress, reviewed food and activity diaries, addressed any adherence problems, and prepared for transition to the next phase of the diet. Most of the topics were accompanied by a homework assignment, found in the participant hand-outs to be completed before the next visit according to the visit schedule. From weeks 12 to 24, IBT counseling visits decreased to every-other-week, and from weeks 24 to 68 were every 4 weeks (for a total of 30 IBT visits over the 68 weeks). The first three IBT visits lasted for 30–45 minutes, while the remaining visits lasted for 20–30 minutes. Participants received and used an activity tracker and were instructed to record their food intake in order to facilitate behavior change. The activity tracker, food diary/app and content of the participant hand-out from an IBT guide were used for counseling purposes by the dietitian or a similarly qualified healthcare professional at all visits. Data from the activity tracker collected in this trial were used for exploratory purposes. Participants were allowed to keep the activity tracker after approval by the independent ethics committee/institutional review board. Participants could use a food diary of their choice (eg, paper/app/other tool) for dietary recording, provided it could be reviewed during the counseling sessions. All participants were instructed on how to capture food intake and were encouraged to keep the diary on a daily basis.

eAppendix 5. Summary of Assessments

	Screening	Randomization	Dose escalation period														Maintenance period														End of treatment	End of trial
Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
Timing (weeks)	–1	0	1	2	3	4	5	6	7	8	9	10	11	12	14	16	18	20	22	24	28	32	36	40	44	48	52	56	60	64	68	75
Visit window (days)	–7–0	0	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	±3	0–5
Informed consent	X																															
Inclusion/exclusion criteria	X	X																														
Randomization		X																														
Glycemia status		X																		X										X	
Efficacy																																
Body weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Waist circumference	X	X				X				X				X		X		X			X		X		X		X		X		X	
Glycated hemoglobin	X	X																X									X				X	
Fasting plasma glucose		X																X									X				X	
Lipids and biomarkers		X																X													X	
Blood pressure	X	X				X				X				X		X		X			X		X		X		X		X		X	X
SF-36		X								X						X		X					X				X				X	
Safety																																
Adverse events		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pulse	X	X				X				X				X		X		X			X		X		X		X		X		X	X
Other procedures																																
Barriers and motivation interview	X																															
Diet and physical activity counseling		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

Abbreviation: SF-36, Short Form36v2® Health Survey, Acute Version. The table presents a consolidated summary of the assessments performed. For a complete overview of all study assessments and procedures, please see the protocol available in Supplement 2.

eAppendix 6. Statistical Analysis

Analysis and Imputation Methods to Address the Effectiveness and Efficacy Estimands for the Primary and Confirmatory Secondary End Points in the Statistical Testing Hierarchy

Objective	End Point	Test order	End Point type	Estimand	Statistical model	Imputation approach
Co-primary end points						
Primary	% weight	1	Continuous	Treatment policy[a]	ANCOVA	RD-MI
				Trial product[b]	MMRM	—
	5% responders	2	Binary	Treatment policy[a]	Logistic regression	RD-MI
				Trial product[b]	Logistic regression	MMRM
Confirmatory secondary end points						
Primary	10% responders	3	Binary	Treatment policy[a]	Logistic regression	RD-MI
				Trial product[b]	Logistic regression	MMRM
Primary	15% responders	4	Binary	Treatment policy[a]	Logistic regression	RD-MI
				Trial product[b]	Logistic regression	MMRM
Primary	Waist circumference change (cm)	5	Continuous	Treatment policy[a]	ANCOVA	RD-MI
				Trial product[b]	MMRM	—
Secondary	SBP change (mmHg)	6	Continuous	Treatment policy[a]	ANCOVA	RD-MI
Secondary	SF-36 PF score change	7	Continuous	Treatment policy[a]	ANCOVA	RD-MI

Abbreviations: ANCOVA, analysis of covariance; FAS, full analysis set; MMRM, mixed model for repeated measurements; PF, physical functioning; RD-MI, multiple imputation using retrieved participants; SBP, systolic blood pressure; SF-36, Short Form36v2® Health Survey, Acute Version.

Test order refers to the order of the end point in the statistical test hierarchy. All analyses were performed using the full analysis set.

[a]Designated as the primary estimand.

[b]Also known as the hypothetical estimand; designated as the secondary estimand.

eAppendix 7. Patient-Reported Outcome Assessments

Short Form36v2® Health Survey, Acute Version

Short Form36v2® Health Survey, Acute Version (SF-36) is a generic patient-reported outcome (PRO) instrument that measures health-related quality of life and general health status across disease conditions. It consists of 36 questions (items) across eight domains (ie, physical functioning, role limitations due to physical health problems, body pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health). The SF-36 also provides two aggregated scores, the physical component summary (PCS) score and mental component summary (MCS) score, created by aggregating the eight domains according to the scoring algorithm.[2] SF-36 scores are norm-based scores (also referred to as T-score metrics), ie, transformed to a scale where the 2009 US general population has a mean of 50 and an SD of 10. Scores are calculated using PRO-CoRE version 1.5, a scoring software provided by Optum. The range of lowest to highest scores for the physical functioning domain is 19.03 to 57.60, for the physical component summary it is 6.11 to 79.67, and for the mental component summary it is –3.83 to 78.75. An increase in score represents an improvement in health status.

eAppendix 8. Supportive Secondary End Points

Efficacy End Points

- Change from baseline to week 68 in:
    - Body weight (kg) and BMI (kg/m^2)
    - Glycated hemoglobin (%, mmol/mol), fasting plasma glucose (mg/dL), and fasting serum insulin (mIU/L)
    - Diastolic blood pressure (mmHg)
    - Lipids (mg/dL): total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, free fatty acids, and triglycerides
    - High sensitivity C-reactive protein (mg/L)
    - Plasminogen activator inhibitor-1 activity (AU/mL)
    - SF-36 scores: role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health, physical component summary, mental component summary
- Participants who after 68 weeks achieved (yes/no):
    - Body weight reduction ≥20% from baseline
    - Responder definition value for SF-36 physical functioning score
- Change from baseline to week 8 in body weight (%)

Adverse Event End Points

- Number of treatment-emergent adverse events (TEAEs) from baseline to week 75
- Number of serious adverse events (SAEs) from baseline to week 75
- Change from baseline to week 68 in:
    - Pulse (bpm)
    - Amylase (U/L)
    - Lipase (U/L)
    - Calcitonin (ng/L)

Exploratory End Points

- Change from baseline to week 68 in:
    - Glycemic category (normo-glycemia, pre-diabetes, type 2 diabetes)
    - Antihypertensive medication (decrease, no change, increase)
    - Lipid-lowering medication (decrease, no change, increase)
    - Work Productivity and Activity Impairment Questionnaire - Specific Health Problem V2.0 (WPAI-SHP)
        - Work time missed due to weight (%)
        - Impairment while working due to weight (%)
        - Overall work impairment due to weight (%)
        - Activity impairment due to weight (%)
        - Total score (WRSSM)
- Participants who from randomization to week 68 discontinued randomized trial product (yes/no)
- Time to permanent discontinuation of randomized trial product (weeks)

eTable 1. Changes in Secondary End Points from Baseline to Week 68[a]

End Point[b]	Semaglutide 2.4 mg (N = 407)	Placebo (N = 204)	Difference (95% CI)	Odds ratio (95% CI)	*P* value
Co-primary end points[c]					
Body weight, % reduction	–17.6	–5.0	–12.7 (–14.3 to –11.0)		< .001
Body weight reduction ≥5% – proportion of participants at week 68, %	89.8	50.0		11.7 (7.6 to 17.8)	< .001
Confirmatory secondary end points					
Waist circumference, cm	–16.3	–6.2	–10.1 (–11.8 to –8.4)		< .001
Systolic blood pressure, mmHg	–6.21	–3.47	–2.74 (–5.12 to –0.36)		.02
SF-36 physical functioning score[d]	2.4	1.5	1.0 (–0.0 to 1.9)		.05
Body weight reduction ≥10% – proportion of participants at week 68, %	79.3	27.4		14.0 (9.3 to 21.1)	< .001
Body weight reduction ≥15% – proportion of participants at week 68, %	59.6	12.8		13.5 (8.3 to 22.0)	< .001
Supportive secondary end points[e]					
Body weight reduction ≥20% – proportion of participants at week 68, %	38.6	4.3		17.4 (8.3 to 36.4)	< .001
Body weight, kg	–18.4	–5.4	–13.0 (–14.9 to –11.2)		< .001
BMI, kg/m^2	–6.6	–1.9	–4.7 (–5.4 to –4.0)		< .001
Glycated hemoglobin, %-points	–0.56	–0.28	–0.27 (–0.32 to –0.23)		< .001
Fasting plasma glucose, mg/dL	–8.01	–0.60	–7.41 (–9.13 to –5.68)		< .001
Diastolic blood pressure, mmHg	–3.61	–1.86	–1.75 (–3.42 to –0.08)		.04
SF-36[d]					
Physical component summary score	3.0	2.0	1.0 (0.0 to 2.0)		.049
Mental component summary score	–1.0	–1.8	0.9 (–0.4 to 2.1)		.168
Fasting lipid profile, % change at week 68[f]					
Cholesterol					
Total	–4.5	2.1	–6.4 (–8.8 to –4.0)[f]		< .001
HDL	6.2	6.5	0.2 (–2.5 to 3.0)[f]		.860
LDL	–5.0	2.8	–7.6 (–11.1 to –3.9)[f]		< .001
vLDL	–24.7	–11.6	–14.8 (–20.3 to –9.0)[f]		< .001
Free fatty acids	–12.1	2.4	–14.2 (–23.2 to –4.1)[f]		.007
Triglycerides	–24.6	–11.4	–14.9 (–20.5 to –8.9)[f]		< .001

C-reactive protein, % change at week 68[f]	–63.4	–25.6	–50.8 (–58.0 to –42.4)[f]		< .001

Abbreviations: BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SF-36, Short Form36v2® Health Survey, Acute Version; vLDL, very low-density lipoprotein.
[a]Values are estimated mean change from baseline to week 68 and estimated treatment difference (unless stated otherwise), based on the trial product estimand for the on-treatment period for the full analysis set, which assesses the treatment effect in all randomized participants assuming they adhered to treatment and did not receive rescue intervention.
[b]Continuous end points were analyzed using a mixed model for repeated measurements (MMRM). Categorical end points were assessed using logistic regression with treatment as the only factor (for missing data, categorization was based on values predicted from an MMRM).
[c]Baseline body weight was 106.9 kg (SD 22.8) in the semaglutide group and 103.7 kg (SD 22.9) in the placebo group.
[d]SF-36 is a measure of health-related quality of life and general health status. The SF-36 uses a norm-based score. Norm-based scores above and below 50 are above and below the average, respectively, found in the 2009 US general population. Further information on the SF-36 is provided in eAppendix 7 in Supplement 1.
[e]Supportive secondary end point analyses were not adjusted for multiplicity.
[f]These parameters were initially analyzed on a log scale as estimated ratio to baseline (within treatment groups) and estimated treatment ratios (between treatment groups). For interpretation, these data are expressed as relative percent change and estimated relative percent difference between groups, respectively, and were calculated using the formula: (estimated ratio–1)*100.

eTable 2. Supportive Secondary Safety End Points

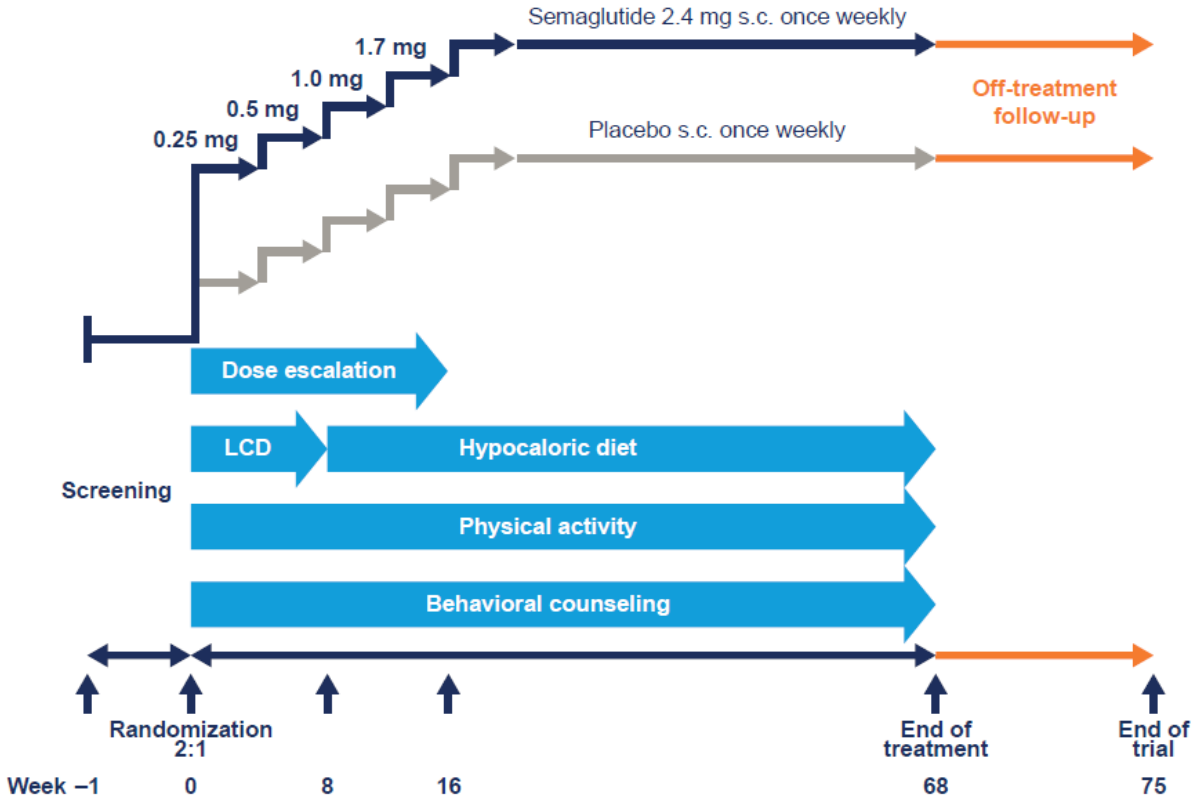
End Point	Semaglutide 2.4 mg		Placebo	
	N	Mean	N	Mean
Pulse, bpm				
Baseline	407	71 ± 10	204	71 ± 10
Week 68	334	74 ± 10	163	73 ± 10
Change from baseline to week 68[a]	407	3.1	204	2.1
Estimated treatment difference for semaglutide vs placebo (95% CI)[a]	1.0 (–0.7 to 2.6); *P* = .26			
Amylase, U/L				
Baseline	407	52 (38.5)	204	49 (34.9)
Week 68	332	59 (40.0)	161	52 (34.0)
% change at week 68[b]	332	11.5	161	7.3
Lipase, U/L				
Baseline	407	24 (55.5)	204	24 (55.8)
Week 68	332	31 (68.2)	161	22 (67.1)
% change at week 68[b]	332	30.9	161	–6.0
Calcitonin, ng/L				
Baseline	407	1.4 (79.0)	204	1.2 (61.8)
Week 68	332	1.3 (69.1)	162	1.2 (53.1)
% change at week 68[b]	332	–7.4	162	–5.6

Unless indicated otherwise, values are descriptive statistics presenting arithmetic mean ± standard deviation for the on-treatment period (during treatment with trial product, including any dose of trial medication administered within the previous 2 weeks).

[a]Pulse changes are for the trial product estimand (assesses treatment effect assuming all participants continued treatment without rescue intervention) analyzed using a mixed model for repeated measurements.

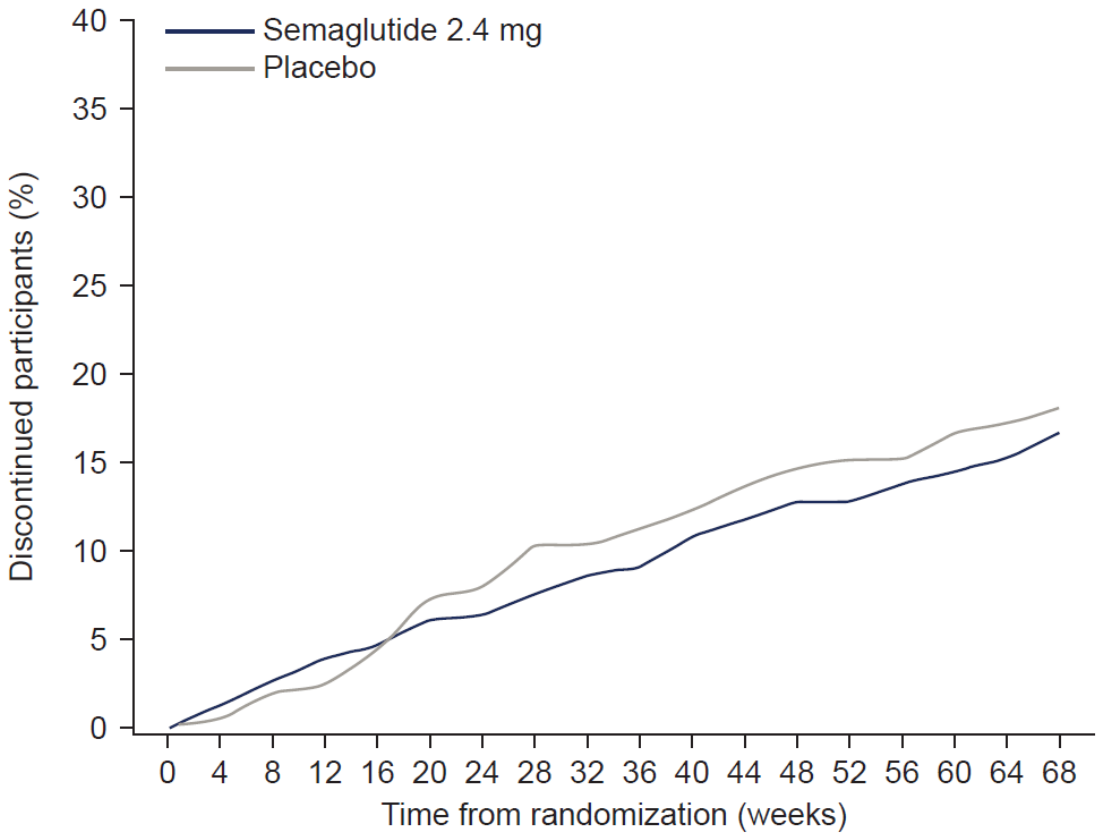
[b]Relative percent change was calculated based on the estimated ratio to baseline. The formula for calculation was: (estimated ratio –1)*100.

eFigure 1. Trial Design



Abbreviations: LCD, low-calorie diet; s.c., subcutaneous.

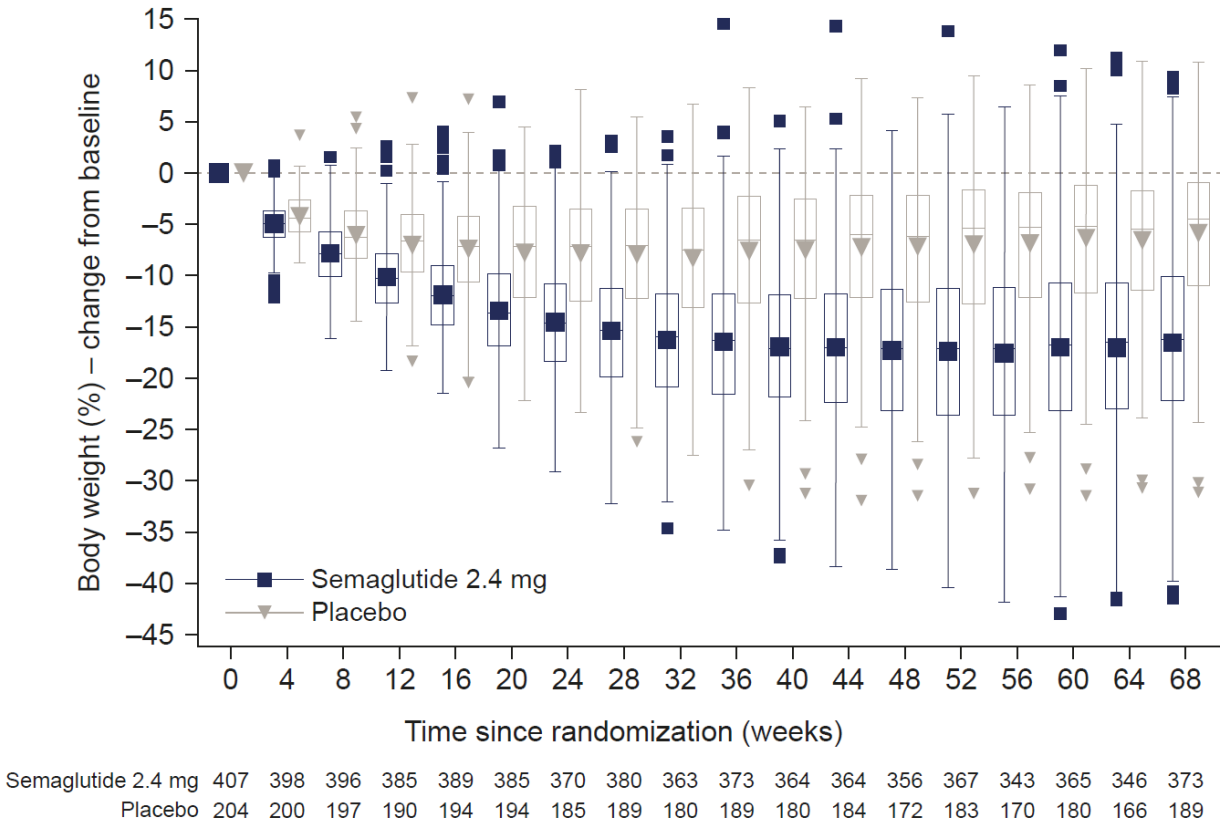
eFigure 2. Time to Permanent Discontinuation of Trial Product (Weeks)



Semaglutide 2.4 mg	407	402	396	391	388	382	381	376	372	370	363	359	355	355	351	348	345	339
Placebo	204	203	200	199	195	189	188	183	183	181	179	176	174	173	173	170	169	167

Numbers shown in the lower panel are participants who have not discontinued trial product permanently. Permanent discontinuation is when a participant stopped taking trial product, did not resume treatment, and is therefore not considered as 'on-treatment' at week 68. A timepoint is considered as 'on-treatment' if any dose of trial product has been administered within the prior 14 days. Permanent discontinuations after week 68 are not shown.

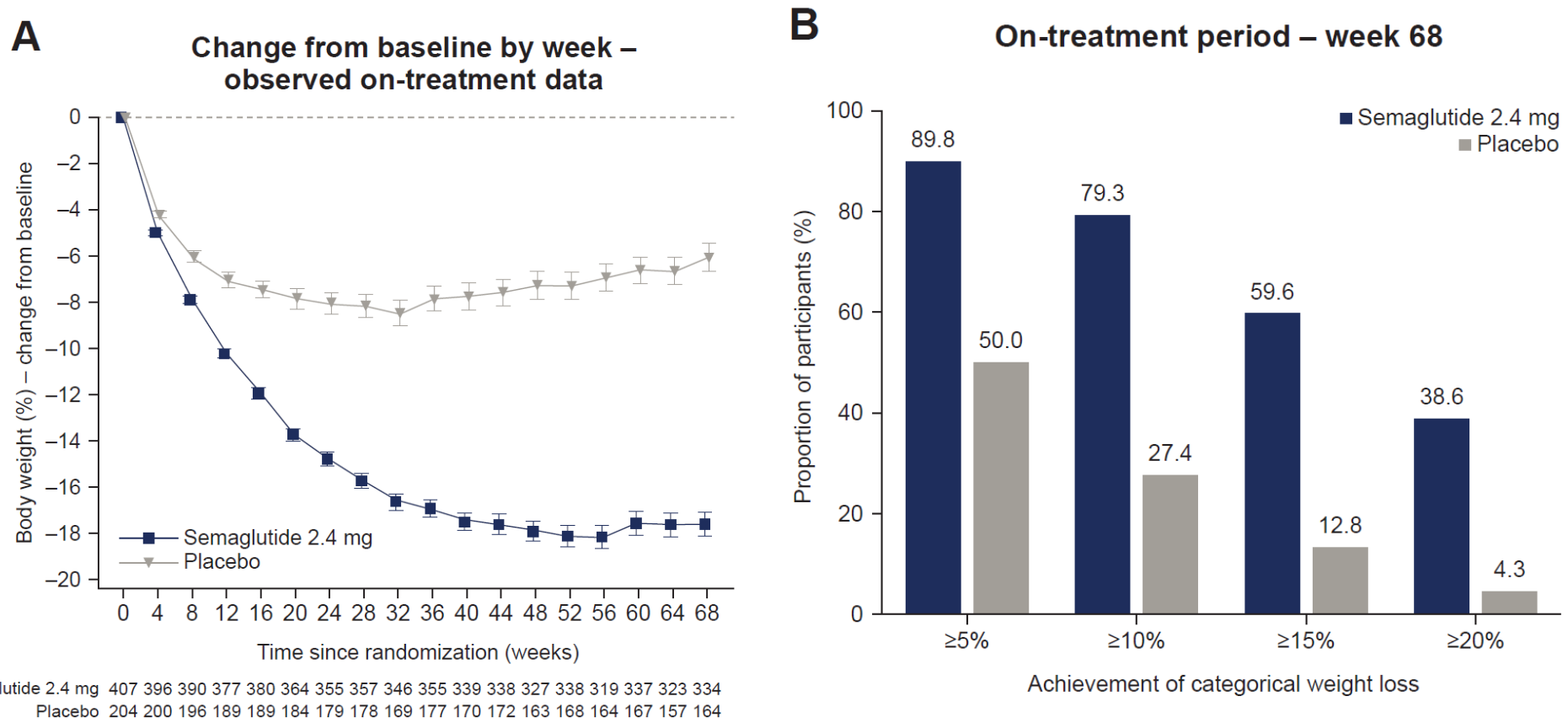
eFigure 3. Variability in Body Weight Change from Baseline by Week



Semaglutide 2.4 mg	407	398	396	385	389	385	370	380	363	373	364	364	356	367	343	365	346	373
Placebo	204	200	197	190	194	194	185	189	180	189	180	184	172	183	170	180	166	189

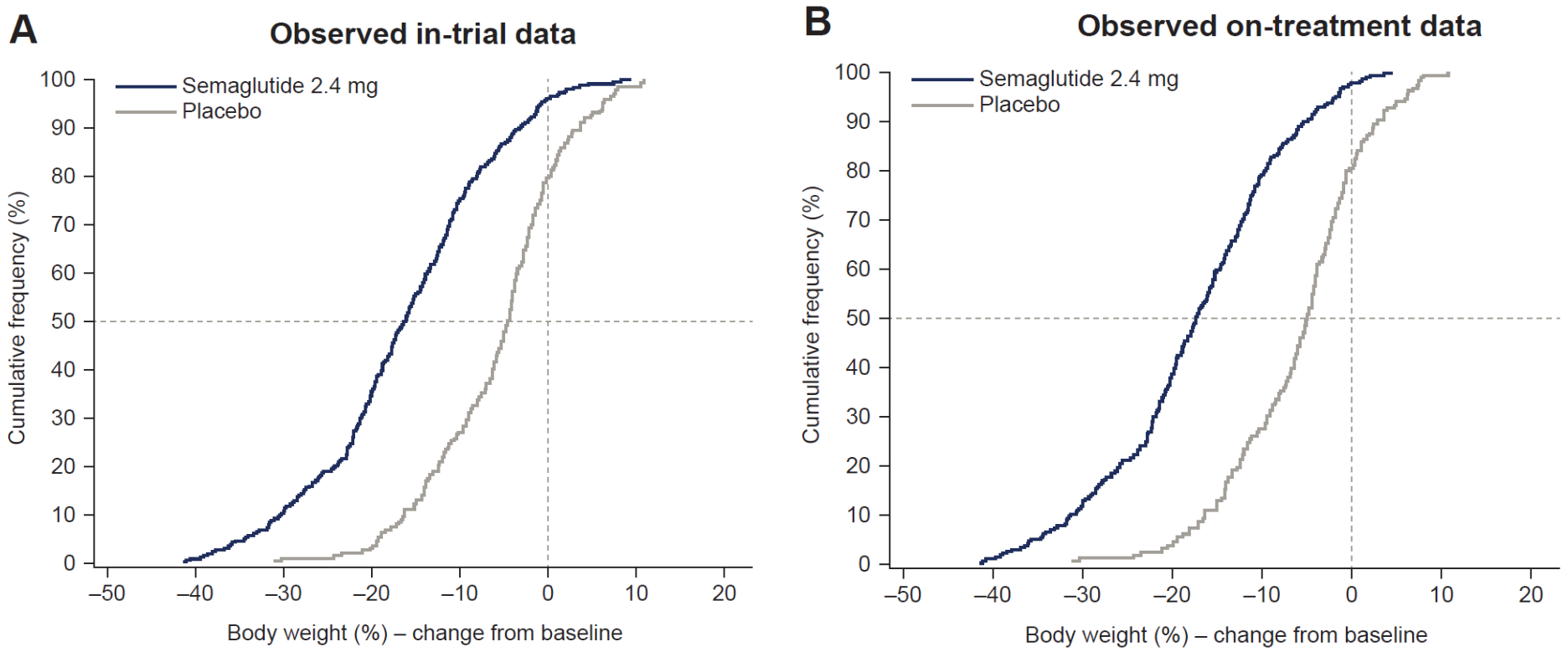
Data presented are observed data for the in-trial period. The middle lines represent median observed percentage change in body weight from baseline, symbols in the boxes represent mean observed percentage change, box tops and bottoms represent interquartile range, whiskers extend to the most extreme observed values with 1.5 times the interquartile range of the nearer quartile, and symbols beyond these points represent observed values outside that range. More negative values indicate greater weight loss.

eFigure 4. Body Weight-Related Efficacy End Points



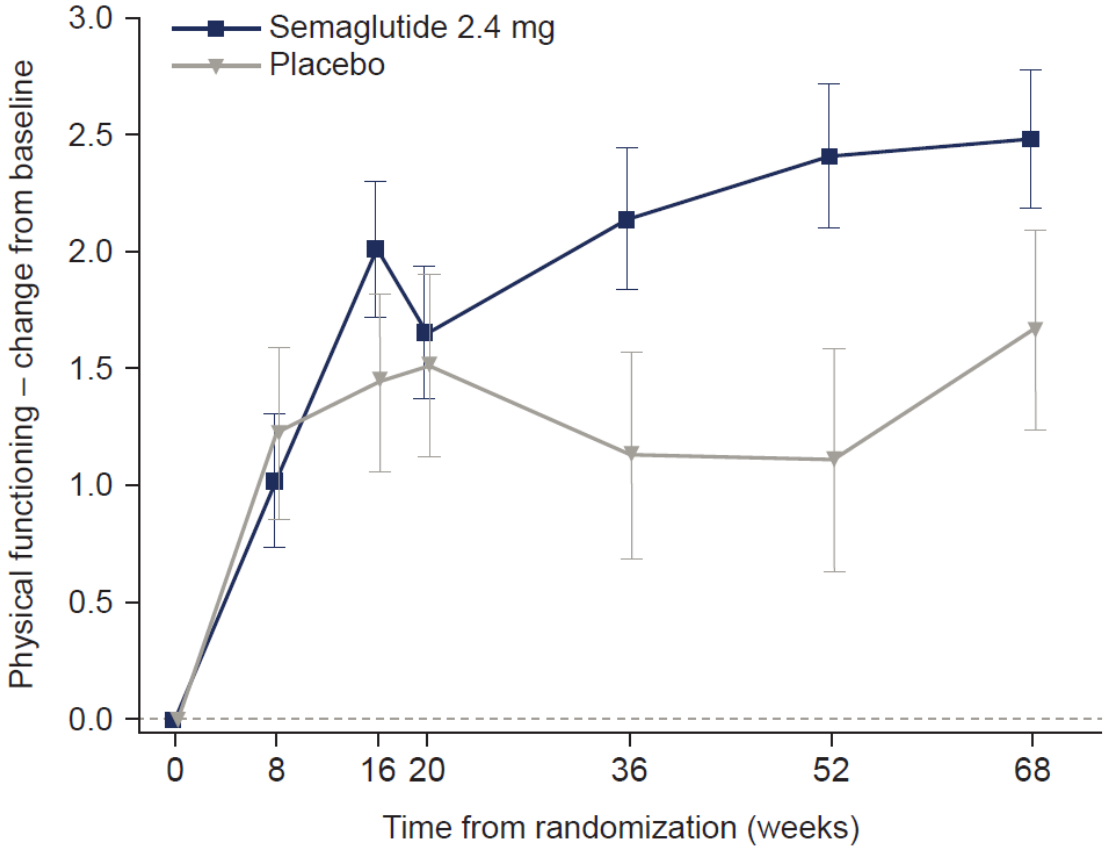
Panel A shows the observed mean percentage change in body weight over time for participants in the full analysis set for the on-treatment period. Panel B shows the observed proportions of participants attaining at least 5% (co-primary end point), 10%, 15%, and 20% reduction in body weight since baseline at week 68 in the full analysis set.
Error bars represent standard error of the mean.
N numbers represent the number of participants with available data contributing to the means at each visit.
On-treatment period: during treatment with trial product (any dose of trial medication administered within the previous 2 weeks).

eFigure 5. Cumulative Distribution Plots of Change from Baseline to Week 68 in Body Weight



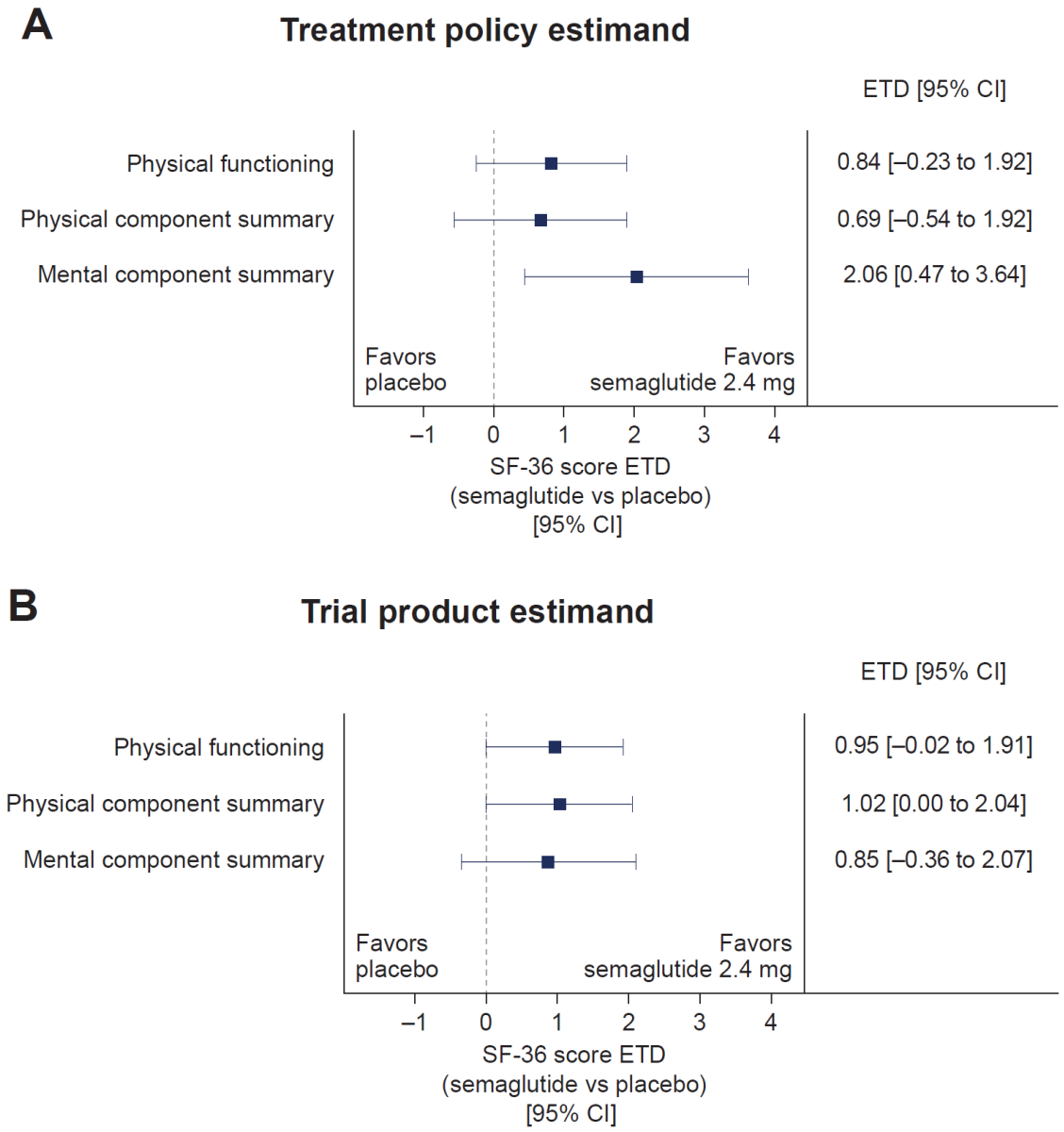
Cumulative distribution plot of observed percentage change from baseline over time in body weight for participants in the full analysis set during the in-trial observation period (Panel A) and on-treatment observation period (Panel B).
In-trial period: from randomization to last contact with trial site, irrespective of treatment discontinuation or rescue intervention.
On-treatment period: during treatment with trial product (any dose of trial medication administered within the previous 14 days).

eFigure 6. Change from Baseline by Week in SF-36 Physical Functioning Score (Treatment Policy Estimand)



Abbreviation: SF-36, Short Form36v2® Health Survey, Acute Version.
Data presented are the observed mean change from baseline in SF-36 physical functioning score over time for participants in the full analysis set during the in-trial observation period (from randomization to last contact with trial site, regardless of treatment discontinuation or rescue intervention). Error bars represent standard error of the mean. Numbers shown in the lower panel are participants contributing to the mean. The SF-36 uses a US 2009 norm-based score.

eFigure 7. SF-36 Change from Baseline to Week 68



Abbreviations: CI, confidence interval; ETD, estimated treatment difference; SF-36, Short Form36v2® Health Survey, Acute Version.
Data presented as estimated treatment differences for semaglutide vs placebo (boxes) and associated 95% CIs (whiskers) for participants in the full analysis set based on the treatment policy estimand (A) and the trial product estimand (B). The SF-36 uses a US 2009 norm-based score. Only SF-36 physical functioning scores were adjusted for multiplicity.
Treatment policy estimand: assesses treatment effect among all randomized participants, regardless of adherence to treatment or initiation of rescue interventions.
Trial product estimand: assesses treatment effect assuming all participants adhered to treatment and did not receive rescue interventions.

eFigure 8. Prevalence, Duration, and Severity of Selected Gastrointestinal Events

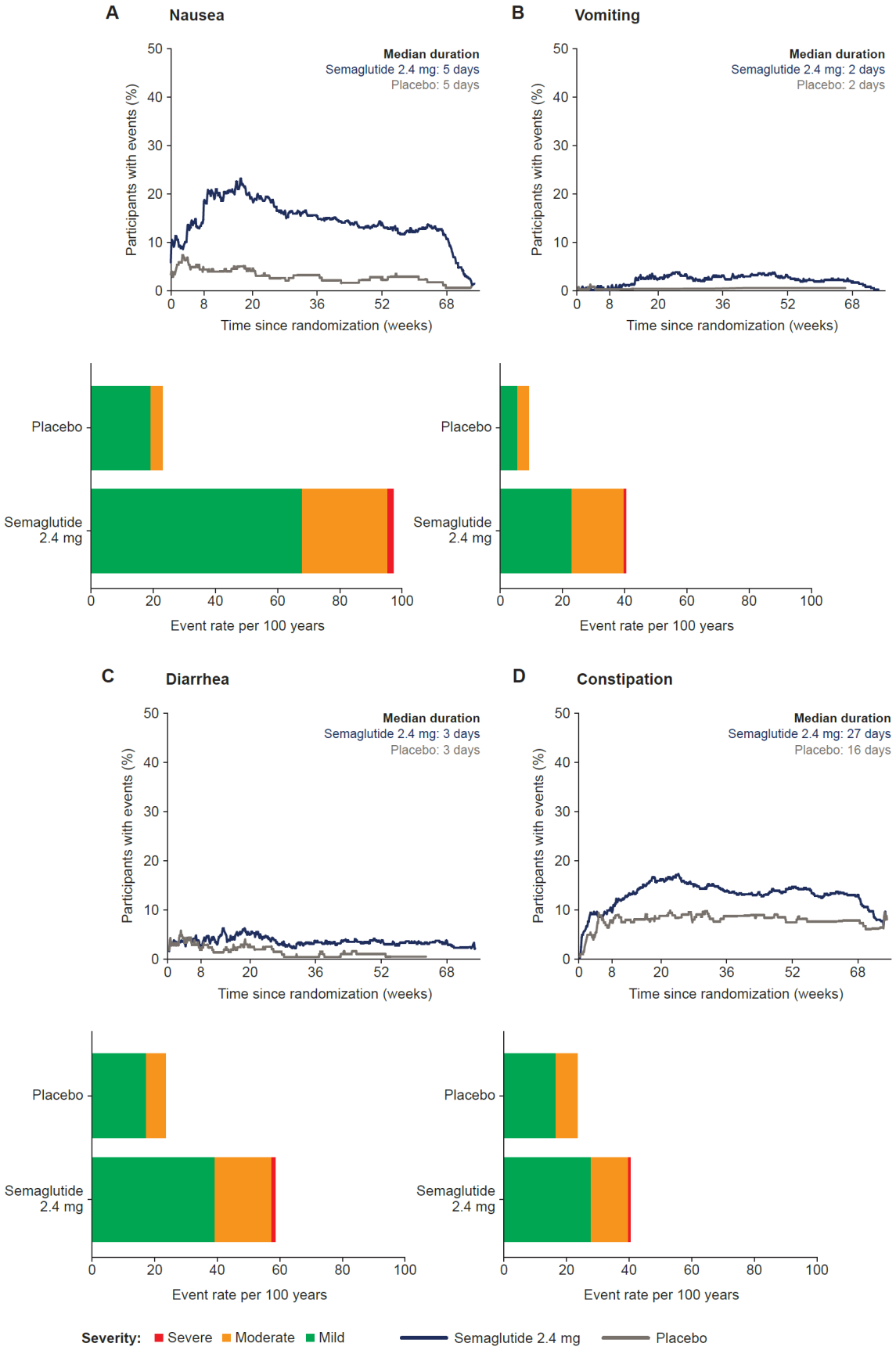


Figure presents the proportion of participants receiving semaglutide or placebo who reported nausea (A), vomiting (B), diarrhea (C), or constipation (D) events over the course of the treatment period, the median duration of the event, and the severity of such events. Data are on-treatment period data (defined as any dose of trial medication administered within the prior 49 days for safety analyses).

eReferences

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2. Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) project. *J Clin Epidemiol*. 1998;51(11):903-912.