Tri-City Cardiovascular Symposium

August 17, 2024

Praneet K. Sharma, MD

- Board Certified in Cardiovascular Disease, Interventional Cardiology, Echocardiography, and Internal Medicine, having received his Cardiology training at the Cleveland Clinic.
- Specializes in performing coronary interventions for heart artery blockages, peripheral vascular interventions for blockages in arteries to limbs, peripheral arterial interventions to open blockages in arteries of the limb, and structural interventions for heart valve damage using catheter-based techniques.
- Dr. Sharma has a particular interest in catheter-based treatment of heart artery blockages from the wrist (Radial catheterization). Additionally, he provides venous care, performing interventions for patients with venous insufficiency, such as varicose veins and leg ulcers.
- He is committed to promoting health among people at risk for heart disease through primary prevention before heart and vascular disease occurs, as well as secondary prevention for those who have developed heart disease.

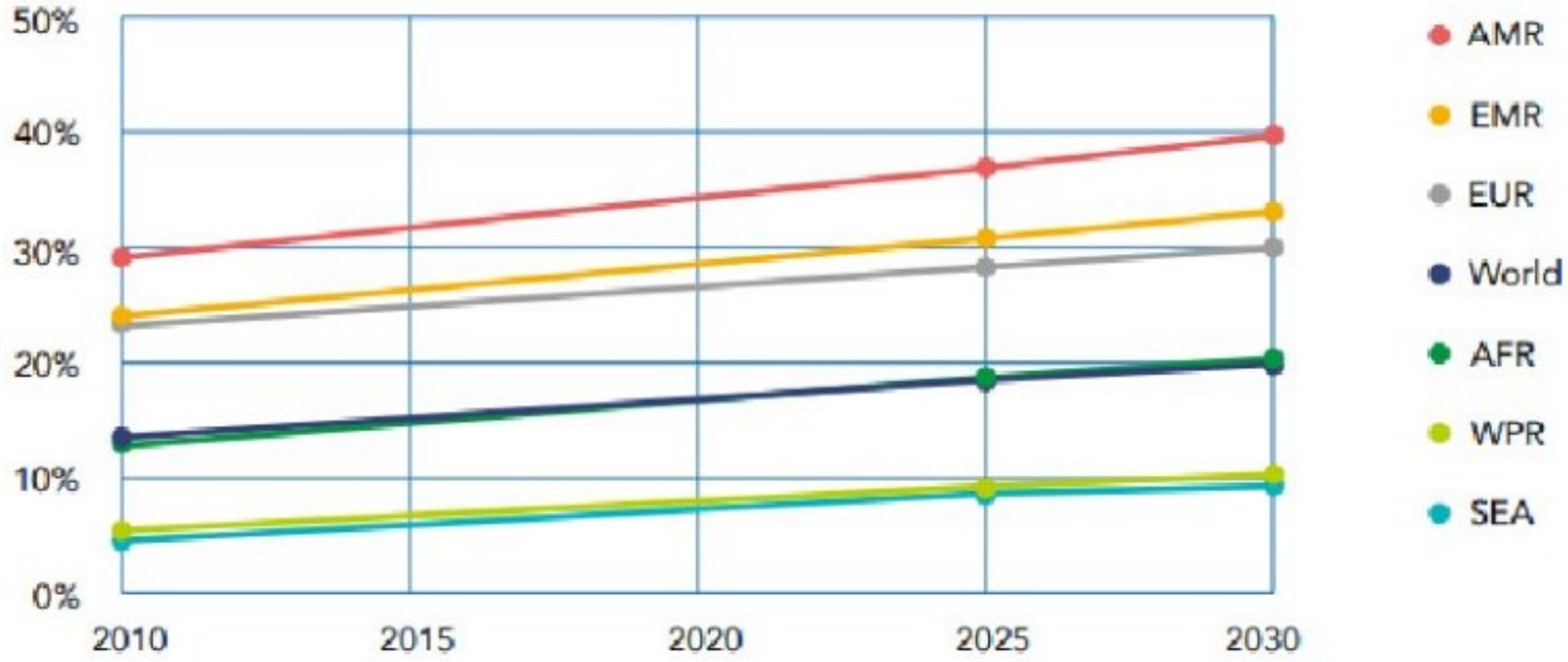
TRI-CITY CARDIOLOGY

Weight Loss Medications and the Effects on Cardiovascular Health

TRI-CITY CARDIOLOGY

Burden of Obesity

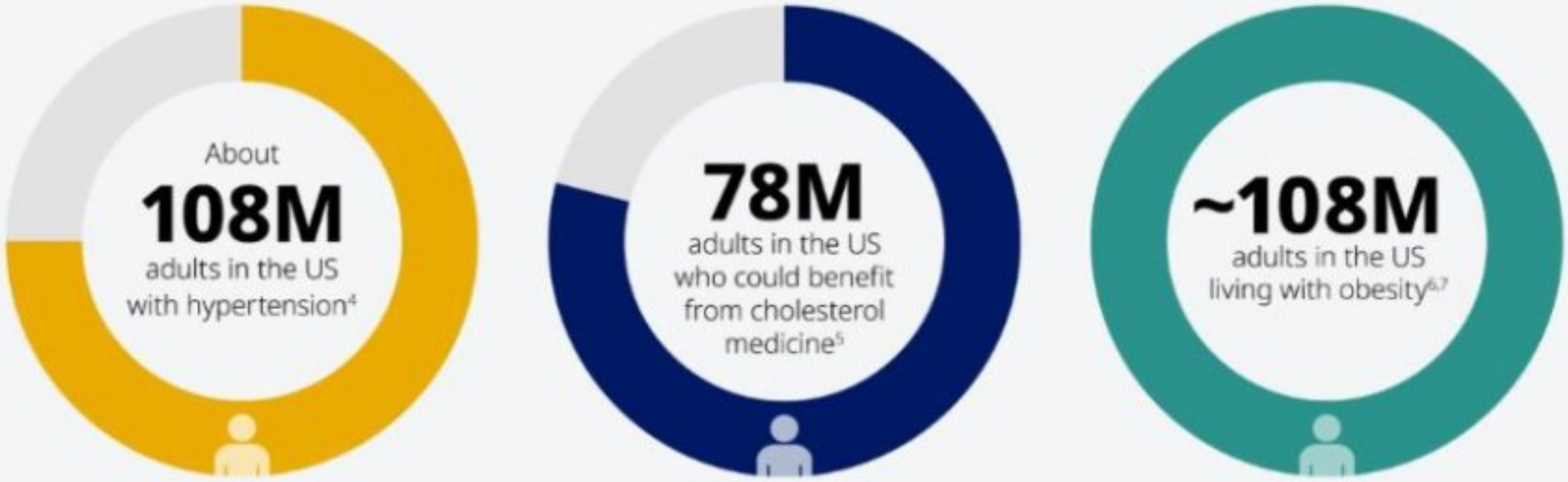
Prevalence of obesity (BMI ≥30kg/m2) amongst women by regions in 2010– 2030



Source: NCD Risk Factor Collaboration (2017) and World Obesity Federation projections

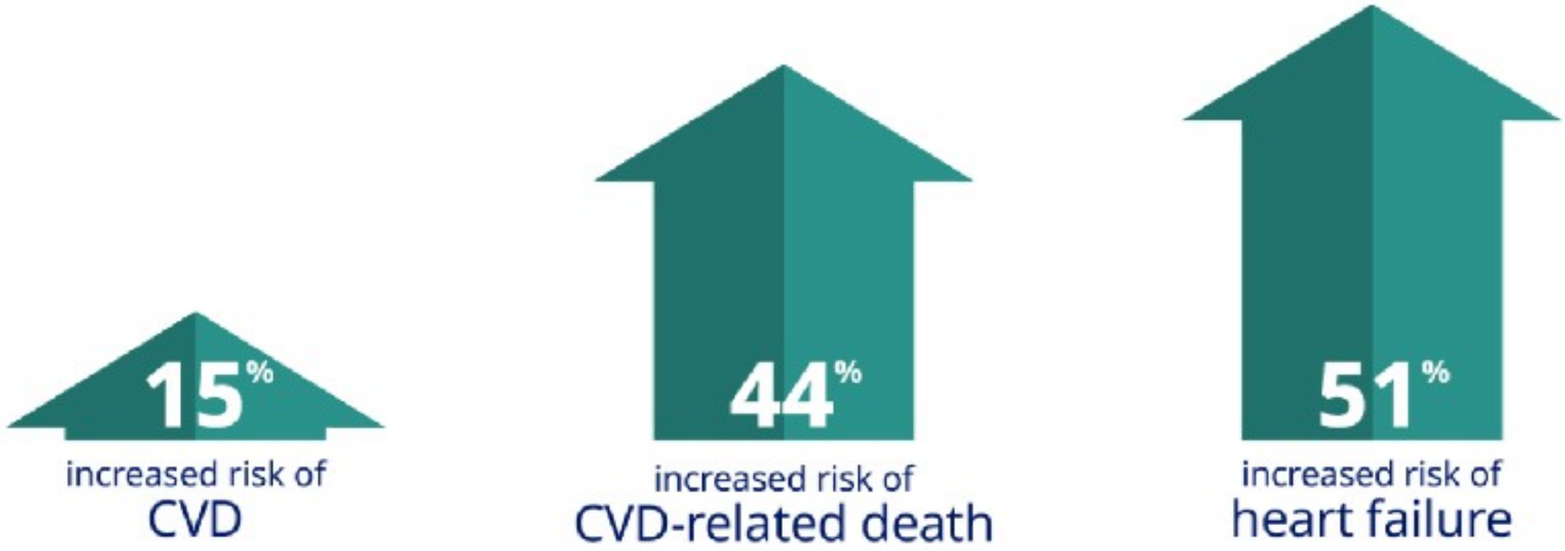
Obesity is not treated in the same way that other chronic and progressive diseases are treated[1]

Millions of adults have health challenges. Obesity is one of the most prevalent.



1. Bray GA, Kim KK, Wilding JPH. Obesity: a chronic relapsing progressive disease. A position statement of the World Obesity Federation. *Obes Rev*. 2017;18(7):715-723.

CVD risks related to Obesity



Iyen B, Weng S, Vinogradova Y, Akyea RK, Qureshi N, Kai J. Long-term body mass index changes in overweight and obese adults and the risk of heart failure, cardiovascular disease and mortality: a cohort study of over 260,000 adults in the UK. BMC Public Health. 2021;21(1):576.

Figure 5. Diagnosis and Medical Management of Obesity

DIAGNOSIS		COMPLICATION-SPECIFIC STAGING AND TREATMENT		
Anthropometric Component (BMI kg/m²)	**Clinical Component**	**Disease Stage**	**Chronic Disease Phase of Prevention**	**Suggested Therapy (based on clinical judgment)**
<25 <23 in certain ethnicities waist circumference below regional/ ethnic cutoffs		**Normal weight** (no obesity)	**Primary**	• **Healthy lifestyle:** healthy meal plan/ physical activity
25–29.9 23–24.9 in certain ethnicities	Evaluate for presence or absence of adiposity-related complications and severity of complications • Metabolic syndrome • Prediabetes • Type 2 diabetes • Dyslipidemia • Hypertension • Cardiovascular disease • Nonalcoholic fatty liver disease • Polycystic ovary syndrome • Female infertility • Male hypogonadism • Obstructive sleep apnea • Asthma/reactive airway disease • Osteoarthritis • Urinary stress incontinence • Gastroesophageal reflux disease • Depression	**Overweight stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions
≥30 ≥25 in certain ethnicities		**Obesity stage 0** (no complications)	**Secondary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to prevent progressive weight gain. (BMI ≥27)
≥25 ≥23 in certain ethnicities		**Obesity stage 1** (1 or more mild-moderate complications)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Weight-loss medications:** Consider after lifestyle therapy fails to achieve therapeutic target or initiate concurrent with lifestyle therapy. (BMI ≥27)
≥25 ≥23 in certain ethnicities		**Obesity stage 2** (at least 1 severe complication)	**Tertiary**	• **Lifestyle therapy:** Reduced-calorie healthy meal plan/physical activity/ behavioral interventions • **Add weight-loss medications:** Initiate concurrent with lifestyle therapy. (BMI ≥27) • **Consider bariatric surgery:** (BMI ≥35)

a. All patients with BMI ≥25 have either overweight stage 0, obesity stage 0, obesity stage 1, or obesity stage 2, depending on the initial clinical evaluation for presence and severity of complications. These patients should be followed over time and evaluated for changes in both anthropometric and clinical diagnostic components. The diagnoses of overweight/obesity stage 0, obesity stage 1, and obesity stage 2 are not static, and disease progression may warrant more aggressive weight-loss therapy in the future. BMI values ≥25 have been clinically confirmed to represent excess adiposity after evaluation for muscularity, edema, sarcopenia, etc.

b. Stages are determined using criteria specific to each obesity-related complication; stage 0 = no complication; stage 1 = mild-to-moderate; stage 2 = severe.

c. Treatment plans should be individualized; suggested interventions are appropriate for obtaining the sufficient degree of weight loss generally required to treat the obesity-related complication(s) at the specified stage of severity.

d. BMI ≥27 is consistent with the prescribing information mandated by the US Food and Drug Administration for weight-loss medications.

Abbreviation: BMI = body mass index.

Endocrine Practice 2016 221-203DOI: (10.4158/EP161365.GL)

Once-Weekly Semaglutide in Adults with Overweight or Obesity

Wilding JPH. et al. DOI: 10.1056/NEJMoa2032183

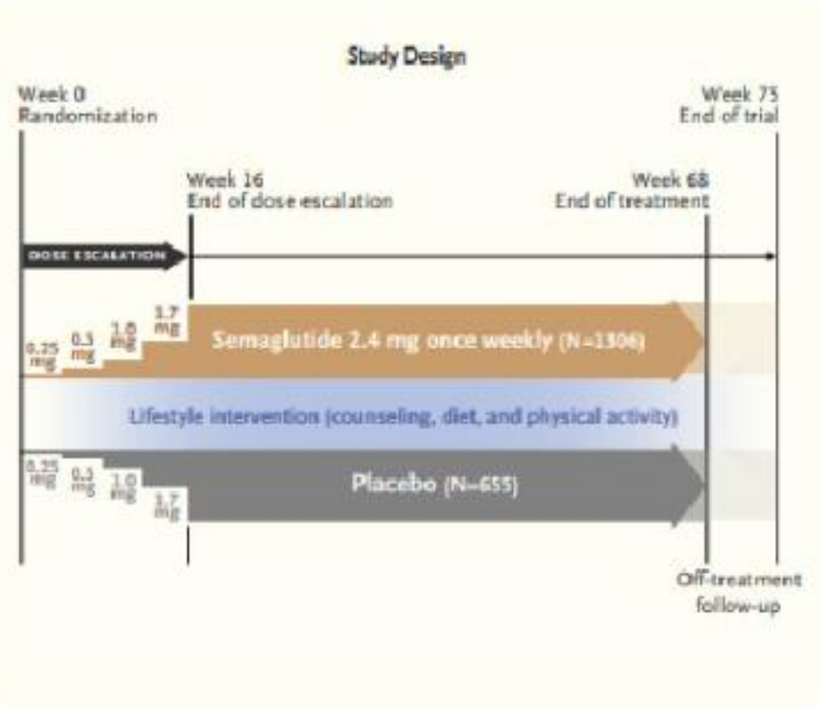
CLINICAL PROBLEM

Clinical guidelines suggest pharmacologic intervention in addition to diet and exercise to promote weight loss among adults with BMI ≥30 (or ≥27 in those with coexisting conditions). Barriers to medication use include limited efficacy, adverse effects, and cost. Subcutaneous semaglutide, a glucagon-like peptide-1 analogue FDA-approved to treat type 2 diabetes in adults, has been accompanied by weight loss in previous clinical trials.

CLINICAL TRIAL

A phase 3, double-blind, randomized, controlled trial comparing semaglutide with placebo, plus lifestyle changes, in overweight or obese adults without diabetes.

1961 participants were assigned to receive 2.4 mg of subcutaneous semaglutide (with gradual increase to the 2.4 mg dose) or placebo weekly for 68 weeks; both groups received a counseling intervention involving diet and exercise. Coprimary end points were percentage change in body weight and weight reduction ≥5%.



TRI-CITY CARDIOLOGY

RESULTS

Efficacy:

By week 68, mean weight declined more with semaglutide than with placebo (14.9% vs. 2.4%; estimated difference, −12.4 percentage points; 95% CI, −13.4 to −11.5). In addition, more participants in the semaglutide group than in the placebo group had weight loss of ≥5% (86.4% vs. 31.5%).

Safety:

Adverse events, mainly gastrointestinal, were most often mild to moderate but led to treatment discontinuation in 7.0% of the semaglutide group and 3.1% of the placebo group. Serious adverse events, primarily gastrointestinal and hepatobiliary events, were reported more often with semaglutide.

LIMITATIONS AND REMAINING QUESTIONS

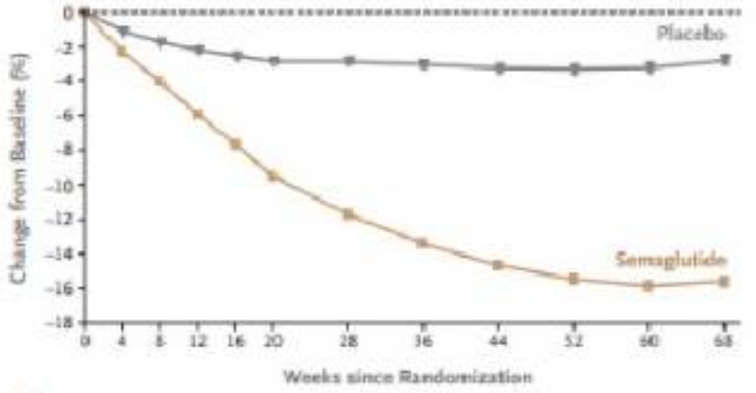
Limitations:

- 43.7% of participants had prediabetes and might have responded differentially to the effects of semaglutide on weight gain.

Further study is required to understand the following:

- Whether results would be similar in persons who differ from the study participants, who were mainly female, White, and potentially highly motivated to lose weight
- Longer-term outcomes
- The mechanism by which semaglutide affects weight-related measures of health (e.g., body composition and glycated hemoglobin) in patients without diabetes

Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk

Placebo	655	649	641	639	635	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

CONCLUSIONS

Adults without diabetes who were overweight or obese had clinically relevant weight loss with weekly injections of semaglutide (2.4 mg) added to lifestyle changes.

TRI-CITY CARDIOLOGY

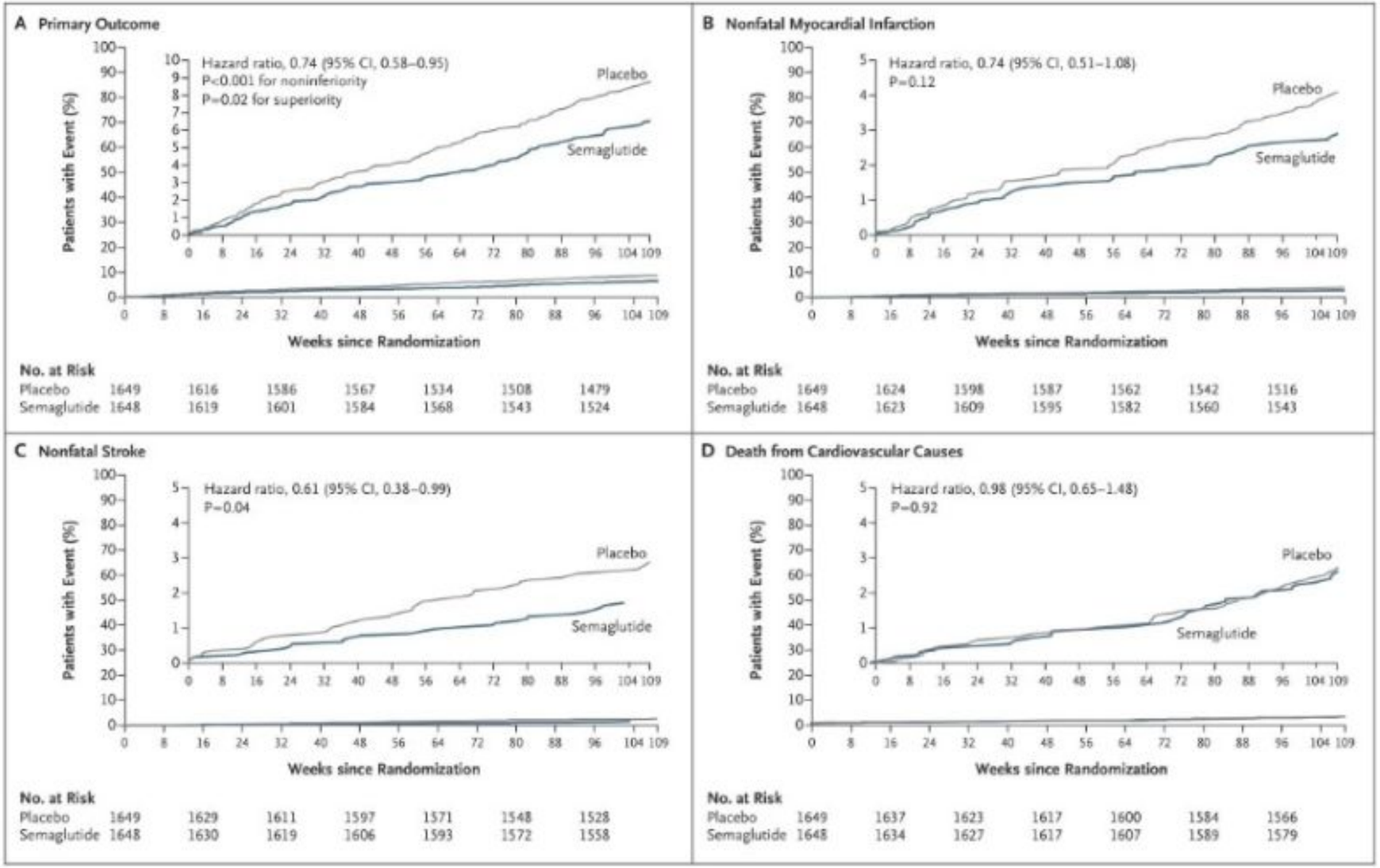
Original Article

Steven P. Marso, M.D., Stephen C. Bain, M.D., Agostino Consoli, M.D., Freddy G. Eliaschewitz, M.D., Esteban Jódar, M.D., Lawrence A. Leiter, M.D., Ildiko Lingvay, M.D., M.P.H., M.S.C.S., Julio Rosenstock, M.D., Jochen Seufert, M.D., Ph.D., Mark L. Warren, M.D., Vincent Woo, M.D., Oluf Hansen, M.Sc., Anders G. Holst, M.D., Ph.D., Jonas Pettersson, M.D., Ph.D., Tina Vilsbøll, M.D., D.M.Sc., for the SUSTAIN-6 Investigators

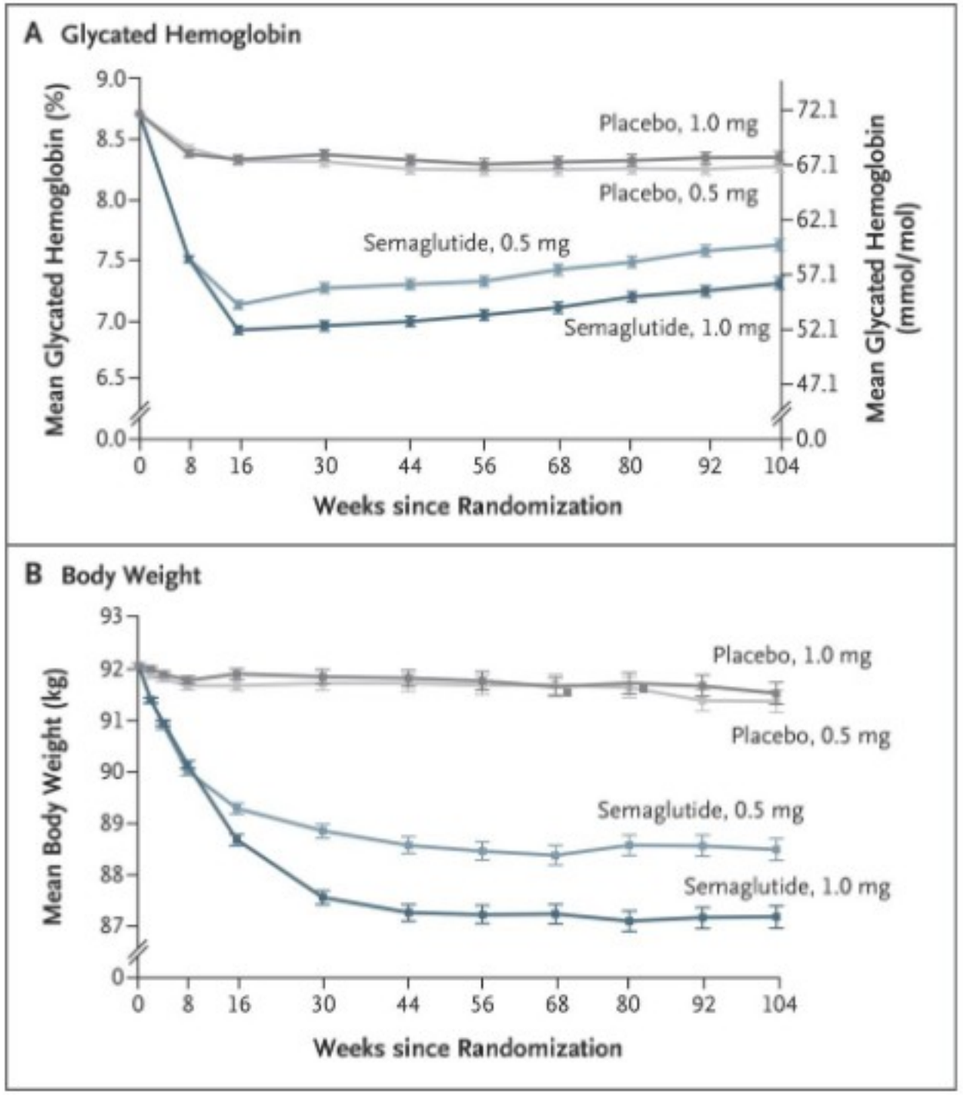
N Engl J Med

- Patients with type 2 diabetes at high cardiovascular risk received either once-weekly semaglutide, a glucagon-like peptide 1 analogue, or placebo.
- Randomly assigned 3297 patients with type 2 diabetes who were on a standard-care regimen to receive once-weekly semaglutide (0.5 mg or 1.0 mg) or placebo for 104 weeks.
- The primary composite outcome was the first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

Cardiovascular Outcomes.



Glycated Hemoglobin and Body Weight.



Characteristics of the Patients at Baseline.

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Semaglutide (N=1648)		Placebo (N=1649)		Total (N=3297)
	0.5 mg (N=826)	1.0 mg (N=822)	0.5 mg (N=824)	1.0 mg (N=825)	
Age — yr	64.6±7.3	64.7±7.1	64.8±7.6	64.4±7.5	64.6±7.4
Male sex — no. (%)	495 (59.9)	518 (63.0)	482 (58.5)	507 (61.5)	2002 (60.7)
Body weight — kg	91.8±20.3	92.9±21.1	91.8±20.3	91.9±20.8	92.1±20.6
Type 2 diabetes					
Duration — yr	14.3±8.2	14.1±8.2	14.0±8.5	13.2±7.4	13.9±8.1
Glycated hemoglobin — %	8.7±1.4	8.7±1.5	8.7±1.5	8.7±1.5	8.7±1.5
Cardiovascular risk factors					
Systolic blood pressure — mm Hg	136.1±18.0	135.8±17.0	135.8±16.2	134.8±17.5	135.6±17.2
Diastolic blood pressure — mm Hg	77.1±9.8	76.9±10.2	77.5±9.9	76.7±10.2	77.0±10.0
Low-density lipoprotein cholesterol — mg/dl†	81.6±47.1	83.3±41.2	80.9±48.1	83.6±45.9	82.3±45.6
Never smoked — no. (%)	390 (47.2)	364 (44.3)	391 (47.5)	348 (42.2)	1493 (45.3)
History of cardiovascular disease — no. (%)					
Ischemic heart disease	493 (59.7)	495 (60.2)	510 (61.9)	496 (60.1)	1994 (60.5)
Myocardial infarction	266 (32.2)	264 (32.1)	267 (32.4)	275 (33.3)	1072 (32.5)
Heart failure	201 (24.3)	180 (21.9)	190 (23.1)	206 (25.0)	777 (23.6)
Ischemic stroke	89 (10.8)	89 (10.8)	96 (11.7)	109 (13.2)	383 (11.6)
Hemorrhagic stroke	28 (3.4)	24 (2.9)	27 (3.3)	29 (3.5)	108 (3.3)
Hypertension	772 (93.5)	771 (93.8)	756 (91.7)	760 (92.1)	3059 (92.8)

* Plus–minus values are means ±SD unless otherwise indicated. Differences in baseline characteristics were assessed with the use of analysis of covariance for continuous characteristics and logistic regression for categorical characteristics. There were no significant differences between the groups except for the duration of type 2 diabetes (P=0.048). To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

† Values are geometric means and coefficients of variation.

Secondary Cardiovascular and Microvascular Outcomes.

Table 2. Primary and Secondary Cardiovascular and Microvascular Outcomes.

Outcome	Semaglutide (N=1648)		Placebo (N=1649)		Hazard Ratio (95% CI)*	P Value
	no. (%)	*no./100 person-yr*	*no. (%)*	*no./100 person-yr*		
Primary composite outcome†	108 (6.6)	3.24	146 (8.9)	4.44	0.74 (0.58–0.95)	<0.001 for noninferiority; 0.02 for superiority
Expanded composite outcome‡	199 (12.1)	6.17	264 (16.0)	8.36	0.74 (0.62–0.89)	0.002
All-cause death, nonfatal myocardial infarction, or nonfatal stroke	122 (7.4)	3.66	158 (9.6)	4.81	0.77 (0.61–0.97)	0.03
Death						
From any cause	62 (3.8)	1.82	60 (3.6)	1.76	1.05 (0.74–1.50)	0.79
From cardiovascular cause	44 (2.7)	1.29	46 (2.8)	1.35	0.98 (0.65–1.48)	0.92
Nonfatal myocardial infarction	47 (2.9)	1.40	64 (3.9)	1.92	0.74 (0.51–1.08)	0.12
Nonfatal stroke	27 (1.6)	0.80	44 (2.7)	1.31	0.61 (0.38–0.99)	0.04
Hospitalization for unstable angina pectoris	22 (1.3)	0.65	27 (1.6)	0.80	0.82 (0.47–1.44)	0.49
Revascularization	83 (5.0)	2.50	126 (7.6)	3.85	0.65 (0.50–0.86)	0.003
Hospitalization for heart failure	59 (3.6)	1.76	54 (3.3)	1.61	1.11 (0.77–1.61)	0.57
Retinopathy complications§	50 (3.0)	1.49	29 (1.8)	0.86	1.76 (1.11–2.78)	0.02
New or worsening nephropathy¶	62 (3.8)	1.86	100 (6.1)	3.06	0.64 (0.46–0.88)	0.005

* Hazard ratios and P values were estimated with the use of a Cox proportional-hazards model with the study treatments as fixed factors and stratified according to all combinations of stratification factors used in the randomization.

† The primary composite outcome was the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

‡ The expanded composite outcome included death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, revascularization (coronary or peripheral), and hospitalization for unstable angina or heart failure.

§ Retinopathy complications include vitreous hemorrhage, onset of diabetes-related blindness, and the need for treatment with an intravitreal agent or retinal photocoagulation.

¶ New or worsening nephropathy includes persistent macroalbuminuria, persistent doubling of the serum creatinine level and a creatinine clearance of less than 45 ml per minute per 1.73 m^2 of body-surface area (according to the Modification of Diet in Renal Disease criteria), or the need for continuous renal-replacement therapy.

Selected Adverse Events.

Table 3. Selected Adverse Events.*

Event	Semaglutide		Placebo	
	0.5 mg (N=816)	1.0 mg (N=822)	0.5 mg (N=824)	1.0 mg (N=825)
	number of patients (percent)			
Adverse event	740 (80.6)	732 (80.1)	748 (90.8)	736 (89.2)
Serious adverse event†	289 (33.8)	276 (33.6)	329 (39.9)	298 (36.1)
Severe adverse event‡	200 (24.2)	207 (25.2)	216 (26.2)	194 (23.5)
Adverse event leading to treatment discontinuation	95 (11.5)	119 (14.5)	47 (5.7)	63 (7.6)
Nausea	18 (2.2)	38 (4.6)	2 (0.2)	2 (0.2)
Vomiting	14 (1.7)	23 (2.8)	3 (0.4)	2 (0.2)
Diarrhea	15 (1.8)	19 (2.3)	5 (0.6)	2 (0.2)
Gastrointestinal disorder§	419 (50.7)	430 (52.3)	294 (35.7)	290 (35.2)
Diarrhea	148 (17.9)	151 (18.4)	98 (11.9)	87 (10.5)
Nausea	143 (17.3)	180 (21.9)	62 (7.5)	67 (8.1)
Vomiting	87 (10.5)	122 (14.8)	43 (5.2)	34 (4.1)
Cardiac disorder§	173 (20.9)	150 (18.2)	189 (22.9)	173 (21.0)
Atrial fibrillation	27 (3.3)	23 (2.8)	32 (3.9)	26 (3.2)
Acute pancreatitis¶	6 (0.7)	3 (0.4)	3 (0.4)	9 (1.1)
Gallbladder disorder§	32 (3.9)	26 (3.2)	38 (4.6)	23 (2.8)
Cholelithiasis	21 (2.5)	17 (2.1)	19 (2.3)	12 (1.5)
Acute cholecystitis	4 (0.5)	0	6 (0.7)	2 (0.2)
Severe or symptomatic hypoglycemic event‖**	191 (23.1)	178 (21.7)	177 (21.5)	173 (21.0)
Acute renal failure§	42 (5.1)	23 (2.8)	34 (4.1)	35 (4.2)
Allergic reaction§	49 (5.9)	49 (6.0)	46 (5.6)	57 (6.9)
Injection-site reaction§	8 (1.0)	9 (1.1)	9 (1.1)	12 (1.5)
Neoplasm¶	66 (8.0)	89 (10.8)	70 (8.5)	69 (8.4)
Benign	40 (4.8)	54 (6.6)	36 (4.4)	34 (4.1)
Premalignant	4 (0.5)	6 (0.7)	3 (0.4)	2 (0.2)
Malignant				
Any	26 (3.1)	40 (4.9)	35 (4.2)	35 (4.2)
Pancreatic	0	1 (0.1)	2 (0.2)	2 (0.2)

* Adverse events were selected on the basis of the safety areas of interest for GLP-1–receptor agonists. All data are based on investigator-reported adverse events unless otherwise specified. All data were reported during the trial, except for adverse events leading to treatment discontinuation, which are reported on an as-treated basis. A complete list of serious adverse events according to system organ class is provided in Table S10 in the Supplementary Appendix.

† A serious adverse event was defined as death, a life-threatening episode, hospitalization or prolongation of existing hospitalization, a persistent or substantial disability or incapacity, or an event otherwise considered to be an important medical event.

‡ A severe adverse event was defined as an event that considerably interferes with the patient's daily activities and is unacceptable.

§ This category was defined according to the system organ class in the *Medical Dictionary for Regulatory Activities* (MedDRA).

¶ This event was confirmed by the event-adjudication committee.

‖ This category was based on the group of preferred terms in MedDRA.

** This category of hypoglycemic event includes episodes of severe hypoglycemia (defined according to the American Diabetes Association criteria) or symptomatic hypoglycemia as confirmed on plasma glucose testing (≤56 mg per deciliter [3.1 mmol per liter]).

- In patients with type 2 diabetes who were at high cardiovascular risk, the rate of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke was significantly lower among patients receiving semaglutide than among those receiving placebo, an outcome that confirmed the noninferiority of semaglutide.

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Lincoff AM et al. DOI: 10.1056/NEJMoa2307563

CLINICAL PROBLEM

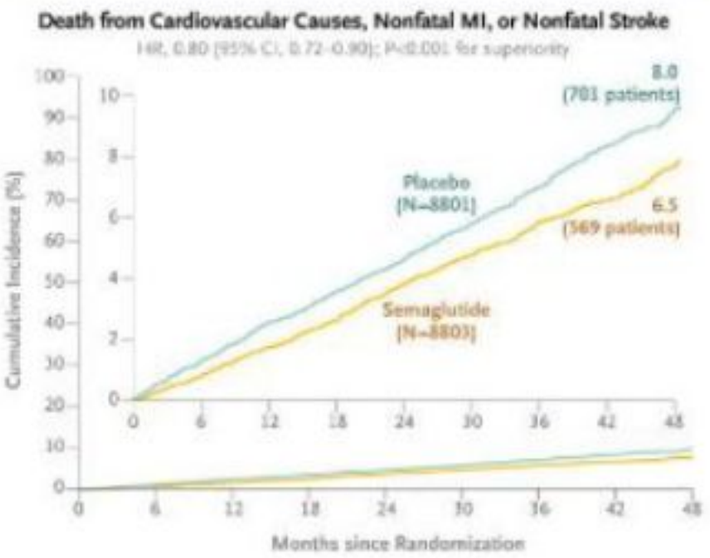
Glucagon-like peptide-1 (GLP-1) receptor agonists can reduce the risk of adverse cardiovascular events in patients with diabetes. Whether the GLP-1 receptor agonist semaglutide can also reduce cardiovascular risk in patients with overweight or obesity but without diabetes is unknown.

CLINICAL TRIAL

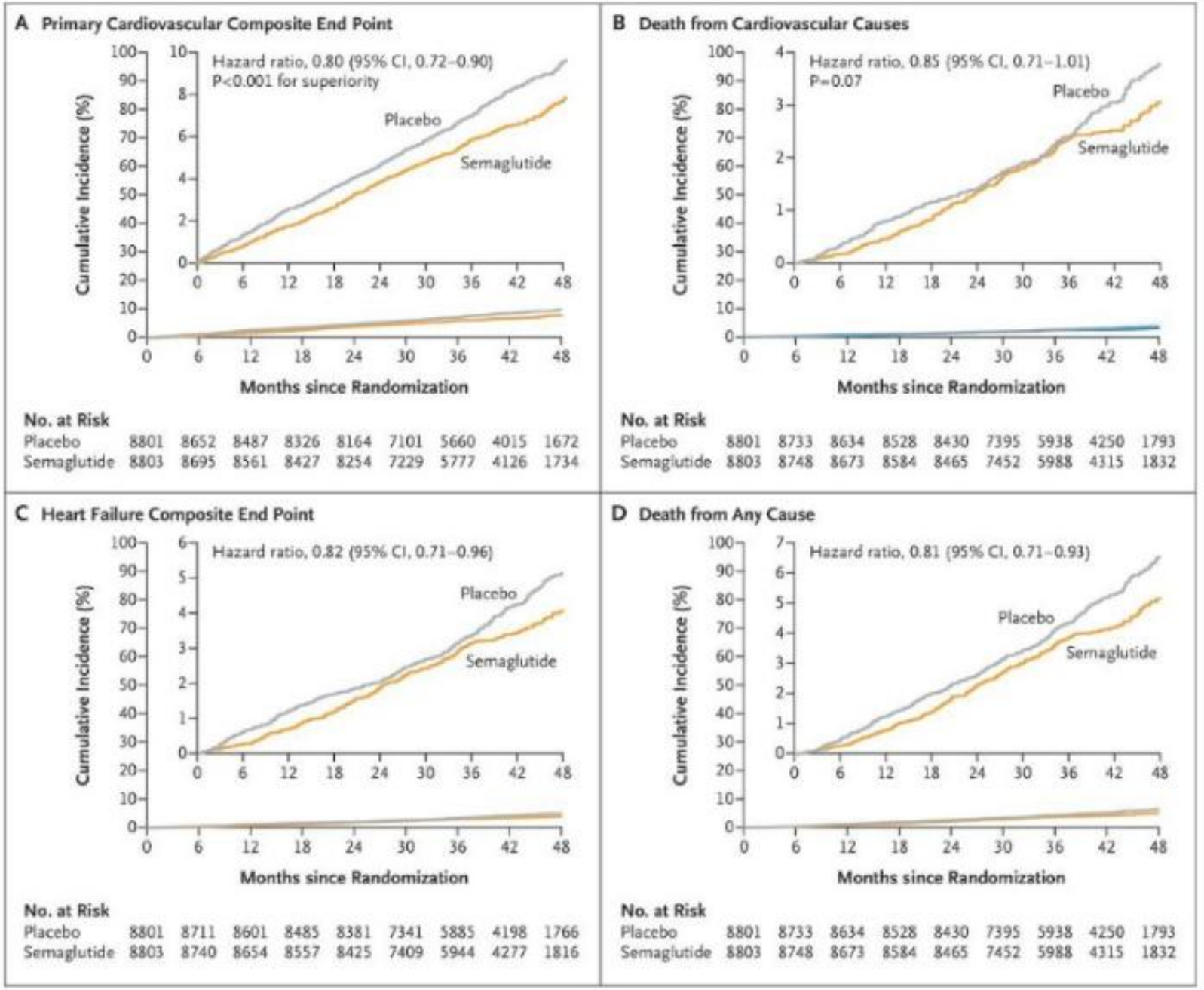
Design: An international, double-blind, event-driven, randomized, placebo-controlled, superiority trial assessed the safety and efficacy of semaglutide in patients with preexisting cardiovascular disease, overweight or obesity (body-mass index, ≥27), and no history of diabetes.

Intervention: 17,604 adults ≥45 years of age were assigned to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo. The primary cardiovascular end point was a composite of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in a time-to-event analysis.

RESULTS



TRI-CITY CARDIOLOGY



TRI-CITY CARDIOLOGY

Event	Semaglutide (N=8803)	Placebo (N=8801)	P Value†
	no. of patients (%)		
Serious adverse events‡	2941 (33.4)	3204 (36.4)	<0.001
Cardiac disorders	1008 (11.5)	1184 (13.5)	<0.001
Infections and infestations	624 (7.1)	738 (8.4)	0.001
Nervous system disorders	444 (5.0)	496 (5.6)	0.08
Surgical and medical procedures	433 (4.9)	548 (6.2)	<0.001
Neoplasms benign, malignant, and unspecified	405 (4.6)	402 (4.6)	0.91
Gastrointestinal disorders	342 (3.9)	323 (3.7)	0.48
Adverse events leading to permanent discontinuation of trial product, irrespective of seriousness‡	1461 (16.6)	718 (8.2)	<0.001
Gastrointestinal disorders	880 (10.0)	172 (2.0)	<0.001
Nervous system disorders	124 (1.4)	92 (1.0)	0.03
Metabolism and nutrition disorders	108 (1.2)	27 (0.3)	<0.001
General disorders and administration-site conditions	105 (1.2)	47 (0.5)	<0.001
Neoplasms benign, malignant, and unspecified	80 (0.9)	105 (1.2)	0.07
Infections and infestations	75 (0.9)	84 (1.0)	0.47
Prespecified adverse events of special interest, irrespective of seriousness§			
Covid-19–related events	2108 (23.9)	2150 (24.4)	0.46
Malignant neoplasms	422 (4.8)	418 (4.7)	0.92
Gallbladder-related disorders	246 (2.8)	203 (2.3)	0.04
Acute kidney failure	171 (1.9)	200 (2.3)	0.13
Acute pancreatitis¶	17 (0.2)	24 (0.3)	0.28

Tirzepatide Once Weekly for the Treatment of Obesity

Jastreboff AM et al. DOI: 10.1056/NEJMoa2206038

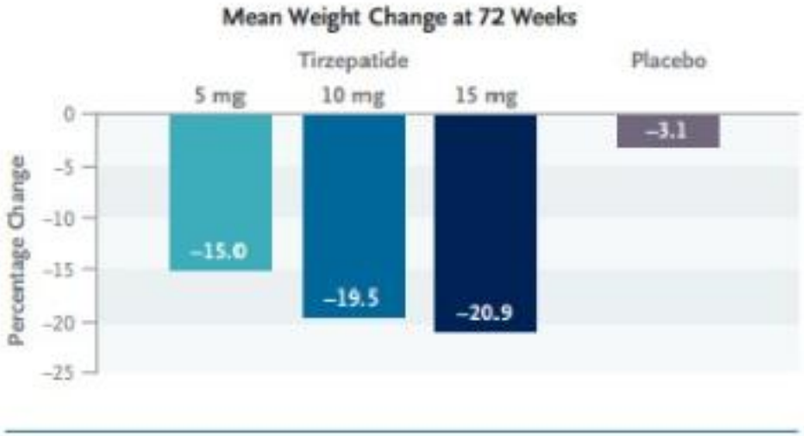
CLINICAL PROBLEM

Several clinical guidelines recommend pharmacotherapy for obesity. Tirzepatide — a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist recently approved in the United States to treat type 2 diabetes — induced clinically relevant weight reduction in phase 2 studies of people with diabetes. However, its efficacy for weight reduction in those without diabetes is unknown.

CLINICAL TRIAL

Design: An international, phase 3, double-blind, randomized, placebo-controlled trial examined the efficacy and safety of tirzepatide in adults with obesity or overweight who did not have diabetes.

Intervention: 2539 adults with a body-mass index of 30 or higher, or 27 or higher with at least one weight-related complication, were assigned to once-weekly subcutaneous tirzepatide at one of three doses (5 mg, 10 mg, or 15 mg) or placebo, in addition to lifestyle intervention. Treatment included a dose-escalation phase and lasted for 72 weeks. The coprimary end points were the percentage change in weight from baseline to week 72 and weight reduction of at least 5% by week 72.



TRI-CITY CARDIOLOGY

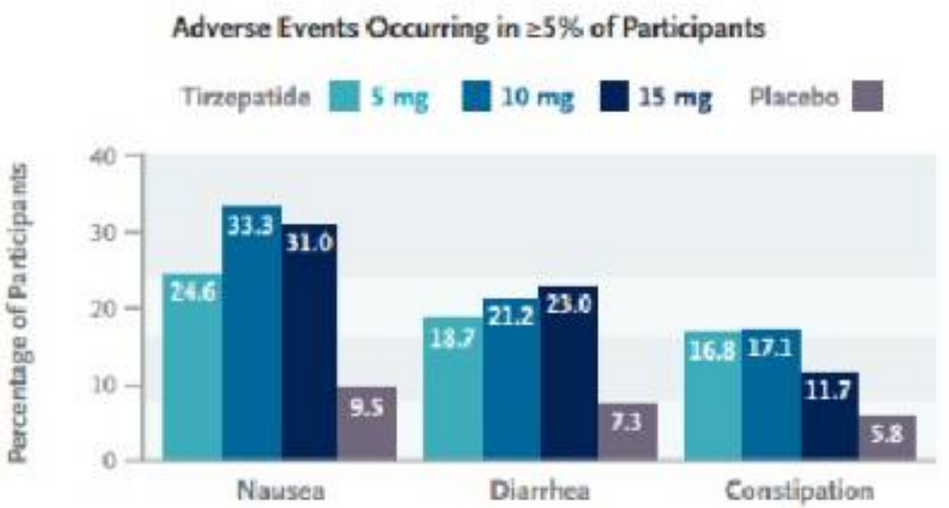
RESULTS

Efficacy: Both the percentage change in weight and the percentage of participants with at least 5% weight reduction were significantly greater with all three doses of tirzepatide than with placebo.

Safety: Gastrointestinal events, including nausea, diarrhea, and constipation, were the most common adverse events seen with tirzepatide; the majority of events were transient and mild to moderate in severity.

LIMITATIONS AND REMAINING QUESTIONS

- Enrolled participants may have been more committed to weight management than many people with obesity.
- Cardiometabolic variables (e.g., blood pressure and lipid levels) were relatively normal at baseline, so the ability to show a potential improvement within the time frame of this study was limited.
- The number of participants with overweight plus at least one weight-related complication was small (140 of the 2539 participants; 5.5%), which prevented definitive conclusions in this subgroup.



CONCLUSIONS

All three doses of once-weekly subcutaneous tirzepatide led to clinically meaningful and sustained weight reduction in obese adults who did not have diabetes.

TRI-CITY CARDIOLOGY

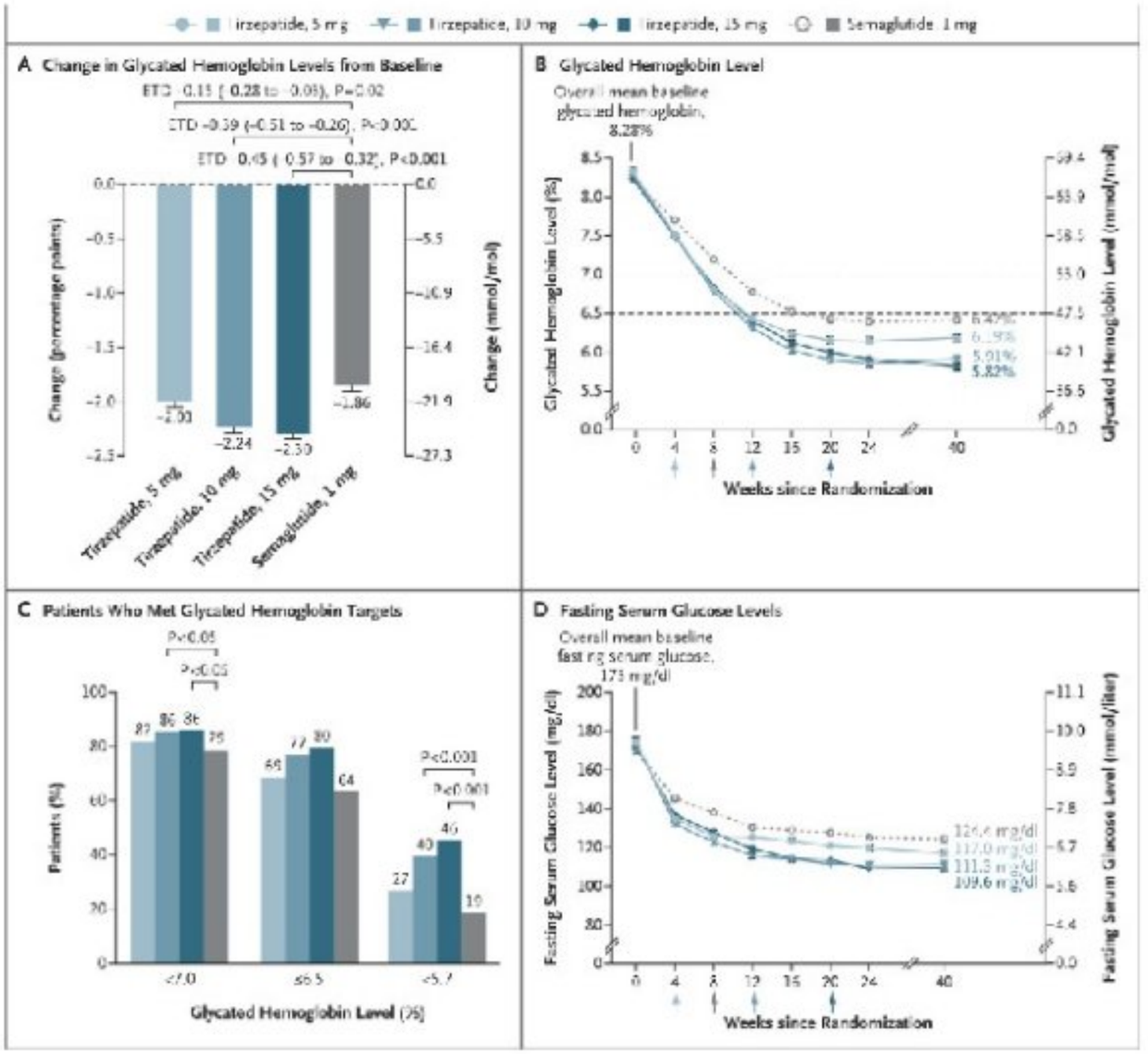
Tirzepatide vs. Semaglutide Once Weekly in Patients with Type 2 Diabetes

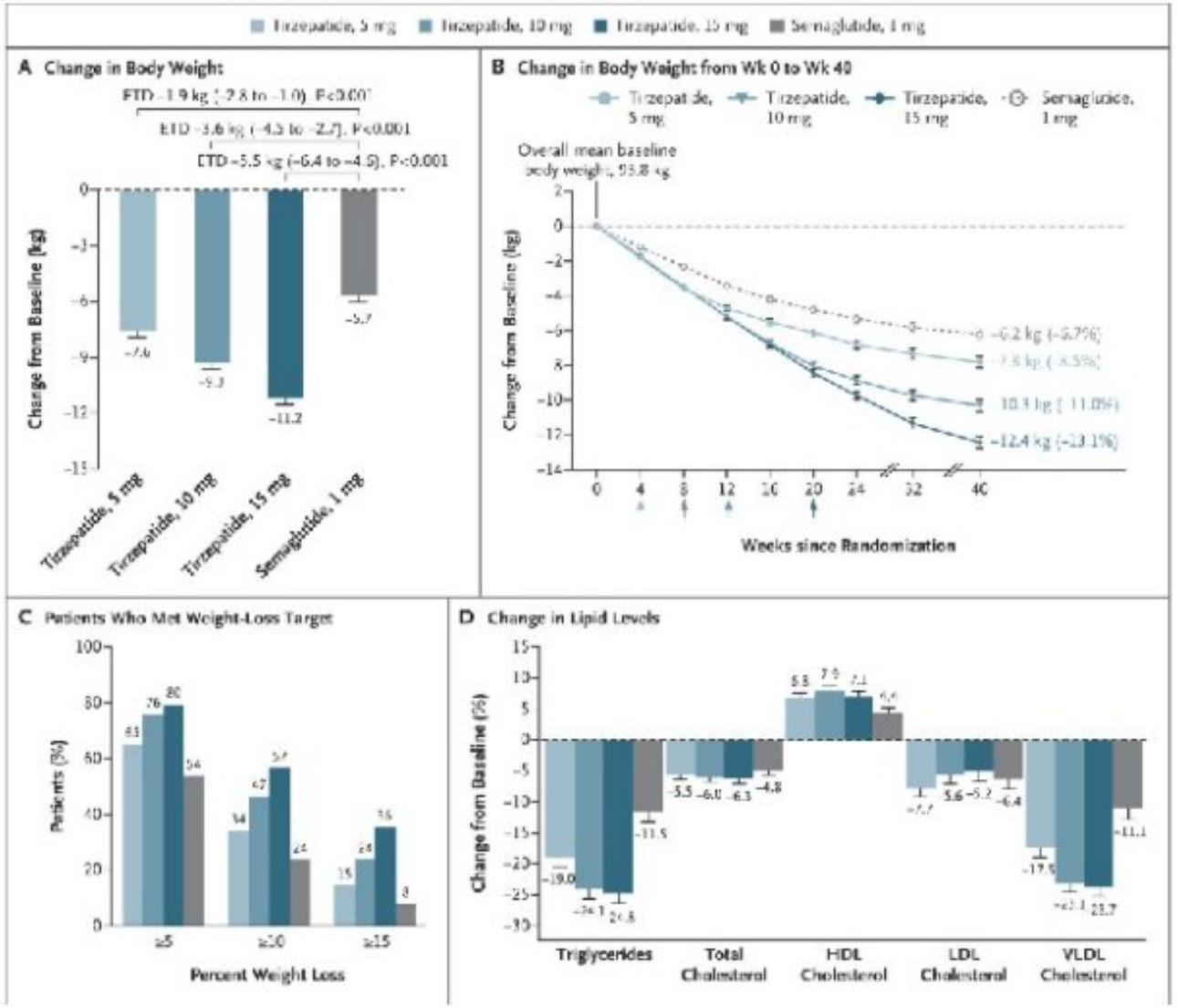
Frías JP et al. DOI: 10.1056/NEJMoa2107519

CLINICAL PROBLEM

Not all patients with type 2 diabetes have adequate glucose control with metformin monotherapy. Tirzepatide is a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist under development for treatment of diabetes; how it compares with the selective GLP-1 receptor agonist semaglutide is unknown.

TRI-CITY CARDIOLOGY


Tirzepatide, 5 mg
Tirzepatide, 10 mg
Tirzepatide, 15 mg
Semaglutide, 1 mg
A Change in Glycated Hemoglobin Levels from Baseline
ETD −0.15 (−0.28 to −0.03), P=0.02
ETD −0.39 (−0.51 to −0.26), P<0.001
ETD −0.45 (−0.57 to −0.32), P<0.001
Change (percentage points)
Change (mmol/mol)
0.0
−0.5
−1.0
−1.5
−2.0
−2.5
0.0
−5.5
−10.9
−16.4
−21.9
−27.3
−2.00
−2.24
−2.30
−1.86
B Glycated Hemoglobin Level
Overall mean baseline glycated hemoglobin, 8.28%
Glycated Hemoglobin Level (%)
Glycated Hemoglobin Level (mmol/mol)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
59.4
53.9
48.5
43.0
37.5
32.1
26.5
21.0
6.40%
6.19%
5.91%
5.82%
0
4
8
12
16
20
24
40
Weeks since Randomization
C Patients Who Met Glycated Hemoglobin Targets
P<0.05
P<0.05
P<0.001
P<0.001
Patients (%)
100
80
60
40
20
0
87
86
88
75
66
77
80
64
27
40
46
19
<7.0
≤6.5
<5.7
Glycated Hemoglobin Level (%)
D Fasting Serum Glucose Levels
Overall mean baseline fasting serum glucose, 175 mg/dl
Fasting Serum Glucose Level (mg/dl)
Fasting Serum Glucose Level (mmol/liter)
200
180
160
140
120
100
80
0
11.1
10.0
8.9
7.8
6.7
5.6
4.4
0.0
126.4 mg/dl
117.0 mg/dl
111.3 mg/dl
109.6 mg/dl
0
4
8
12
16
20
24
40
Weeks since Randomization



TRI-CITY CARDIOLOGY

The role of GLP-1 RAs in achieving weight loss and improving cardiovascular outcomes in people with overweight and obesity

In the United States:[1,2]

31% have overweight (BMI ≥25 kg/m²)

42% have obesity (BMI ≥30 kg/m²)

Obesity is associated with an increased risk of CVD and CVD-associated mortality[4]

Improving the recognition and understanding of GLP-1 RA therapy among HCPs may re-motivate them to support patients in losing weight[16]

Pancreas[49,105]
- ↑ β-cell function
- ↑ Glucose-dependent insulin secretion
- ↑ Insulin biosynthesis
- ↓ Post-prandial glucagon secretion
- ↓ β-cell apoptosis

Brain[49]
- ↓ Body weight
- ↑ Satiety
- ↓ Appetite
- ↓ Energy intake
- ↓ Food cravings
- ↑ Eating control

Effects of GLP-1 RAs

GI tract[49,105]
- ↓ Gastric emptying
- ↓ GI motility

Cardiovascular[64,106,107]
- ↑ Fatty acid metabolism
- ↓ Inflammation
- ↓ Systolic BP
- ↓ CV risk

GLP-1 RAs approved by the FDA for treatment of:

T2D[62–64,89,108]
Dulaglutide, exenatide, liraglutide semaglutide and tirzepatide

Overweight and obesity[76,77]
Liraglutide and semaglutide

MACE reduction[62–64]
Liraglutide, semaglutide (s.c.) and dulaglutide in patients with T2D

GLP-1 RAs currently under investigation for MACE reduction
- *Oral semaglutide and s.c. tirzepatide in patients with and without T2D*
- *s.c. semaglutide in patients with obesity/overweight*

		Liraglutide (s.c. 3 mg)[68] – (s.c. 0.5 and 1.0 mg)[63]	Semaglutide (s.c. 2.4 mg)[71] – (s.c. 0.5 and 1.0 mg)[64]	Tirzepatide (s.c. 5, 10 and 15 mg)[78]	Dulaglutid (s.c. 1.5 mg)[6]
Weight loss *(mean % change in body weight)* **Data from people with obesity/overweight without T2D**	GLP-1 RA / Placebo	–8.0% / –2.6%	–14.9% / –2.4%	–15.0% –19.5% / –3.1% –20.9%	— / —
MACE *(% of patients with primary composite outcome of time to first occurrence of MACE)* **Data from people with T2D**	GLP-1 RA / Placebo	13.0% / 14.9%	6.6% / 8.9%	— / —	12.0% / 13.

GLP-1 RAs have a tolerable safety profile

Mild-to-moderate GI side effects associated with therapy initiation and dose escalation[70–74,78]

Despite pre-clinical warnings, clinical evidence suggests no increased risk of psychiatric or metabolic adverse effects or cancer with GLP-1 RA therapy[70–74,78]

As obesity increases the risk of CVD in patients with and without T2 cardiologists should take an active role in obesity management

Despite guidelines recommending GLP-1 RA use in patients with T2D at risk of CVD, GLP-1 RAs are under-prescribed among these patients[99,100,109,110]

GLP-1 RAs should be considered by cardiologists as a treatment option for obesity and to reduce CVD risk in patien with T2D

Any Questions?

Please use the QR code to submit your questions.

TRI-CITY CARDIOLOGY

Thank You For Attending the Tri-City Cardiovascular Symposium

TRI-CITY
CARDIOLOGY