Semaglutide 2.4mg : A New Era in Obesity Management

Tuesday, 23rd April 2024

Dr. Elamin Abdelgadir
Endocrinologist-Dubai Hospital- Dubai Academic Health Corporation

- Dr. Abdelgadir is a fellow of the American College of Endocrinology, the American college of physician, and the Royal college of physicians of Edinburgh.

- He is licensed Thyroid and neck sonographer from the American College of Endocrinology.

- He is a member of an active research group and he has published over 80 original articles and abstracts.

- Dr. Abdelgadir is a member of various regional and international conferences scientific committees. And he is the former secretary general of the Sudan Diabetes Association – Gulf Chapter.

Disclaimer

- This presentation is purely for educational purposes and for the purpose of scientific update only
- Please refer to your local approved label and indication in your respective country
- Some presented data are yet unpublished.

Disclosures

- I have been engaged with Novo Nordisk to chair this session
- I have no actual or potential conflict of interest in relation to this presentation

Introduction & Epidemiology of Obesity

Dr. Elamin Abdelgadir

Global prevalence of obesity

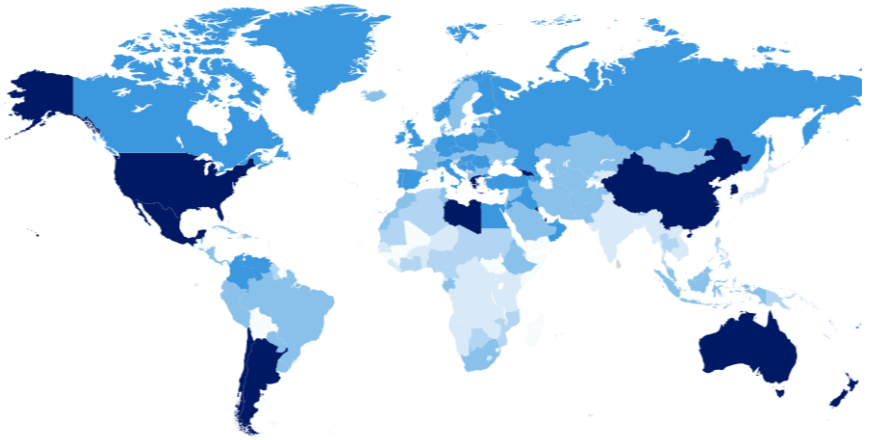
Among adults

764

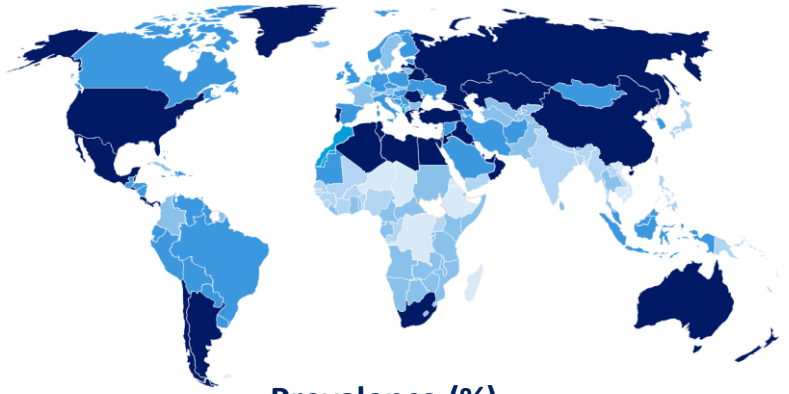
million people

live with obesity[1]

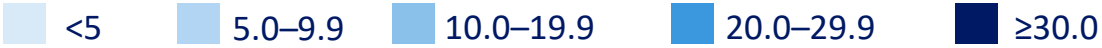
Men[2]



Women[3]



Prevalence (%)



1. World Obesity Federation: World Obesity Atlas, 2022. Available from: https://s3-eu-west-1.amazonaws.com/wof-files/World_Obesity_Atlas_2022.pdf. Accessed October 2022; 2. World Obesity Federation: Men living with obesity. Newest available data. Available from: https://data.worldobesity.org/maps/?area=trends&group=M&year=2020. Accessed October 2022; 3. World Obesity Federation: Women living with obesity. Newest available data. Available from: https://data.worldobesity.org/maps/?area=trends&group=F&year=2020. Accessed October 2022.

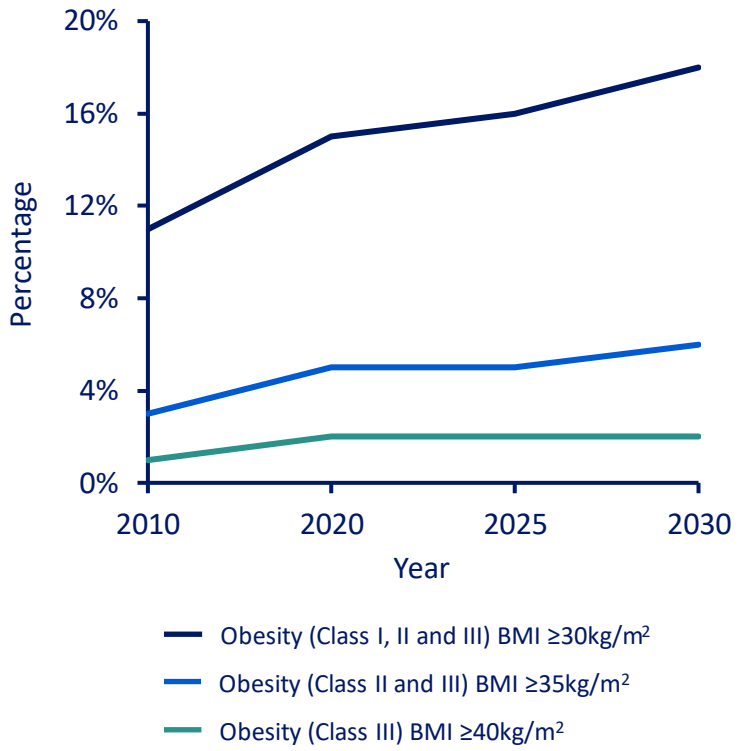
Predictions for global prevalence of obesity

1bn

people with **obesity** predicted by 2030

Prevalence over time[1]

Global obesity prevalence is predicted to steadily increase over the next decade



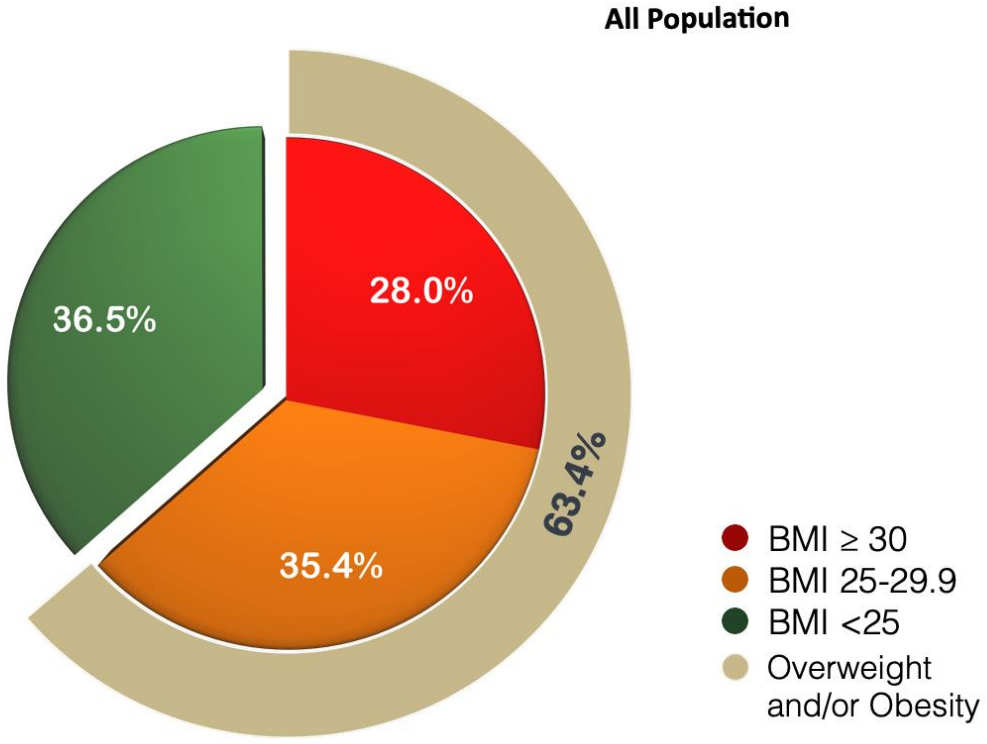
BMI, body mass index; bn, billion.

1. World Obesity Federation: World Obesity Atlas, 2022. Available from: https://s3-eu-west-1.amazonaws.com/wof-files/World_Obesity_Atlas_2022.pdf. Accessed October 2022.


NO
PHOTOGRAPHY

Overweigh & obesity (All population)

- Dubai obesity Study
- 440,590 individuals
- > 18 years old



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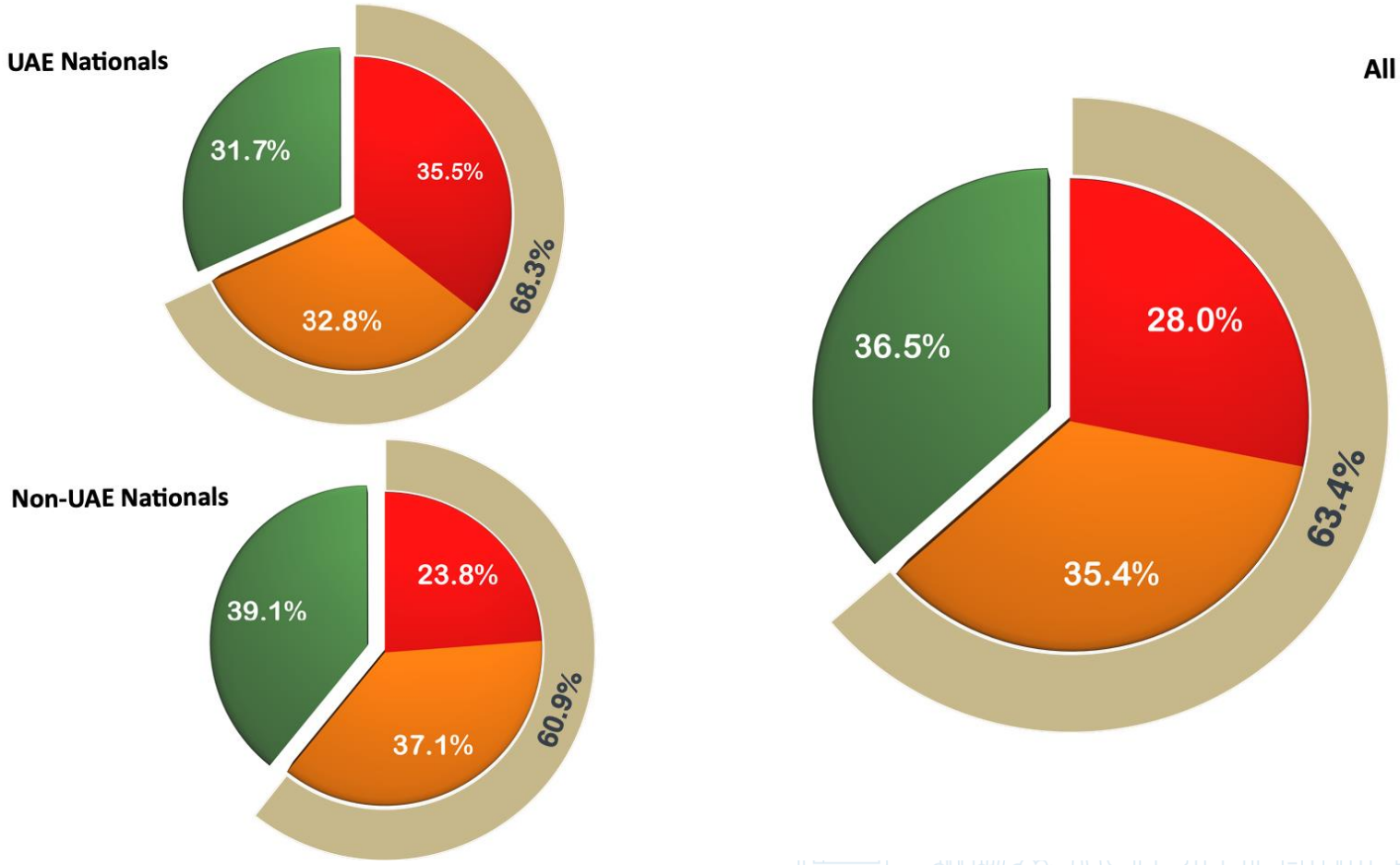
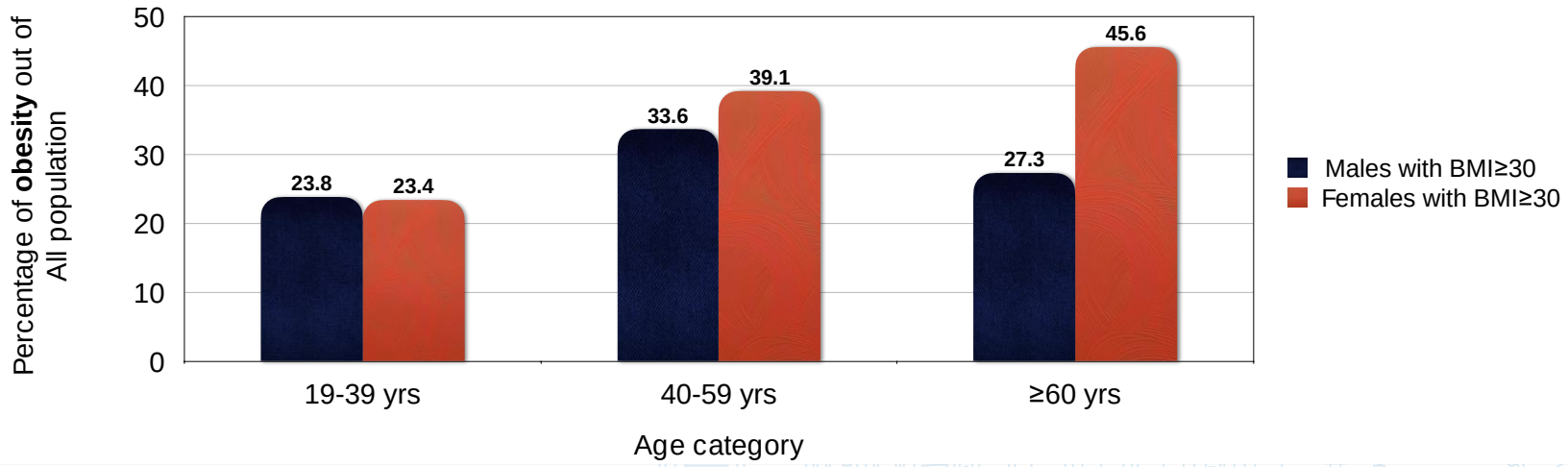


Overweight & Obesity as per gender at different age groups (All population)

- Dubai obesity Study
- 440,590 individuals
- > 18 years old



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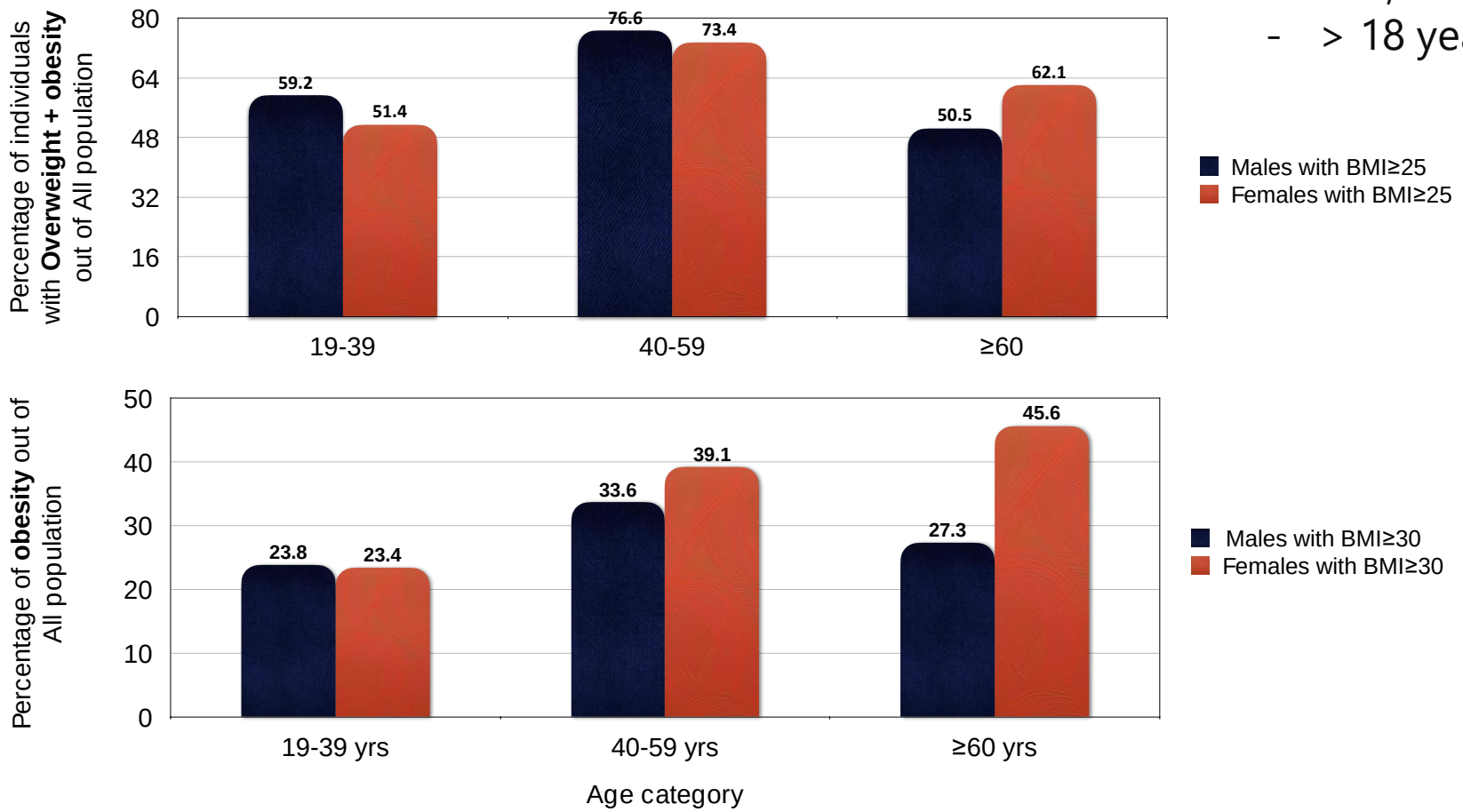
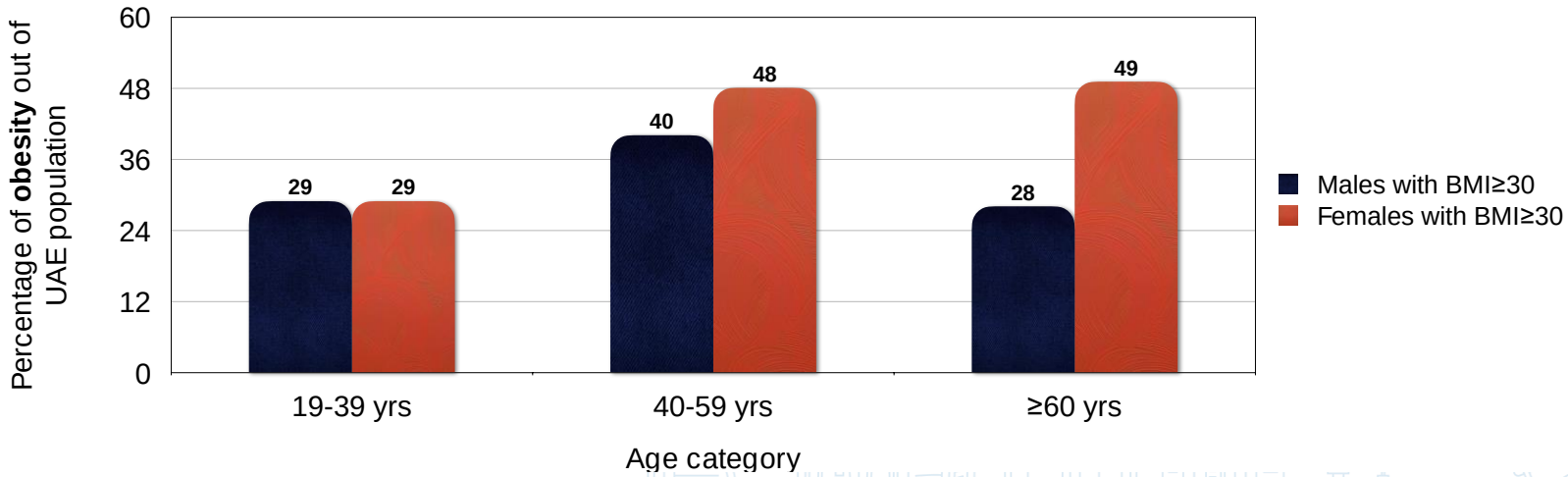


Overweight & Obesity as per gender at different age groups (UAE Nationals)

- Dubai obesity Study
- 440,590 individuals
- > 18 years old



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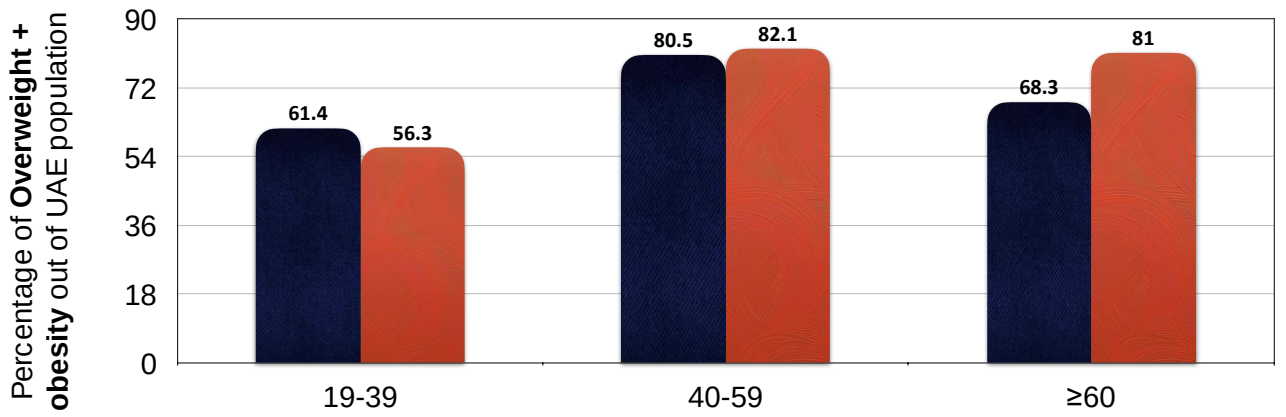
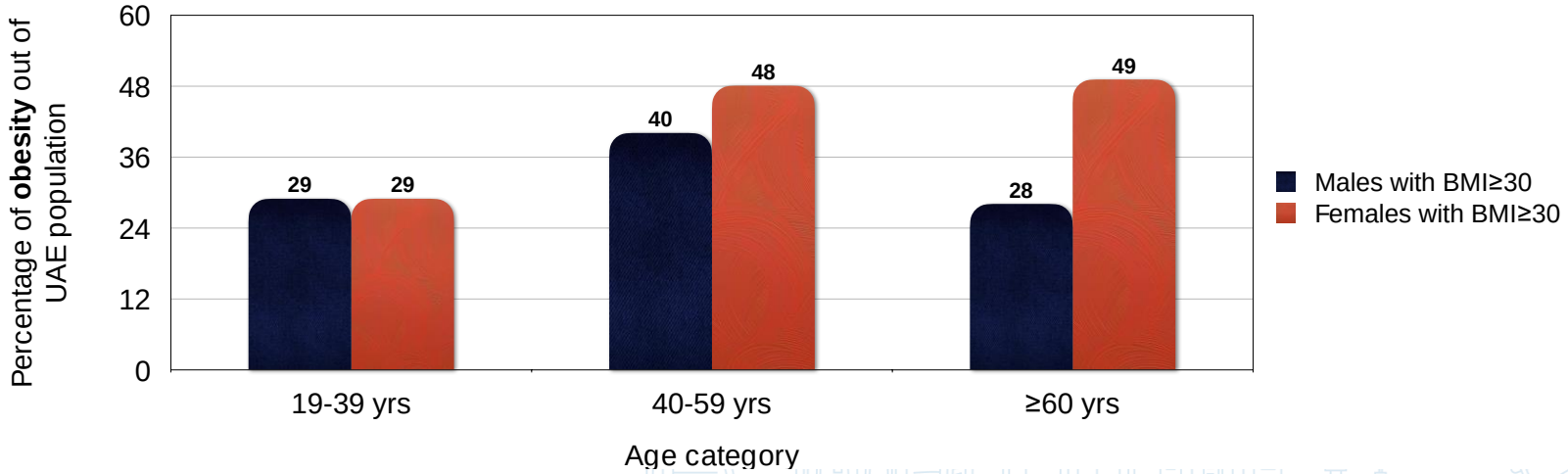
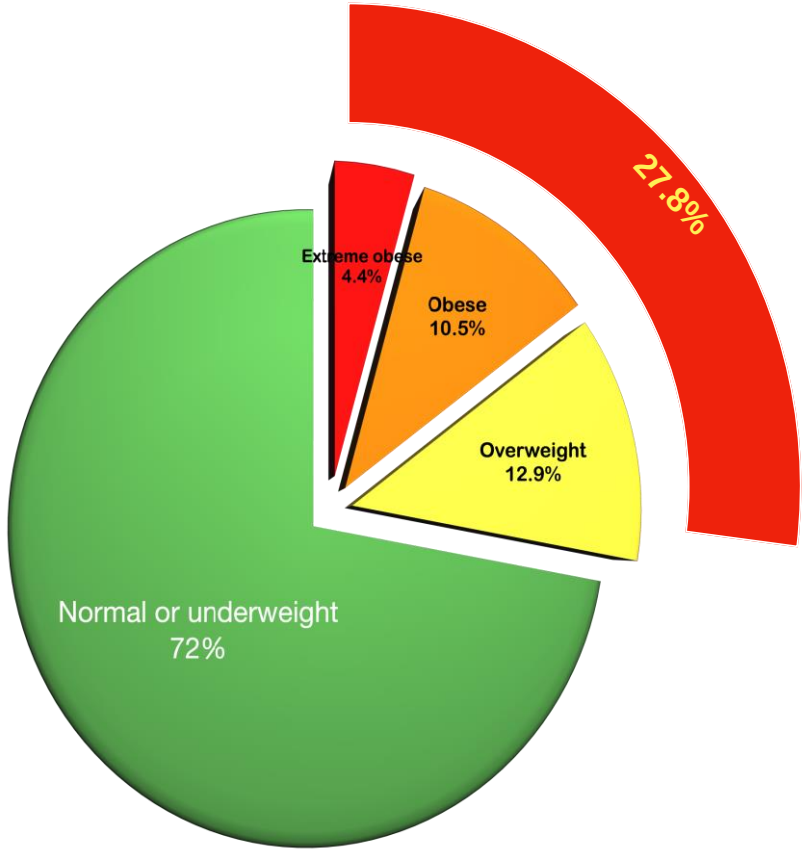




Dubai Obesity study .. Children & adolescents

Overweigh & obesity (Aage 3-18 years)

- Dubai obesity Study
- 162,300 individuals
- > 18 years old



Dubai Obesity study .. Children & adolescents

- Dubai obesity Study
- 162,300 individuals
- > 18 years old

		Underweight	Normal	Overweight	Obese	Extreme obese	Total
3 to 8 years	Count	9234	54684	14325	12209	1522	91974
	%	10.00%	59.50%	15.60%	13.30%	1.70%	100.00%
9 to 12 years	Count	6379	19809	3335	2312	949	32784
	%	19.50%	60.40%	10.20%	7.10%	2.90%	100.00%
13 to 18 years	Count	5936	20623	5686	4179	2389	38813
	%	15.30%	53.10%	14.60%	10.80%	6.20%	100.00%
Total	Count	21549	95116	23346	18700	4860	163571
	%	13.20%	58.10%	14.30%	11.40%	3.00%	100.00%

Obesity : Is it a disease?

Dr. Elamin Abdelgadir

Obesity is recognized as a Chronic relapsing disease and a health issue

"Obesity is a chronic, relapsing, progressive disease process ….need for immediate action for prevention and control of this global epidemic"

World Obesity Federation[1]

"Obesity is a progressive chronic disease, similar to diabetes or high blood pressure, …"

Obesity Canada[3]

"A progressive disease, impacting severely on individuals and society alike,… obesity is the gateway to many other disease areas…"

European Association for the Study of Obesity[4]

"Obesity and overweight as a chronic medical condition (de facto disease state) and urgent public health problem…"

American Medical Association[2]

"It (obesity) is not a lifestyle choice caused by individual greed but a disease caused by health inequalities, genetic influences and social factors.."

Royal College of Physicians UK[5]

"The Treat and Reduce Obesity Act would allow a variety of qualified practitioners, including registered dietitian nutritionists, to more effectively treat this disease, which impacts more than one-third of our nation."

Academy of nutrition and dietetics[6]

"Obesity is a chronic relapsing disease, which in turn acts as a gateway to a range of other non-communicable diseases, such as diabetes, cardiovascular diseases and cancer."[3]

European Commission[7]

"A pathological state (obesity disease) in which a person suffers health problems caused by or related to obesity thus making weight loss clinically desirable …"

Asia Oceania Association for the Study of Obesity[8]

1. Bray et al. Obes Rev 2017;18:715–23; 2. AMA resolutions. June 2012. Available at https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/hod/a12-resolutions_0.pdf. Accessed October 2022; 3. Obesity Canada. Available at https://obesitycanada.ca/guidelines/. Accessed October 2022; 4. EASO: 2015 Milan Declaration: A Call to Action on Obesity. Available at https://easo.org/2015-milan-declaration-a-call-to-action-on-obesity/. Accessed October 2022; 5. Royal College of Physicians. Anon. BMJ 2019;364:l45; 6. Raynor et al. J Acad Nutr Diet 2016;116:129–47; 7. European Commission. Obesity prevention. Available from https://knowledge4policy.ec.europa.eu/health-promotion-knowledge-gateway/obesity_en. Accessed October 2022; 8. AOASO position statement, Nagoya Declaration 2015.

Consequences of Obesity

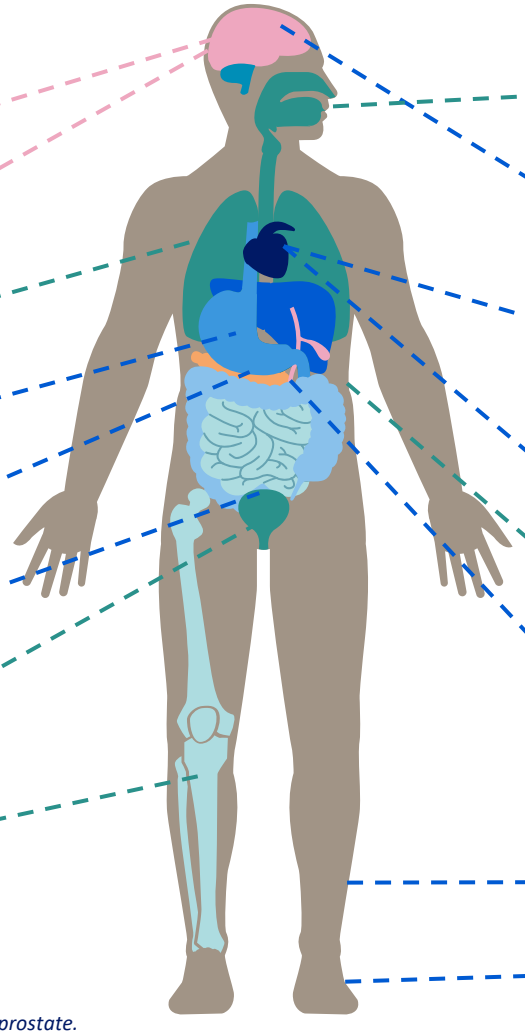
Novo Nordisk®

Metabolic

Mechanical

Mental

- GERD
- Cancers*
- Physical functioning
- Depression
- Anxiety
- Asthma
- NAFLD
- Gallstones
- Infertility
- Incontinence
- Knee osteoarthritis



- Sleep apnoea
- **Cardiovascular diseases**
  - Stroke
  - Dyslipidaemia
  - Hypertension
  - Coronary artery disease
  - Pulmonary embolism
  - HFpEF
- Coronary heart disease
- Chronic back pain
- T2D
  Prediabetes
- Thrombosis
- Gout

**Including postmenopausal breast, colorectal, endometrial, oesophageal, kidney, ovarian, pancreatic and prostate.*
CVD, cardiovascular disease; GERD, gastro-oesophageal reflux disease; HFpEF, heart failure with preserved ejection fraction; NAFLD, non-alcoholic fatty liver disease; T2D, type 2 diabetes.
Adapted from Sharma AM. Obes Rev 2010;11:808–9; Guh DP et al. BMC Public Health 2009;9:88; Luppino FS et al. Arch Gen Psychiatry 2010;67:220–9; Simon GE et al. Arch Gen Psychiatry 2006;63:824–30; Church TS et al. Gastroenterology 2006;130:2023–30; Li C et al. Prev Med 2010;51:18–23; Hosler AS. Prev Chronic Dis 2009;6:A48; Lammert F et al. Nat Rev Dis Primers 2016;2:16024; Powell-Wiley TM et al. Circulation 2021;143:e984–1010; Larsson SC et al. Metabolism 2022;137:155326.

Semaglutide 2.4mg (Wegovy®) : A New Era in Obesity Management

Dr. Rahila Bhatti

Dr. Rahila Bhatti

Endocrinologist- Genesis Healthcare

- Dr Rahila has over 15 years of experience in Endocrinology and Diabetes in Dubai, the UK and Pakistan.
- She undertook her specialty training in London UK and achieved dual CCT in General Internal Medicine/Diabetes & Endocrinology. She is currently a fellow of Royal College of Physicians, UK.
- Dr Rahila is SCOPE certified and has led a successful weight management program in a multidisciplinary setting to deal with the obesity epidemic in UAE. It was accredited as a 'clinical centre of excellence' by the European Association for study of obesity (EASO) in August 23.
- She is an adjunct clinical assistant professor for Diabetes and Endocrinology at University of Sharjah, UAE and teaches at postgraduate 'Masters of Science in Diabetes Management' there.
- She has presented her work at national and international conferences

Semaglutide 2.4mg (Wegovy®) : A New Era in Obesity Management

Dr. Rahila Bhatti

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Why people living with obesity need pharmacotherapy

- Obesity is a progressive disease, centred in the brain and influenced by the complex interaction between inherited genes and the environment[1,2,3]

- Obesity is a global pandemic associated with decrease in life expectancy and severe complications[4,5]

- Complications arising from obesity can be improved by weight loss[4,6,7]

- Weight loss achieved with diet, physical activity and behavioural modifications is limited and difficult to maintain

- Maintenance of weight loss is challenging due to metabolic adaptation: a physiological process characterised by changes in the levels of appetite regulating hormones and a decrease in energy expenditure[9,10]

Pharmacotherapies that combine weight loss efficacy, long-term safety, weight loss maintenance, and reduce complications are needed

1. Bray GA et al. Obes Rev 2017;18:715–23; 2. Badman MK et al. Science 2005;307:1909–14; 3. Herrera BM and Lindgren CM. Curr Diab Rep 2010;10:498–505; 4. Rose F et al. Expert Opin Drug Discov 2019;14(11):1151–9; 5. Prospective Studies Collaboration. Lancet 2009;373:1083–96; 6. Magkos F et al. Cell Metab 2016;23:591–601; 7. Cefalu WT et al. Diabetes Care 2015;38:1567–828. Saunders KH et al. Med Clin North Am 2018;102:135–48; 9. Nordmo M et al. Obes Rev 2019. doi: 10.1111/obr.12949; 10. Fothergill E et al. Obesity (Silver Spring). 2016;24:1612–19.

1 Ask permission

"Would it be all right if we discussed your weight?"

Asking permission
- Shows compassion and empathy
- Builds patient–provider trust

2 Assess their story

- Goals that matter to the patient
- Obesity classification (BMI and waist circumference)
- Disease severity (Edmonton Obesity Staging System)

Patient at the clinic

3 Advise on management

Medical nutrition therapy
- Personalized counselling by a registered dietitian with a focus on healthy food choices
- and evidence-based nutrition therapy

Exercise
- 30-60 min of moderate to vigorous activity most days

Psychological
- Cognitive approach to behaviour change
- Manage sleep, time and stress
- Psychotherapy if appropriate

Medications
- For weight loss and to help maintain weight loss

Bariatric surgery
- Surgeon–patient discussion

4 Agree on goals

Collaborate on a personalized, sustainable action plan

5 Assist with drivers and barriers

Pharmacotherapy for Obesity in Adults

Medications Approved in Canada

Agent	Populations Showing Weight Loss Benefit in Clinical Trials*	Average Weight Loss at 1 year	Benefits in adiposity related health parameters	Cost	Provincial Coverage for Obesity Pharmacotherapy
Liraglutide 3mg SC daily	Overweight and Obesity PreDM T2DM NASH OSA	-8.6% vs -2.6% placebo	remission of preDM A1C NASH parameters apnea-hypopnea index BP QoL	$$$$	None
Naltrexone-Bupropion 16/180mg PO bid	Overweight and Obesity T2DM	-6.1% vs -1.3% placebo	A1C Depression scores Cravings QoL	$$$	None
Orlistat 120mg PO tid	Overweight and Obesity preDM T2DM	-10.2% vs -6.1% placebo	Remission of PreDM A1C	$$	None
Semaglutide 2.4mg SC weekly	Overweight and Obesity PreDM T2DM NASH	-14.9% vs -2.4% placebo	A1C NASH parameters BP Cravings QoL	TBD	None

* Clinical trials conducted in populations with overweight and obesity, and trials conducted in populations with overweight/obesity and specific comorbidities (preDM, T2DM, NASH, OSA)

Abbreviations: preDM = prediabetes; T2DM = type 2 diabetes mellitus; NASH = nonalcoholic steatohepatitis; OSA = obstructive sleep apnea; A1C = hemoglobin A1c; BP = blood pressure; QoL = quality of life

GLP-1RAs and semaglutide have CV and metabolic effects

Effects of GLP-1 and GLP-1 receptor agonists

Appetite[1]

- ↑ Satiety
- ↑ Fullness
- ↓ Hunger
- ↓ Prospective food consumption
- ↓ Energy intake

Cardiovascular[3–6]

- ↓ SBP
- ↓ Lipids
- ↓ Inflammation
- ↓ Atherosclerosis
- ↓ MACE

Glucose regulation[2]

(glucose-dependent)

- ↑ Insulin secretion
- ↓ Glucagon secretion

Gastric effects[7–9]

- ↓ Gastric acid
- ↓ Gastric emptying

Semaglutide: a GLP-1 receptor agonist

Has 94% homology to human GLP-1[10] and t½ of approximately 1 week[11]

Reduces body weight, and improves glucose metabolism and lipid profile[3,5]

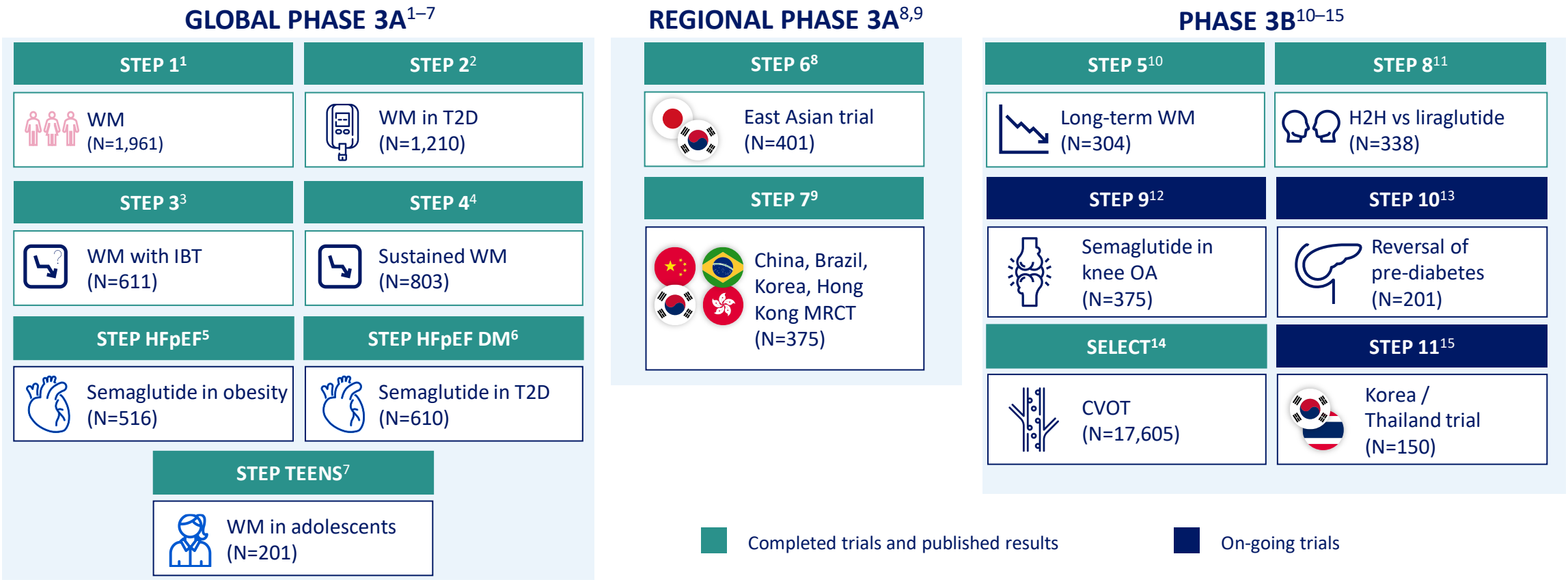
Has anti-inflammatory and anti-atherosclerotic effects (mouse models)[12]

Associated with CV benefits in T2D[3,5]

CV, cardiovascular; GLP-1, glucagon-like peptide-1; GLP-1RA, glucagon-like peptide-1 receptor agonist; MACE, major cardiovascular event; SBP, systolic blood pressure; t½, half-life; T2D, type 2 diabetes.

1. Flint A et al. J Clin Invest 1998;101:515–20; 2. Nauck MA et al. Diabetologia 1993;36:741–4; 3. Marso SP et al. N Engl J Med 2016;375:1834–44; 4. Marso SP et al. N Engl J Med 2016;375:311–22; 5. Husain M, et al. N Engl J Med 2019; 381:841–51; 6. Newsome PN et al. Aliment Pharmacol Ther 2019;50(2):193–203; 7. Hjerpsted JB et al. Diabetes Obes Metab 2018;20:610–9 8. O'Halloran DJ et al. J Endocrinol 1990;126:169–73; 9. Nauck MA et al. Am J Physiol 1997;273:E981–8; 10. Lau J et al. J Med Chem 2015;58:7370–80; 11. Granhall C et al. Clin Pharmacokinet 2019;58:781–91; 12. Rakipovski G et al. JACC Basic Transl Sci 2018; 3:844–57; 13. Husain M, et al. N Engl J Med 2019; 381:841–51.

The STEP programme investigated semaglutide for weight management in people with overweight or obesity



See slide notes for references. STEP 7: China, Brazil, Korea, Hong Kong (left to right) multi-regional clinical trial; Novo Nordisk. Data on file.
CVOT, cardiovascular outcomes trial; DM, diabetes mellitus; H2H, head-to-head; HFpEF, heart failure with preserved ejection fraction; IBT, intensive behavioural therapy; MRCT, multi-regional clinical trial (including China and ≥1 additional East Asian country); OA, osteoarthritis; T2D, type 2 diabetes; WM, weight management.

STEP 1–4: key baseline characteristics

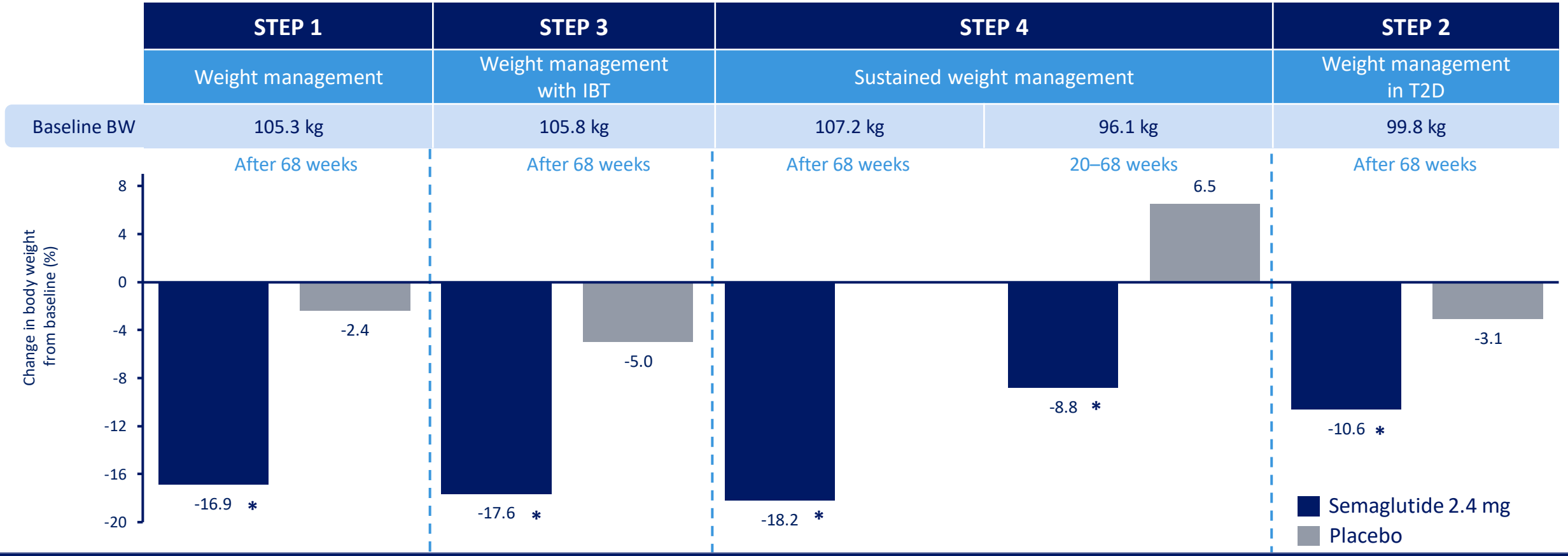
	STEP 1 WM (N=1,961)	**STEP 2** WM in T2D (N=1,210)	**STEP 3** WM with IBT (N=611)	**STEP 4** Sustained WM (N=902)
Sex, female, n (%)	1,453 (74.1)	616 (50.9)	495 (81.0)	717 (79.5)
Age, years	46.5 (12.7)	55.3 (10.6)	46.2 (12.7)	46.4 (11.9)
BMI, kg/m^2	37.9 (6.7)	35.7 (6.3)	38.0 (6.7)	38.3 (7.0)
Waist circumference, cm	114.7 (14.7)	114.6 (14.1)	113.0 (15.5)	115.1 (15.6)
HbA_{1c}, %	5.7 (0.32)	8.1 (0.8)	5.7 (0.3)	5.7 (0.3)
Diabetes duration, years	N/A	8.6 (6.2)	N/A	N/A
Systolic blood pressure, mmHg	126.5 (14.3)	130.0 (13.5)	124.4 (14.8)	126.4 (14.3)
FPG, mmol/L	5.3 (0.6)	8.6 (2.2)	5.2 (0.5)	5.4 (0.6)

Data are mean (±SD) unless otherwise stated. FPG, fasting plasma glucose; HbA_{1c}, glycated haemoglobin; IBT, intensive behavioural therapy; WM, weight management.

Kushner RF et al. Obesity 2020;28:1050–61.

Weight loss across STEP 1-4

Effects of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity



Trial product estimand: Evaluates the treatment effect under the assumption that the trial product is taken as intended

**Statistically significant vs placebo. BW, body weight; IBT, intensive behavioural therapy.*

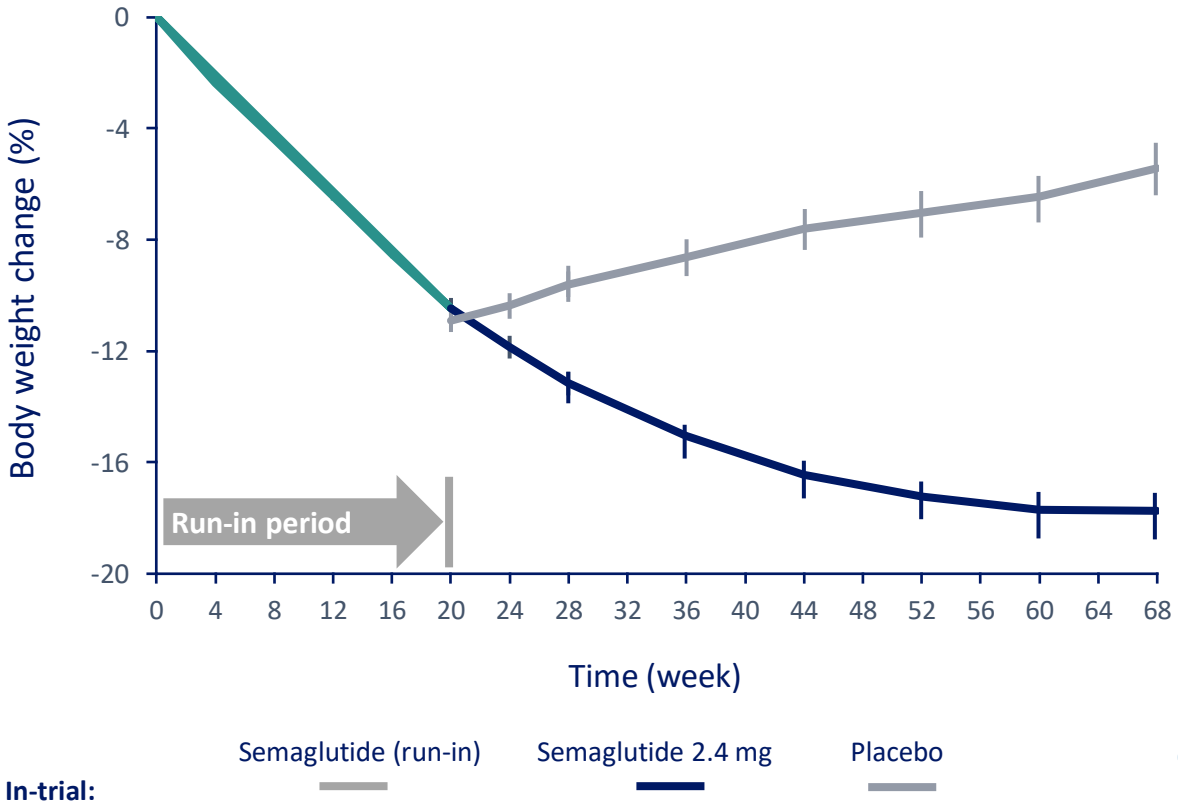
Wilding JPH et al. NEJM 2021; doi: 10.1056/NEJMoa2032183. Online ahead of print; Davies M et al. Lancet 2021; doi: 10.1016/S0140-6736(21)00213-0. Online ahead of print; Wadden TA et al. JAMA 2021; doi: 10.1001/jama.2021.1831. Online ahead of print; Rubino DM et al. Presented at the Endocrine Society (ENDO) virtual meeting, March 20-23, 2021.

Body weight change (week 0–68)

STEP 4

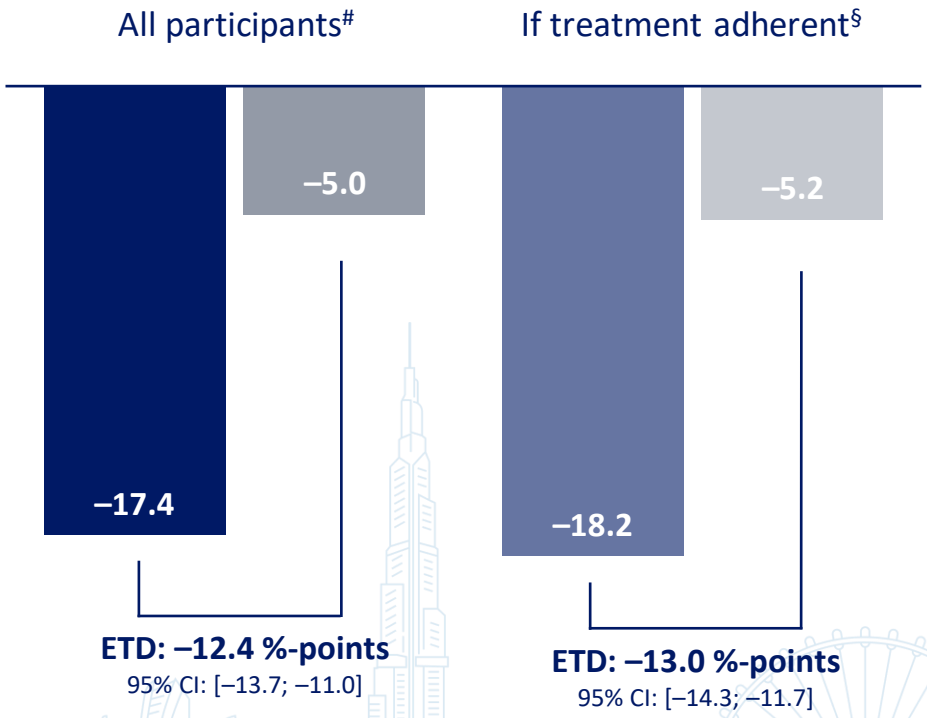
Observed body weight change over time

(Mean at week 0: 107.2 kg)



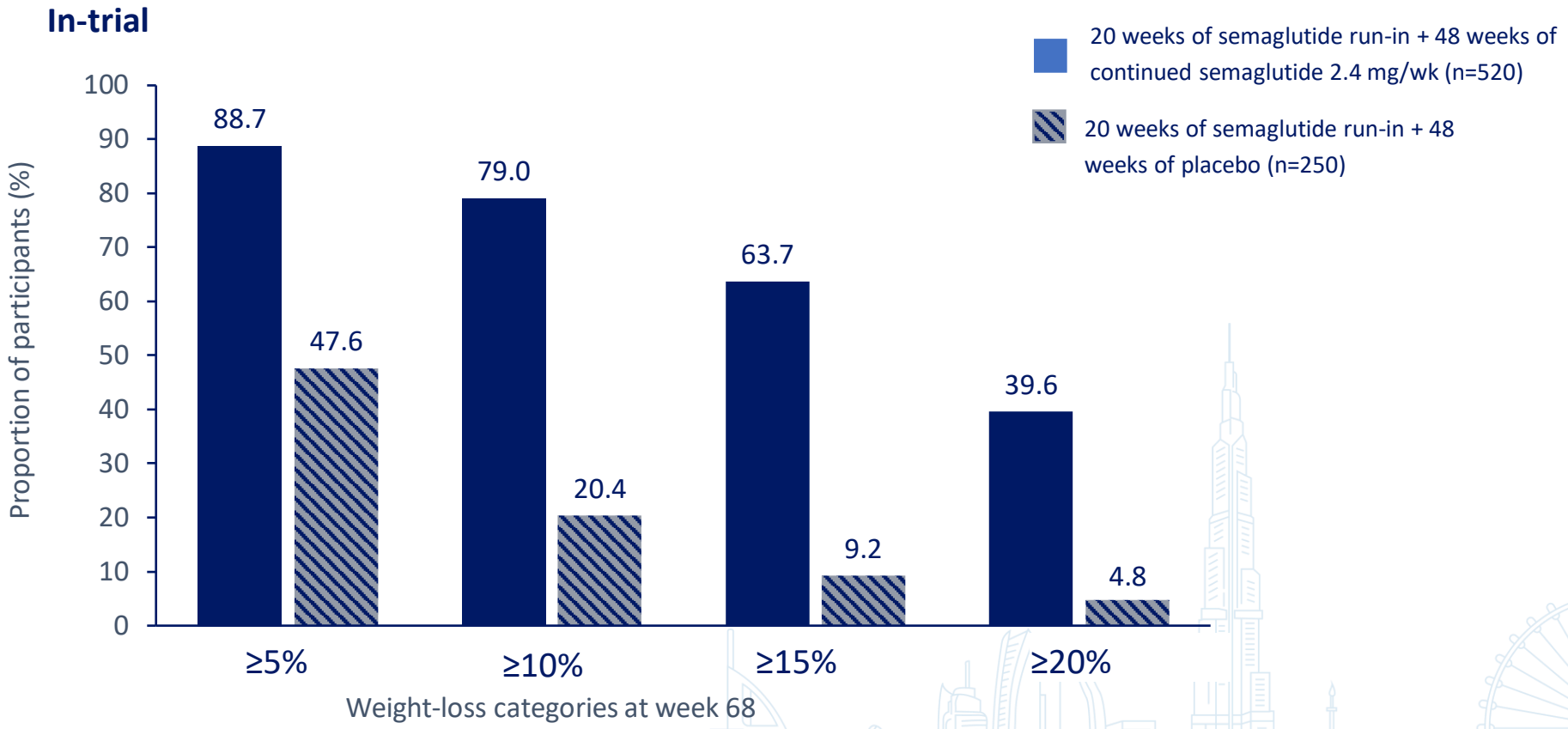
#Treatment policy estimand (regardless of treatment adherence). §Trial product estimand.
Error bars are +/- standard error of the mean.
CI, confidence interval; ETD, estimated treatment difference; IT, in-trial; OT, on-treatment.
Rubino et al. JAMA. 2021;325:1414-25.

Estimated change from week 0 to week 68



Categorical body weight loss (week 0–68)

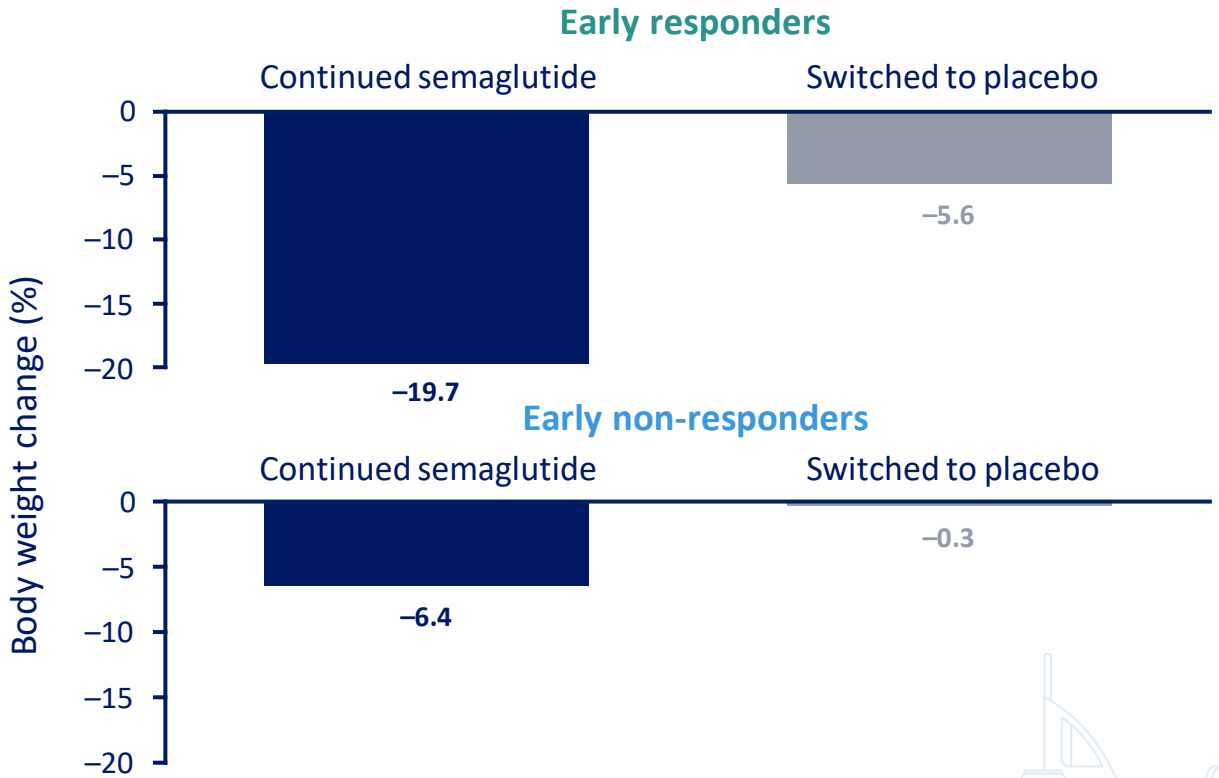
STEP 4



Rubino et al. JAMA. 2021;325:1414-25.

STEP 4: Mean weight loss from week 0 to 68 by week 20 responder status (≥ or <5% weight loss)

Mean weight loss at week 68 with continued semaglutide vs switched to placebo



- **Early response** was associated with **greater mean weight loss** by week 68 with continued semaglutide vs early non-response
- **Early non-responders** still achieved **clinically-relevant weight loss** by week 68 with continued semaglutide, compared with the switch to placebo

Analysed in all participants using a mixed model for repeated measurements analysis with treatment, responder status and the interaction of these as factors, and baseline body weight as a covariate, all nested within visit. The analysis assumed all participants were treatment adherent (the trial product estimand).

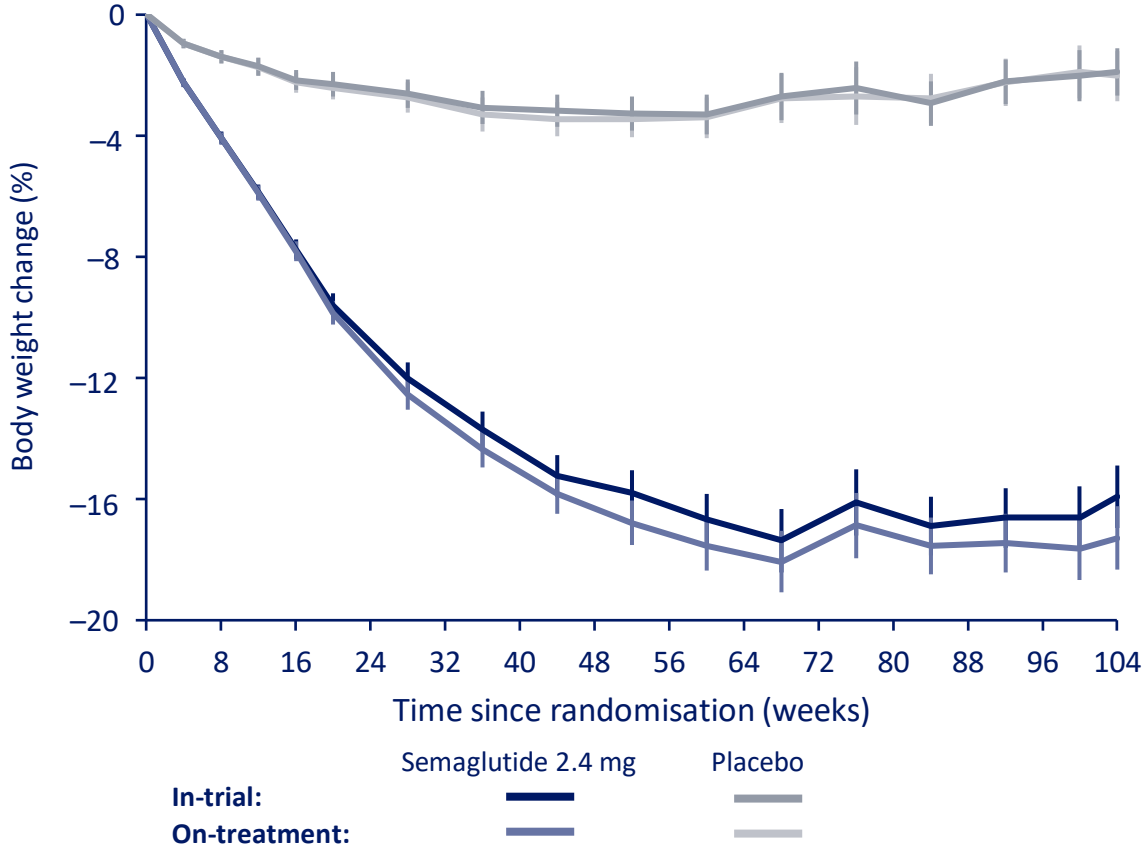
Mosenzon O et al. Presented at the Endocrine Society (ENDO) virtual meeting, March 20–23, 2021.

Body weight change

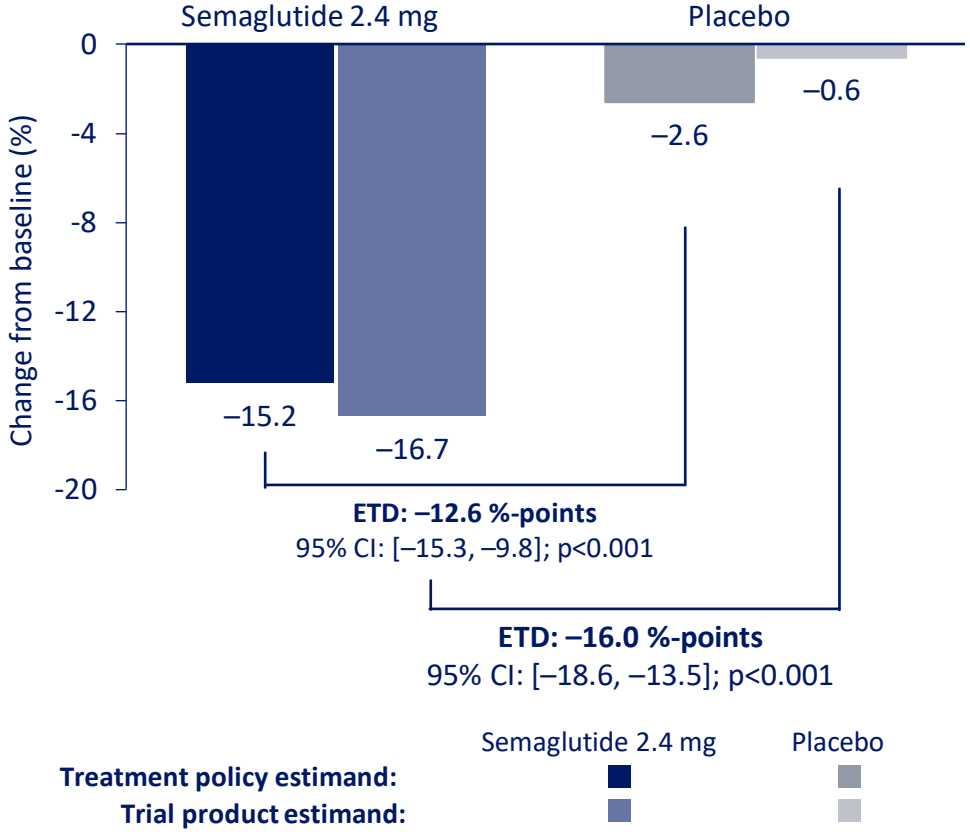
STEP 5

Observed mean change over time

(Mean at baseline: 106.0 kg)



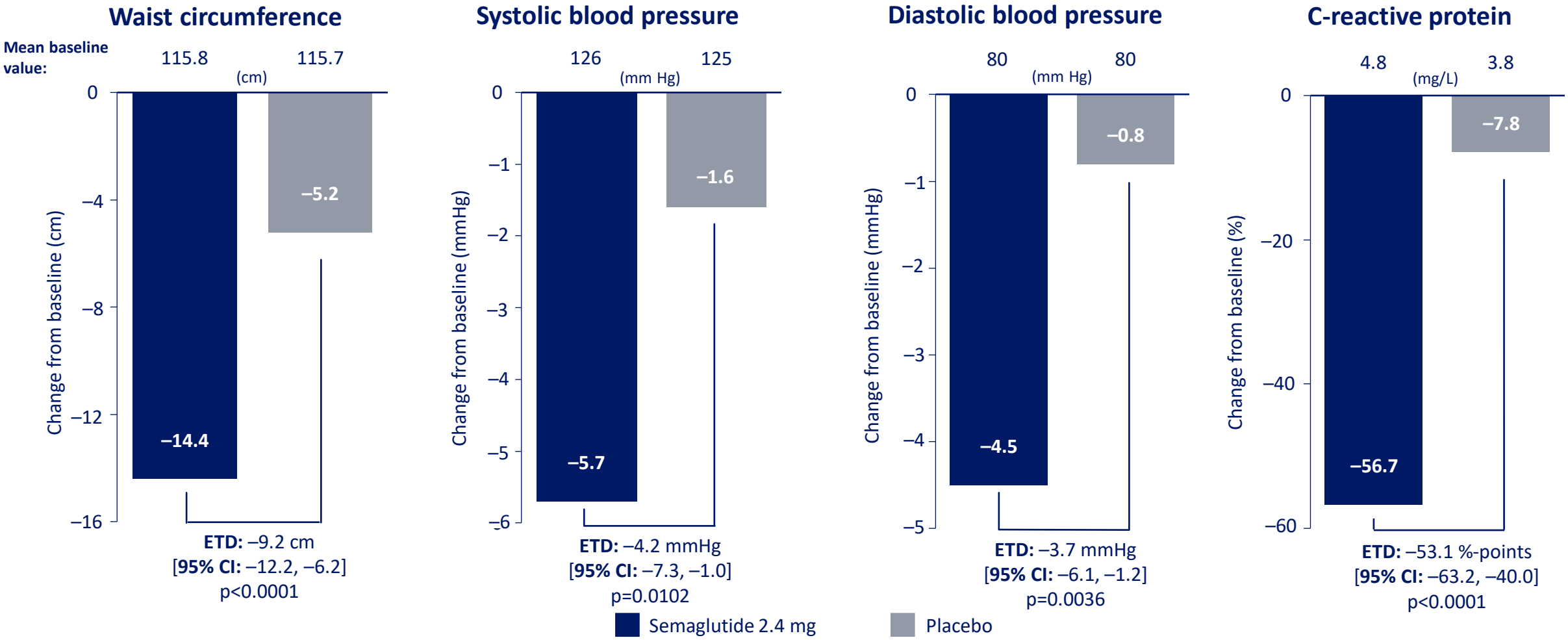
Estimated mean change from baseline to week 104



Treatment policy estimand assesses treatment effect regardless of treatment discontinuation or rescue intervention); Trial product estimand assesses treatment effect if trial product was taken as intended.
CI, confidence interval; ETD, estimated treatment difference.
Garvey et al. Nature Medicine 2022; 28(10): 2083-2091

Cardiovascular risk factors

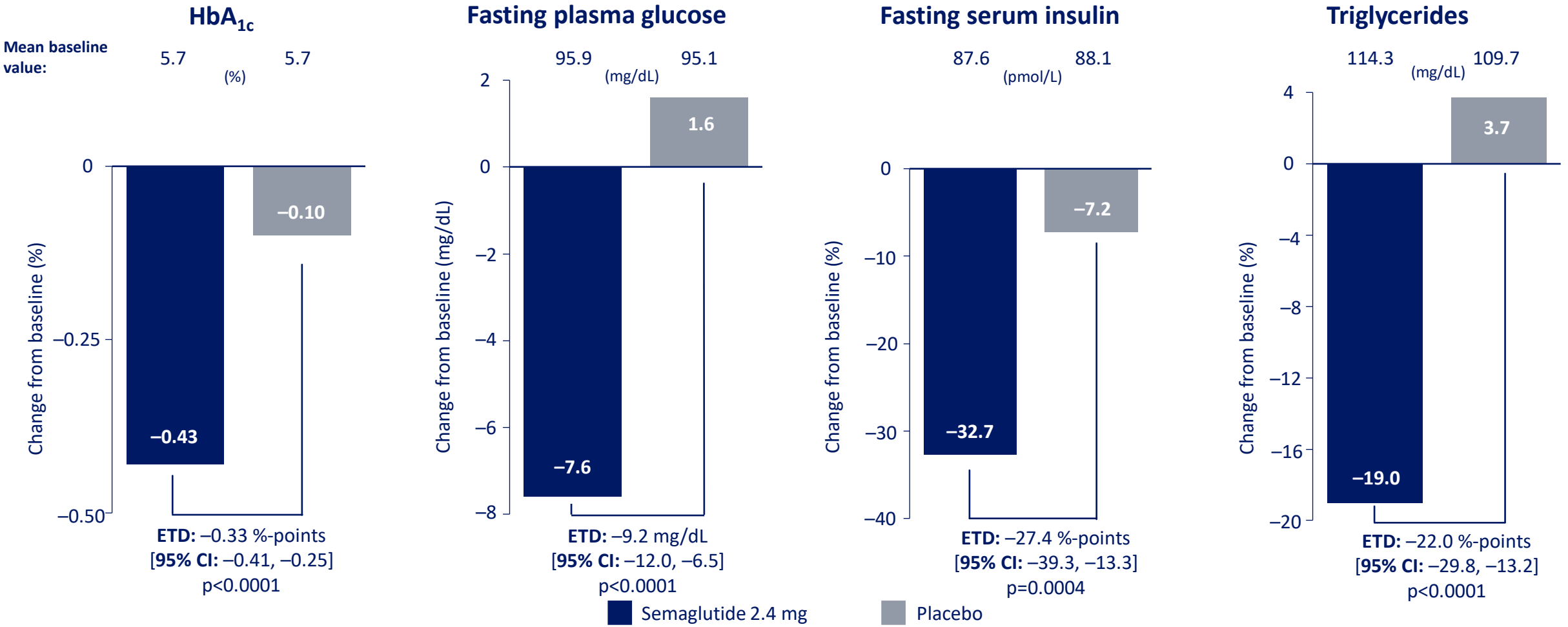
STEP 5



Change from baseline to week 104 based on the treatment policy estimand (assesses treatment effect regardless of treatment discontinuation or rescue intervention). CI, confidence interval; ETD, estimated treatment difference. Garvey et al. Nat Med 28, 2083–2091 (2022).

Metabolic risk factors

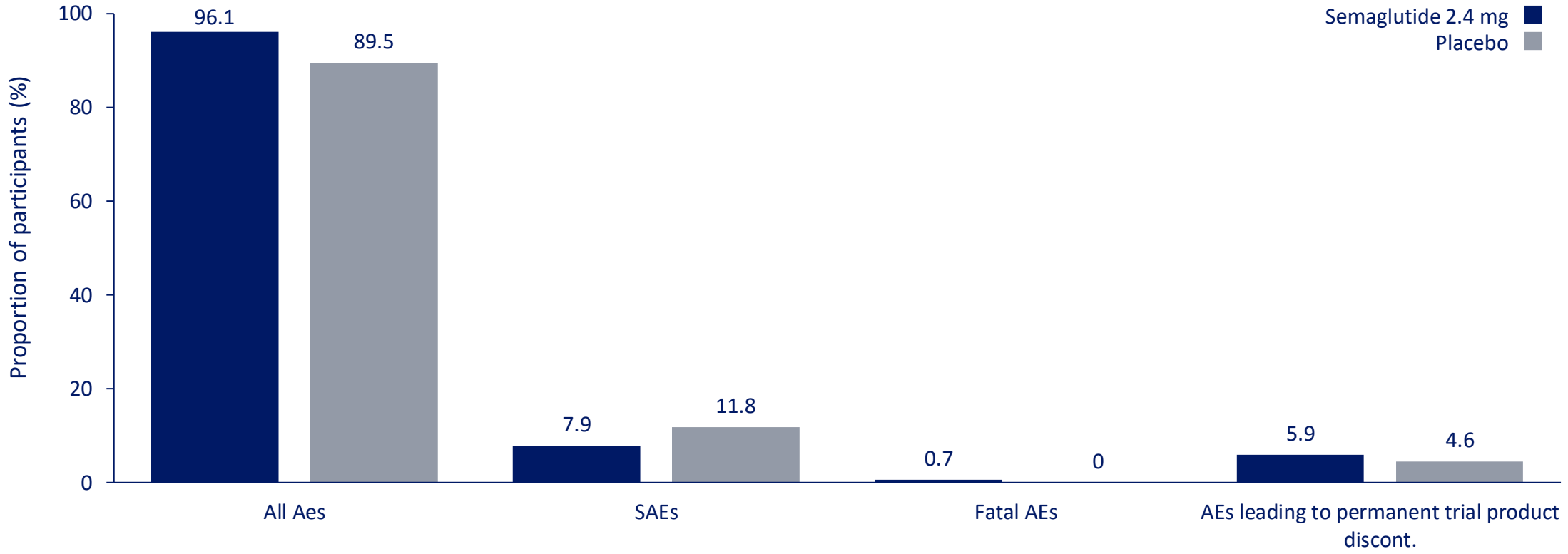
STEP 5



Change from baseline to week 104 based on the treatment policy estimand (assesses treatment effect regardless of treatment discontinuation or rescue intervention).
CI, confidence interval; ETD, estimated treatment difference.
Garvey et al. Nat Med 28, 2083–2091 (2022).

Adverse events overview

STEP 5



On-treatment data.
AE, adverse event; discont., discontinuation; N, number of participants with event(s); SAE, serious adverse event; %, proportion of participants with event(s).
Garvey et al. Nature Medicine 2022; 28(10): 2083-2091

Overview of safety focus areas

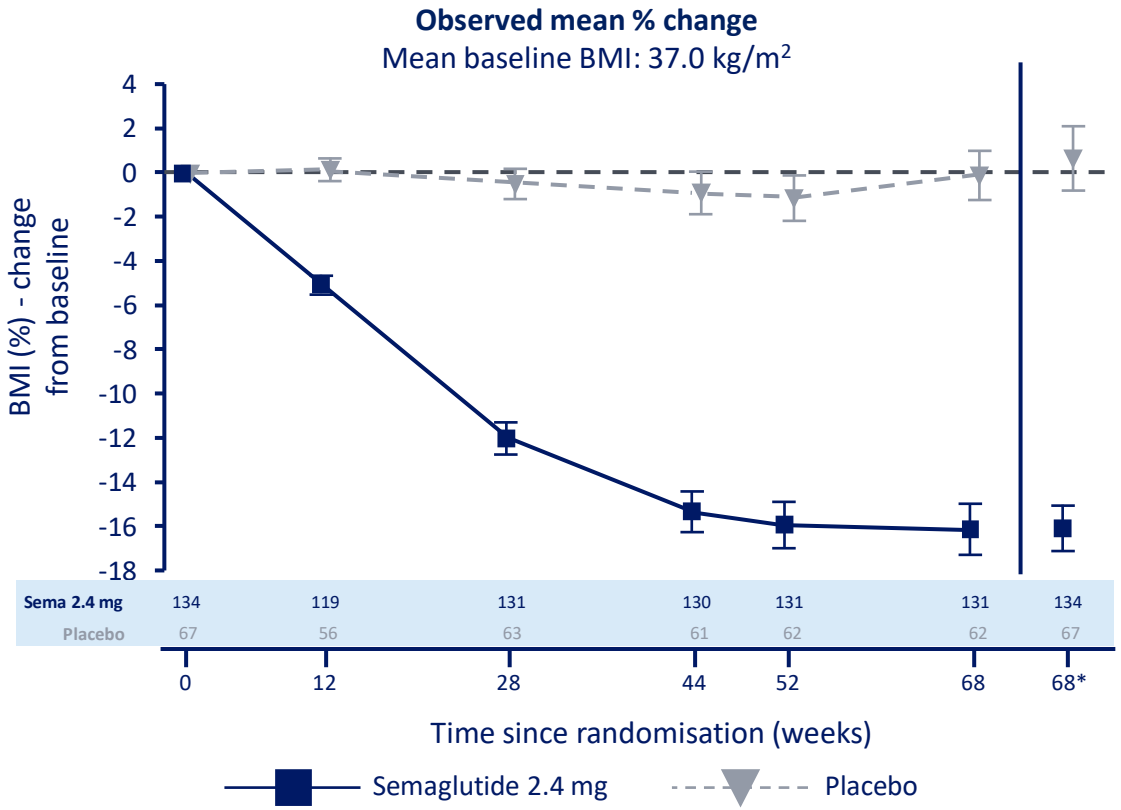
STEP 5

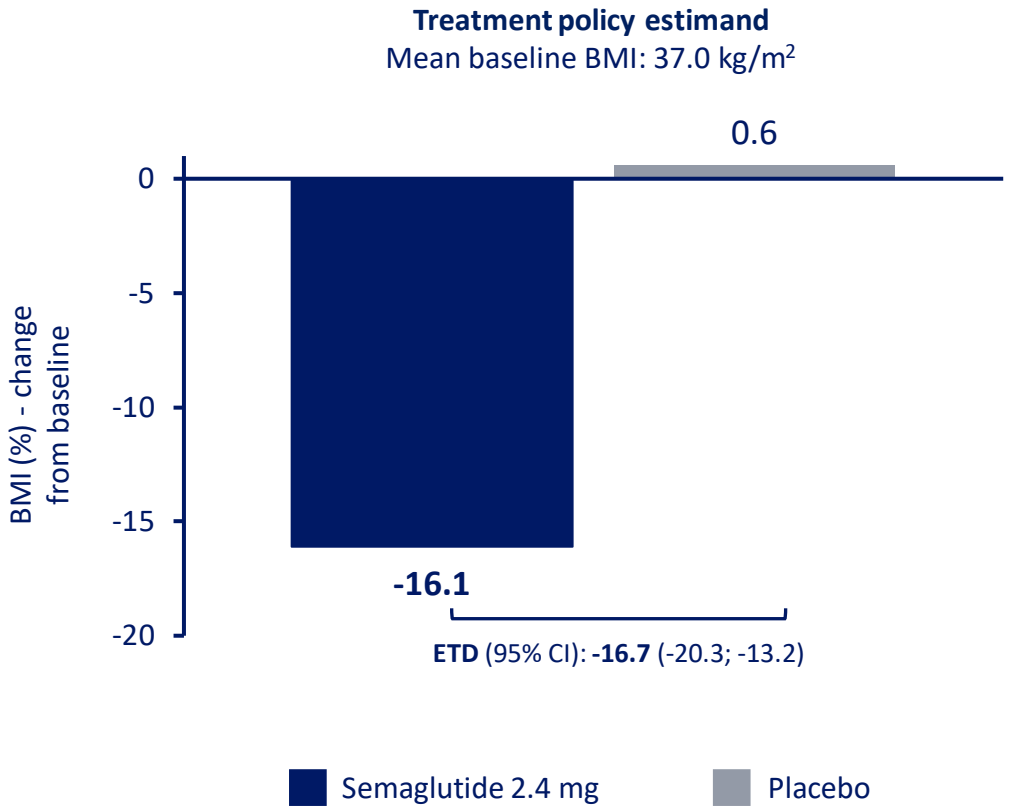
Adverse events within safety focus areas	Semaglutide 2.4 mg (N=152)		Placebo (N=152)	
	N	%	N	%
Gastrointestinal disorders	125	82.2	82	53.9
Gallbladder-related disorders	4	2.6	2	1.3
Hepatic disorders	3	2.0	3	2.0
Acute pancreatitis	0		0	
Cardiovascular disorders*	17	11.2	30	19.7
Allergic reactions	23	15.1	8	5.3
Injection site reactions	10	6.6	15	9.9
Malignant neoplasms*	2	1.3	4	2.6
Psychiatric disorders	26	17.1	25	16.4
Acute renal failure	0		0	
Hypoglycaemia	4	2.6	0	
Rare events	0		1	0.7
Overdose	0		1	0.7

**Events occurred during the in-trial period.*

Garvey et al. Nature Medicine 2022; 28(10): 2083-2091

STEP TEENS : Change in BMI (%)





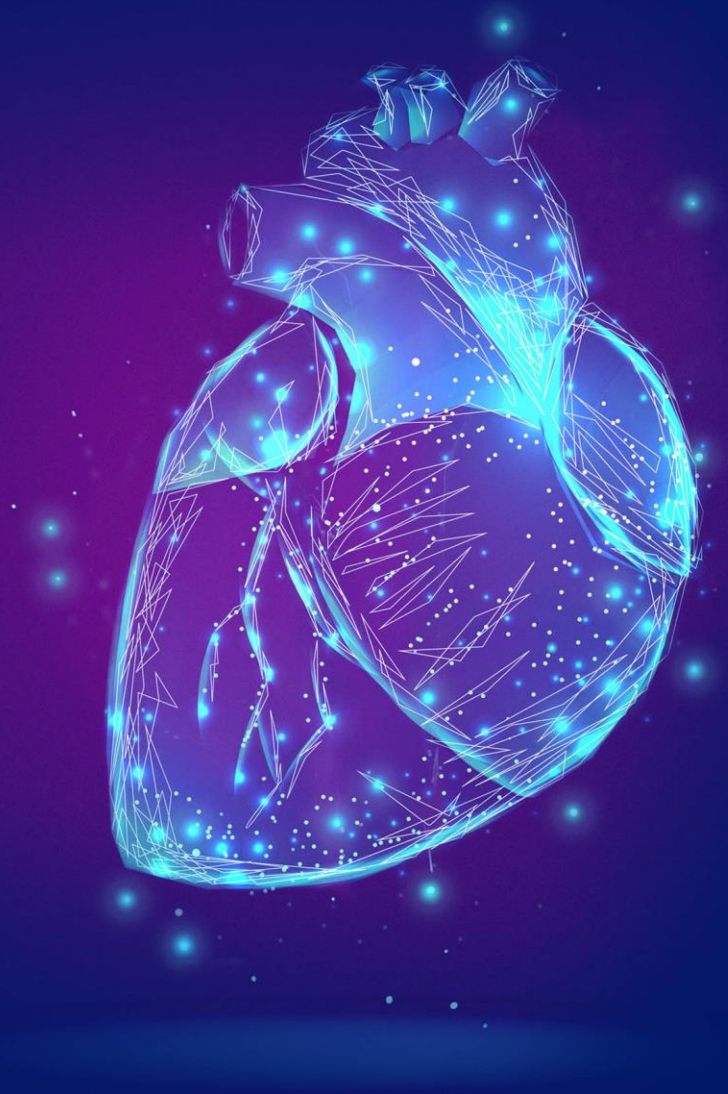
Analysis at week 68	ETD	95% CI	P-value
Sema 2.4 mg vs placebo	-16.7 %-points	[-20.3; -13.2]	<0.0001

68: Estimated means. Error bars are +/- standard error of the mean. Numbers shown in the lower panel of the left-hand figure are number of subjects contributing to the mean.*
ETD, estimated treatment difference; CI, confidence interval; Sema, semaglutide.
Weghuber et al. N Engl J Med 2022; 387(24): 2245-2257

*Semaglutide is not approved for the treatment of cardiovascular disease in UAE

SELECT *

Semaglutide | effects on cardiovascular outcomes in people with overweight or obesity



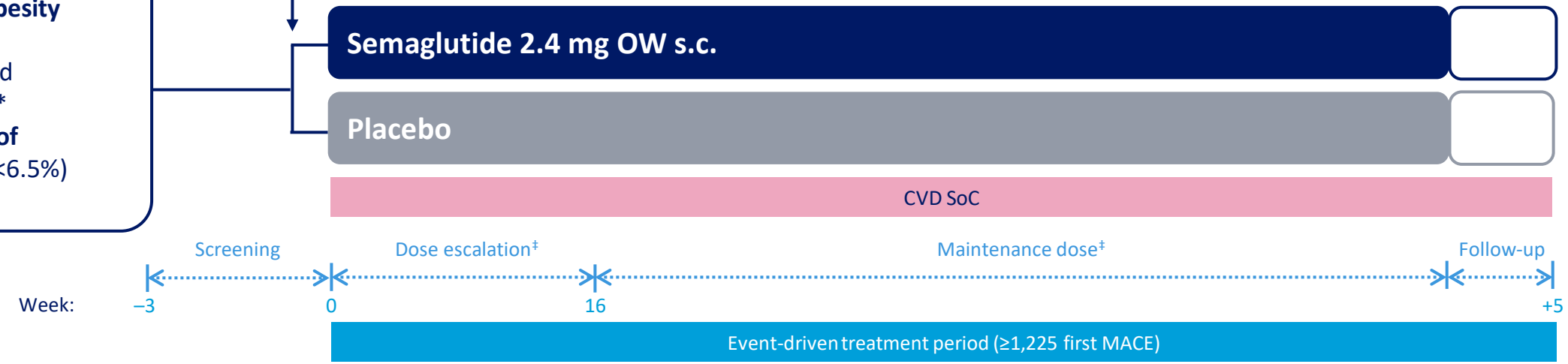
Trial design

SELECT

- **Overweight** or **obesity** (BMI ≥27 kg/m^2)
- Age ≥45 years and **established CVD***
- **No prior history of diabetes** (HbA_{1c} <6.5%)

Randomisation (1:1)
N=17,604†

Trial information[1–3]
- FPFV 24 October 2018
- Double-blind, placebo-controlled, superiority trial



Three-component MACE consisted of non-fatal MI, non-fatal stroke and CV death.
**Established CVD: MI ≥60 days prior to screening, stroke ≥60 days prior to screening or symptomatic PAD; NYHA class IV excluded. †Number of enrolled participants differs from number reported in baseline publication (17,605) as one participant was randomised twice in error and subsequently removed for the primary analysis. ‡Dose escalation is from week 4 to 16 with intervals of 4 weeks, and maintenance dose is event-driven to end of treatment period.*
BMI, body mass index; CV, cardiovascular; CVD, cardiovascular disease; FPFV, first patient first visit; HbA_{1c}, glycated haemoglobin; MACE, major adverse cardiovascular event; MI, myocardial infarction; NYHA, New York Heart Association; OW, once weekly; PAD, peripheral artery disease; s.c., subcutaneous; SoC, standard of care.
1. Ryan DH et al. Am Heart J 2020;229:61–9; 2. Lingvay I et al. Obesity (Silver Spring) 2023;31:111–22; 3. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

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Main inclusion/exclusion criteria

SELECT

Key inclusion criteria[1–3]

Prior MI*
Prior stroke*
Symptomatic PAD†

Male or female individuals aged ≥45 years

BMI ≥27 kg/m^2

Key exclusion criteria[1–3]

HbA_{1c} ≥6.5%

History of type 1 or type 2 diabetes‡

Treatment with glucose-lowering agents within the past 90 days

Presently classified as having NYHA class IV heart failure

>60 days prior to the day of screening. †Symptomatic PAD evidenced by intermittent claudication with ankle-brachial index less than 0.85 (at rest), or peripheral arterial revascularisation procedure or amputation due to atherosclerotic disease. ‡Gestational diabetes was allowed.

BMI, body mass index; HbA_{1c}, glycated haemoglobin; MI, myocardial infarction; NYHA, New York Heart Association; PAD, peripheral artery disease.

1. Ryan DH et al. Am Heart J 2020;229:61–9; 2. Lingvay I et al. Obesity (Silver Spring) 2023;31:111–22; 3. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

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Primary and confirmatory secondary endpoints

SELECT

Primary endpoint[1–3]

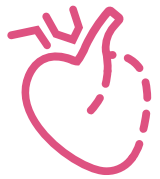
Time from randomisation to first occurrence of composite endpoint consisting of:

- CV death
- Non-fatal MI
- Non-fatal stroke

Confirmatory secondary endpoints[1–3]

Time from randomisation to occurrence of:

- CV death
- Composite HF endpoint consisting of HF hospitalisation, urgent HF visit or CV death
- All-cause death



A hierarchical testing procedure required statistical significance to be established for the primary endpoint before confirmatory secondary and supportive secondary endpoints could be tested.
CV, cardiovascular; HF, heart failure; MI, myocardial infarction.
1. Ryan DH et al. Am Heart J 2020;229:61–9; 2. Lingvay I et al. Obesity (Silver Spring) 2023;31:111–22; 3. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

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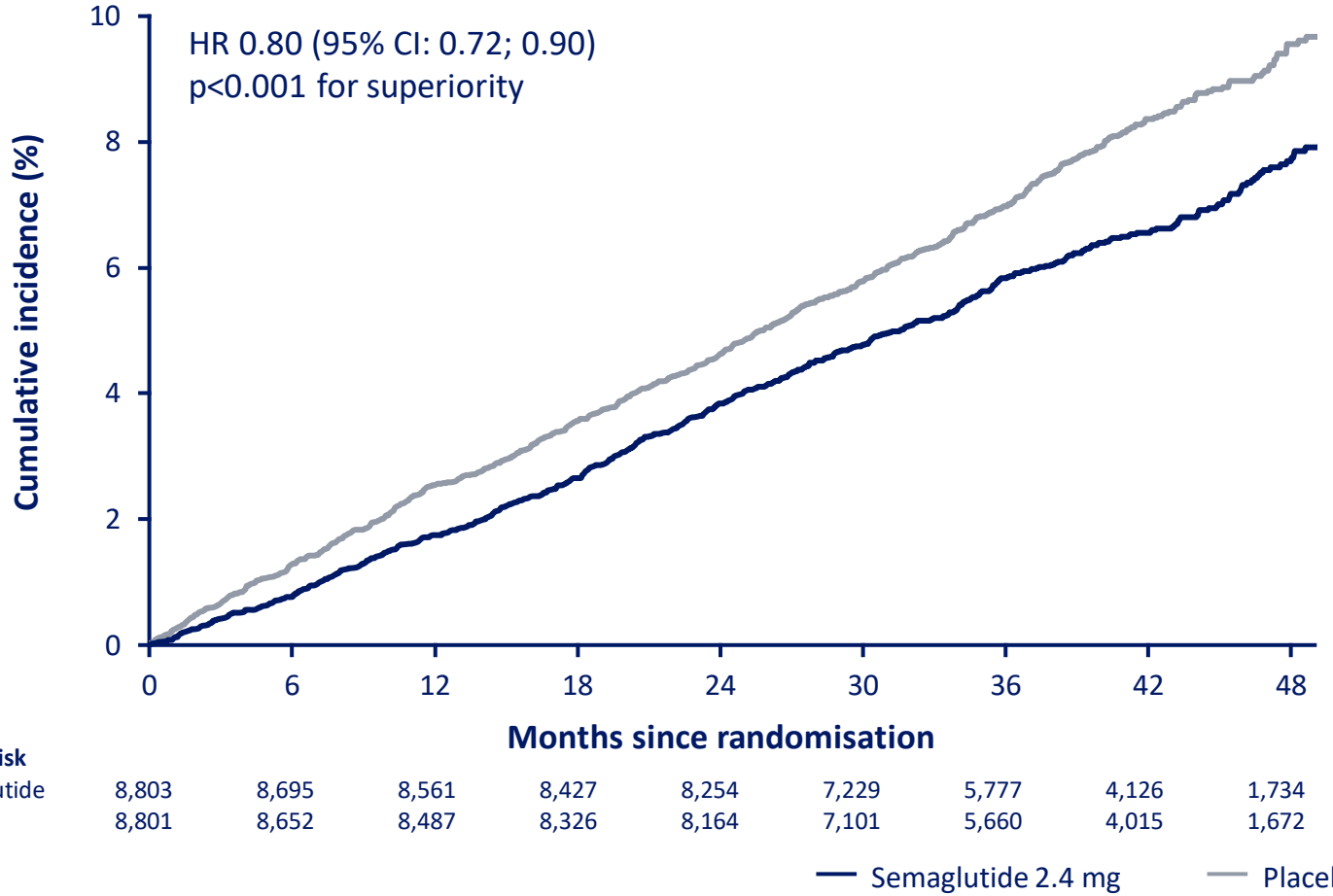
Cumulative incidence of MACE

SELECT: Primary cardiovascular composite endpoint



No. at risk									
Semaglutide	8,803	8,695	8,561	8,427	8,254	7,229	5,777	4,126	1,734
Placebo	8,801	8,652	8,487	8,326	8,164	7,101	5,660	4,015	1,672

— Semaglutide 2.4 mg — Placebo

20%
reduction in risk of MACE*

Semaglutide 2.4 mg significantly reduced
the risk of MACE by 20%
compared with placebo in people with obesity and established CVD, without T2D[1,2]

All three components (death from CV causes, non-fatal MI and non-fatal stroke) contributed to MACE risk reduction

Mean follow-up time was 39.8 months

Cumulative incidence (using the Aalen–Johansen method) of the composite MACE primary endpoint. The HR was estimated using a Cox proportional hazards regression model. The proportion of participants with MACE was 6.5% with semaglutide 2.4 mg and 8.0% with placebo. MACE was defined as death from CV causes, non-fatal myocardial infarction, or non-fatal stroke.
CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction.
1. Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563; 2. Novo Nordisk A/S. Company announcement, 8 August 2023. Available at: https://www.novonordisk.com/content/nncorp/global/en/news-and-media/news-and-ir-materials/news-details.html?id=166301. Accessed October 2023.

*Semaglutide is not approved for the treatment of cardiovascular disease in UAE

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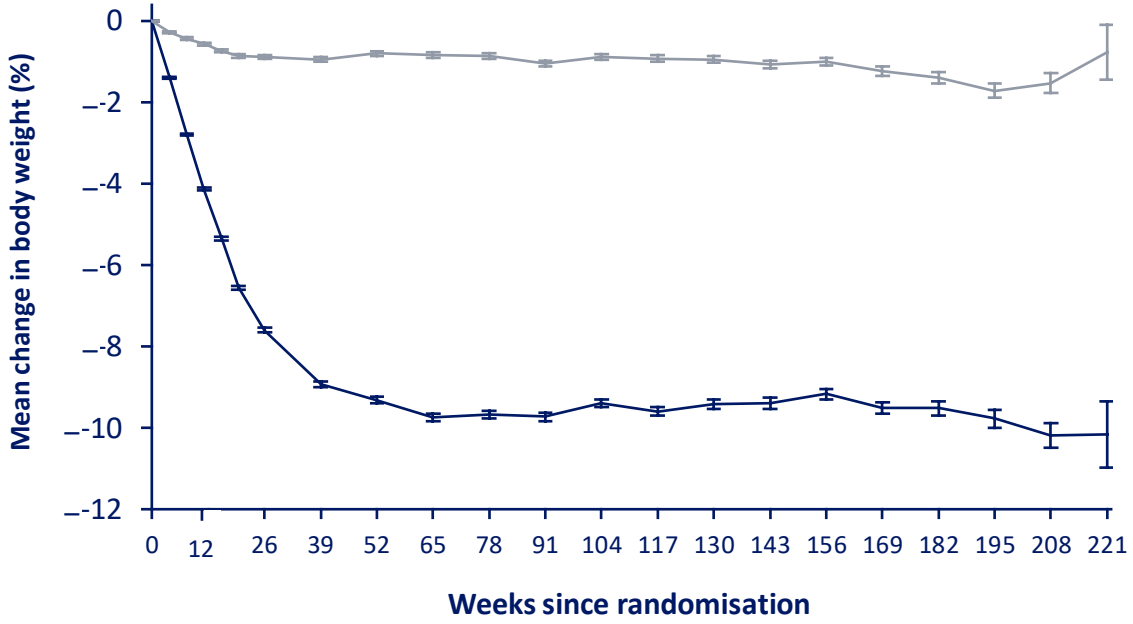
Change in body weight (%)

SELECT

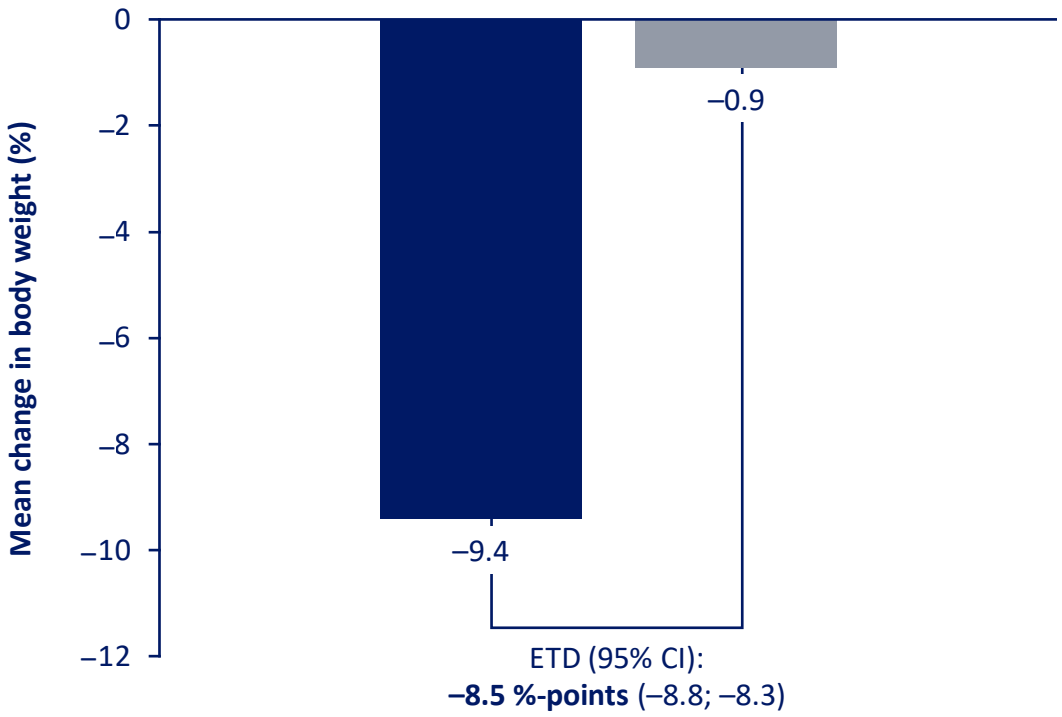
Observed change from baseline over time

Mean baseline body weight, kg:
Semaglutide 2.4 mg: 96.5 Placebo: 96.8



No. of participants																	
Semaglutide	8,803	7,647	7,493	6,690	7,290	6,447	7,282	6,460	7,474	5,991	5,898	4,686	5,085	3,650	2,954	1,737	921	157
Placebo	8,801	7,715	7,516	6,704	7,269	6,340	7,272	6,392	7,378	5,871	5,879	4,583	5,014	3,560	2,890	1,698	898	152

Estimated change from baseline to week 104*

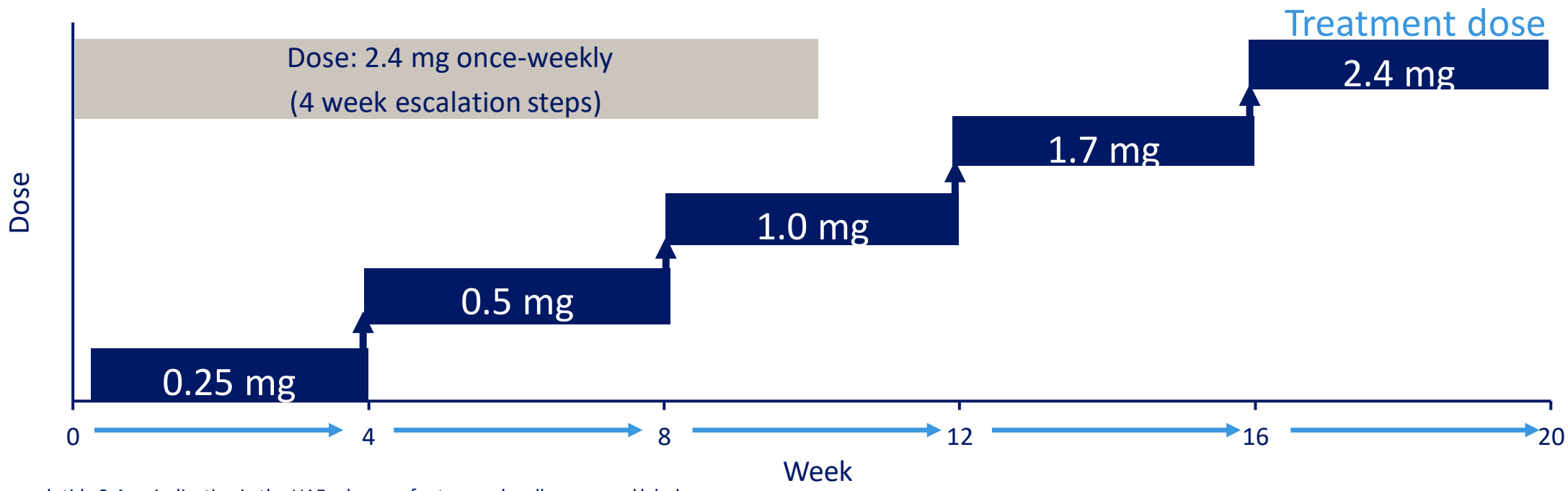


Semaglutide 2.4 mg Placebo

*Error bars in the left-hand figure are 95% CI as calculated by 1.96 times the standard error. *Estimated using an ANCOVA with treatment as factor and the baseline value as covariate, using multiple imputation for missing values under a missing-at-random assumption. CIs have not been adjusted for multiplicity. ANCOVA, analysis of covariance; CI, confidence interval; ETD, estimated treatment difference; SD, standard deviation.*
Lincoff AM et al. N Engl J Med 2023;DOI:10.1056/NEJMoa2307563.

Semaglutide 2.4 mg (Wegovy®) indications & dose escalation*

- **Semaglutide 2.4 mg** is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in **adult patients with an initial BMI of ≥30 kg/m2 or ≥27 kg/m2 + at least one weight-related comorbidity** such: dysglycaemia (pre-diabetes or T2D), hypertension, dyslipidaemia, OSA
- Also indicated as an adjunct to a healthy nutrition and increased physical activity for weight management in **adolescent patients from the age of 12 years** and above with:
  - ✓ Obesity (BMI corresponding to ≥30 kg/m^2 for adults by international cut-off points) and
  - ✓ Body weight above 60 kg



* Semaglutide 2.4mg indication in the UAE, please refer to your locally approved label

Summary

Semaglutide 2.4 mg (Wegovy®), a GLP-1RA , is currently approved for weight management and has been shown to energy intake and control of appetite

STEP trials showed a mean weight loss of 17-18% in adults and 16.7% in adolescents

Semaglutide 2.4 mg (Wegovy®) improved multiple modifiable risk factors known to drive CV events, such as body weight, waist circumference, blood pressure, lipids and hsCRP

Semaglutide 2.4 mg **significantly reduced risk of MACE by 20%** vs placebo in people with established CVD and overweight or obesity without T2D, with consistent effects across participant subgroups

This is the **first time** a weight management medication has **shown a reduction in CV events** in people with established CVD and overweight or obesity, without T2D

Q&A