DiabeteScan

Episode 3

Presented by **Professor Melanie Davies, CBE**
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Presenter Disclosure: Melanie J. Davies

Advisory Panel:	AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck Sharp & Dohme, Novo Nordisk, Sanofi-Aventis, Servier
Board Member:	AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck Sharp & Dohme, Novo Nordisk, Sanofi-Aventis
Consultant:	AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck Sharp & Dohme, Novo Nordisk, Sanofi-Aventis, Intarcia
Employee:	None
Research Support:	Eli Lilly and Company, Novo Nordisk, Sanofi-Aventis
Speaker Bureau:	AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Janssen, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma Corporation, Novo Nordisk, Sanofi-Aventis
Stock/Shareholder:	None in any device or pharmaceutical company

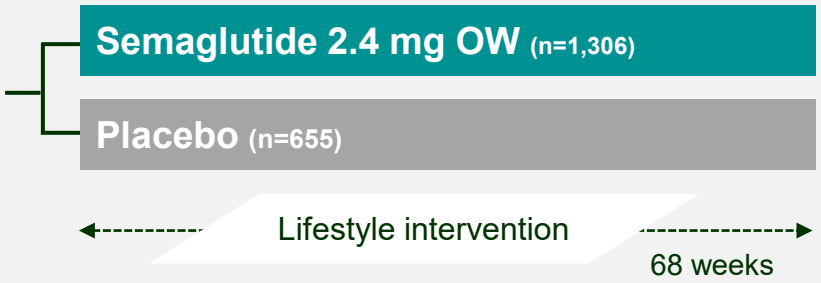
STEP Trials – Semaglutide in obesity

Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with T2D

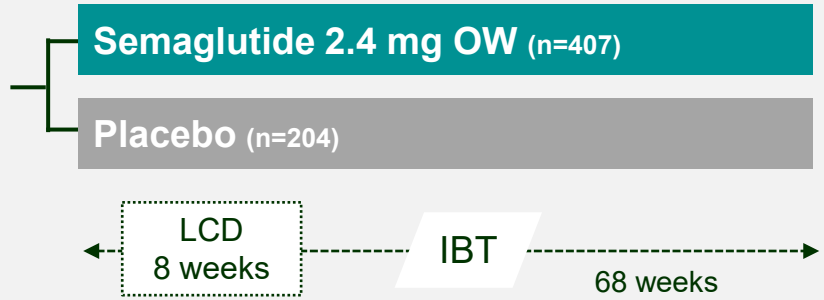
STEP program: Pivotal trials at a glance

4,700 patients in total

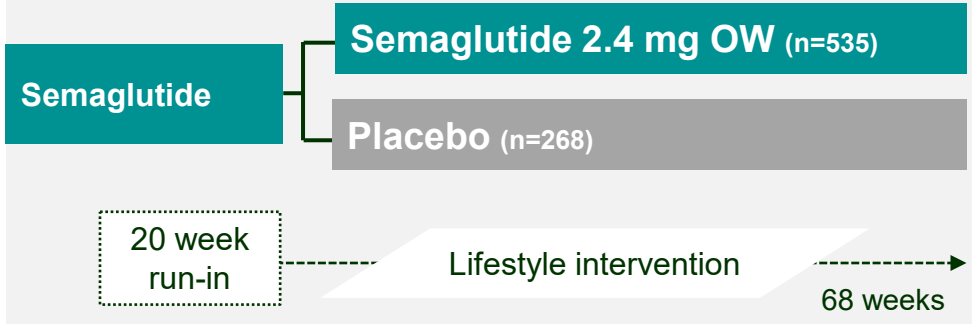
STEP-1 Weight management[1]



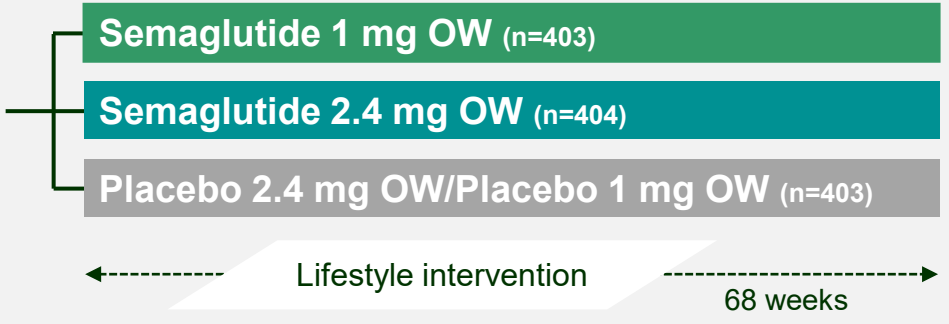
STEP-3 Weight management with IBT[2]



STEP-4 Sustained weight management[3]



STEP-2 Weight management in T2D not on insulin[4]



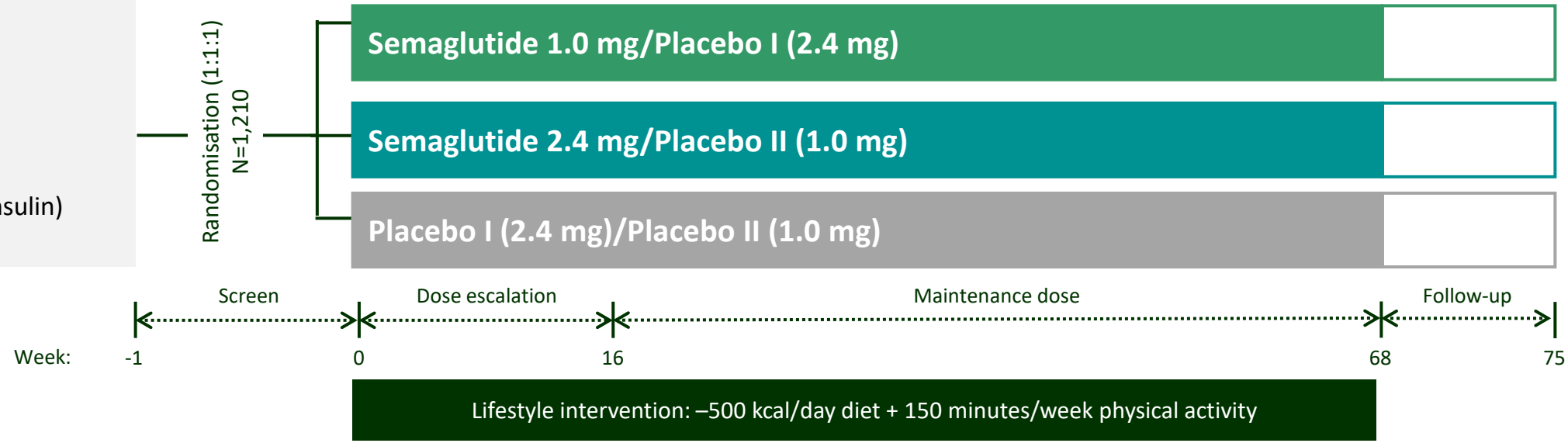
Lifestyle intervention: –500 kcal/day diet + 150 min/week physical activity. *Participants on sulfonylurea: semaglutide 1.0 mg: 24.6%; semaglutide 2.4 mg: 26.7%; placebo: 24.1%

IBT, intensive behavioural therapy; LCD, low-calorie diet; OW, once-weekly; STEP, Semaglutide Treatment Effect in People with obesity; T2D, type 2 diabetes.

1. Wilding et al. N Engl J Med 2021;384:989; 2. Wadden et al. JAMA 2021; doi:10.1001/jama.2021.1831; 3. Rubino et al. JAMA 2021; doi:10.1001/jama.2021.3224; 4. Davies et al. Lancet 2021;397:971–84.

STEP-2: Weight management in T2D
Trial design (NN9536-4374)

- Male or female
- Age ≥18 years
- BMI ≥27 kg/m^2
- T2D
  - HbA1c 7–10%
  - ≤3 OAD (and no insulin)



Trial information
Double-blind, double-dummy multicentre, placebo-controlled trial

Trial objective
To show superiority of semaglutide 2.4 mg vs placebo and vs semaglutide 1.0 mg OW on weight loss and to compare the safety and tolerability in adults with T2D and either obesity or overweight

Key endpoints in test hierarchy

Primary: % weight loss, achievement of ≥5% weight loss

Secondary: Achievement of ≥10% and ≥15% weight loss, waist circumference, % weight loss (vs 1.0 mg OW), HbA1c, systolic blood pressure, SF-36, IWQOL-Lite

*Anticipated. BMI, body mass index; HbA1c, glycated haemoglobin IWQOL-Lite, Impact of Weight on Quality Of Life-Lite for clinical trials; OAD, oral anti-diabetes medication; OW, once-weekly; SF-36, 36-item Short Form health survey; T2D, type 2 diabetes. 1. NCT03552757. Available from https://clinicaltrials.gov/ct2/show/NCT03552757?term=NN9536-4374&draw=2&rank=1. Accessed June 2020; 2. Davies et al. Lancet 2021;397:971–84.

Baseline demographics and clinical characteristics

Characteristic	Semaglutide 2.4 mg (N=404)	Semaglutide 1.0 mg (N=403)	Placebo (N=403)	Total (N=1210)
Age, years	55 ± 11	56 ± 10	55 ± 11	55 ± 11
Female, n (%)	223 (55.2)	203 (50.4)	190 (47.1)	616 (50.9)
Race or ethnicity, n (%)				
Asian	112 (27.7)	97 (24.1)	108 (26.8)	317 (26.2)
Black or African American	35 (8.7)	28 (6.9)	37 (9.2)	100 (8.3)
White	237 (58.7)	272 (67.5)	242 (60.0)	751 (62.1)
Body weight, kg	99.9 ± 22.5	99.0 ± 21.1	100.5 ± 20.9	99.8 ± 21.5
BMI, kg/m^2				
Mean	35.9 ± 6.4	35.3 ± 5.9	35.9 ± 6.5	35.7 ± 6.3

All data presented as mean ± standard deviation, unless indicated otherwise. There were no marked differences between treatment groups at baseline.
*Including American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander. BMI, body mass index.
Adapted from Table 1. Baseline characteristics. Davies et al. Lancet 2021;397:971–84.

Baseline demographics and clinical characteristics

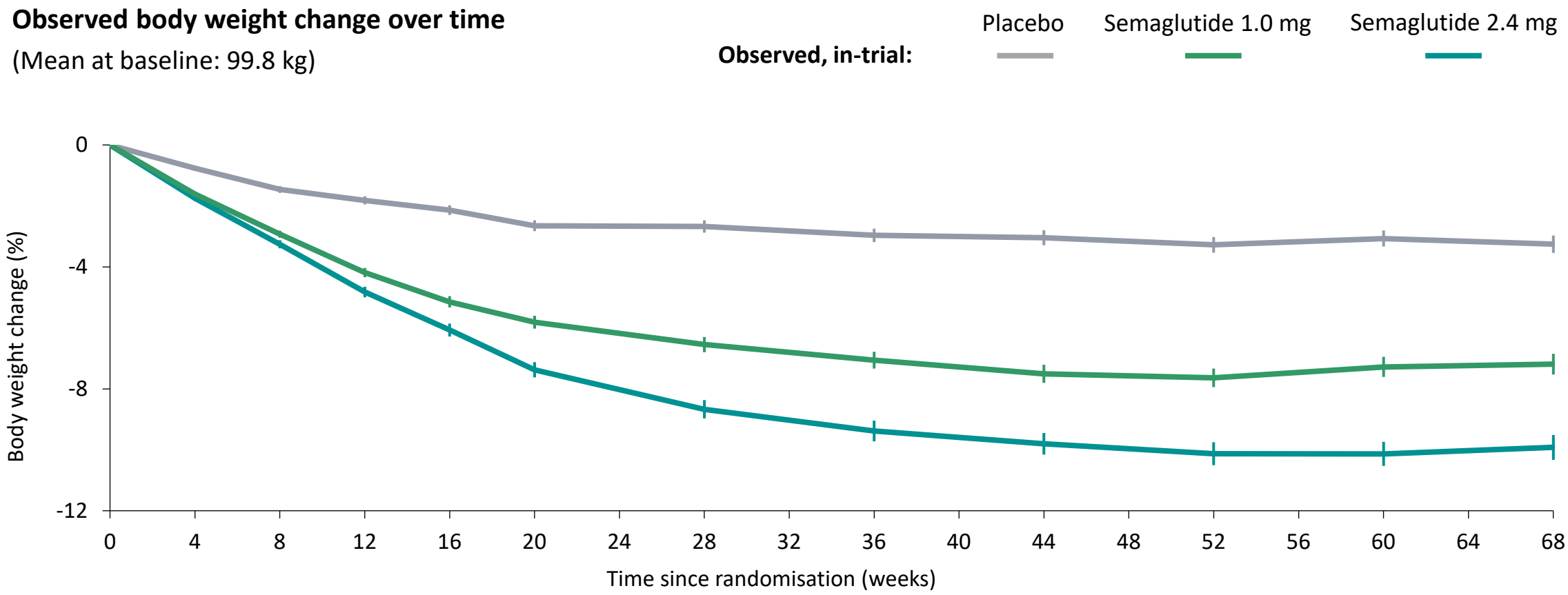
Characteristic	Semaglutide 2.4 mg (N=404)	Semaglutide 1.0 mg (N=403)	Placebo (N=403)	Total (N=1210)
Waist circumference, cm	114.5 ± 14.3	113.9 ± 14.0	115.5 ± 13.9	114.6 ± 14.1
HbA1c, %	8.1 ± 0.8	8.1 ± 0.8	8.1 ± 0.8	8.1 ± 0.8
Duration of diabetes, years	8.2 ± 6.2; n=404	7.7 ± 5.9; n=403	8.2 ± 6.2; n=402	8.0 ± 6.1; n=1209
Glucose-lowering drug class, n (%)				
Biguanides	370 (91.6)	379 (94.0)	362 (89.8)	1111 (91.8)
Sulphonylureas	110 (27.2)	99 (24.6)	99 (24.6)	308 (25.5)
SGLT2 inhibitors	99 (24.5)	96 (23.8)	105 (26.1)	300 (24.8)

Semaglutide is not approved for weight management.
*HbA1c, glycated haemoglobin; SGLT2, sodium–glucose co-transporter 2.
Adapted from Table 1. Baseline characteristics. Davies et al. Lancet 2021;397:971–84.

Co-primary endpoint: Body weight change (%)

Observed body weight change over time

(Mean at baseline: 99.8 kg)



Observed, in trial period and on-treatment period. In-trial period: from randomisation to last contact with trial site, regardless of treatment discontinuation or rescue intervention; on-treatment period: during which participants received trial product within the previous 2 weeks, excluding any period of temporary treatment interruption. Error bars are +/- standard error of the mean. Davies et al. Lancet 2021;397:971–84.

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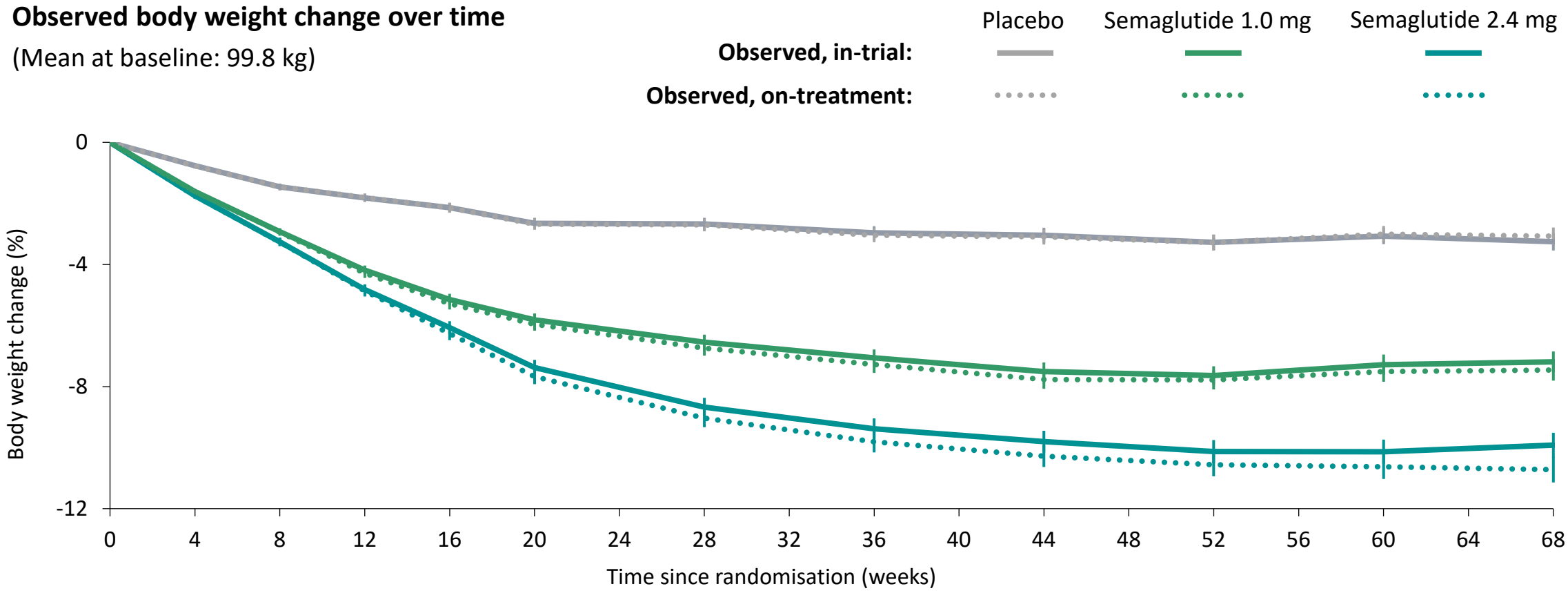

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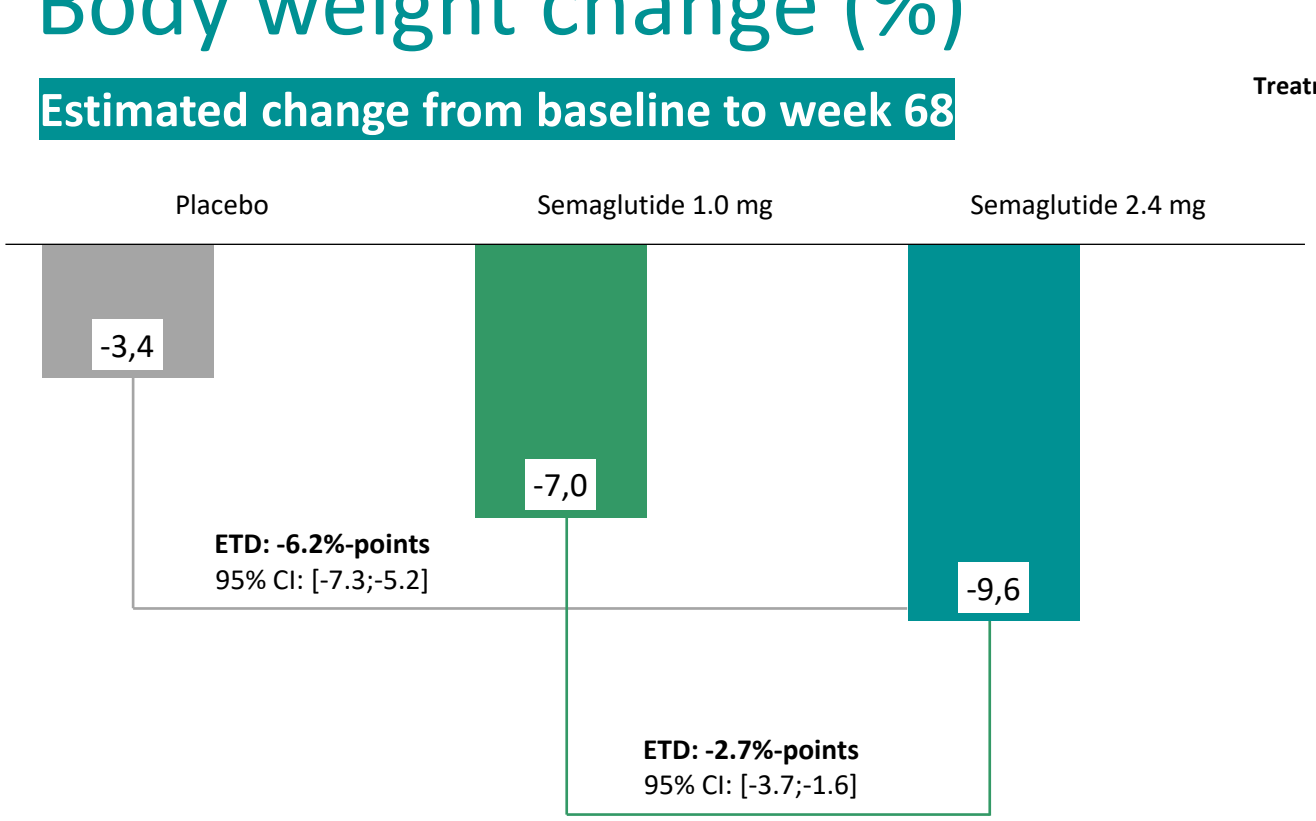
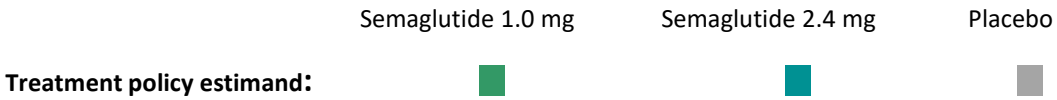
Estimated treatment differences: Body weight change (%)

Estimated change from baseline to week 68





P<0.0001 for all ETD comparisons

Note: comparison between semaglutide 1.0 mg and semaglutide 2.4 mg was not a primary endpoint

Treatment policy estimand assesses treatment effect regardless of treatment discontinuation or rescue intervention. Trial product estimand assesses treatment effect assuming treatment adherence and without rescue intervention. Primary and secondary endpoints were assessed for the treatment policy estimand (other analyses not controlled for multiplicity).
Error bars are +/- standard error of the mean. ETD, estimated treatment difference; CI, confidence interval. Davies et al. Lancet 2021;397:971–84.

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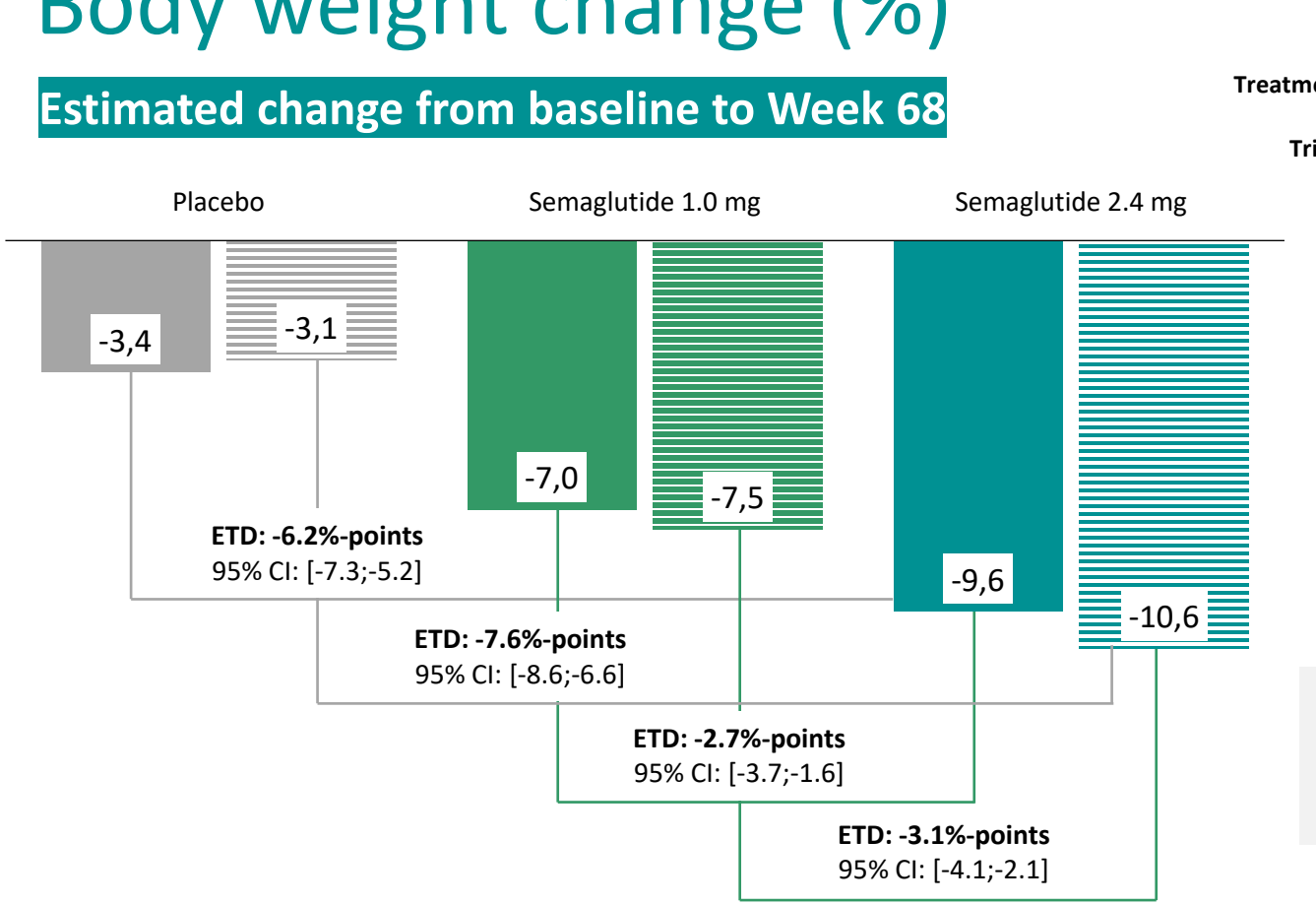

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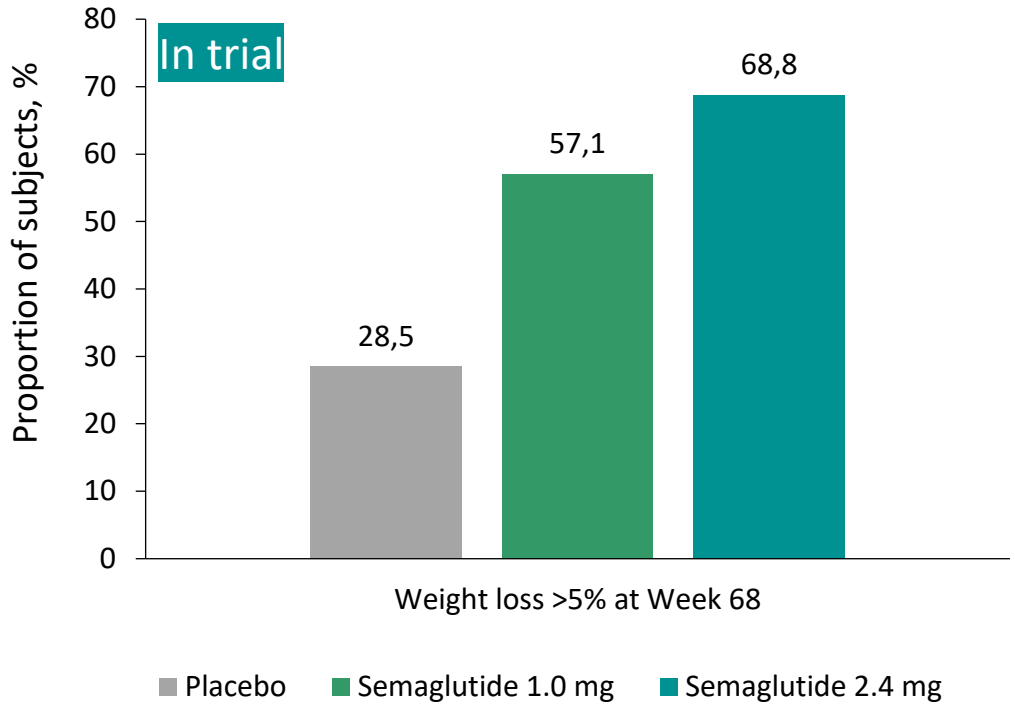
Categorical body weight loss: ≥5%



P<0.0001 for comparisons between semaglutide 2.4 mg and placebo

Observed, in-trial period and on-treatment period. In-trial period: from randomisation to last contact with trial site, regardless of treatment discontinuation or rescue intervention; on-treatment period: during which participants received trial product within the previous 2 weeks, excluding any period of temporary treatment interruption.
Davies et al. Lancet 2021;397:971–84.

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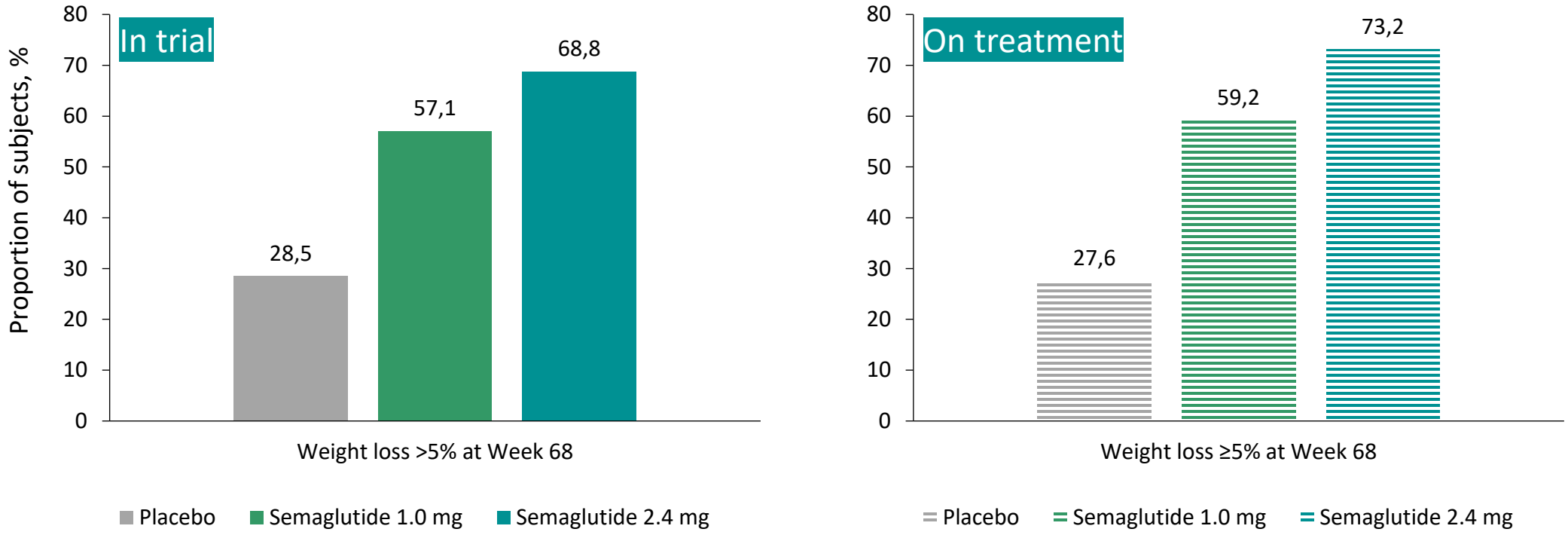
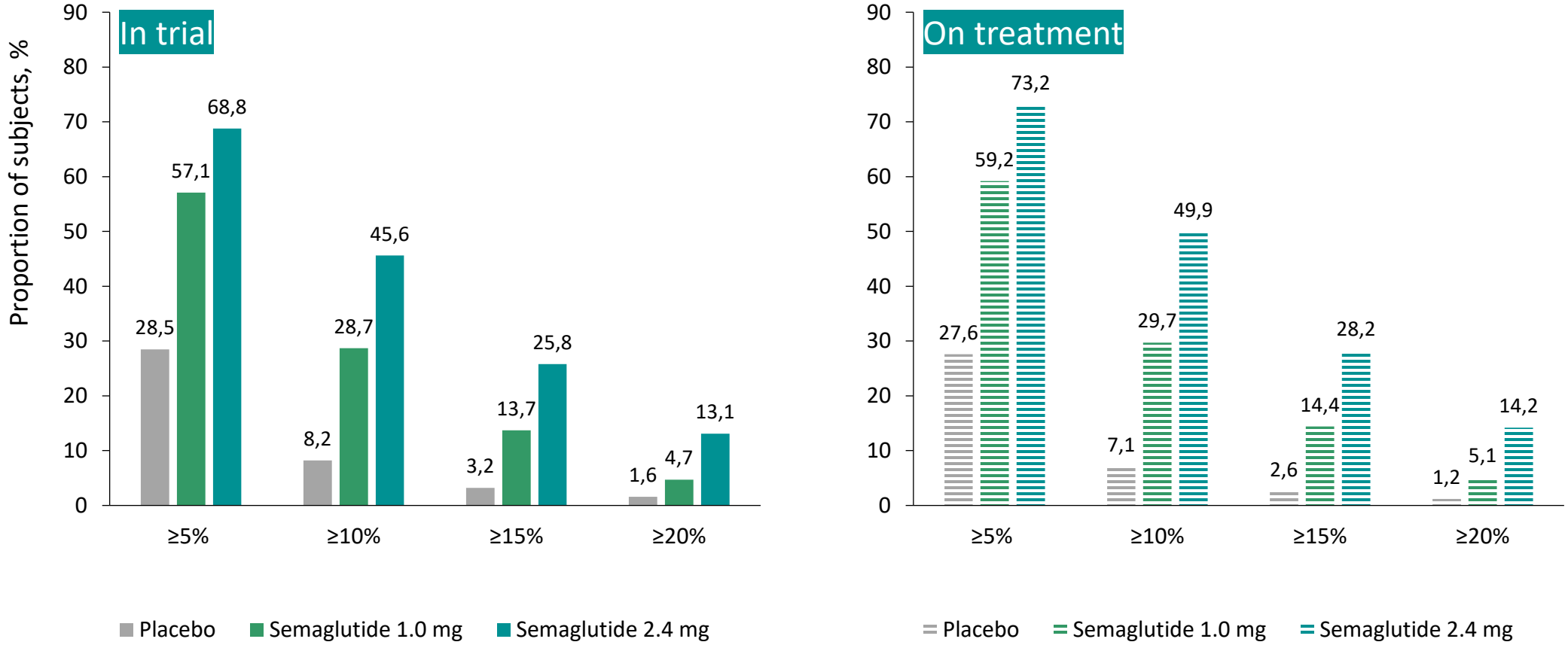


P<0.0001 for comparisons between semaglutide 2.4 mg and placebo

Observed, in-trial period and on-treatment period. In-trial period: from randomisation to last contact with trial site, regardless of treatment discontinuation or rescue intervention; on-treatment period: during which participants received trial product within the previous 2 weeks, excluding any period of temporary treatment interruption.
Davies et al. Lancet 2021;397:971–84.

STEP-2: Categorical body weight loss



Semaglutide is not approved for weight management.

Full analysis set. Davies et al. Lancet 2021;397:971–84.

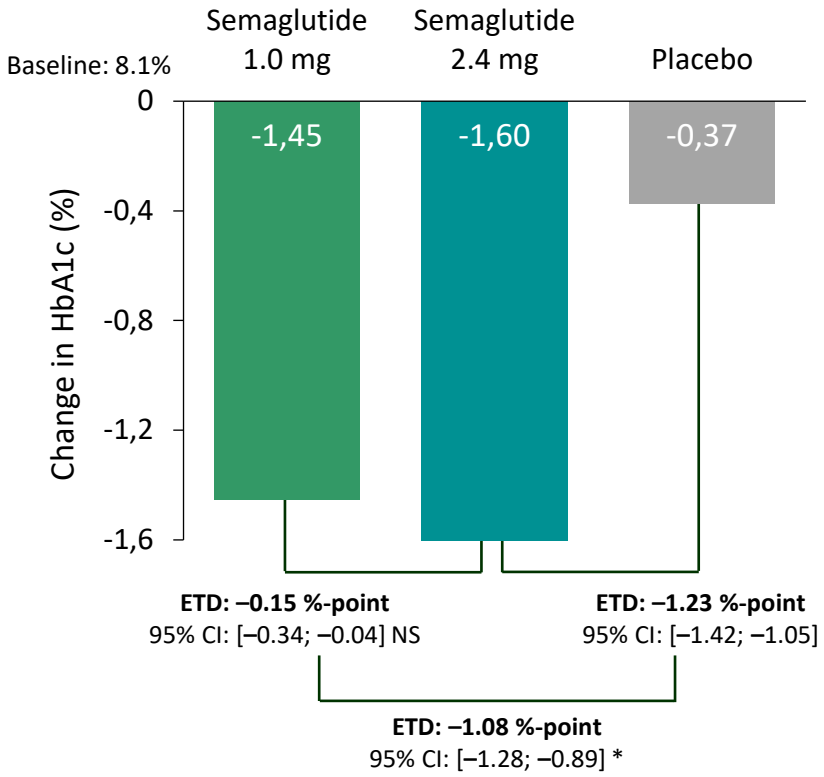
Confirmatory endpoints: Summary

Endpoint	Placebo (N=403)	Semaglutide 1.0 mg (N=403)	Semaglutide 2.4 mg (N=404)	Treatment comparison
Body weight reduction ≥10%: % of patients at Week 68	8.2	28.7	45.6	• Semaglutide 2.4 mg / placebo: OR: 7.4 [4.9 to 11.2]; P<0.0001 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: OR: 2.1 [1.5 to 2.8]
Body weight reduction ≥15%: % of patients at Week 68	3.2	13.7	25.8	• Semaglutide 2.4 mg / placebo: OR: 7.7 [4.1 to 14.2]; P<0.0001 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: OR: 2.2 [1.5 to 3.2]
Waist circumference (cm): • Week 68 mean ± SD • Change from baseline to Week 68	111.0 ±13.7 –4.5	107.2 ± 14.6 –6.7	104.4 ± 14.7 –9.4	• Semaglutide 2.4 mg / placebo: ETD: –4.9 cm [–6.0 to –3.8]; P<0.0001 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: ETD: –2.7 cm [–3.7 to –1.7]

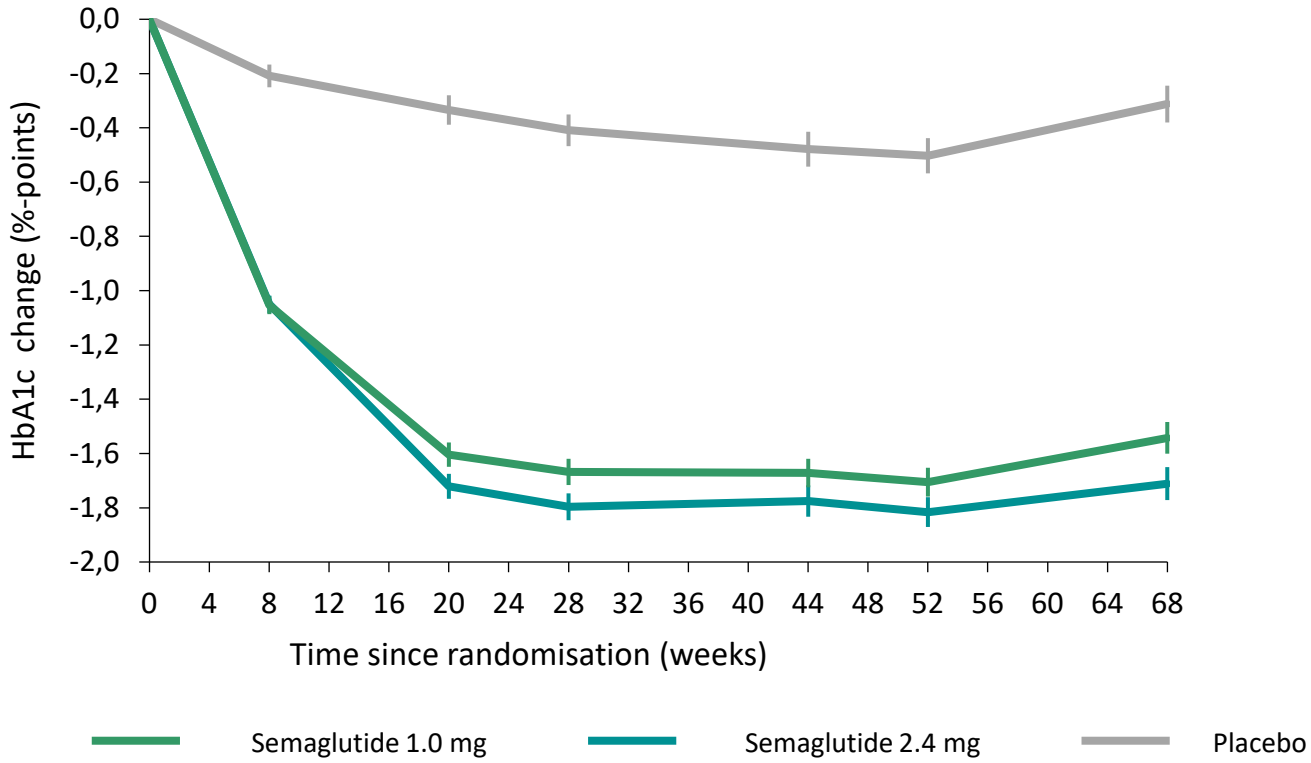
ETD, estimated treatment difference; OR, odds ratio; SD, standard deviation.
Davies et al. Lancet 2021;397:971–84.

STEP-2: Glycaemic control: change in HbA1c

Estimated change from baseline to Week 68†



Observed change over time‡



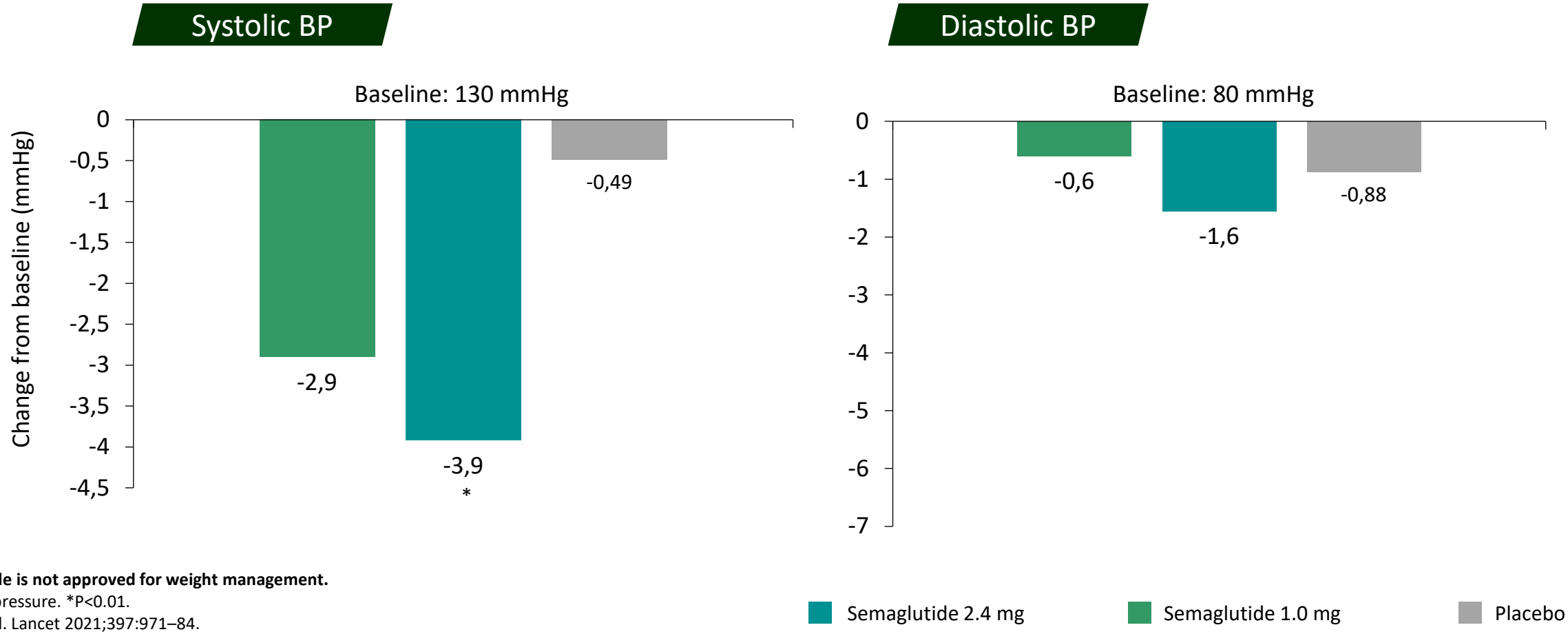
Semaglutide is not approved for weight management

Mean HbA1c at baseline: 8.1%, 65.3 mmol/mol. *P<0.0001. †Estimated change from baseline for treatment policy estimand. ‡Observed mean data for patients in the full analysis set during the in-trial period. Error bars are ± standard error of the mean. CI, confidence interval; ETD, estimated treatment difference; HbA1c, glycated haemoglobin; NS, not significant.

Davies et al. Lancet 2021;397:971–84; Data on file.

STEP-2: Change in blood pressure at Week 68

Treatment policy estimand



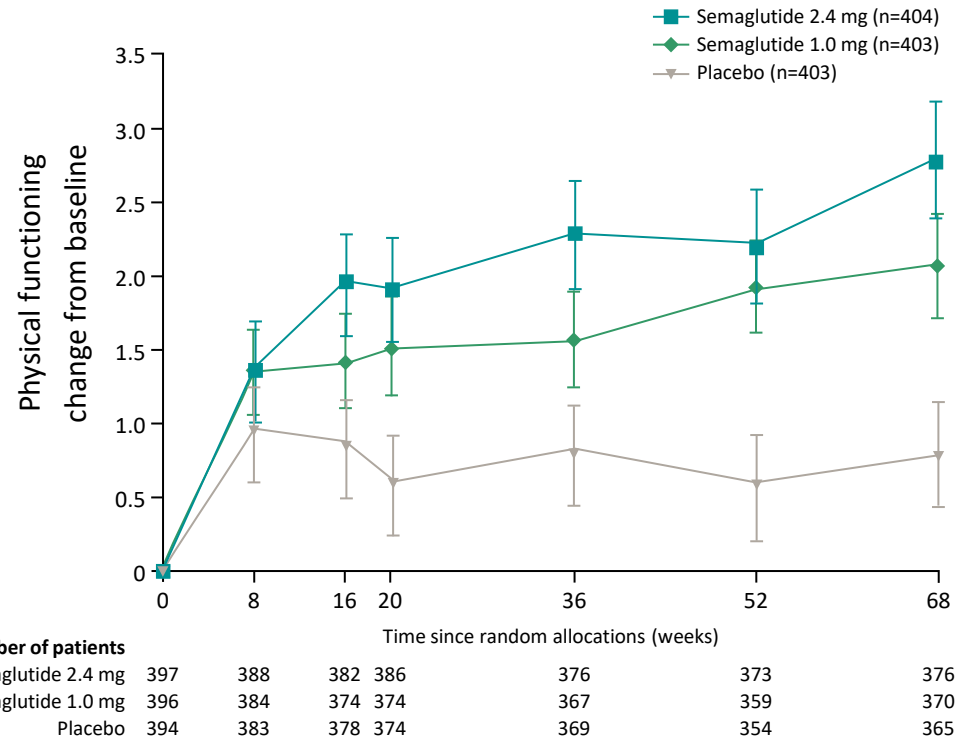
Semaglutide is not approved for weight management.

BP, blood pressure. *P<0.01.

Davies et al. Lancet 2021;397:971–84.

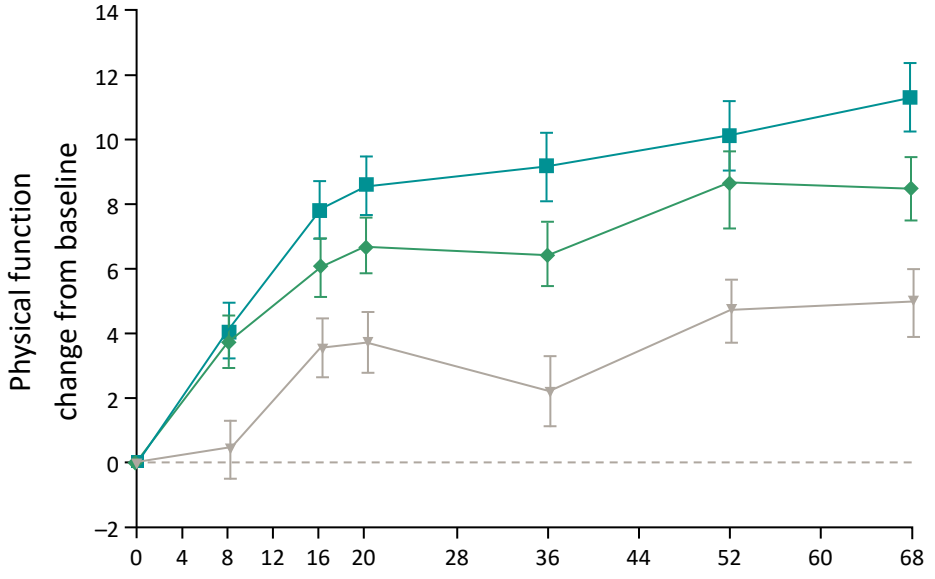
STEP-2: Change from baseline by week for selected confirmatory secondary endpoints

SF-36 physical functioning score – observed in-trial data



Number of patients							
Semaglutide 2.4 mg	397	388	382	386	376	373	376
Semaglutide 1.0 mg	396	384	374	374	367	359	370
Placebo	394	383	378	374	369	354	365

IWQOL-Lite-CT physical function score – observed in-trial data



	397	388	380	386	376	373	376
	395	381	373	373	365	358	369
	394	382	378	374	369	354	365

Semaglutide is not approved for weight management.

Observed mean change from baseline over time for patients in the full analysis set during the in-trial observation period. Error bars are standard error of the mean. Numbers shown below the panel are patients contributing to the mean. IWQOL-Lite-CT, Impact of Weight on Quality of Life-Lite Clinical Trials Version; SF-36, Short Form36v2® Health Survey, Acute Version. Davies et al. Lancet 2021;397:971–84.

Confirmatory endpoints: Summary

Endpoint	Placebo (N=403)	Semaglutide 1.0 mg (N=403)	Semaglutide 2.4 mg (N=404)	Treatment comparison
HbA1c (%): • Week 68 mean ± SD • Change from baseline to Week 68 (%-points)	7.8 ±1.3 –0.4	6.6 ±1.1 –1.5	6.4 ±1.2 –1.6	• Semaglutide 2.4 mg / placebo: ETD (%-points): –1.2 [–1.4 to –1.1]; P<0.0001 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: ETD (%-points): –0.2 [–0.3 to 0.0] • Semaglutide 1.0 mg / placebo: ETD (%-points): –1.1 [–1.3 to –0.9]
Systolic blood pressure (mmHg): • Week 68 mean ± SD • Change from baseline to Week 68 (mmHg)	130 ±14 –0.5	127 ±15 –2.9	126 ±14 –3.9	• Semaglutide 2.4 mg / placebo: ETD (mmHg): –3.4 [–5.6 to –1.3]; P=0.0016 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: ETD (mmHg): –1.0 [–3.3 to 1.2]
SF-36 Physical Functioning score: • Week 68 mean ± SD • Change from baseline to Week 68	50.5 ±9.0 1.0	52.6 ±7.1 2.4	52.1 ±7.9 2.5	• Semaglutide 2.4 mg / placebo: ETD: 1.5 [0.4 to 2.6]; P=0.0061 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: ETD: 0.1 [–1.0 to 1.2]
IWQOL-Lite CT Physical Function score: • Week 68 mean ± SD • Change from baseline to Week 68	74.8 ±24.6 5.3	79.6 ±20.8 8.7	79.0 ±23.3 10.1	• Semaglutide 2.4 mg / placebo: ETD: 4.8 [1.8 to 7.9; P=0.0018 • Semaglutide 2.4 mg / Semaglutide 1.0 mg: ETD: 1.4 [–1.5 to 4.3]

ETD, estimated treatment difference; HbA1c, glycated haemoglobin; IWQOL-Lite-CT, Impact of Weight on Quality of Life-Lite Clinical Trials Version; SD, standard deviation; SF-36, Short Form36v2® Health Survey, Acute Version. Davies et al. Lancet 2021;397:971–84.

Safety summary

GI AEs

Nausea the most common GI AE with semaglutide 2.4 mg but of mild-to-moderate severity and generally transient

Serious AEs

Comparable frequency with semaglutide 2.4 mg versus placebo

Discontinuations

Semaglutide 2.4 mg was associated with a higher frequency of AEs leading to permanent treatment discontinuation, mostly due to GI AEs

Other safety

Retinal disorders, severe or BG-confirmed hypoglycaemic episodes and psychiatric disorders more frequent with semaglutide 2.4 mg

No other unexpected safety findings

Semaglutide is not approved for weight management.

AE, adverse event; GI, gastrointestinal. Davies et al. Lancet 2021;397:971–84.

Summary

In adults with overweight or obesity and type 2 diabetes, once a week semaglutide 2.4 mg as adjunct to lifestyle intervention led to:

- Body weight: 9.6%
- Waist circumference: 9.4 cm
- HbA1c: 1.6%
- Blood pressure: 3.9 mmHg (systolic)

- Safety profile consistent with known effects
- Gastrointestinal AEs
- No unexpected safety findings

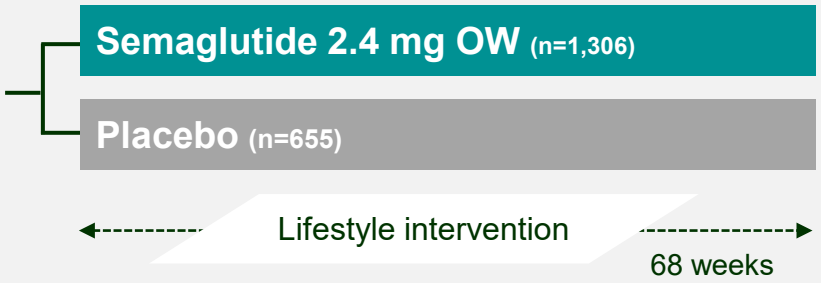
Semaglutide is not approved for weight management.

AE, adverse event; HbA1c, glycated haemoglobin; T2D, type 2 diabetes. Davies et al. Lancet 2021;397:971–84.

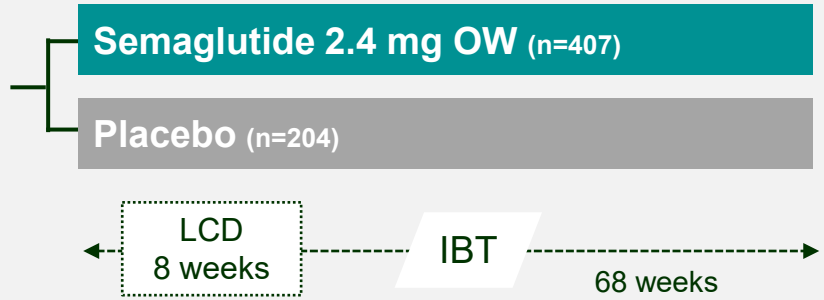
STEP program: Pivotal trials at a glance

4,700 patients in total

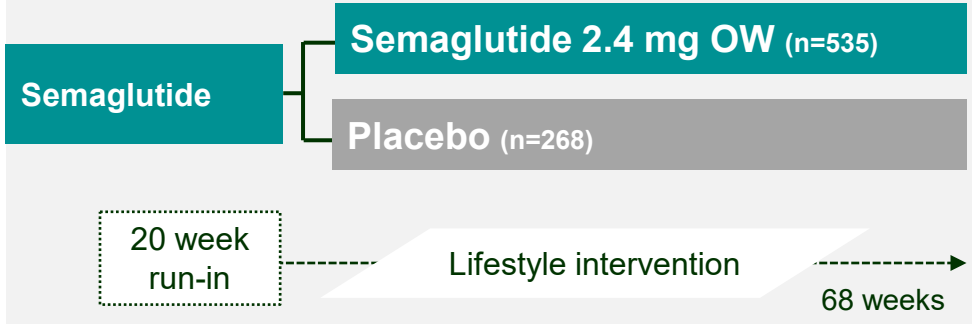
STEP-1 Weight management[1]



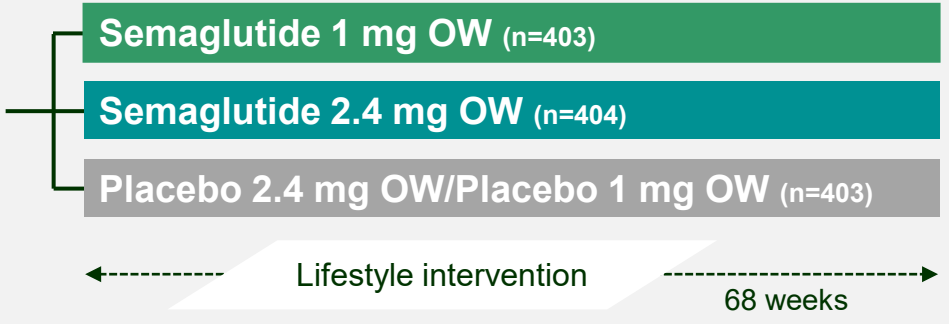
STEP-3 Weight management with IBT[2]



STEP-4 Sustained weight management[3]



STEP-2 Weight management in T2D not on insulin[4]



Lifestyle intervention: –500 kcal/day diet + 150 min/week physical activity. *Participants on sulfonylurea: semaglutide 1.0 mg: 24.6%; semaglutide 2.4 mg: 26.7%; placebo: 24.1%

IBT, intensive behavioural therapy; LCD, low-calorie diet; OW, once-weekly; STEP, Semaglutide Treatment Effect in People with obesity; T2D, type 2 diabetes.

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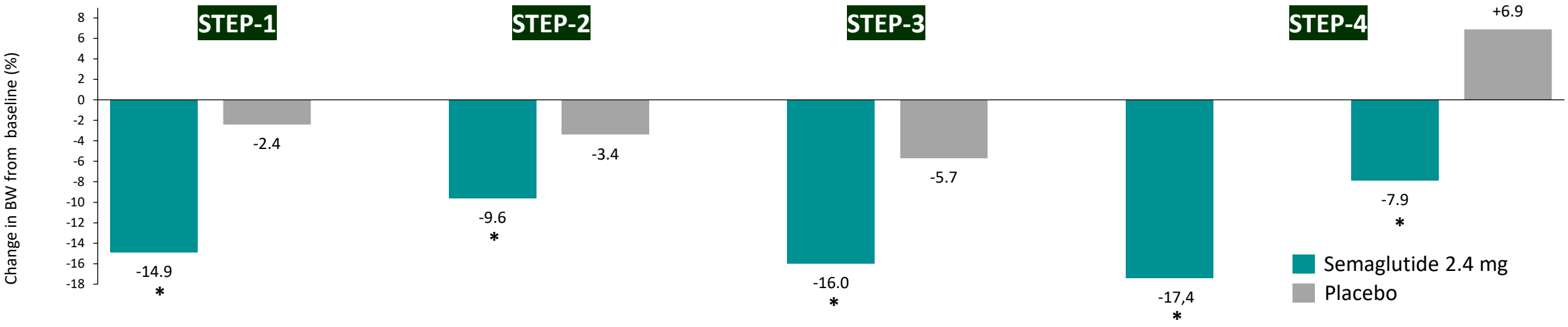
Primary endpoint summary for STEP1–4

	Weight management	Weight management in T2D	Weight management with IBT	Sustained weight management	
Trial details	Adults with obesity or overweight without T2D (n=1961)	Adults with obesity or overweight with T2D (n=1210)	Adults with obesity or overweight, without diabetes adjunct to IBT (n=611)	Adults with obesity or overweight without diabetes reaching target dose during run-in (n=902)	Adults with obesity or overweight without diabetes after run-in (n=803)
Duration and baseline BW	0–68 weeks 105.3 kg	0–68 weeks 99.8 kg	0–68 weeks 105.8 kg	0–68 weeks 107.2 kg	20–68 weeks 96.1 kg



Treatment policy estimand: Evaluates treatment effect regardless of trial product discontinuation and use of rescue medication

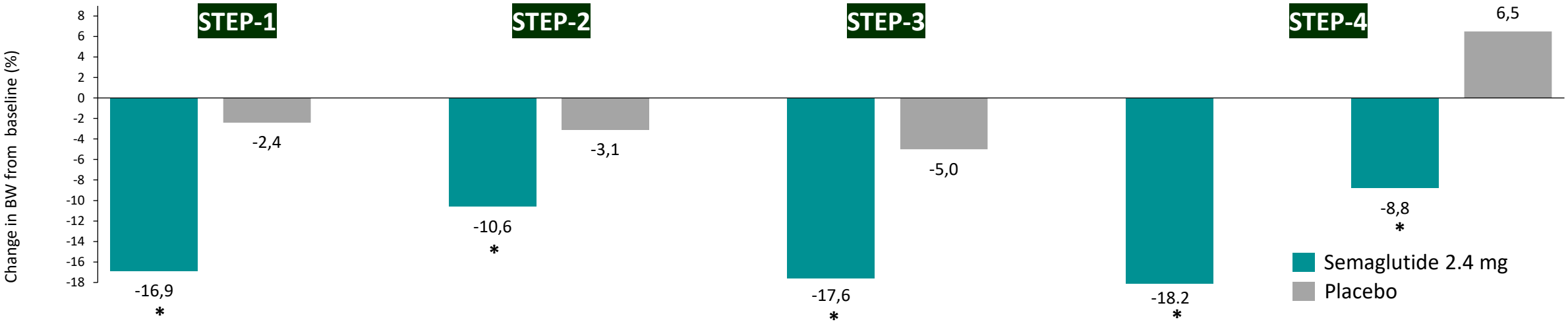
*Lifestyle intervention: –500 kcal/day diet + 150 min/week physical activity. *Participants on sulfonylurea: semaglutide 1.0 mg: 24.6%; semaglutide 2.4 mg: 26.7%; placebo: 24.1%

BW, body weight; IBT, intensive behavioural therapy; LCD, low-calorie diet; OW, once-weekly; STEP, Semaglutide Treatment Effect in People with obesity; T2D, type 2 diabetes.

1. Wilding et al. N Engl J Med 2021;384:989; 2. Wadden et al. JAMA 2021; doi:10.1001/jama.2021.1831; 3. Rubino et al. JAMA 2021; doi:10.1001/jama.2021.3224; 4. Davies et al. Lancet 2021;397:971–84.

Primary endpoint summary for STEP1–4

	Weight management	Weight management in T2D	Weight management with IBT	Sustained weight management	
Trial details	Adults with obesity or overweight without T2D (n=1961)	Adults with obesity or overweight with T2D (n=1210)	Adults with obesity or overweight, without diabetes adjunct to IBT (n=611)	Adults with obesity or overweight without diabetes reaching target dose during run-in (n=902)	Adults with obesity or overweight without diabetes after run-in (n=803)
Duration and baseline BW	0–68 weeks 105.3 kg	0–68 weeks 99.8 kg	0–68 weeks 105.8 kg	0–68 weeks 107.2 kg	20–68 weeks 96.1 kg



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

*Lifestyle intervention: –500 kcal/day diet + 150 min/week physical activity. *Participants on sulfonylurea: semaglutide 1.0 mg: 24.6%; semaglutide 2.4 mg: 26.7%; placebo: 24.1%
BW, body weight; IBT, intensive behavioural therapy; LCD, low-calorie diet; OW, once-weekly; STEP, Semaglutide Treatment Effect in People with obesity; T2D, type 2 diabetes.
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STEP Trials –
Semaglutide in obesity

Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with T2D

Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with type 2 diabetes: A nationwide observational study in England

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Lancet Diabetes Endocrinol 2021
https://doi.org/10.1016/ S2213-8587(21)00050-4

Evidence before this study

- From March 1 to Nov 30, 2020, we did weekly searches of PubMed and medRxiv using the search terms “COVID-19”, “SARS-CoV-2”, “coronavirus”, “SARS virus”, and “diabetes”, restricted to English-language publications
- Smaller retrospective studies from the USA, China, and France have all reported lower or neutral risk of COVID-19-related mortality in people previously or currently prescribed metformin
- A recent meta-analysis of 5 observational studies showed use of metformin before hospital admission in people with diabetes and sepsis (non-COVID-19 related) was associated with lower mortality
- In a small French multicentre observational study, investigators reported no association between use of sulfonylureas, meglitinides, DPP-4 inhibitors, or GLP-1 receptor agonists and COVID-19-related mortality, but higher mortality associated with insulin therapy
- Most previous studies were done at a single centre with a small number of people with T2D, and most studies investigated a small number of glucose-lowering drugs

DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide 1; T2D, type 2 diabetes.
Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Methods

A nationwide observational cohort study

- Data from the National Diabetes Audit for people with T2D and registered with a general practice in England since 2003

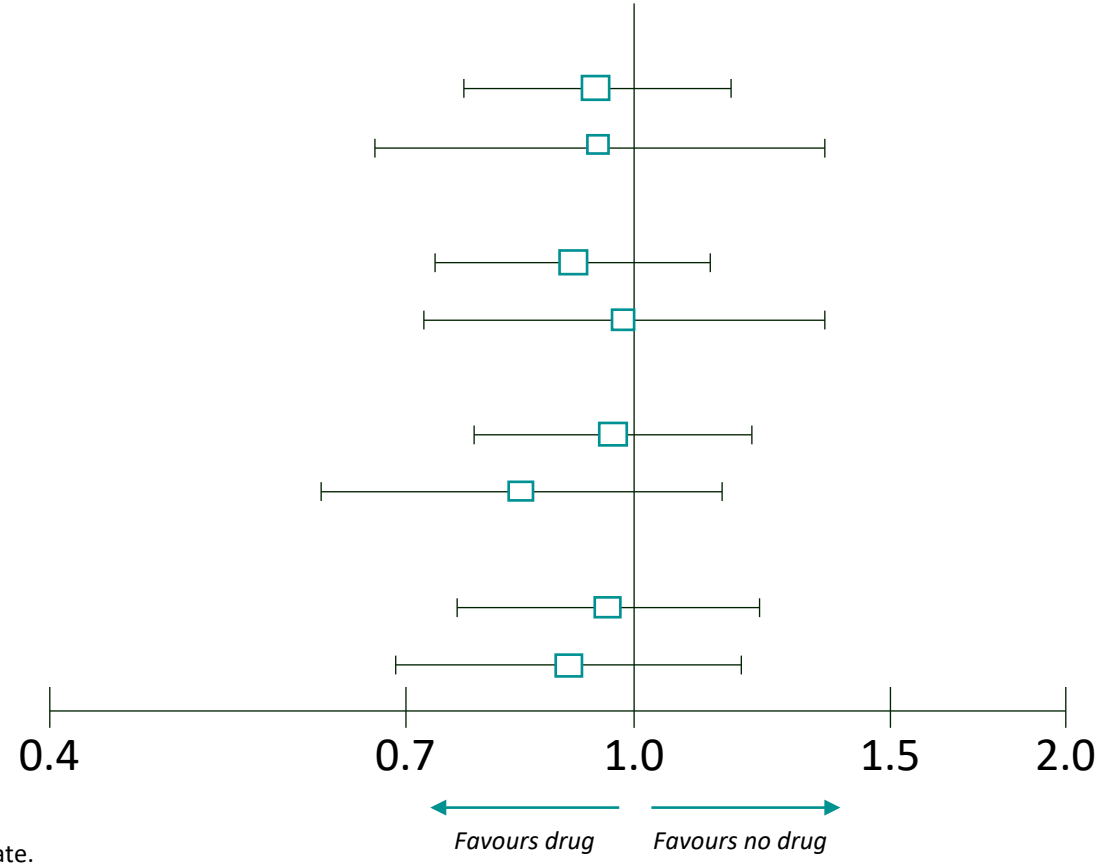
- Cox regression to estimate HR of COVID-19-related mortality in people prescribed each class of glucose-lowering drug
- Covariate adjustment with propensity score to address confounding by demographic, socioeconomic, and clinical factors

HR, hazard ratio; T2D, type 2 diabetes.

Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Results: Thiazolidinediones

	n/N	Adjusted HR (99% CI)
Age, years		
≥70	57/25305	0.94 (0.77–1.16)
<70	169/34775	0.94 (0.66–1.34)
Sex		
Men	154/38095	0.91 (0.73–1.13)
Women	72/21990	0.98 (0.72–1.32)
CV disease history		
No	155/50405	0.97 (0.78–1.20)
Yes	71/9680	0.84 (0.61–1.14)
eGFR, mL/min per 1.73 m^2		
≥60	96/47330	0.96 (0.76–1.22)
<60	128/12030	0.90 (0.69–1.18)

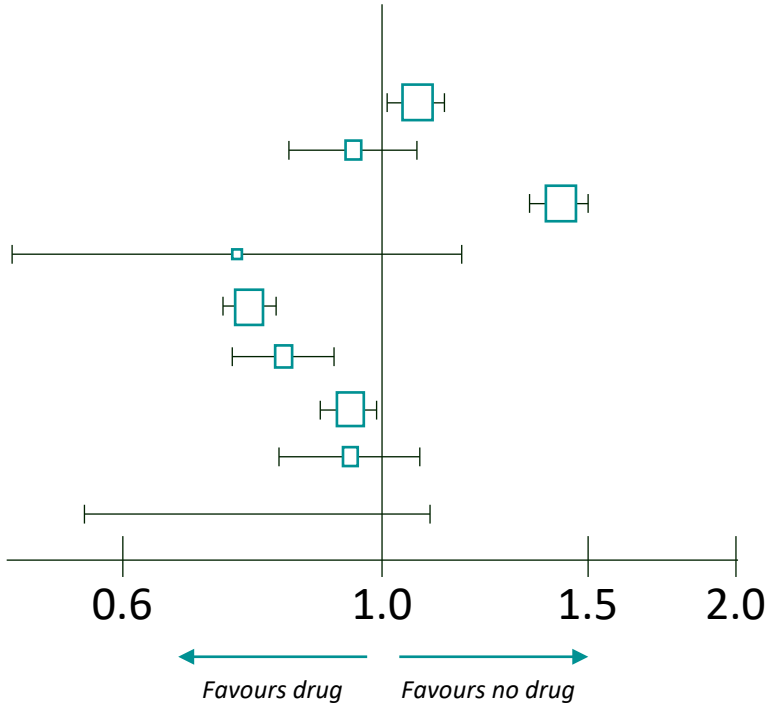


CI, confidence interval; eGFR, estimated glomerular filtration rate.

Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

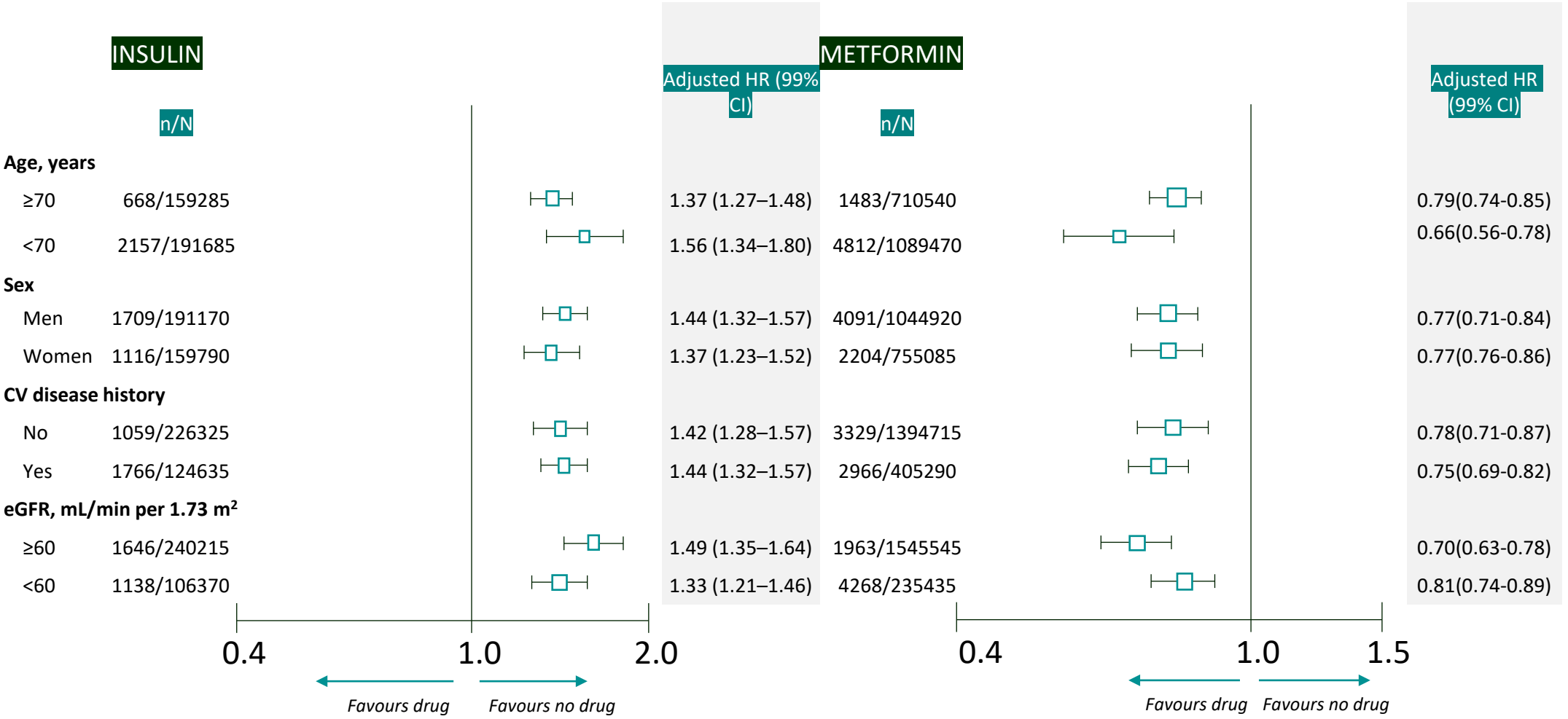
Results: Association between prescription of glucose-lowering drugs and COVID-19 mortality

	n/N	Mortality rate per 1000 person-years		Adjusted HR (95% CI)
		No drug	Drug	
DPP-4 inhibitors	2733/479555	8.5	9.1	1.07 (1.01–1.13)
GLP-1 receptor agonists	279/100820	9.1	8.6	0.94 (0.83–1.07)
Insulin	2825/350960	8.0	11.3	1.42 (1.35–1.49)
Meglitinides	20/4440	8.9	6.7	0.75 (0.48–1.17)
Metformin	6295/1800005	12.9	9.9	0.77 (0.73–0.81)
SGLT2 inhibitors	458/266505	9.5	7.8	0.82 (0.74–0.91)
Sulfonylureas	2628/561290	8.9	8.4	0.94 (0.89–0.99)
Thiazolidinediones	226/60085	8.9	8.3	0.94 (0.82–1.07)
α-Glucosidase inhibitors	15/1665	8.9	11.2	1.26 (0.76–2.09)



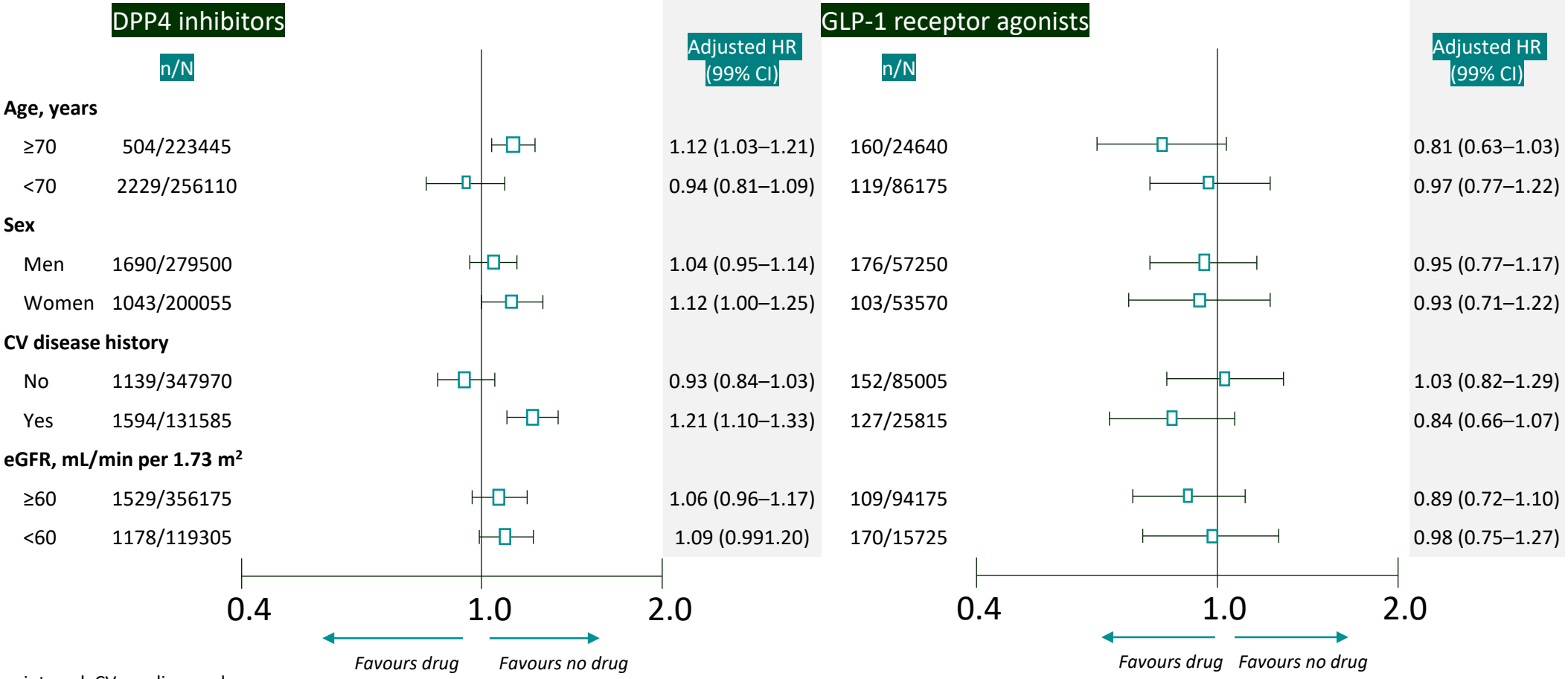
Numbers of people are rounded to the nearest 5 to protect confidentiality. Rates of COVID-19 death in patients prescribed the specific drug are obtained by multiplying the HR by the rate in patients without the prescription of the drug. The size of the box is proportional to the inverse of the variance and the error bars show 95% CIs.
CI, confidence interval; n, number of events (deaths); N, total number of people. Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Results: Insulin and metformin



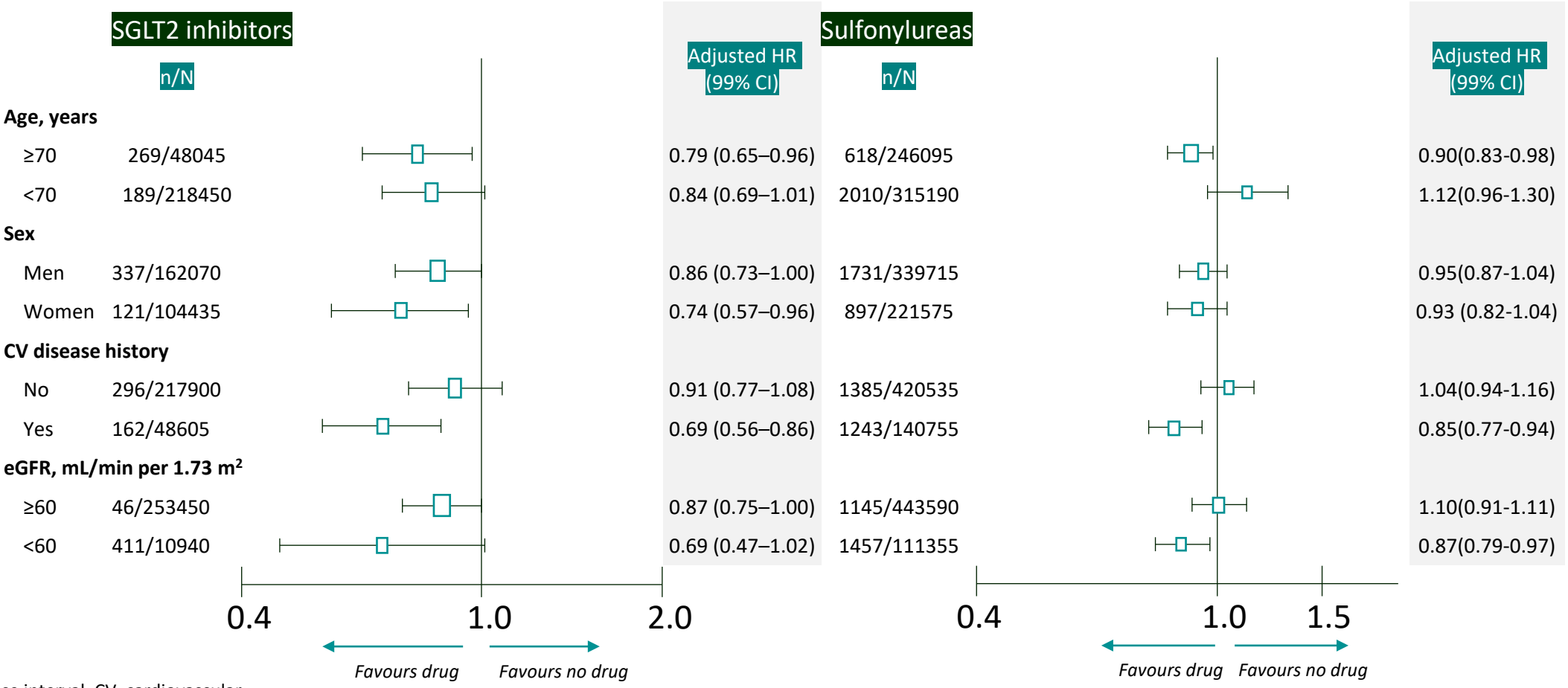
CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio. Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Results: DPP-4i and GLP-1RA



CI, confidence interval; CV, cardiovascular;
DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; GLP-1, glucagon-like peptide 1; HR, hazard ratio. Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Results: SGLT2i and sulfonylurea



CI, confidence interval; CV, cardiovascular;
eGFR, estimated glomerular filtration rate; HR, hazard ratio; SGLT2, Sodium-glucose co-transporter-2. Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Summary

- Among 2,851,465 people with T2D included, 13,479 (0.5%) COVID-19-related deaths occurred during the study period*
  - Corresponding to a rate of 8.9 per 1,000 person-years (95% CI 8.7–9.0)
- Adjusted HR (95% CI) associated with recorded versus no recorded prescription:
  - 0.77 (0.73–0.81) for metformin
  - 1.42 (1.35–1.49) for insulin
  - 0.75 (0.48–1.17) for meglitinides
  - 0.82 (0.74–0.91) for SGLT2 inhibitors
  - 0.94 (0.82–1.07) for thiazolidinediones
  - 0.94 (0.89–0.99) for sulfonylureas
  - 0.94 (0.83–1.07) for GLP-1 receptor agonists
  - 1.07 (1.01–1.13) for DPP-4 inhibitors
  - 1.26 (0.76–2.09) for α-glucosidase inhibitors

*February 16 to August 31, 2020. CI, confidence interval; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide 1; SGLT2, Sodium-glucose co-transporter-2. T2D, type 2 diabetes.
Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Added value of this study

- To our knowledge, this is the largest COVID-19-related population study, covering almost the entire population of people with T2D in England
- We assessed the association of prescriptions for glucose-lowering drugs or drug classes with COVID-related mortality
- People with T2D prescribed metformin, SGLT2 inhibitors, and sulfonylureas had a lower risk of COVID-19-related mortality
- Those prescribed insulin and DPP-4 inhibitors had a higher risk of COVID-19 related mortality (compared with those not prescribed these drugs)
  - These findings are likely due to confounding by indication, in view of the use of different drug classes in early and late stages of the T2D disease trajectory

T2D, type 2 diabetes.
Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

Interpretation

- Our results provide evidence of associations between prescription of some glucose-lowering drugs and COVID-19-related mortality
  - Although the differences in risk are small and these findings are likely to be due to confounding by indication, in view of the use of different drug classes at different stages of T2D disease progression

In the context of the COVID-19 pandemic, there is no clear indication to change prescribing of glucose-lowering drugs in people with T2D

T2D, type 2 diabetes.

Khunti et al. Lancet Diabetes Endocrinol 2021; https://doi.org/10.1016/ S2213-8587(21)00050-4.

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