OBESITÀ COME MALATTIA O FATTORE DI RISCHIO?
I NUOVI ORIZZONTI TERAPEUTICI

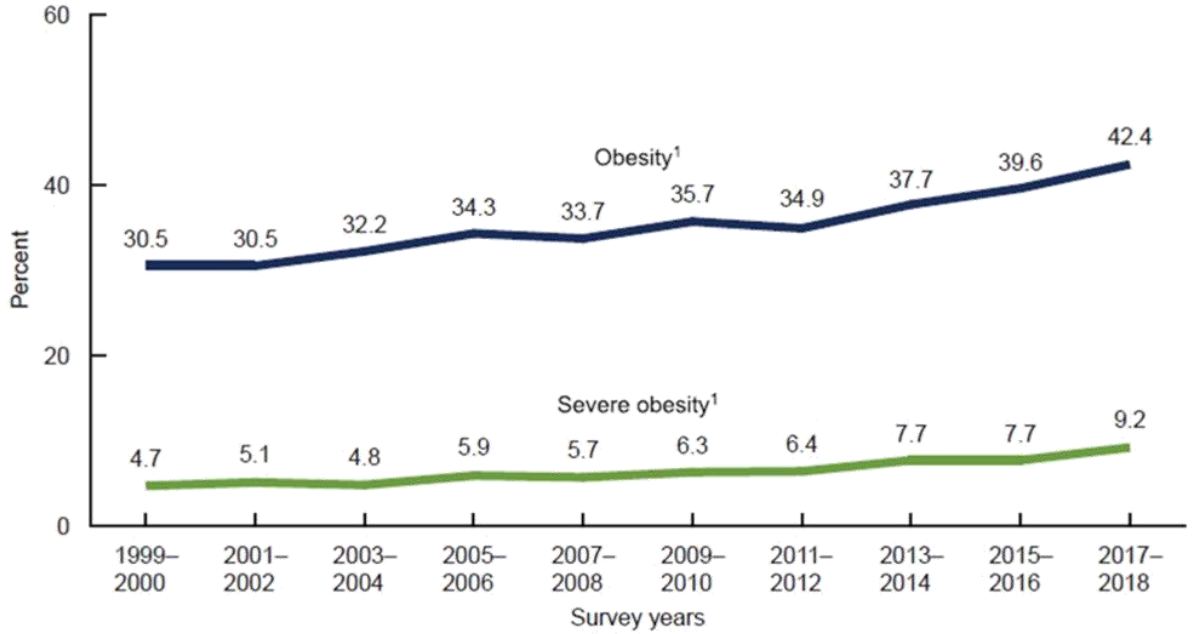
RICCARDO GRANATA

Cardiologia Interventistica
UOC Cardiologia UTIC "D. Rotiroti"
A.O.R.N. "San Giuseppe Moscati" - Avellino

SAN GIUSEPPE MOSCATI - AVELLINO
AZIENDA OSPEDALIERA DI RILIEVO NAZIONALE E DI ALTA SPECIALITÀ

Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017-2018.

Hales CM et al. National Center for Health Statistics (NCHS) Data Brief. 2020



- In 2016, more than 1.9 billion adults aged 18 years and older were overweight. Of these over 650 million adults were obese.
- In 2016, 39% of adults aged 18 years and over (39% of men and 40% of women) were overweight.
- **Overall, about 13% of the world's adult population (11% of men and 15% of women) were obese in 2016.**
- The worldwide prevalence of obesity nearly **tripled** between 1975 and 2016.

World Health Organization

Condizione definita su base anatomica o morfologica come eccesso ponderale per **eccesso di massa grassa** ed individuabile tramite l'analisi delle deviazioni dalla normalità degli indici ponderali.

CLASSIFICAZIONE DEGLI STATI PONDERALI PER BMI

World Health Organization

SOTTOPESO	< 18.5
NORMOPESO	18.5 – 24.9
SOVRAPPESO	25 – 29.9
OBESITÀ CLASSE I	**30 – 34.9**
OBESITÀ CLASSE II	**35 – 39.9**
OBESITÀ CLASSE III	**≥ 40**

Obesity As a Disease: The Obesity Society 2018 Position Statement

Jastreboff AM et al. Obesity 2019

Position Statement

Diseases are defined as "deviations from the normal or healthy structure or function of a part, organ, or system of the body, caused by underlying etiologies, manifested by characteristic symptoms and signs, and resulting in pathologic consequences that affect health, feeling, or functioning" (9-11). Diseases are thus defined by maladaptive changes from "normal" body structure and function that are brought about by underlying pathophysiologic mechanisms and that lead to symptoms and signs that affect health. In this classical context, TOS takes the position that

> [o]besity is a multi-causal chronic disease recognized across the life-span resulting from long-term positive energy balance with development of excess adiposity that over time leads to structural abnormalities, physiological derangements, and functional impairments. The disease of obesity increases the risk of developing other chronic diseases and is associated with premature mortality. As with other chronic diseases, obesity is distinguished by multiple phenotypes, clinical presentations, and treatment responses.

- **Structural abnormalities** such as left ventricular hypertrophy, lymphedema/venous stasis, musculoskeletal derangements, liver steatosis/fibrosis;
- **Functional abnormalities** such as gastrointestinal reflux, urinary incontinence, disability/immobility, and the presence of chronic disease risk factors, including the following: insulin resistance, chronic inflammation, dyslipidemia, and elevated blood pressure; infertility; earlier age at menarche in females; and, with pregnancy, large for age fetus and multiple adverse fetal and neonatal outcomes;
- **Signs** and **symptoms,** including hyperphagia with some conditions, obstructive sleep apnea/obesity hypoventilation syndrome, impaired exercise tolerance, and symptoms related to the structural and functional abnormalities noted above;
- Elevated premature **mortality risk**; and an
- Increased **comorbidity risk**, including providing the conditions favoring the development of more than 200 chronic diseases, including but not limited to the following (#; 2015 ranking of major causes of mortality in the United States): cardiovascular disease (#1); some cancers (#2); cerebrovascular diseases (#5); type 2 diabetes mellitus (#7); hypertension; asthma; psychiatric diseases, including depression; polycystic ovary syndrome; nonalcoholic fatty liver disease; gastrointestinal reflux disease; gallbladder disease; osteoarthritis; during pregnancy, preeclampsia and gestational diabetes mellitus; and, during childhood and adolescence, pseudotumor cerebri.

Association of Overweight With Increased Risk of Coronary Heart Disease Partly Independent of Blood Pressure and Cholesterol Levels

Bogers RP et al. Arch Intern Med. 2007 (JAMA)

Meta-analysis - 21 Cohort Studies - N = 302,296

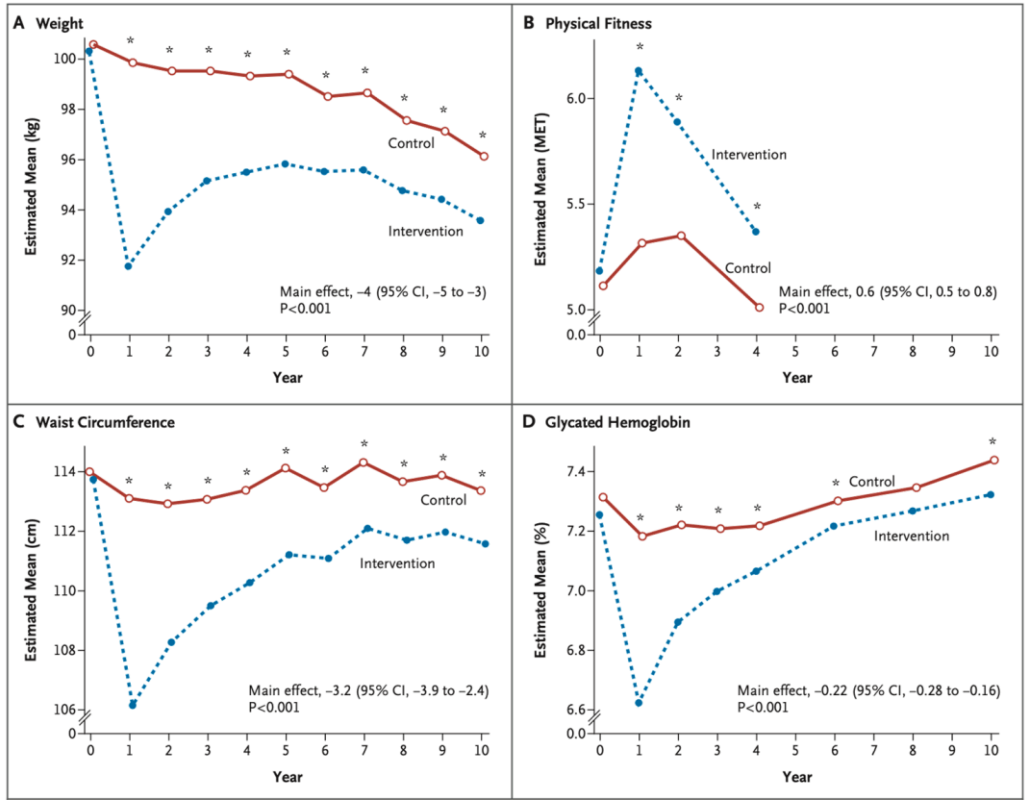
Table 2. Relative Risks (RRs) of Coronary Heart Disease for Moderate Overweight and Obesity Compared With Normal Weight[a] With and Without Adjustments for Blood Pressure and Cholesterol Levels

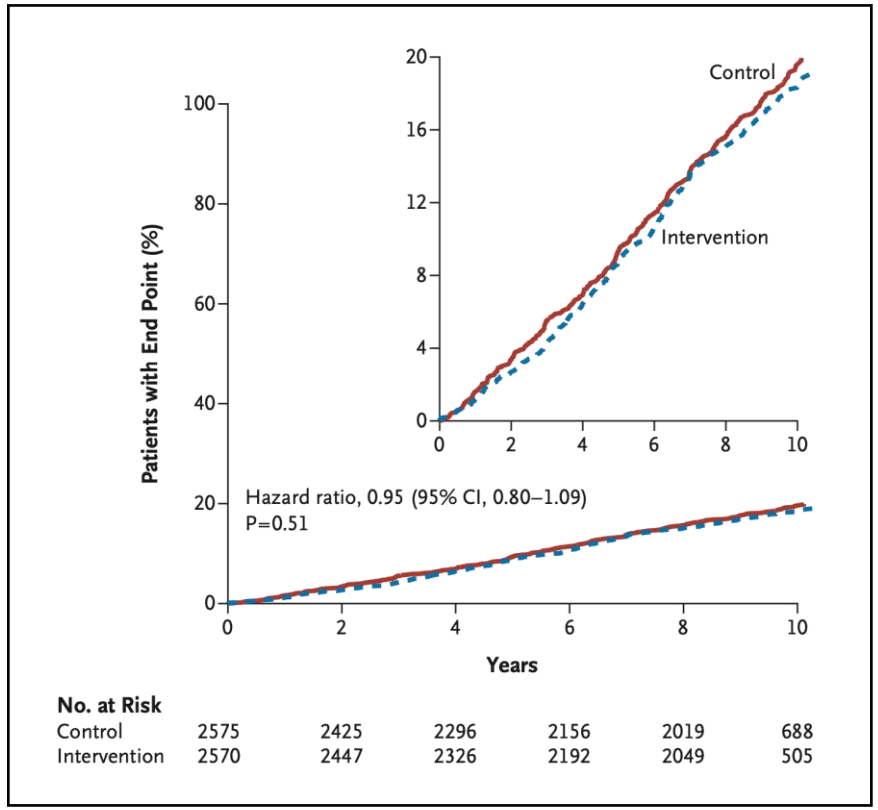
Selection (No. of Studies)	RR (95% CI) for Moderate Overweight	*P* Value for Heterogeneity[b]	RR (95% CI) for Obesity	*P* Value for Heterogeneity[b]
Adjusted for Age, Sex, Physical Activity, and Smoking				
All studies (14)	1.32 (1.24-1.40)	.007	1.81 (1.56-2.10)	<.001
BMI measured (13)	1.29 (1.22-1.37)	.12	1.72 (1.52-1.96)	<.001
BMI measured, systolic blood pressure and total cholesterol (11)[c]	1.32 (1.24-1.40)	.26	1.69 (1.45-1.97)	<.001
Additionally Adjusted for Blood Pressure and Cholesterol				
All studies (14)	1.17 (1.11-1.23)[d]	.15	1.49 (1.32-1.67)[d]	<.001
BMI measured (13)	1.14 (1.09-1.18)[d]	.88	1.41 (1.31-1.53)[d]	.11
BMI measured, systolic blood pressure and total cholesterol (11)[c]	1.16 (1.11-1.21)[d]	.96	1.39 (1.26-1.53)[d]	.10

Conclusions: Adverse effects of overweight on blood pressure and cholesterol levels could account for about 45% of the increased risk of CHD. Even for moderate overweight, there is a significant increased risk of CHD independent of these traditional risk factors, although confounding (eg, by dietary factors) cannot be completely ruled out.

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes – AHEAD Trial

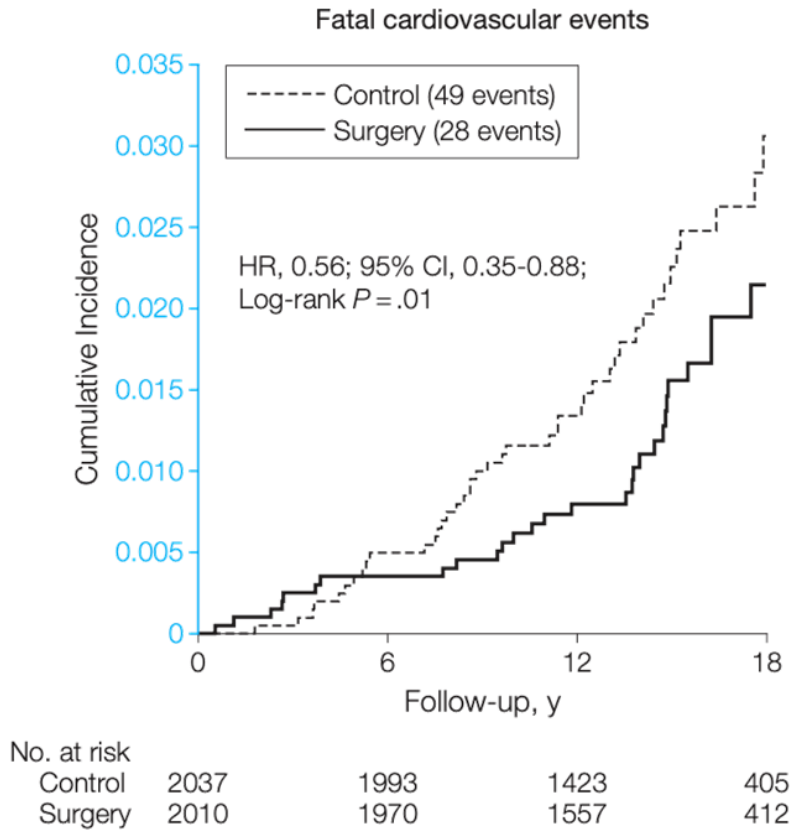
Wing RR et al. NEJM 2013

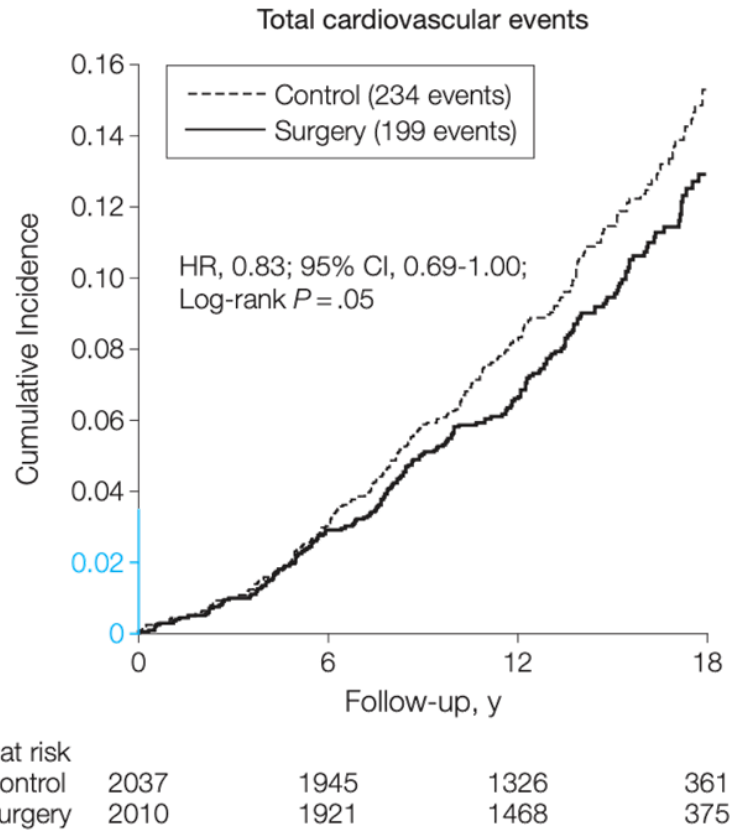




Bariatric Surgery and Long-Term Cardiovascular Events

Sjöström L et al. JAMA 2012





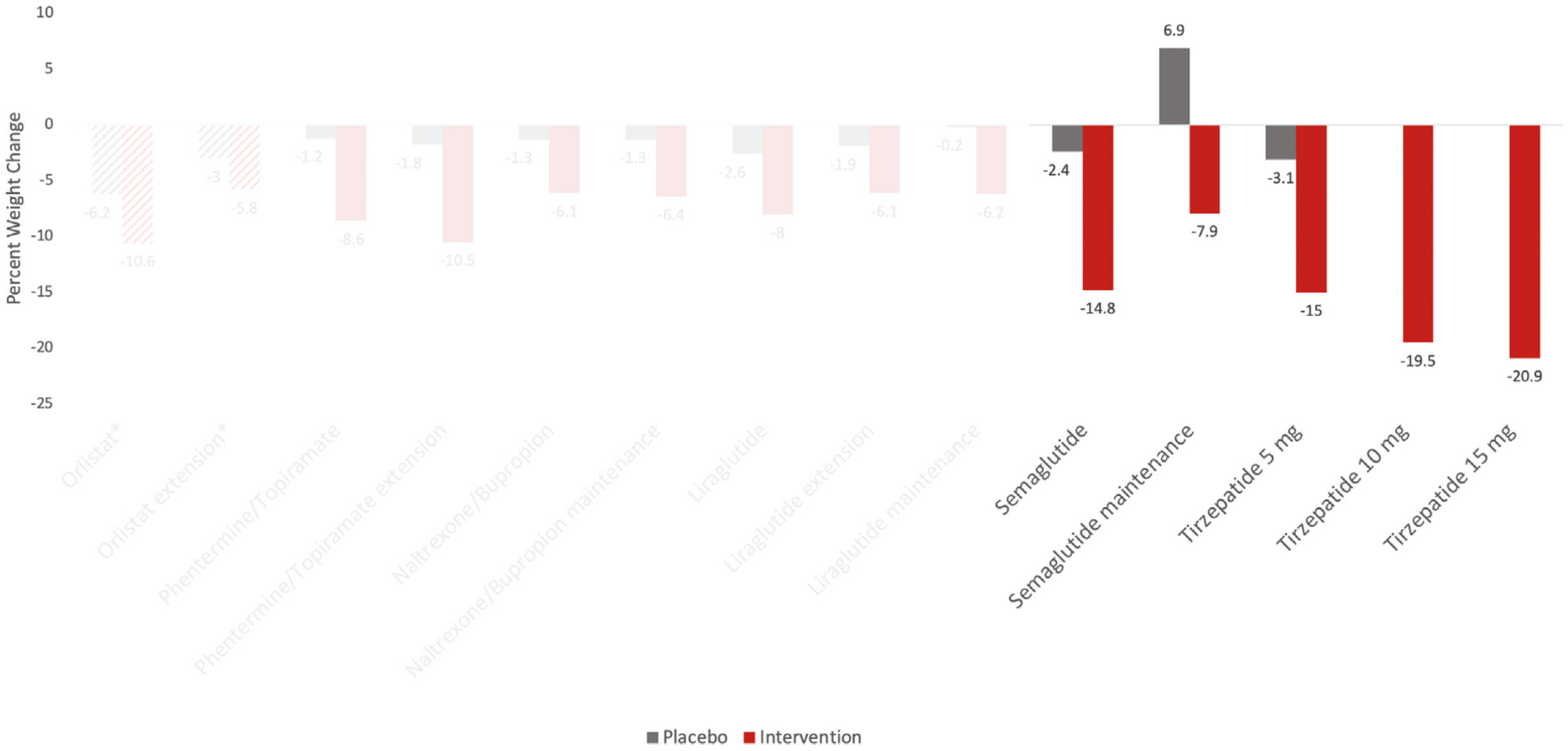
Association of the Magnitude of Weight Loss and Changes in Physical Fitness with Long-Term CVD outcomes in Overweight or Obese People with Type 2 Diabetes: a Post-hoc Analysis of the Look AHEAD RCT

Gregg EW et al. Lancet Diabetes Endocrinol. 2016

	Weight-change categories (percentage weight loss in first year; n=4834)				
	Gain or stable (<2% loss)	Small loss (≥2–<5%)	Medium loss (≥5–<10%)	Large loss (≥10%)	p value
Primary outcome					
Events per person-years	289/17 075	141/7870	154/8570	128/8942	..
Crude rate per 100 person-years	1·69	1·79	1·80	1·43	..
Unadjusted hazard ratio (95% CI)	1·00	1·07 (0·88–1·31)	1·07 (0·88–1·31)	0·83 (0·67–1·02)	0·21
Adjusted hazard ratio†(95% CI)	1·00	1·08 (0·88–1·33)	1·16 (0·95–1·42)	0·79 (0·64–0·98), p=0·034*	0·17
Secondary outcome					
Events per person-years	422/16 699	206/7657	203/8411	186/8792	..
Crude rate per 100 person-years	2·53	2·69	2·41	2·12	..
Unadjusted hazard ratio (95% CI)	1·00	1·08 (0·91–1·27)	0·96 (0·81–1·13)	0·83 (0·70–0·99), p=0·035*	0·04
Adjusted hazard ratio† (95% CI)	1·00	1·05 (0·88–1·25)	0·97 (0·82–1·16)	0·76 (0·63–0·91), p=0·003*	0·006

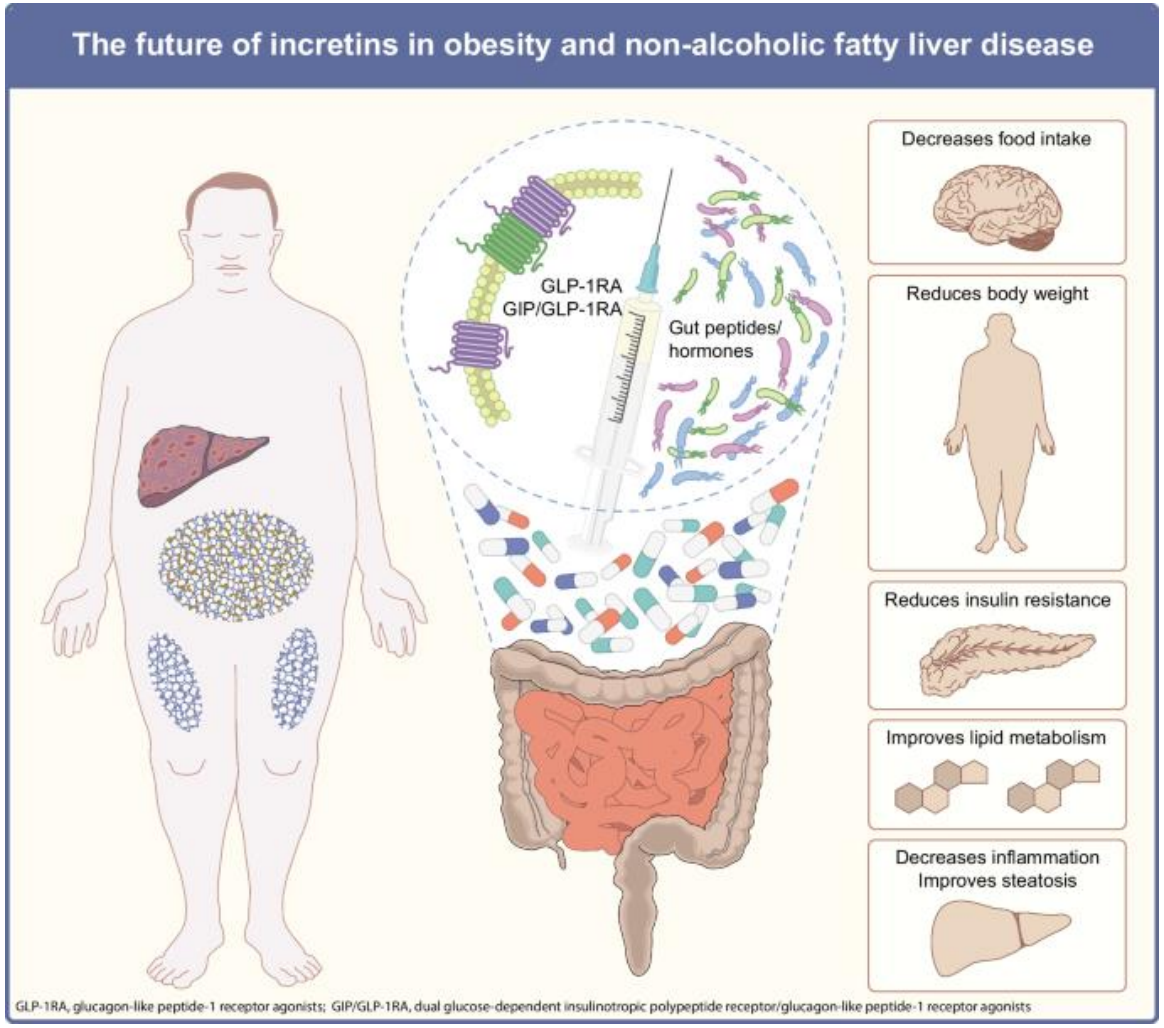
Pharmacotherapy of Obesity: an Update on the Available Medications and Drugs Under Investigation

Chakhtoura M et al. Lancet 2023



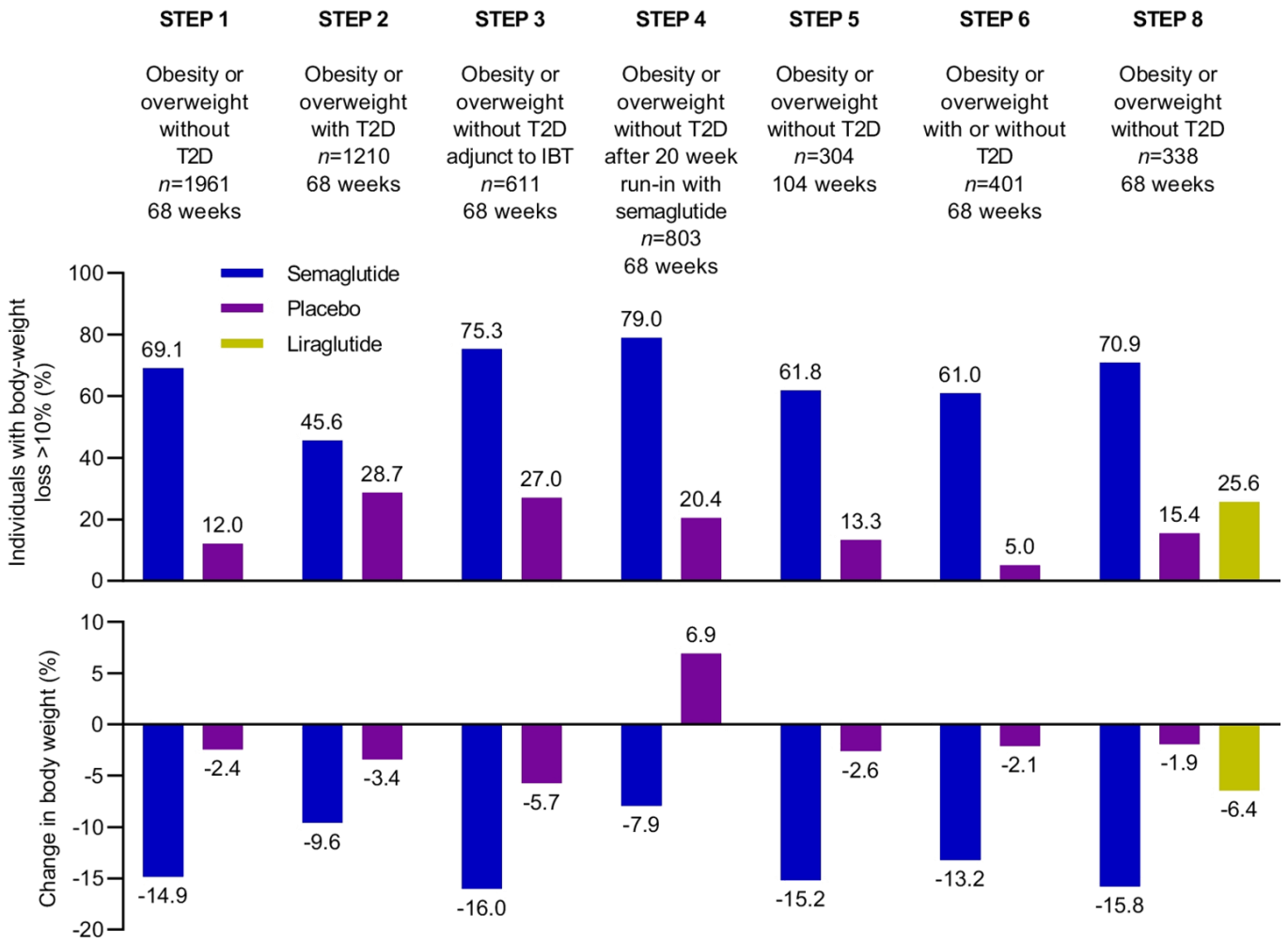
The Future of Incretins in the Treatment of Obesity and Non-Alcoholic Fatty Liver Disease.

Andreasen CR et al. Diabetologia 2023



Overview of Body-Weight Loss in the STEP Trials

Courtesy of Andreasen CR et al. Diabetologia 2023



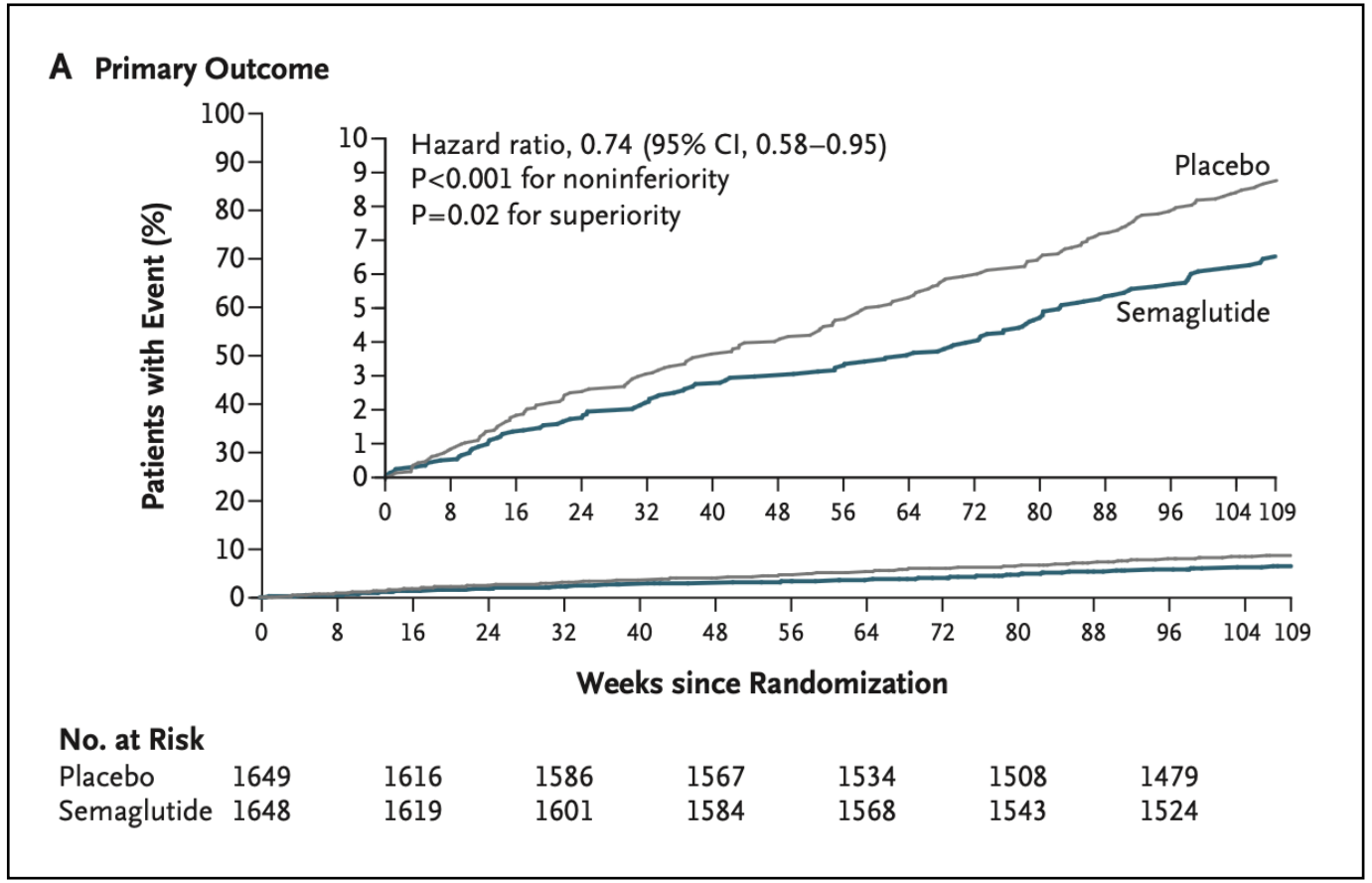
SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES – THE SUSTAIN-6 TRIAL

Marso SP et al. NEJM 2016

RCT – 3,297 patients

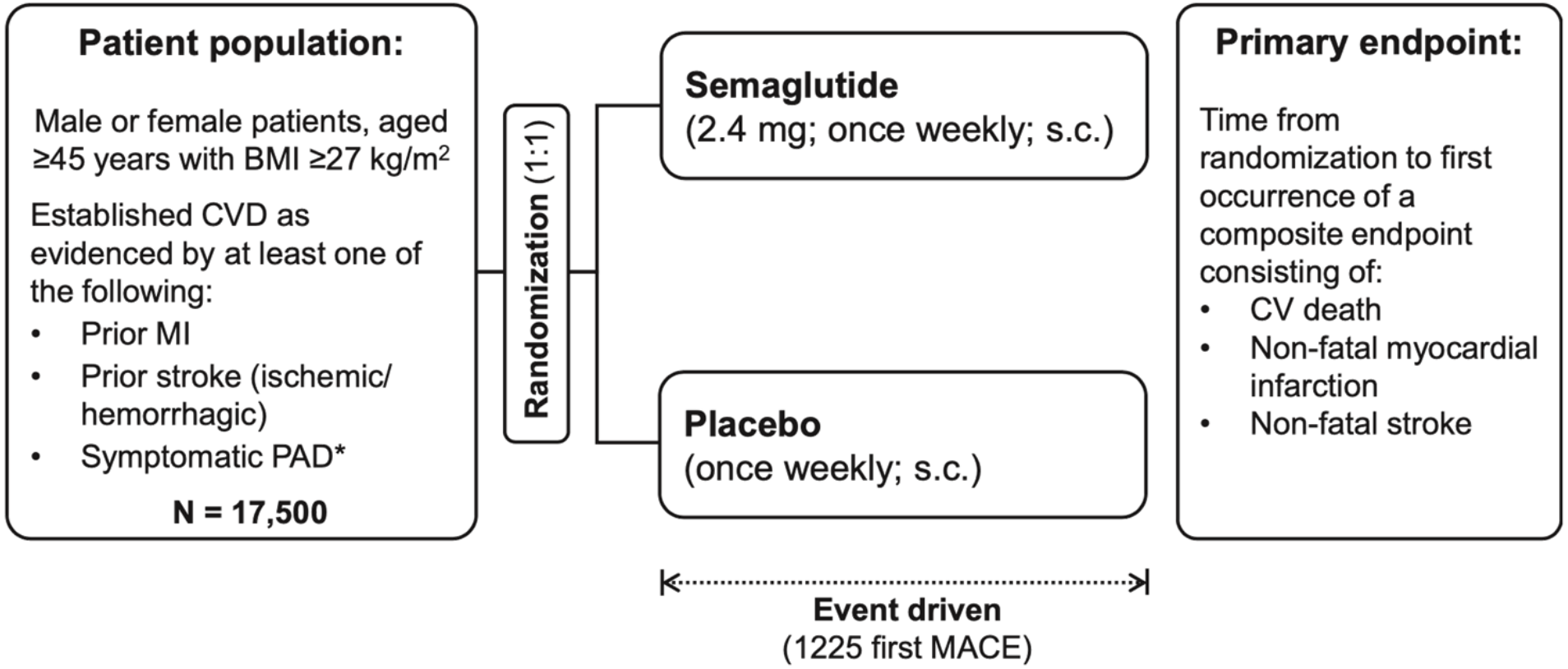
Key inclusion criteria were T2D with baseline HbA_{1c} ≥7% and either:

- ≥ 50 years of age with clinical evidence of CVD
- ≥ 60 years of age with subclinical evidence of CVD



SEMAGLUTIDE EFFECTS ON CARDIOVASCULAR OUTCOMES IN PEOPLE WITH OVERWEIGHT OR OBESITY (SELECT): RATIONALE AND DESIGN
Ryan DH et al. American Heart Journal 2020

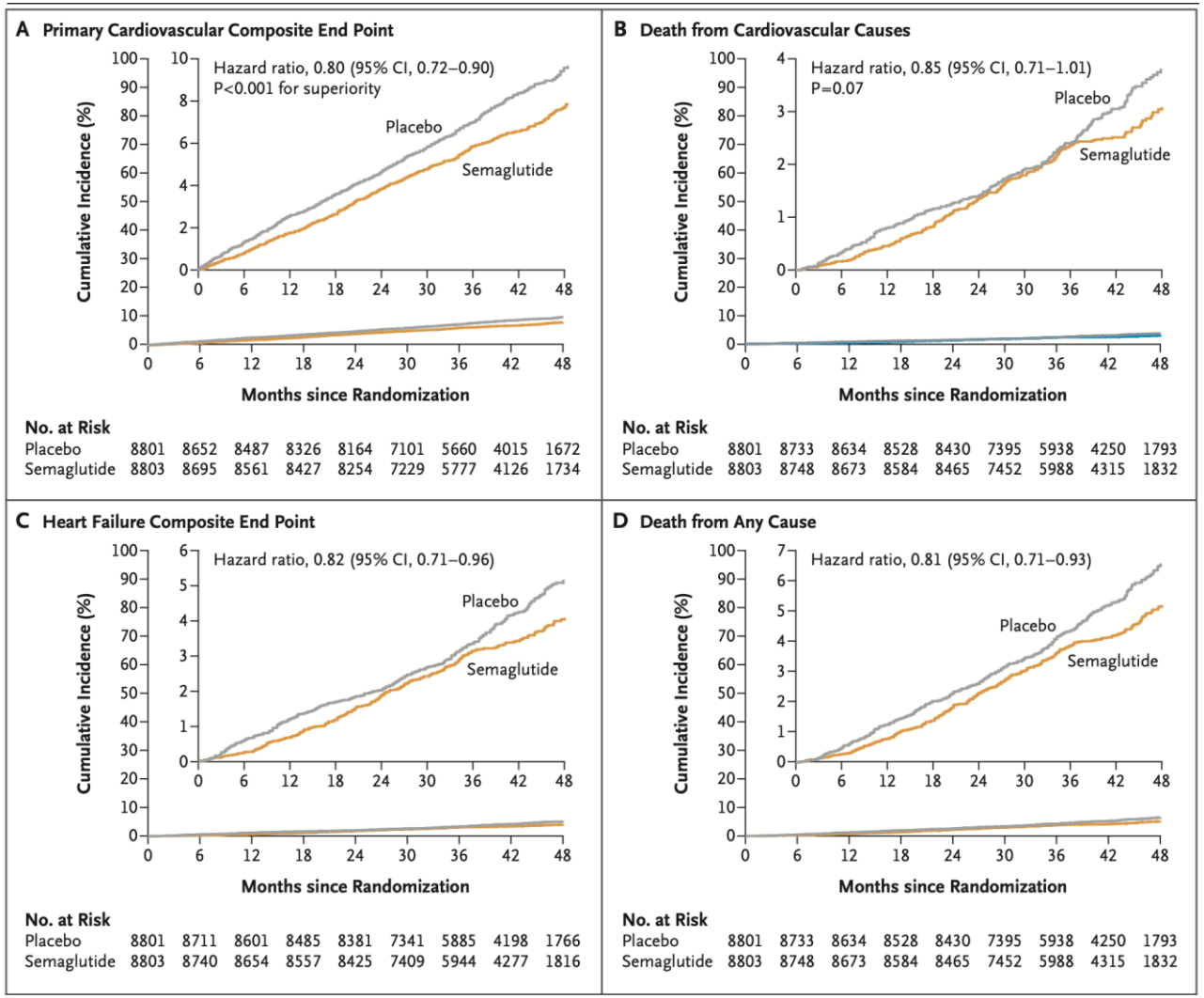
SEMAGLUTIDE FOR CARDIOVASCULAR EVENT REDUCTION IN PEOPLE WITH OVERWEIGHT OR OBESITY: SELECT STUDY BASELINE CHARACTERISTICS
Lingvay I et al. Obesity 2022



SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN OBESITY WITHOUT DIABETES – THE SELECT TRIAL

Lincoff AM. et al N Engl J Med. 2023 Nov 11

RCT – 17,604 patients



SEMAGLUTIDE AND CARDIOVASCULAR OUTCOMES IN OBESITY WITHOUT DIABETES – THE SELECT TRIAL

Lincoff AM. et al N Engl J Med. 2023 Nov 11

RCT – 17,604 patients

Table 3. Supportive Binary and Continuous Secondary End Points.*

End Point	Semaglutide (N=8803)	Placebo (N=8801)	Difference (95% CI)†
Glycated hemoglobin level of <5.7% among patients with baseline glycated hemoglobin level of ≥5.7% — no./total no. (%)‡			
At week 52	3848/5831 (66.0)	1136/5748 (19.8)	10.15 (9.18 to 11.23)
At week 104	3775/5750 (65.7)	1211/5663 (21.4)	8.74 (7.91 to 9.65)
Mean change from randomization to week 104			
Body weight — %	−9.39±0.09	−0.88±0.08	−8.51 (−8.75 to −8.27)
Waist circumference — cm	−7.56±0.09	−1.03±0.09	−6.53 (−6.79 to −6.27)
Glycated hemoglobin level — percentage points	−0.31±0.00	0.01±0.00	−0.32 (−0.33 to −0.31)
Systolic blood pressure — mm Hg	−3.82±0.16	−0.51±0.16	−3.31 (−3.75 to −2.88)
Diastolic blood pressure — mm Hg	−1.02±0.10	−0.47±0.10	−0.55 (−0.83 to −0.27)
Heart rate — beats/min	3.79±0.11	0.69±0.11	3.10 (2.80 to 3.39)
EQ-5D-5L index score§	0.01±0.00	−0.01±0.00	0.01 (0.01 to 0.02)
EQ-5D-VAS score§	2.52±0.16	0.92±0.16	1.60 (1.16 to 2.04)
High-sensitivity CRP level — %	−39.12	−2.08	−37.82 (−39.70 to −35.90)
Total cholesterol level — %	−4.63	−1.92	−2.77 (−3.37 to −2.16)
HDL cholesterol level — %	4.86	0.59	4.24 (3.70 to 4.79)
LDL cholesterol level — %	−5.25	−3.14	−2.18 (−3.22 to −1.12)
Triglyceride level — %	−18.34	−3.20	−15.64 (−16.68 to −14.58)

Table 4. Investigator-Reported Adverse Events.*

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)	0.94
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

Risk of Gastrointestinal Adverse Events Associated With Glucagon-Like Peptide-1 Receptor Agonists for Weight Loss

Sodhi M et al. JAMA. Oct,5 2023

Observational – 16 million patients (2006-2020) from the PharMetrics Plus database (IQVIA)

Outcomes	GLP-1 agonists, HR (95% CI)[a]		Bupropion-naltrexone
	Crude	Adjusted[b]	
Primary analysis			
Biliary disease	1.48 (0.88-2.47)	1.50 (0.89-2.53)	1 [Reference]
Pancreatitis	10.33 (1.44-74.40)	9.09 (1.25-66.00)	1 [Reference]
Bowel obstruction	5.16 (1.27-21.00)	4.22 (1.02-17.40)	1 [Reference]
Gastroparesis	3.31 (1.04-10.50)	3.67 (1.15-11.90)	1 [Reference]
Sensitivity analyses			
Exclusion of hyperlipidemia			
Biliary disease	1.50 (0.88-2.56)	1.46 (0.84-2.51)	1 [Reference]
Pancreatitis	9.80 (1.36-70.79)	7.99 (1.10-58.30)	1 [Reference]
Bowel obstruction	4.43 (1.08-18.20)	3.63 (0.87-15.10)	1 [Reference]
Gastroparesis	3.32 (1.04-10.60)	3.67 (1.14-11.80)	1 [Reference]
Analysis with less-restrictive obesity definition[c]			
Biliary disease	1.29 (0.92-1.80)	1.20 (0.85-1.69)	1 [Reference]
Pancreatitis	6.19 (1.99-19.30)	5.94 (1.90-18.60)	1 [Reference]
Bowel obstruction	3.11 (1.28-7.54)	2.44 (1.00-5.95)	1 [Reference]
Gastroparesis	2.11 (1.09-4.09)	2.35 (1.20-4.58)	1 [Reference]
E-values for adjusted HRs[d]			
Biliary disease	2.36		
Pancreatitis	17.67		
Bowel obstruction	7.91		
Gastroparesis	6.80		

Abbreviations: GLP-1, glucagon-like peptide 1; HR, hazard ratio.

[a] Either semaglutide or liraglutide user.

[b] Hazard ratios adjusted for by age, sex, alcohol use, smoking, hyperlipidemia, and abdominal surgery in the last 30 days.

[c] Analysis that included patients without a diabetes code with or without an obesity code.

[d] E-values represent the HRs for the association of an unmeasured confounder (in this study's case, body mass index) with GLP-1 agonists and the study's 4 outcomes. E-values with HRs at least 2 suggest that such confounders are unlikely to change study results.

MENU

Agenzia Italiana del Farmaco

Home > Accesso al farmaco > Nota Informativa Importante su Ozempic® (semaglutide)

Nota Informativa Importante su Ozempic® (semaglutide)

Ozempic® (semaglutide) soluzione iniettabile in penna preriempita: stato di carenza.

- l'aumento della domanda di Ozempic® ha portato a carenze che si prevede continueranno per tutto il 2023. Sebbene la fornitura continui ad aumentare, non è possibile prevedere con certezza quando risulterà sufficiente a soddisfare completamente la domanda attuale.
- Una tardiva consapevolezza della situazione di esaurimento delle scorte può comportare l'impossibilità per i pazienti di acquisire le dosi necessarie, con possibili conseguenze cliniche come l'iperglicemia.
- La invitiamo ad assicurare che i pazienti che utilizzano Ozempic® siano informati di quanto sopra e che i pazienti, a rischio di esaurimento di Ozempic®, vengano trasferiti in sicurezza ad un altro agonista del GLP-1 o ad altre idonee alternative terapeutiche in base alla Sua valutazione clinica.
- Ozempic® è indicato esclusivamente per il trattamento di adulti affetti da diabete mellito di tipo 2 non adeguatamente controllato in aggiunta alla dieta e all'esercizio fisico. Ogni altro utilizzo, inclusa la gestione del peso, rappresenta un uso off-label e attualmente mette a rischio la disponibilità di Ozempic® per la popolazione indicata.

Pubblicato il: 06 marzo 2023

PUBLISHED WED, NOV 8 2023 12:20 PM EST
UPDATED WED, NOV 8 2023 8:00 PM EST

HEALTH AND SCIENCE

FDA approves Eli Lilly's tirzepatide for weight loss, paving way for wider use of blockbuster drug

Annika Kim Constantino
@ANNIKAKIMC

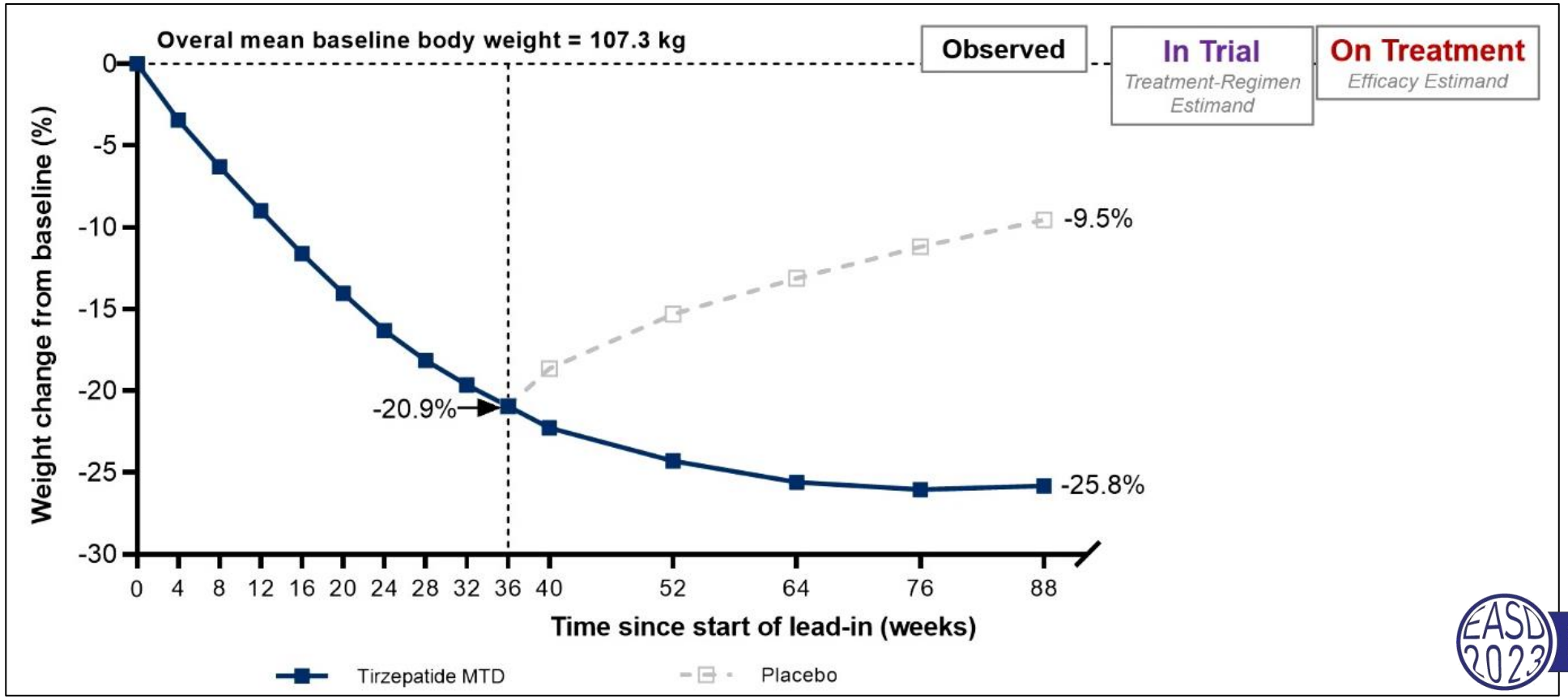
SURMOUNT PROGRAM

TIRZEPATIDE EVALUATED ACROSS A BROAD PATIENT POPULATION

	Expected Read-out Date	Study Size (pts)	Studied Doses	Study Duration	Primary Endpoint	Key Inclusion Criteria
SURMOUNT-1 Weight Management in Participants with Obesity/Overweight*	✓	2,539	5/10/15 mg	72 weeks (2-year additional treatment period**)	1) Percent change in body weight 2) Percentage of participants who achieve ≥5% body weight reduction	BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with ≥1 weight-related comorbidity
SURMOUNT-2 Weight Management in Participants with Obesity/Overweight with T2DM	Mid-2023	~900	10/15 mg	72 weeks		BMI ≥ 27 kg/m^2 with T2D (A1c 7-10%) treated with diet/exercise alone or an oral agent except DPP-4 inhibitors or GLP-1R agonists
SURMOUNT-3 Maximizing Weight Loss Following Intensive Lifestyle Program in Participants with Obesity/Overweight*		~800	MTD (10 or 15 mg)	84 weeks (incl. 12-wk intensive lifestyle lead-in)		BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with ≥1 weight-related comorbidity
SURMOUNT-4 Maintaining Weight Loss with Maximal Tolerated Dose Therapy in Participants with Obesity/Overweight*		~750		88 weeks (incl. 36-wk open-label TZP lead-in)	Percent change in body weight from randomization (week 36) to week 88	

A Study of Tirzepatide in Participants With Obesity or Overweight for the Maintenance of Weight Loss: The SURMOUNT-4 Trial

Chair: Wilding J.



TAKE-HOME MESSAGES

- L'obesità è una **patologia cronica multifattoriale** definita e riconosciuta. Rappresenta, inoltre, un fattore di rischio per le CVD, nonché per patologie oncologiche, respiratorie, metaboliche, ecc. e si associa ad una prematura mortalità

- Gli interventi sullo stile di vita (dieta e attività fisica) rappresentano il caposaldo della terapia per l'obesità

- La **riduzione degli eventi CV** si osserva, secondo i dati oggi disponibili, in presenza di perdite di peso rilevanti (>10%)

- **SEMAGLUTIDE** rappresenta l'unico farmaco con dimostrata efficacia nella perdita di peso e nella riduzione degli eventi CV dei pazienti diabetici e non diabetici, nonostante un profilo di tollerabilità non eccellente (i.e. GI adverse events)

- **TIRZEPATIDE** ha dimostrato grande efficacia nella perdita di peso (> SEMAGLUTIDE), ma non sono ancora disponibili dati riguardo la riduzione degli eventi CV