

**UBERTO PAGOTTO**

**UOC Endocrinologia e Prevenzione e  
Cura del Diabete**

**Dipartimento di Scienze Mediche e  
Chirurgiche**

**Policlinico di S.Orsola IRCCS**

**Alma Mater Università di Bologna**

**Nuovi farmaci:  
effetti clinici  
oltre il peso**

**27 - 29 novembre 2025**

Padova Congress  
Via Carlo Goldoni 8, Cancellò C - Padova



# CONFLITTO DI INTERESSI

**Ai sensi dell'art. 76 del Regolamento applicativo dell'Accordo Stato-Regioni 02.02.2017, dichiaro che negli ultimi tre anni ho avuto i seguenti rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:**

- **Membro di Advisory Board:**

**Novo Nordisk, Sciterion, Boehringer Ingelheim, Pfizer, Lilly Italia**

- **Speaker fee:**

**Novo Nordisk, Astra-Zeneca, Bruno Farmaceutici, Rhythm Pharma, International Medical Press, Lilly Italia, Merck**



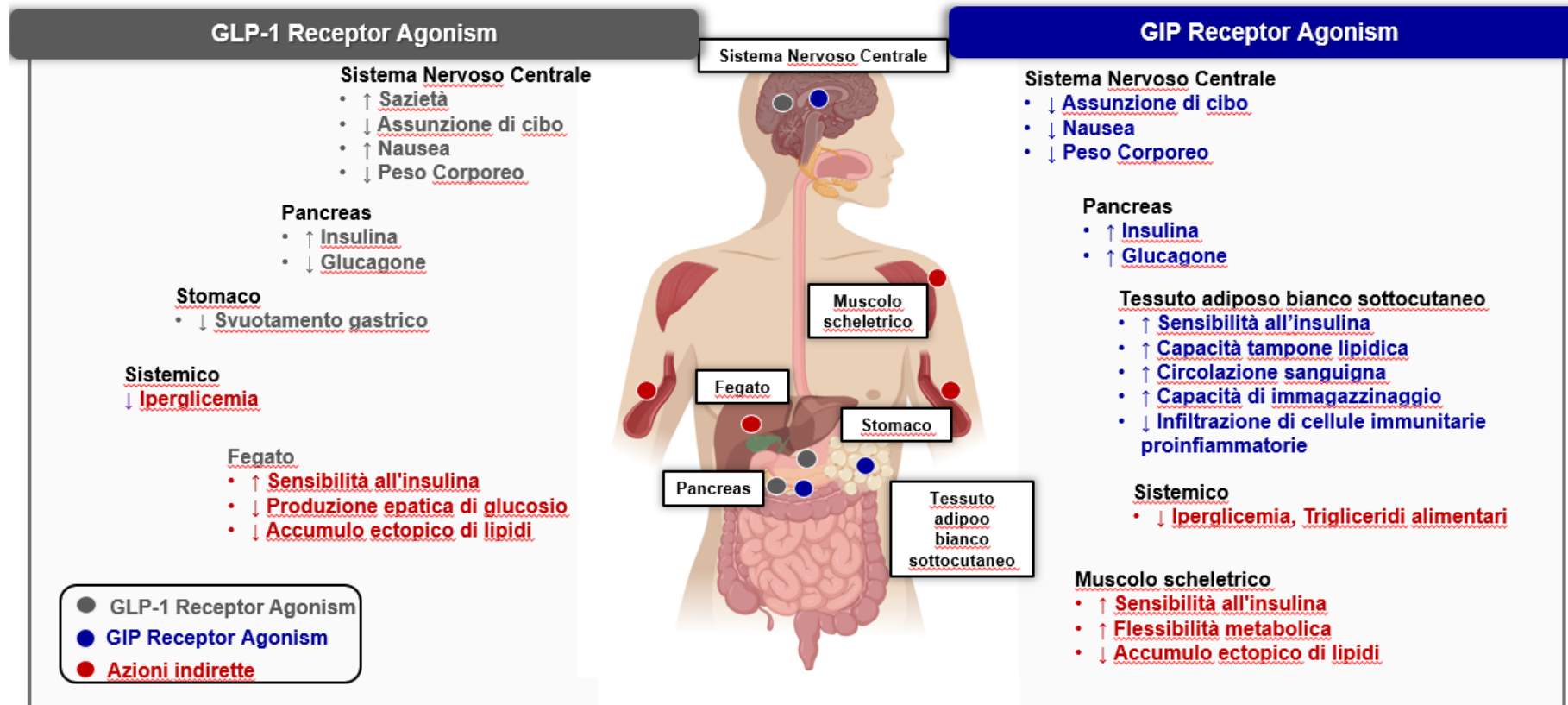
# Terapia farmacologica: analoghi incretinici

Semaglutide

Agonista del GLP1-R

Tirzepatide

Agonista del GLP-1 e del GIP



Congresso Nazionale SINPE 2025

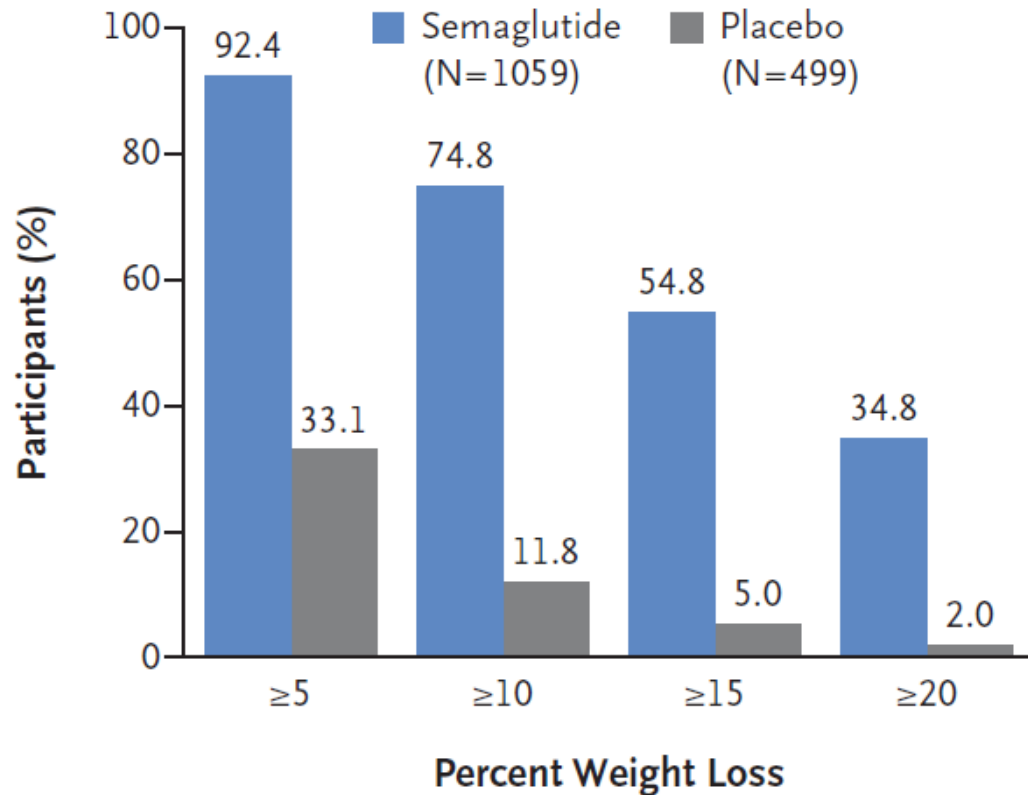
CLINICAL NUTRITION: shaping a better future of health care

# EFFETTI SUL PESO

## SEMAGLUTIDE

Wilding JPH et al. NEJM 2021

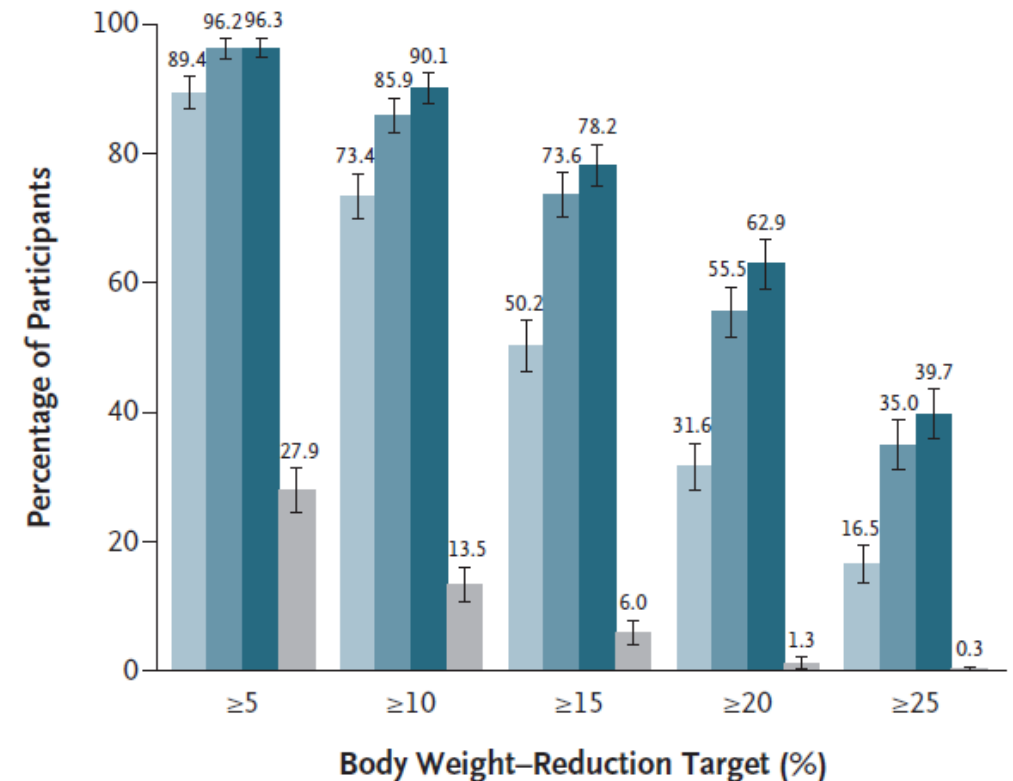
### D On-Treatment Data at Wk 68



## TIRZEPATIDE

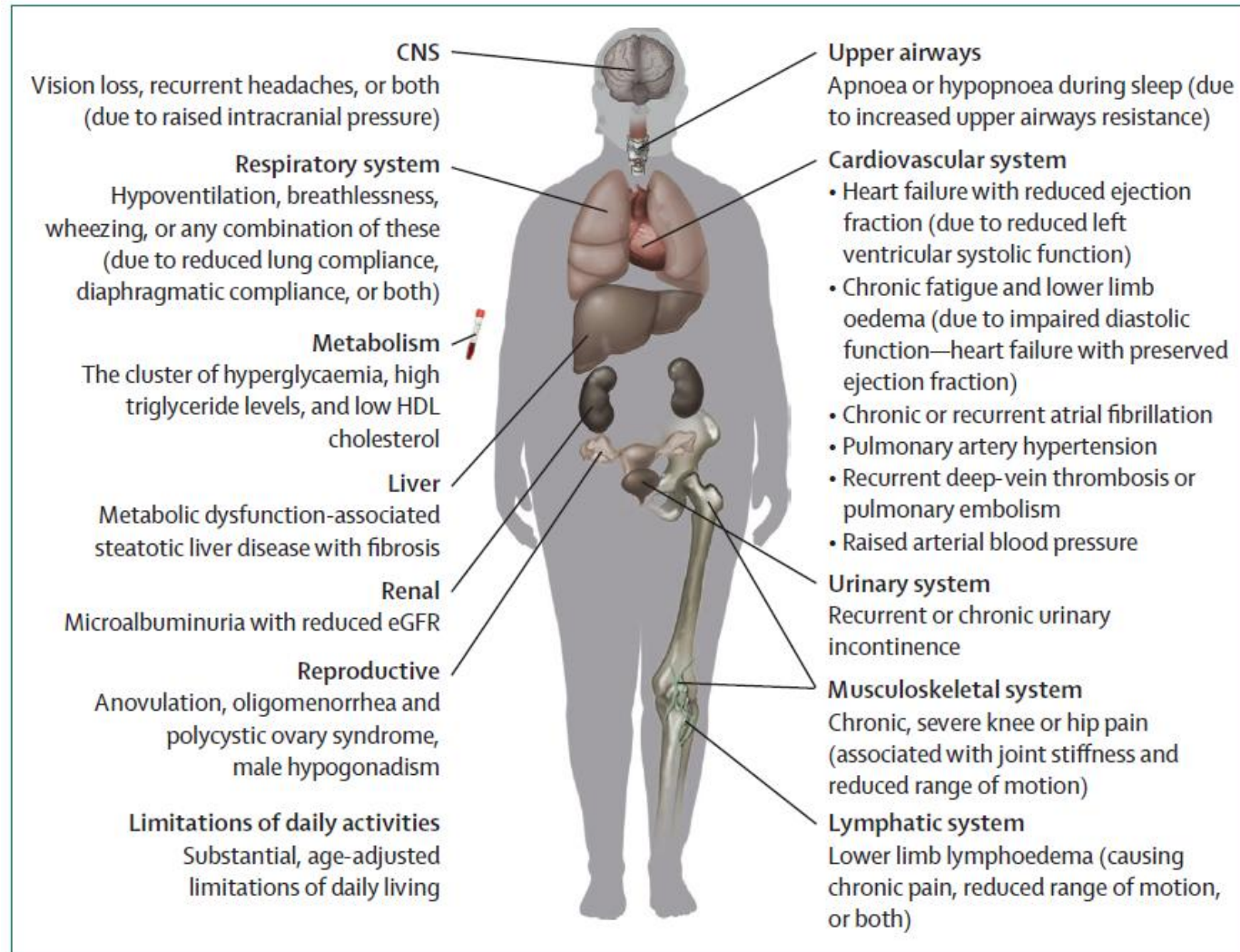
Jastreboff AM et al. NEJM 2022

### D Participants Who Met Weight-Reduction Targets (efficacy estimand)



Convegno Nazionale SINPE 2025

# DIAGNOSTIC CRITERIA FOR CLINICAL OBESITY IN ADULTS



Congresso Nazionale SINPE 2025

# METABOLISMO GLUCIDICO

## Metabolism

The cluster of hyperglycaemia, high triglyceride levels, and low HDL cholesterol

Anovulation, oligomenorrhea and polycystic ovary syndrome, male hypogonadism

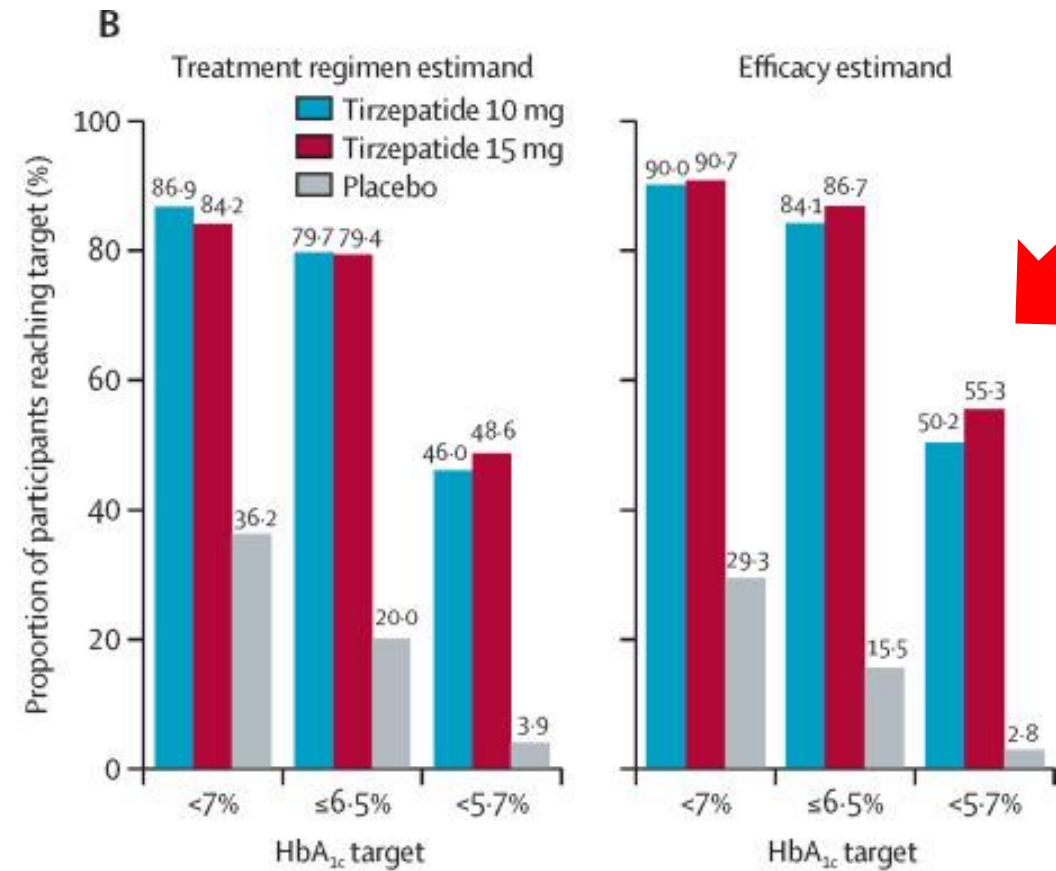
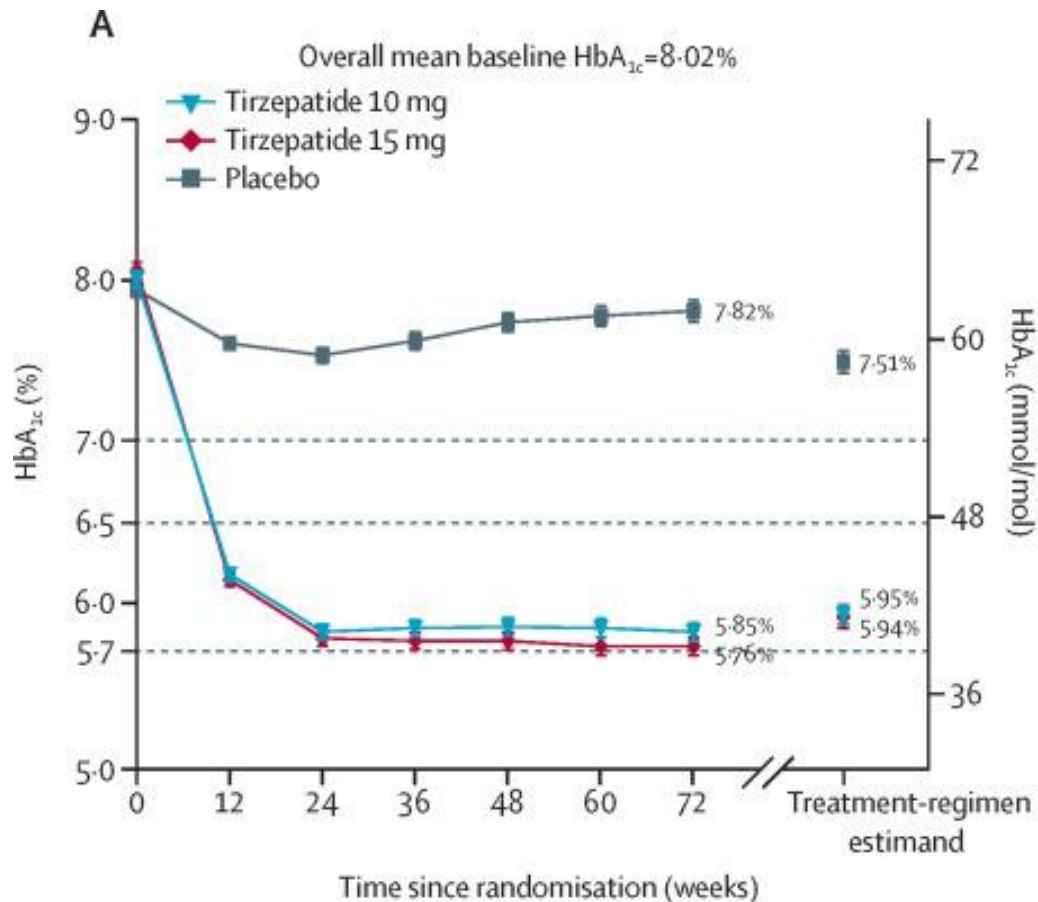
Limitations of daily activities  
Substantial, age-adjusted limitations of daily living



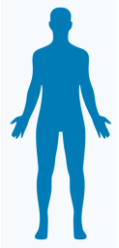
**musculoskeletal system**  
Chronic, severe knee or hip pain (associated with joint stiffness and reduced range of motion)

**Lymphatic system**  
Lower limb lymphoedema (causing chronic pain, reduced range of motion, or both)

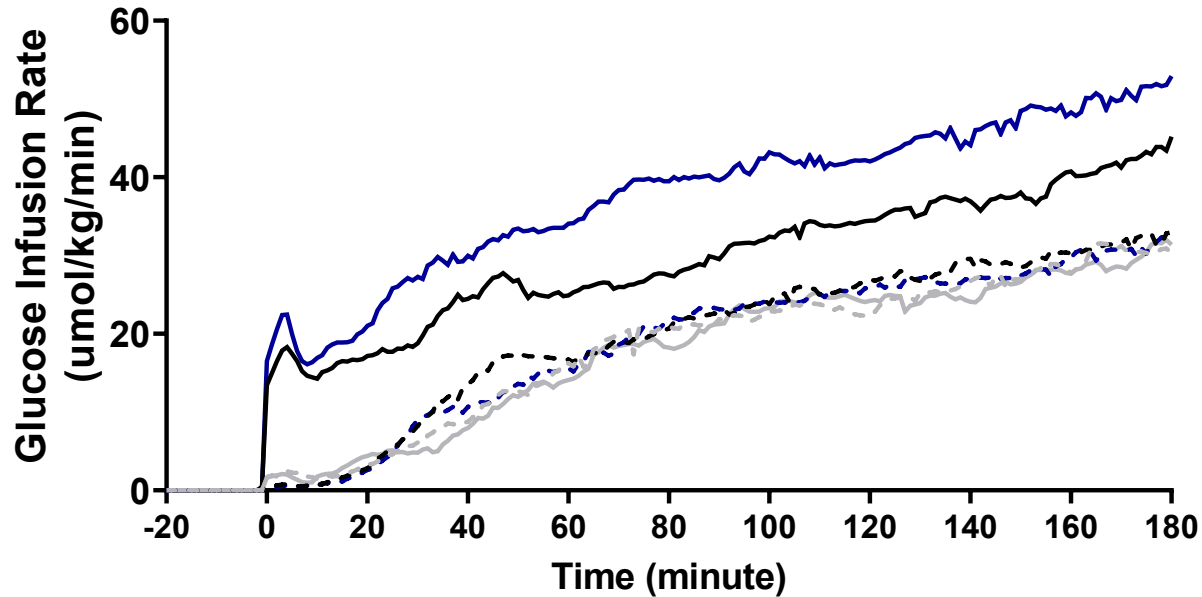
# TIRZEPATIDE MIGLIORA IL CONTROLLO GLICEMICO IN PAZ DIABETICI CON OBESITA': LO STUDIO SURMOUNT 2



# TIRZEPATIDE MIGLIORA LA SENSIBILITÀ ALL'INSULINA NEI PAZIENTI CON T2D

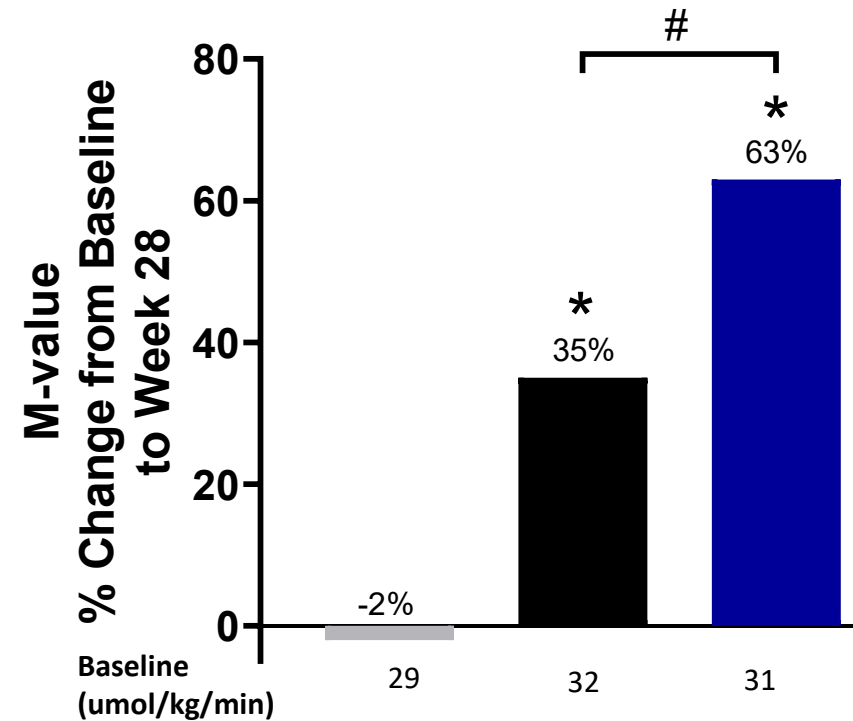


### Velocità di infusione del glucosio



■ Placebo   ■ Semaglutide 1.0mg   ■ Tirzepatide 15mg  
Dashed: baseline   Solid: Week 28

### Sensibilità all'insulina di tutto il corpo, M-value



Heise T et al. Lancet Diabetes Endocr 2022

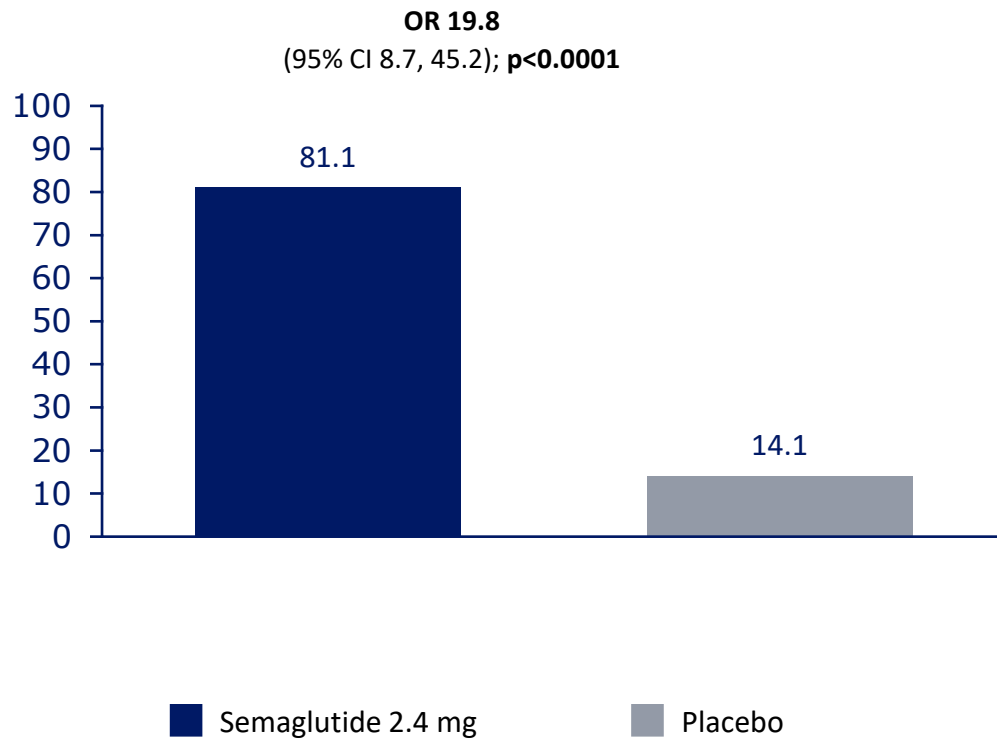
Congresso Nazionale SINPE 2025

CLINICAL NUTRITION: shaping a better future of health care



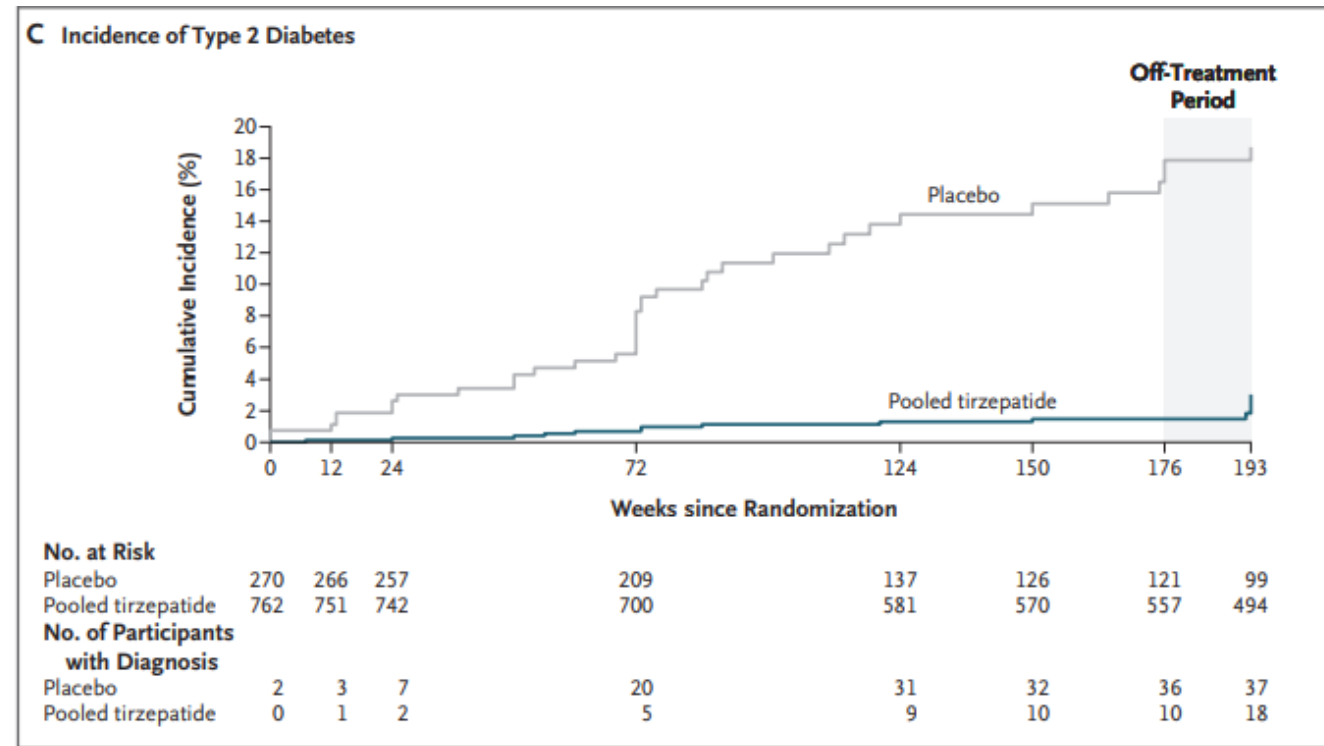
# PROGRESSIONE A DIABETE TIPO 2

## SEMAGLUTIDE: Reversione a normoglicemia alla settimana 52



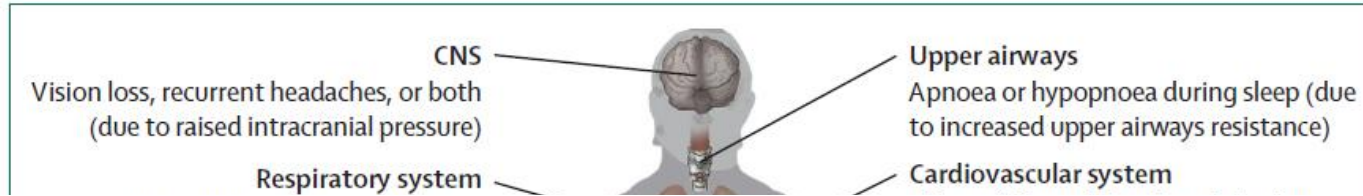
McGowan et al. Lancet Diabetes Endocrinol. 2024 STEP 10

## TIRZEPATIDE: Riduzione dell'incidenza di diabete tipo 2 dopo 3 anni



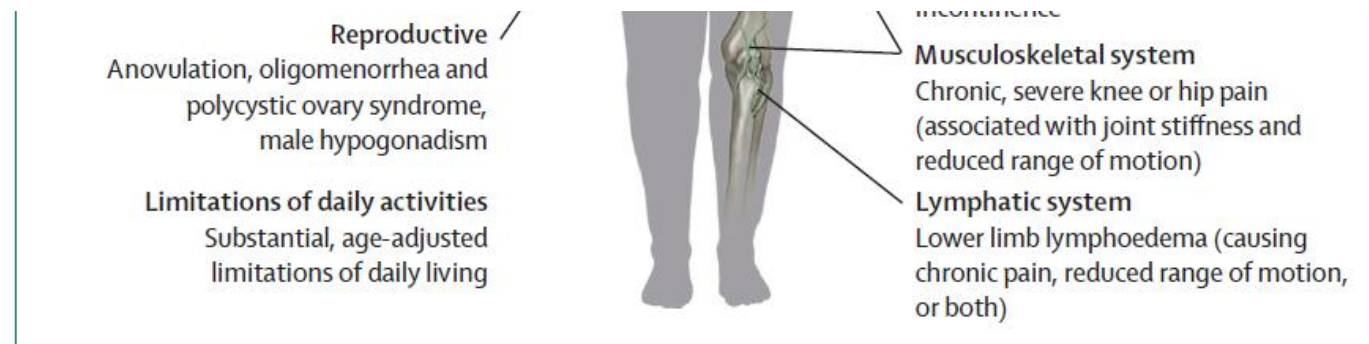
Jastreboff A. M. et al. NEJM 2025 SURMOUNT 1

# FEGATO



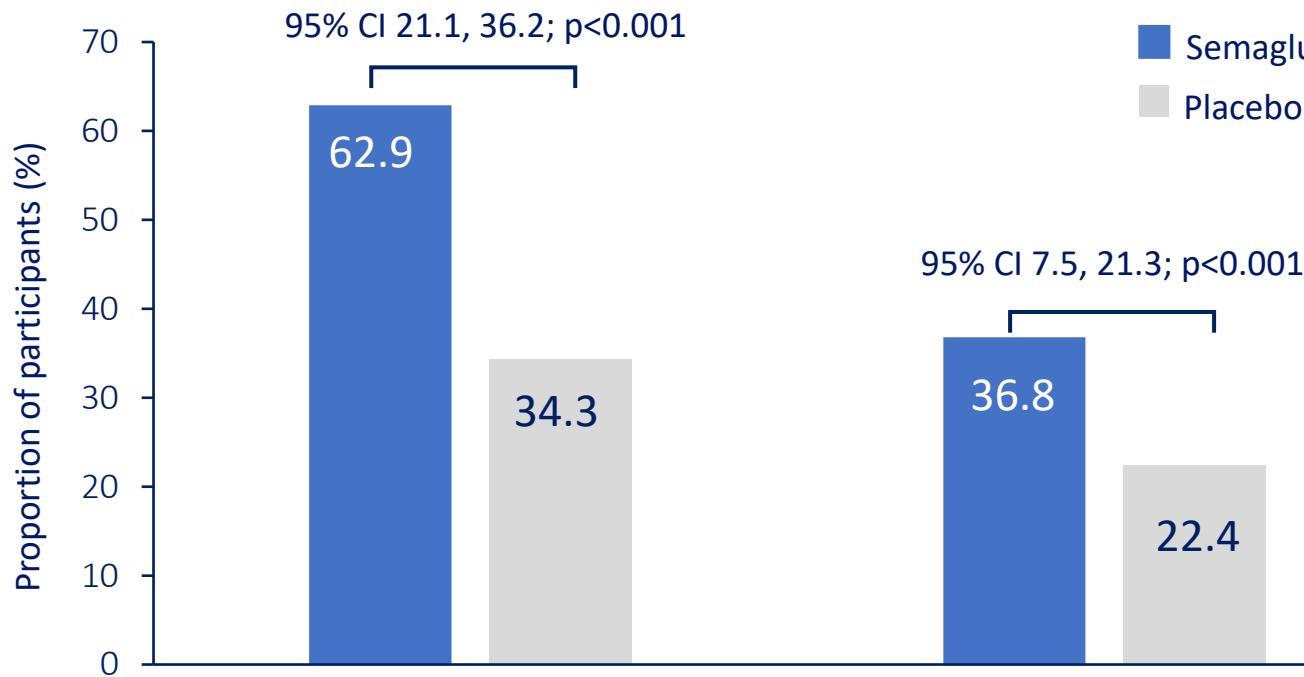
# Liver

## Metabolic dysfunction-associated steatotic liver disease with fibrosis



# SEMAGLUTIDE e MASH: IL TRIAL ESSENCE

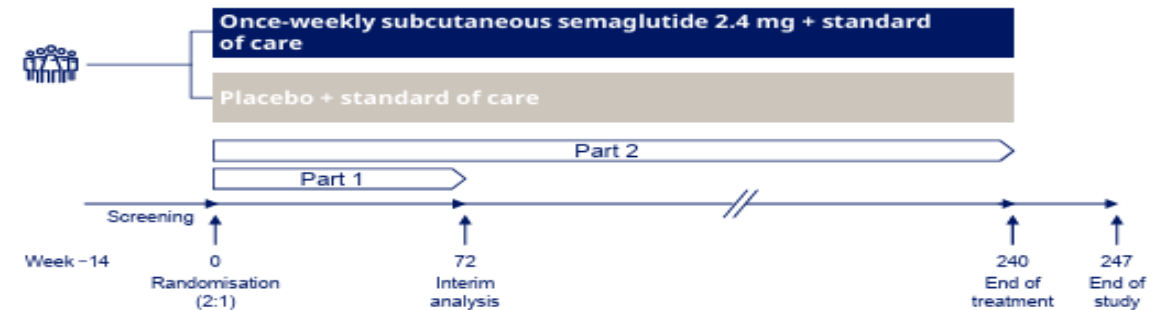
Participants: 800, (56% F), BMI 34,5 kg/m<sup>2</sup>, T2D 56%, Duration 72 weeks (ad interim analysis)



Resolution of steatohepatitis with no worsening of liver fibrosis

Improvement in liver fibrosis with no worsening of steatohepatitis

Figure 1: ESSENCE study design



Sanyal AJ et al. N Engl J Med 2025

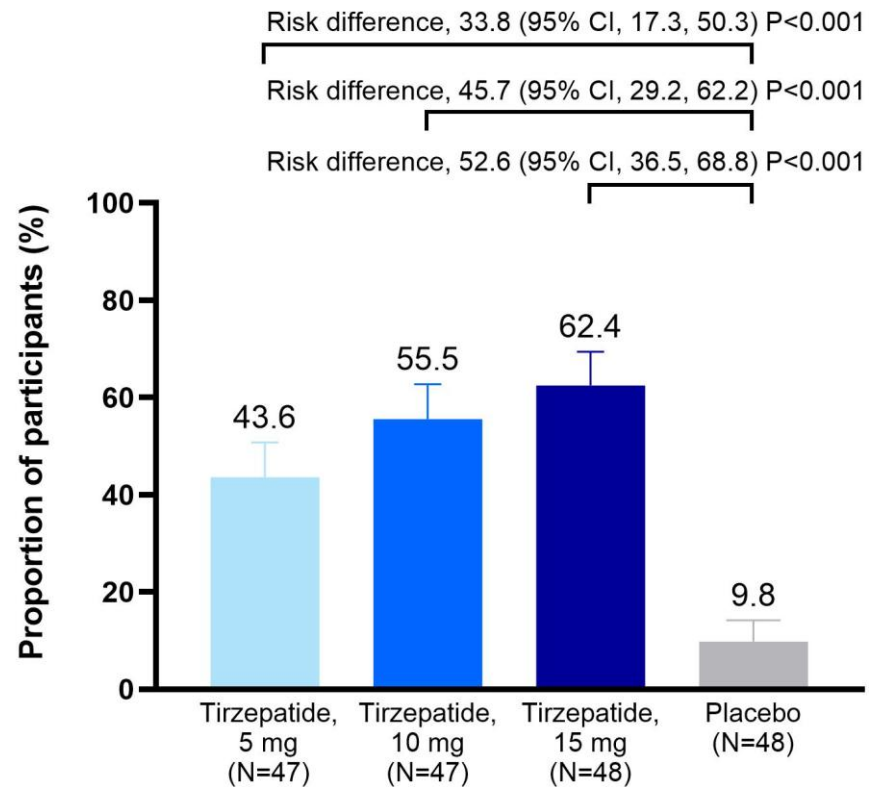
Congresso Nazionale SINPE 2025

CLINICAL NUTRITION: shaping a better future of health care

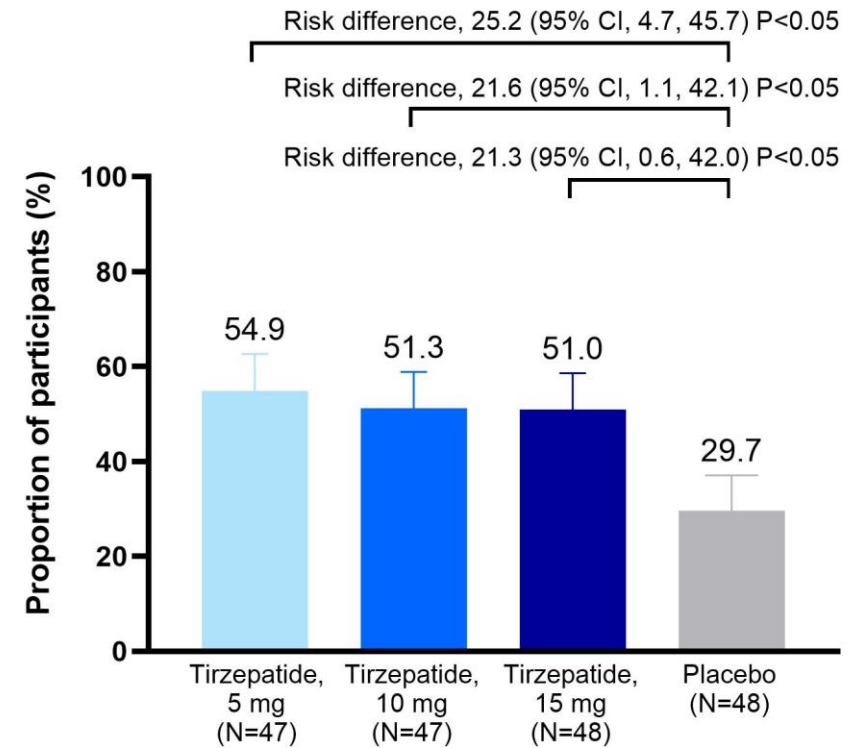
# TIRZEPATIDE e MASH: IL TRIAL SYNERGY

Participants: 190, 57% F, BMI 36.1 kg/m<sup>2</sup>, T2D 58%, Duration 52 weeks

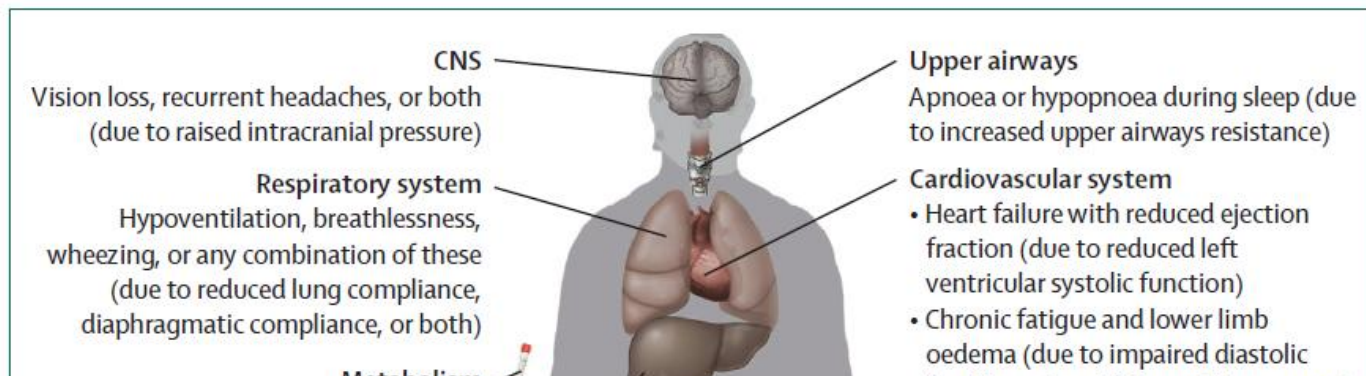
## Resolution of MASH and no worsening of liver fibrosis



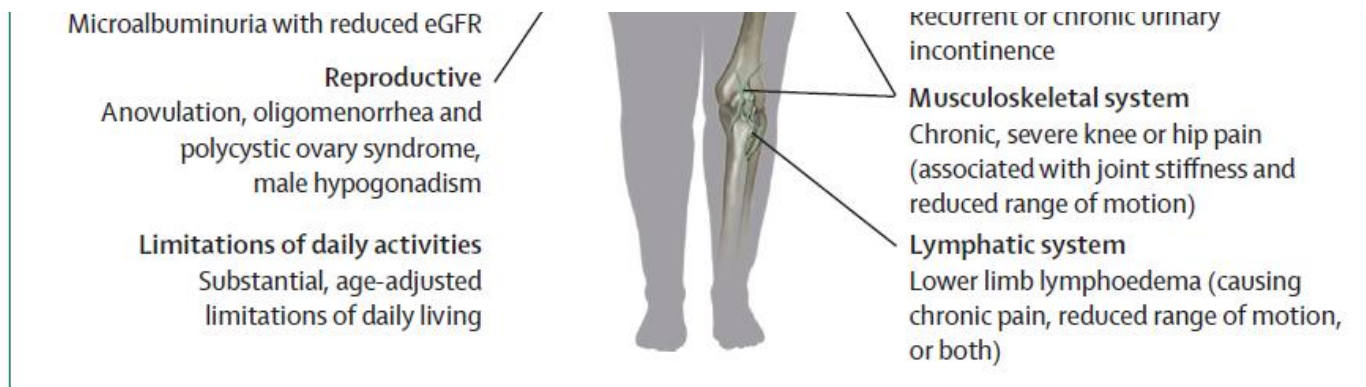
## Improvement in liver fibrosis and no worsening of MASH



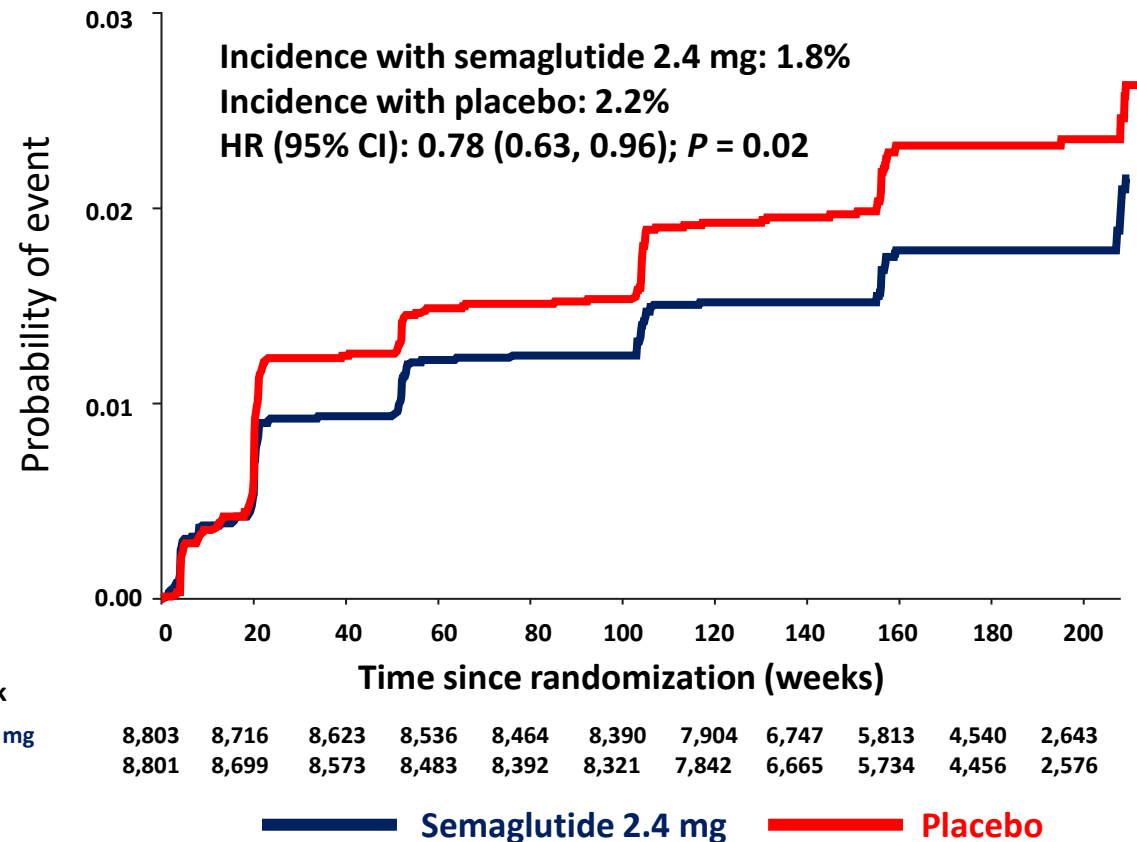
# RENE



## Renal Microalbuminuria with reduced eGFR



# SEMAGLUTIDE SU ENDPOINT COMPOSITO RENALE (STUDIO SELECT)



Patients at risk

Semaglutide 2.4 mg

Placebo

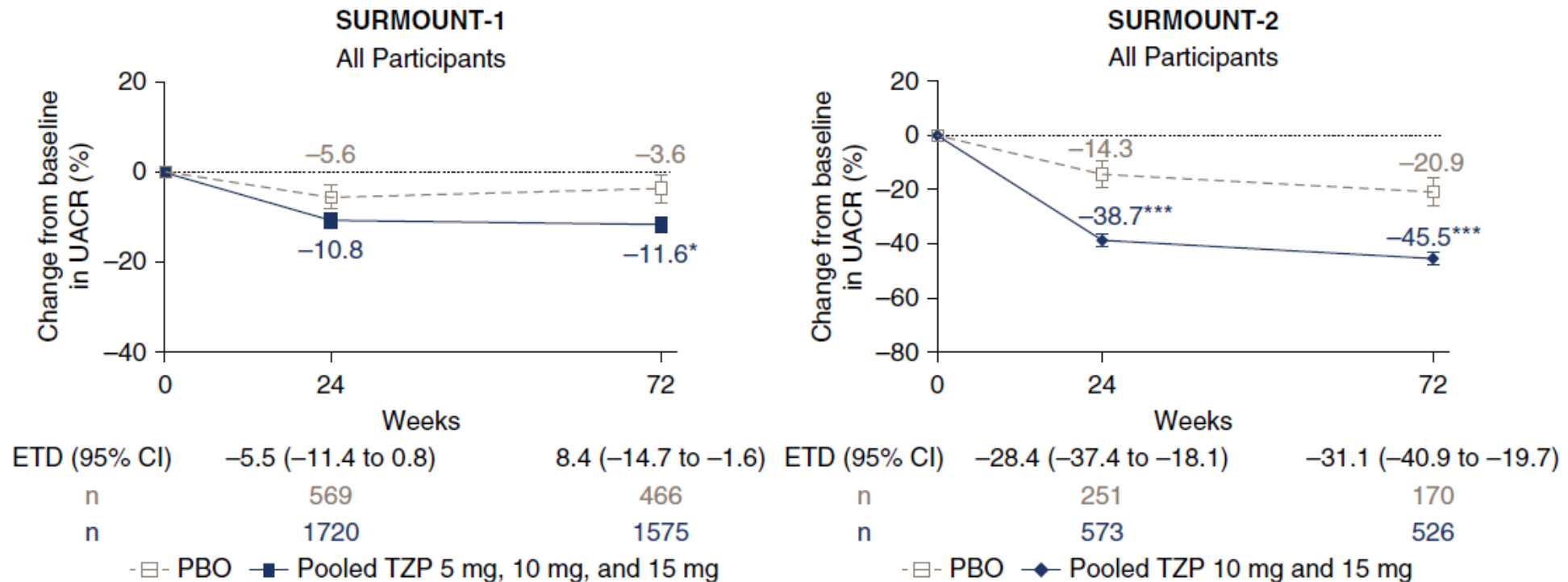
— Semaglutide 2.4 mg — Placebo

Colhoun HM et al. Nat Med. 2024

The main 5-component kidney composite endpoint included death from kidney causes, initiation of chronic kidney replacement therapy (dialysis or transplantation), onset of persistent eGFR <15 ml min<sup>-1</sup> 1.73 m<sup>-2</sup>, persistent ≥50% reduction in eGFR compared with baseline or onset of persistent macroalbuminuria.

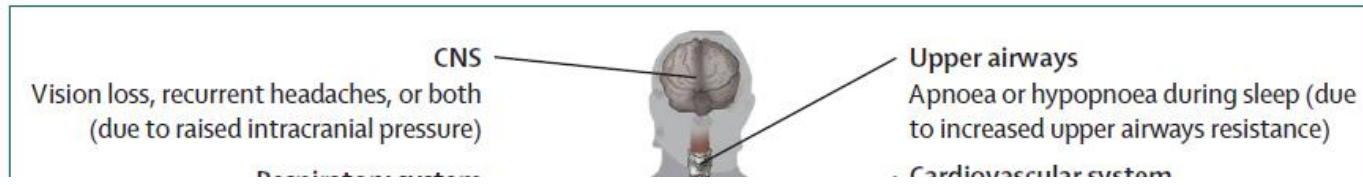
# TIRZEPATIDE SU PARAMETRI RENALI IN PAZIENTI CON SOVRAPPESO/OBESITA' CON O SENZA T2D

A post-hoc analysis of the SURMOUNT-1 and SURMOUNT-2 trials



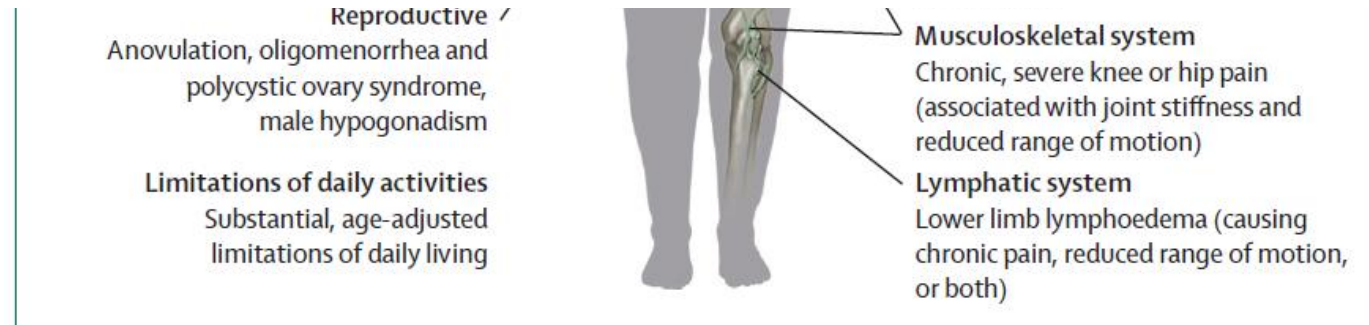
UACR: urine albumin-to-creatinine ratio

# SISTEMA CARDIOVASCOLARE



## Cardiovascular system

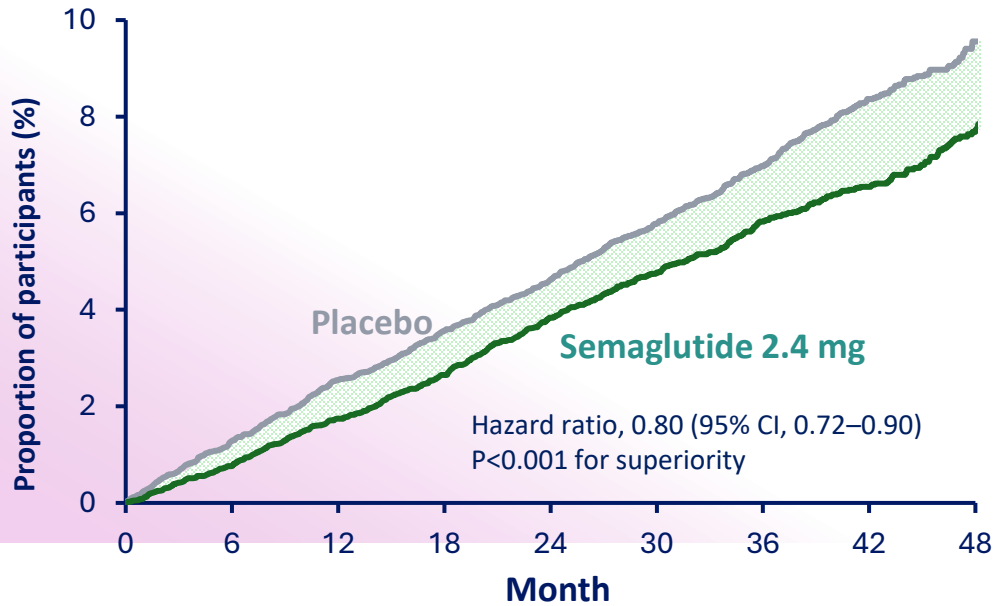
- Heart failure with reduced ejection fraction (due to reduced left ventricular systolic function)



# LO STUDIO SELECT: ENDPOINT PRIMARIO E SECONDARIO

20%

Semaglutide 2.4 mg significantly reduces risk of MACE



Lincoff AM et al. N Engl J Med. 2023

The SELECT trial showed further benefits with semaglutide 2.4 mg vs placebo:

15%

REDUCTION

in risk of CV death

18%

REDUCTION

in risk of composite HF outcome

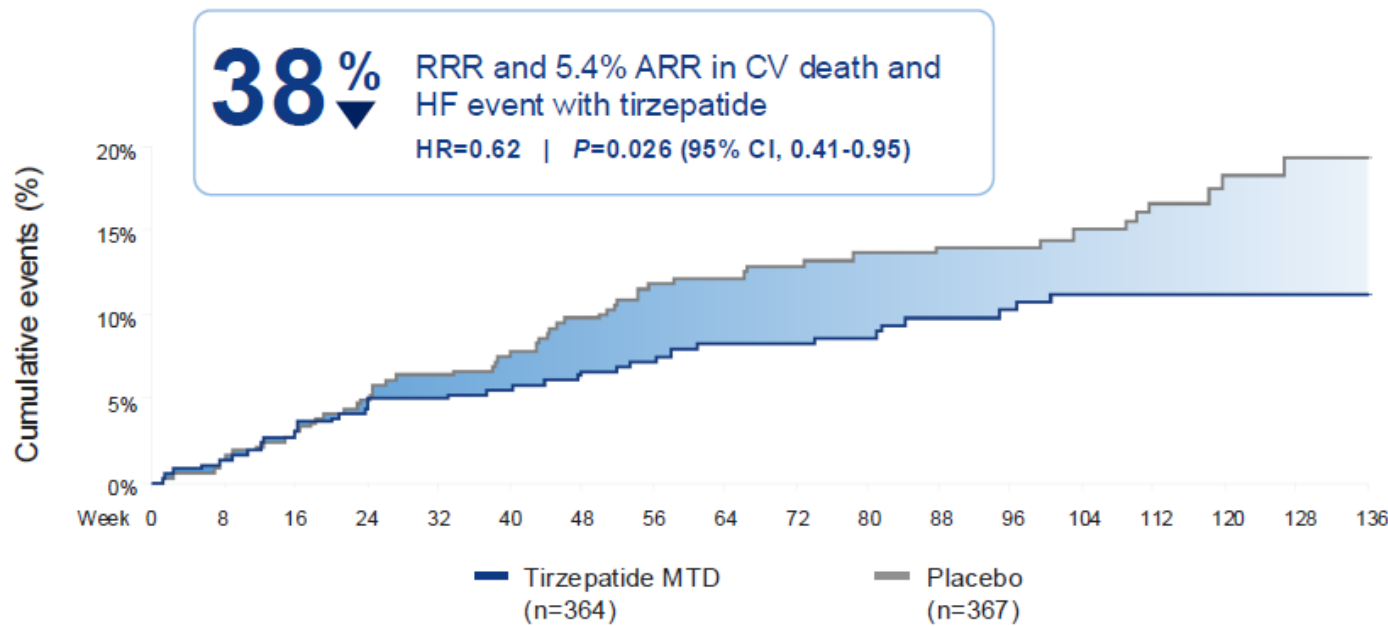
19%

REDUCTION

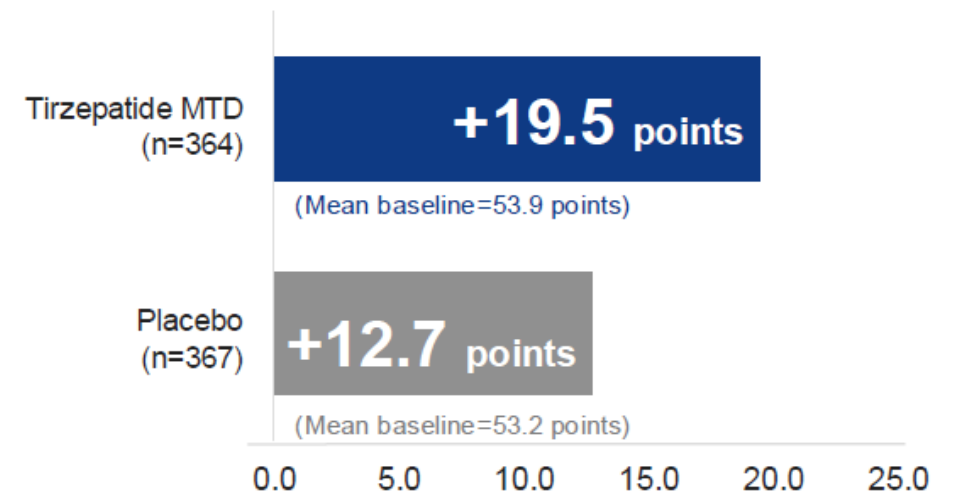
in risk of all-cause death

# TIRZEPATIDE MIGLIORA GLI OUTCOME DI SCOMPENSO IN PAZIENTI CON HFPEF ED OBESITÀ E CON O SENZA DIABETE MELLITO TIPO 2: LO STUDIO SUMMIT

Composite primary endpoint: CV death or worsening HF

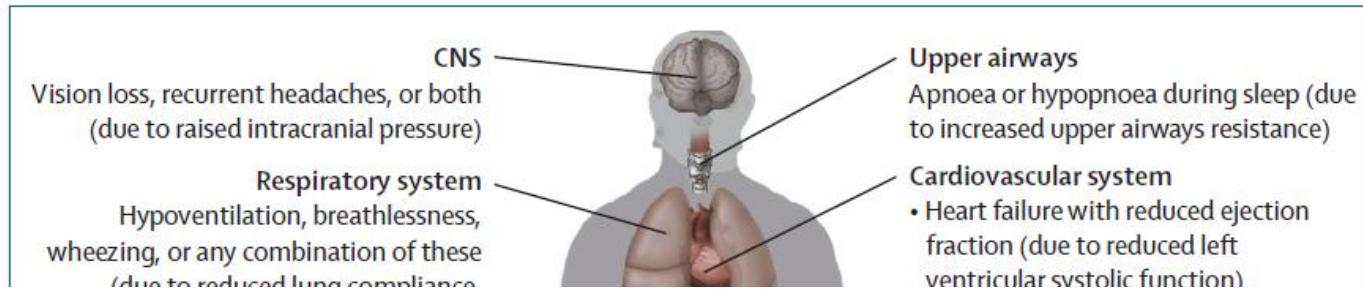


Improvement in physical functioning as measured by the KCCQ-CSS\* self-administered assessment at week 52



**Worsening heart-failure** event was defined as exacerbated symptoms of heart failure resulting in hospitalization, intravenous therapy in an urgent care setting, or intensification of oral diuretic therapy

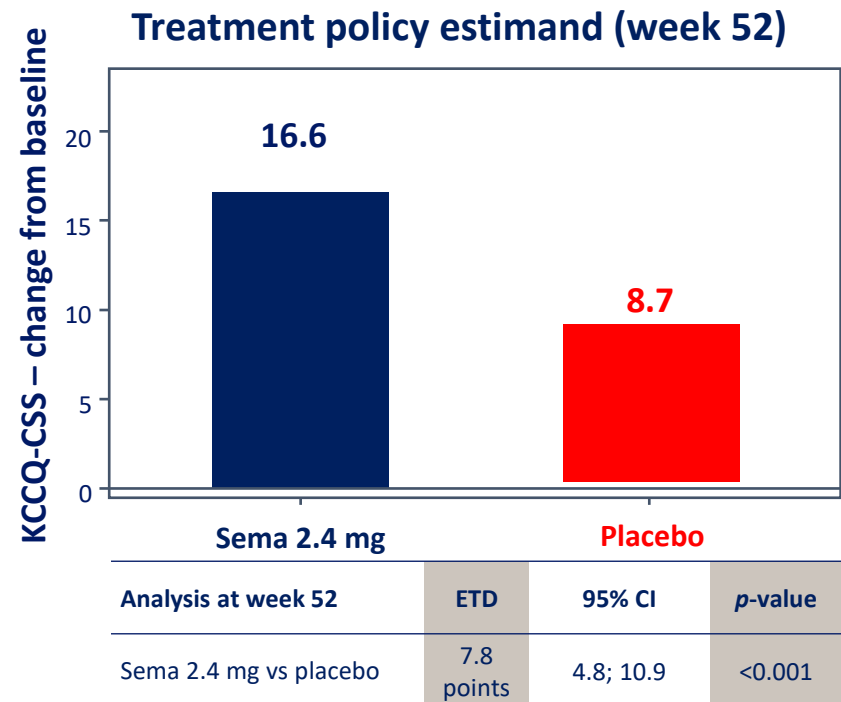
# ATTIVITA' QUOTIDIANE



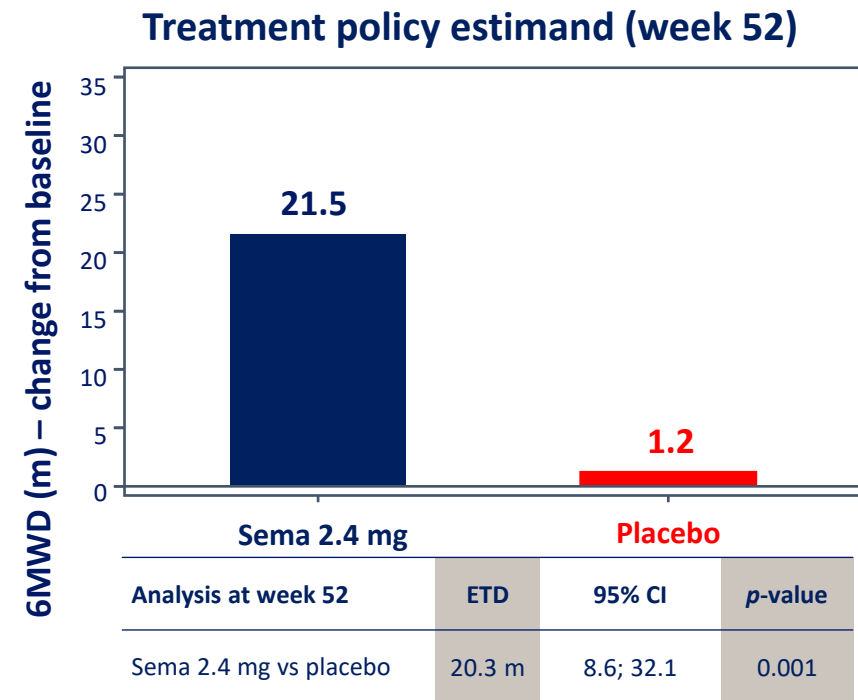
Limitations of daily activities  
Substantial, age-adjusted  
limitations of daily living



# MIGLIORAMENTO CON SEMAGLUTIDE DEL KANSAS CITY QUESTIONNAIRE E DELLA CAMMINATA PER 6 MINUTI IN PORTATORI DI SCOMPENSO A FE CONSERVATA



Baseline median KCCQ-CSS: 58.9 points

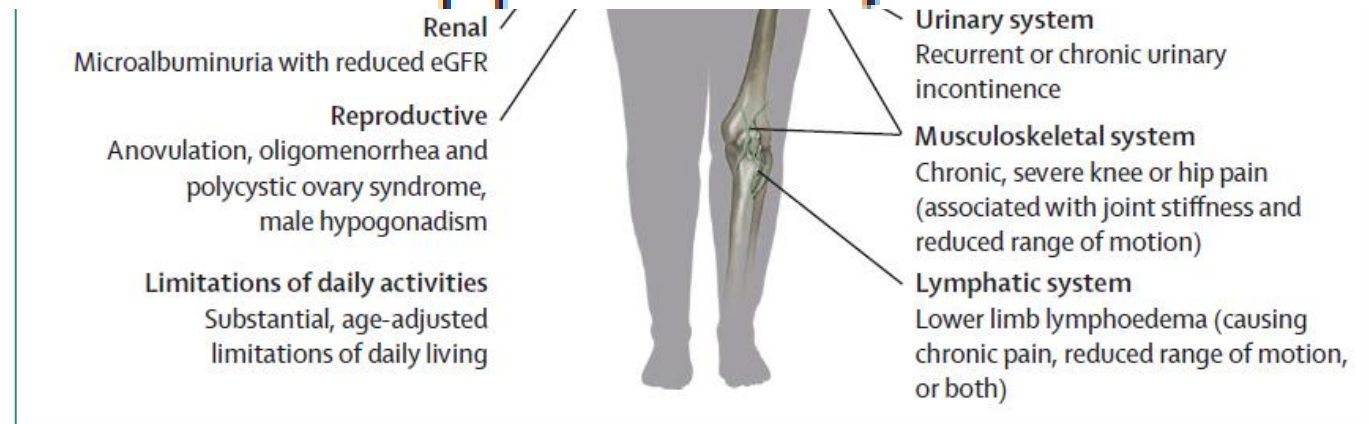


Baseline 6MWD: 320.0 m

# APPARATO RESPIRATORIO

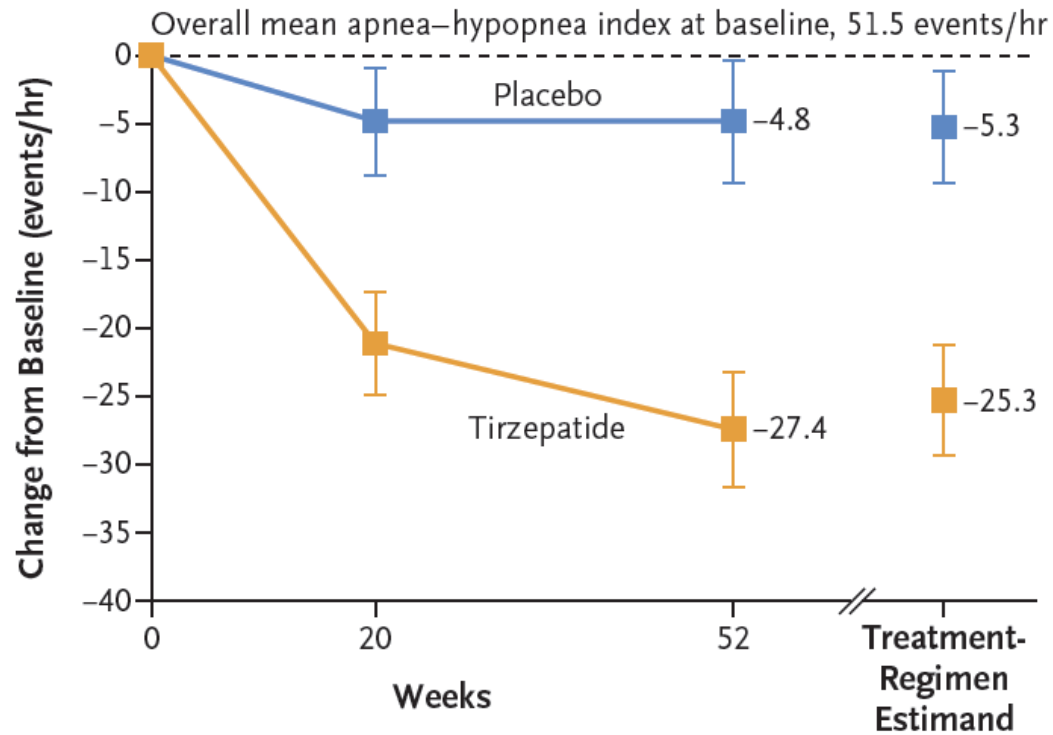


## Upper airways Apnoea or hypopnoea during sleep (due to increased upper airways resistance)

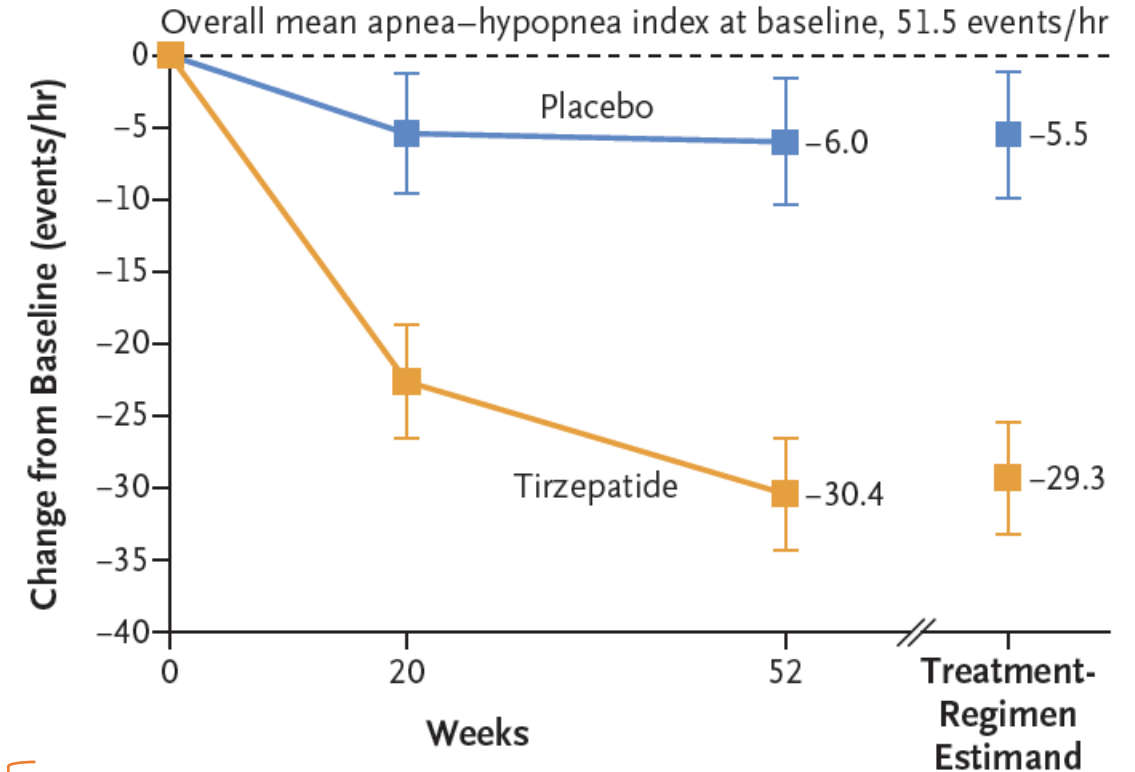


# MIGLIORAMENTO CON TIRZEPATIDE DELLE OSAS SIA IN PAZ SENZA CPAP SIA IN QUELLI CON CPAP

VARIAZIONE DELL'INDICE AHI IN PAZIENTI NON IN TERAPIA PAP



VARIAZIONE DELL'INDICE AHI IN PAZIENTI IN TERAPIA PAP

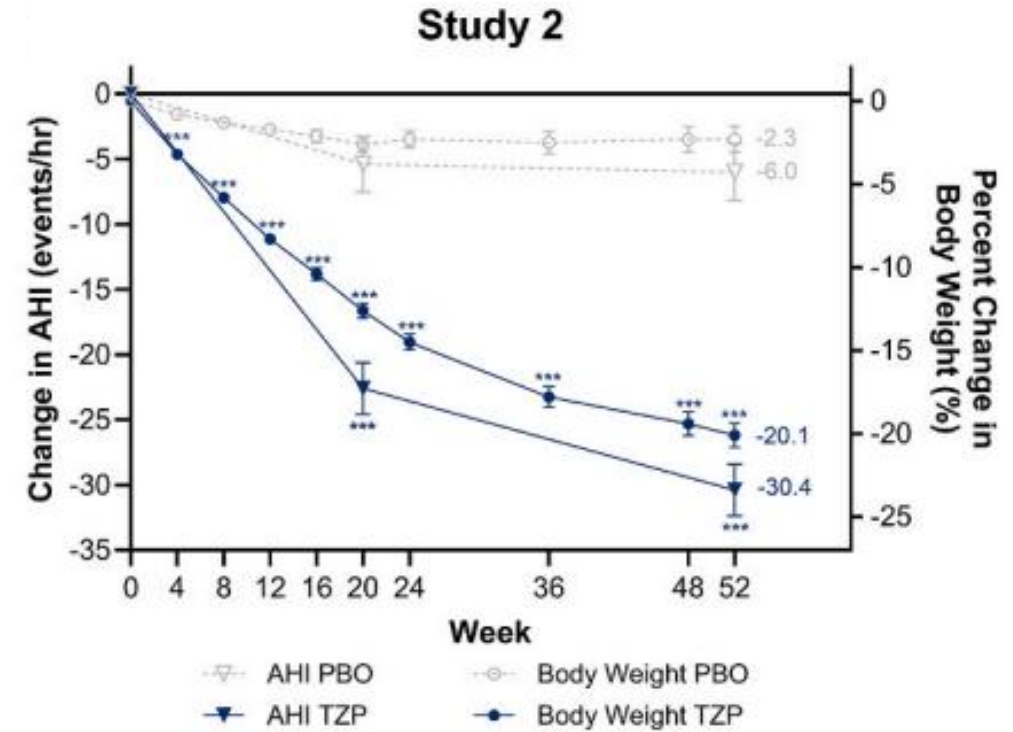
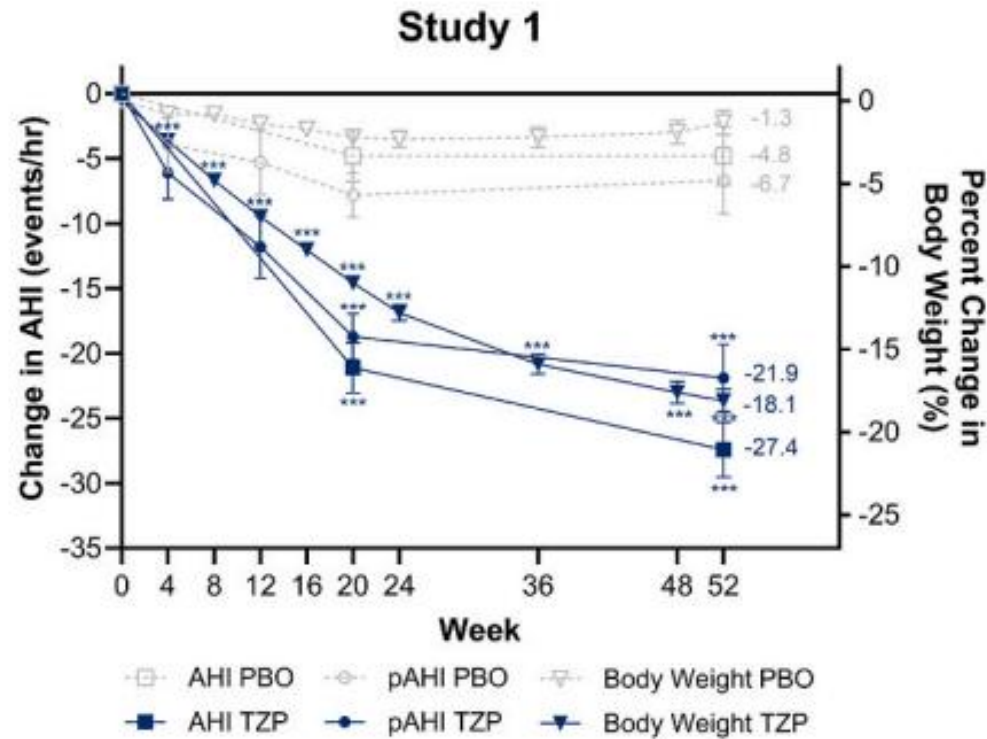


**Indice Apnee/Ipopnee (AHI):**  
numero di apnee e ipopnee per ora di sonno

**OSAS**

< 5	normale
5 - <15	lieve
15 - 30	moderata
> 30	severa

# ASSOCIAZIONE TRA MIGLIORAMENTO DELLE OSAS E PERDITA DI PESO DOPO TIRZEPATIDE



January 24, 2025

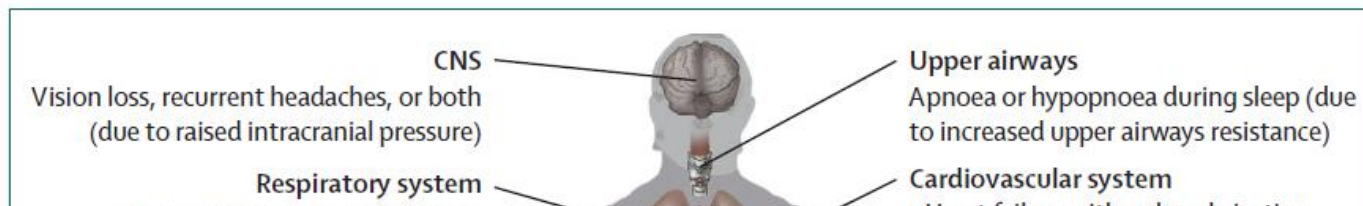
# FDA Approves Tirzepatide as First Drug for Obstructive Sleep Apnea

Samantha Anderer

*JAMA*. 2025;333(8):656. doi:10.1001/jama.2024.28055



# APPARATO MUSCOLO-SCHELETRICO



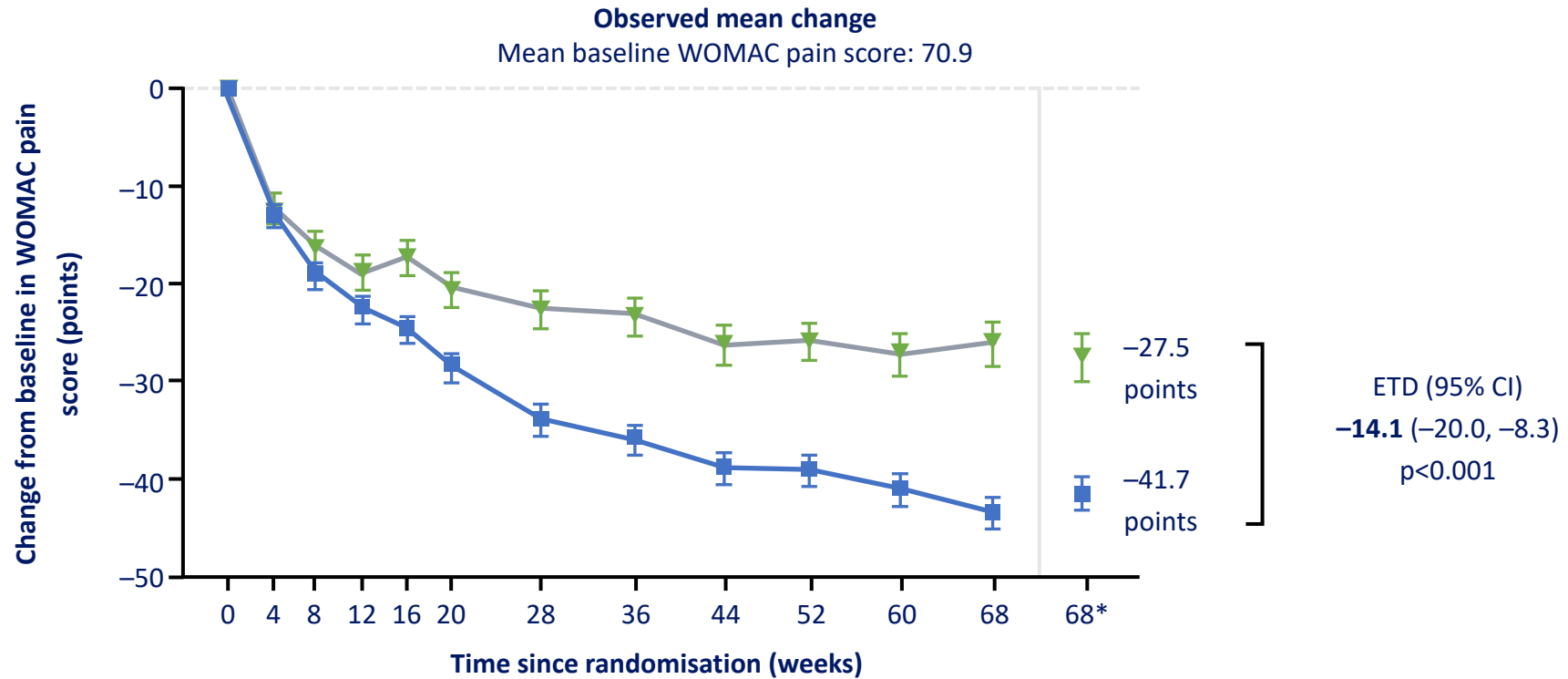
## Musculoskeletal system

Chronic, severe knee or hip pain

(associated with joint stiffness and  
reduced range of motion)



# VARIAZIONE NEL PUNTEGGIO WOMAC PER MONITORARE IL DOLORE DA PARTE DI SEMAGLUTIDE



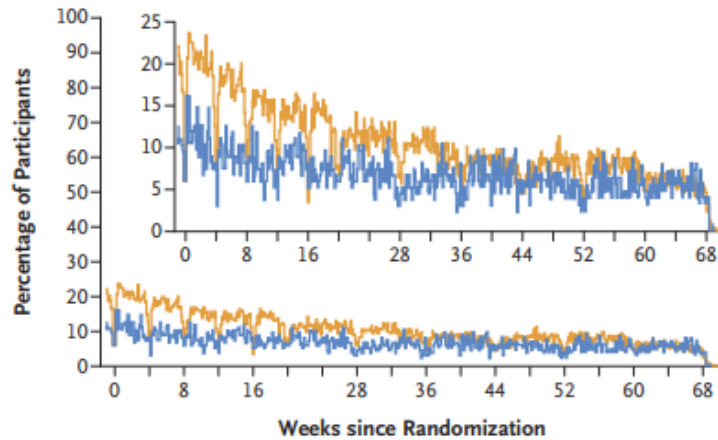
**Number of participants**

Semaglutide 2.4 mg	271	262	260	256	257	256	251	250	245	245	239	245	271
Placebo	136	132	129	126	126	128	126	117	116	118	111	117	136

■ Semaglutide 2.4 mg    ■ Placebo

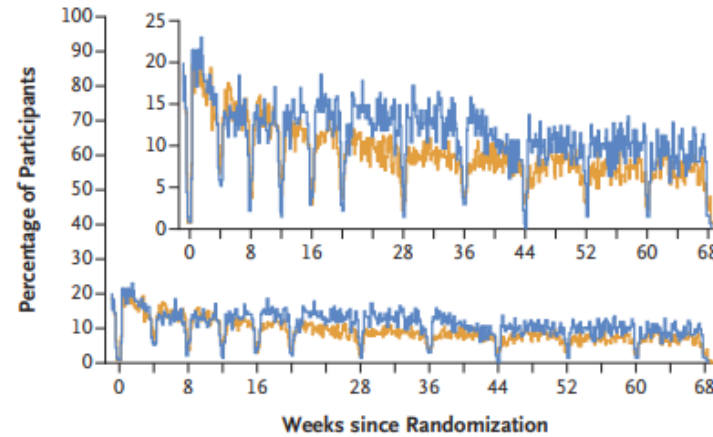
# IMPIEGO DI FARMACI ANTI-DOLORIFICI

**A** Participants Receiving Acetaminophen



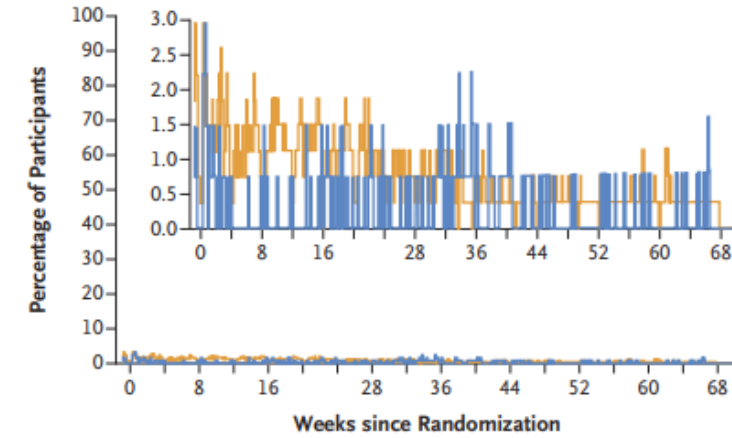
No. of Participants		0	8	16	28	36	44	52	60	68
Placebo		136	135	135	135	133	131	128	126	121
Semaglutide		271	269	267	266	266	265	263	263	258

**B** Participants Receiving NSAIDs



No. of Participants		0	8	16	28	36	44	52	60	68
Placebo		136	135	135	135	133	131	128	126	121
Semaglutide		271	269	267	266	266	265	263	263	258

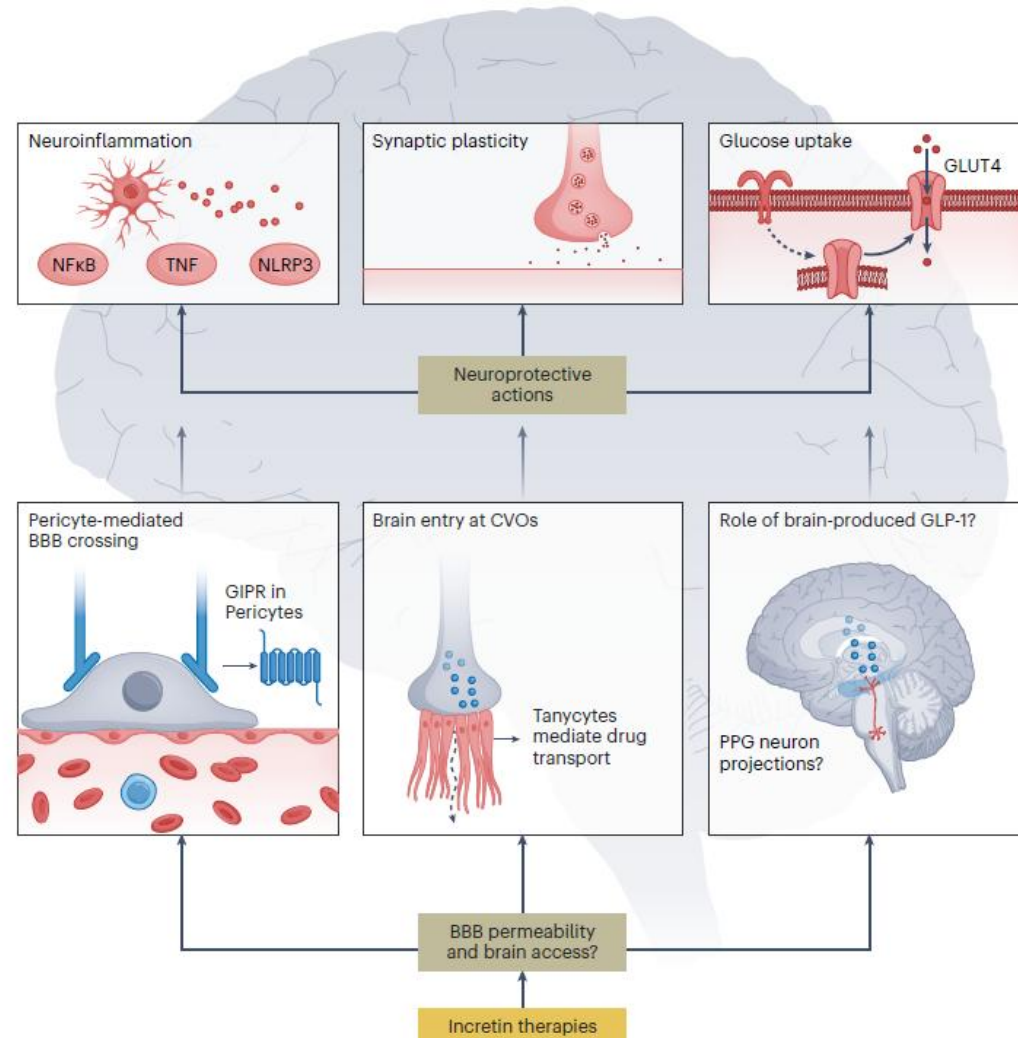
**C** Participants Receiving Opioids



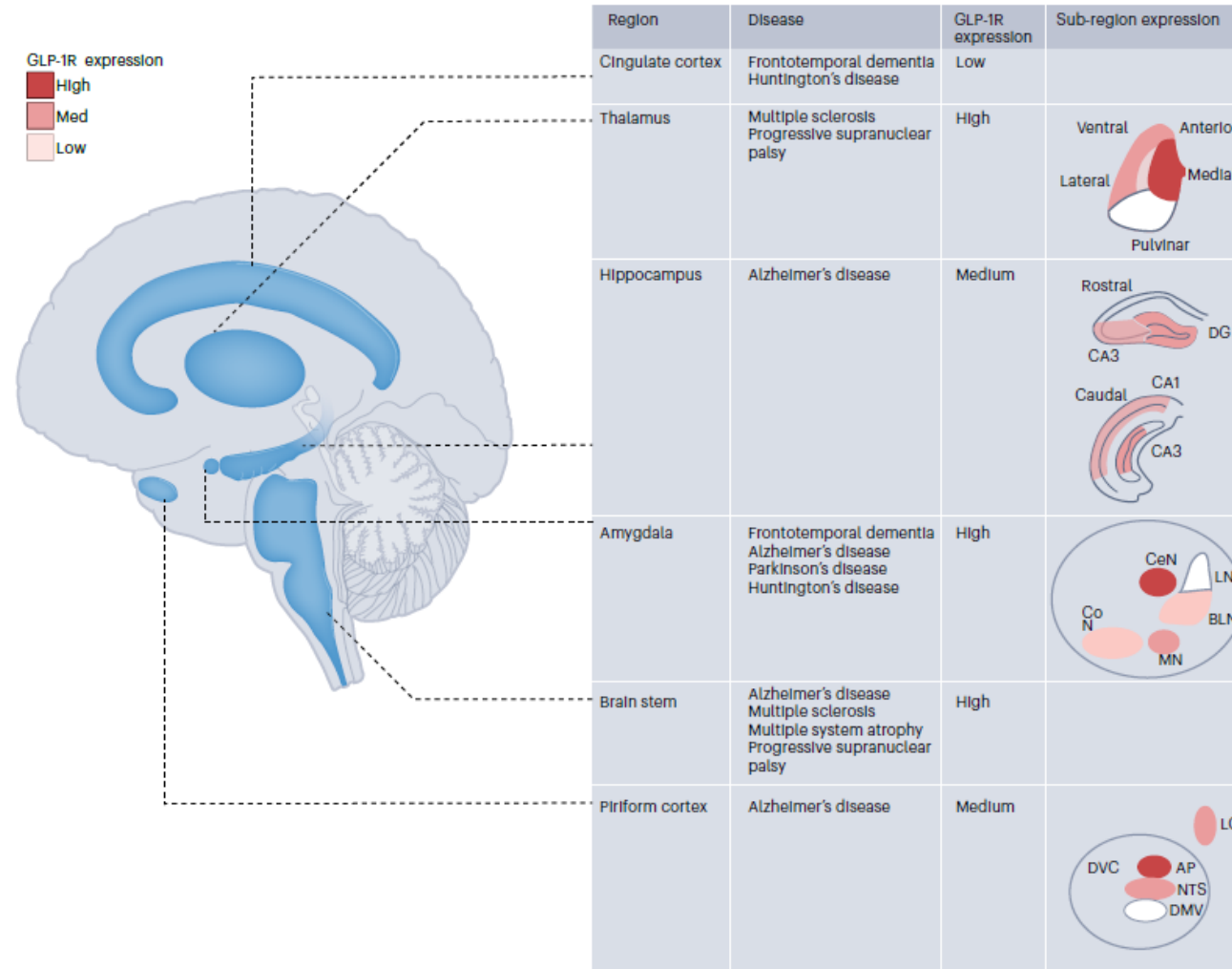
No. of Participants		0	8	16	28	36	44	52	60	68
Placebo		136	135	135	135	133	131	128	126	121
Semaglutide		271	269	267	266	266	265	263	263	258

— Semaglutide — Placebo

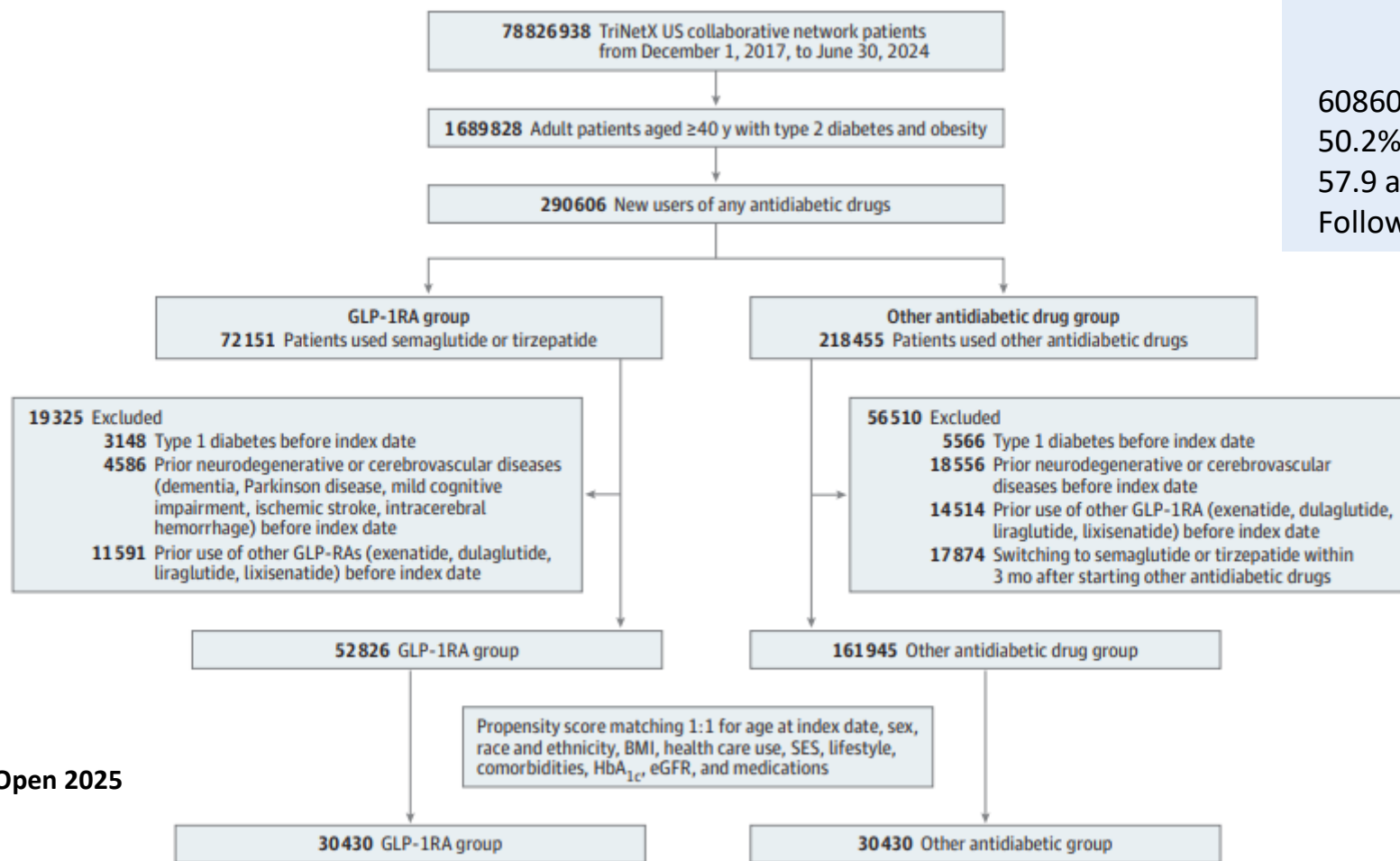
# POTENZIALI VIE D'ACCESSO E SITI DI PRODUZIONE DELLE INCRETINE NEL SNC



# ESPRESSIONE DEL RECETTORE PER IL GLP-1 IN REGIONI CEREBRALI RILEVANTI PER MALATTIE NEURODEGENERATIVE



# GLP1 e GLP1/GIP e ASPETTO COGNITIVO

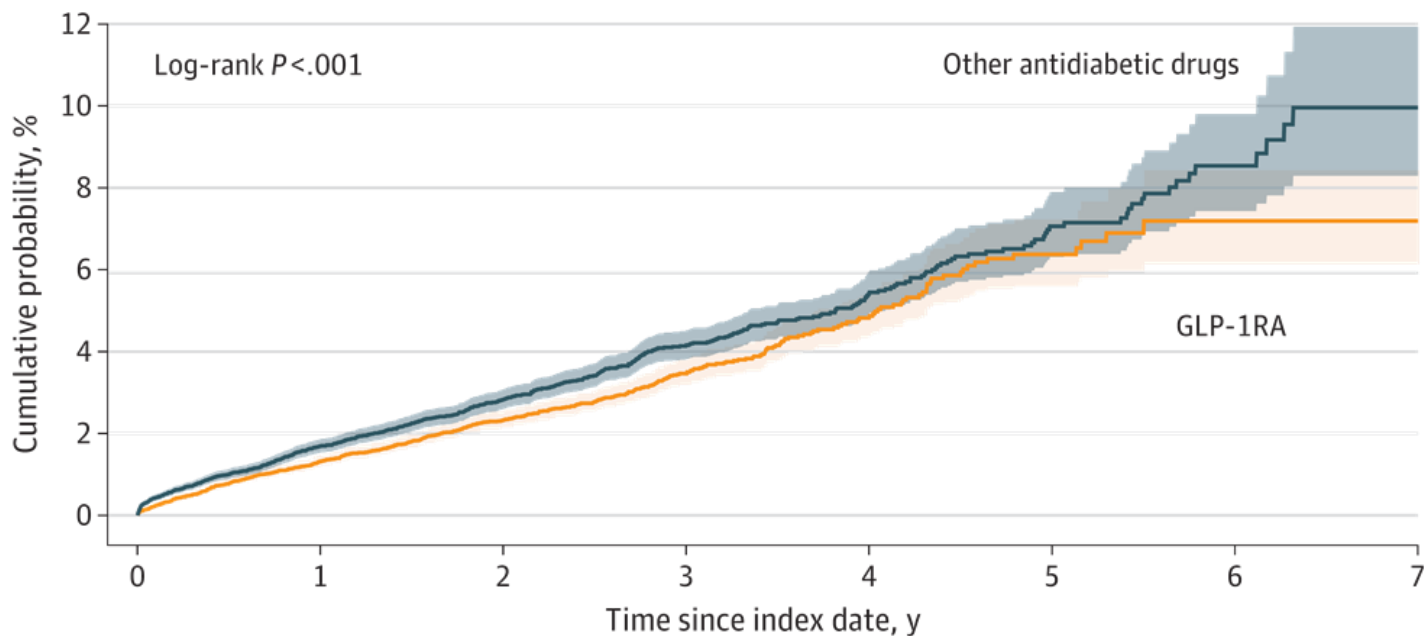


60860 pz con obesità eT2D  
50.2% donne  
57.9 anni  
Follow-up 7 anni

Lin H-T et al. JAMA Net Open 2025

# GLP1 e GLP1/GIP e ASPETTO COGNITIVO

Figure 2. Cumulative Probability of Neurodegenerative and Cerebrovascular Diseases in Glucagon-Like Peptide 1 Receptor Agonist (GLP-1RA) vs Other Antidiabetic Drug Users



No. at risk	0	1	2	3	4	5	6	7
GLP-1RA	30 430	29 968	29 694	29 519	29 445	29 408	29 395	29 395
Other antidiabetic drugs	30 430	29 900	29 642	29 479	29 403	29 359	29 338	29 332

Shading indicates 95% CI.

**Maggiore beneficio nei paz dai 60 anni in su, donne e con BMI tra 30 e 40**

.....”while treatment with semaglutide resulted in improvement of Alzheimer’s disease-related biomarkers in both trials, this did not translate into a delay of disease progression....”

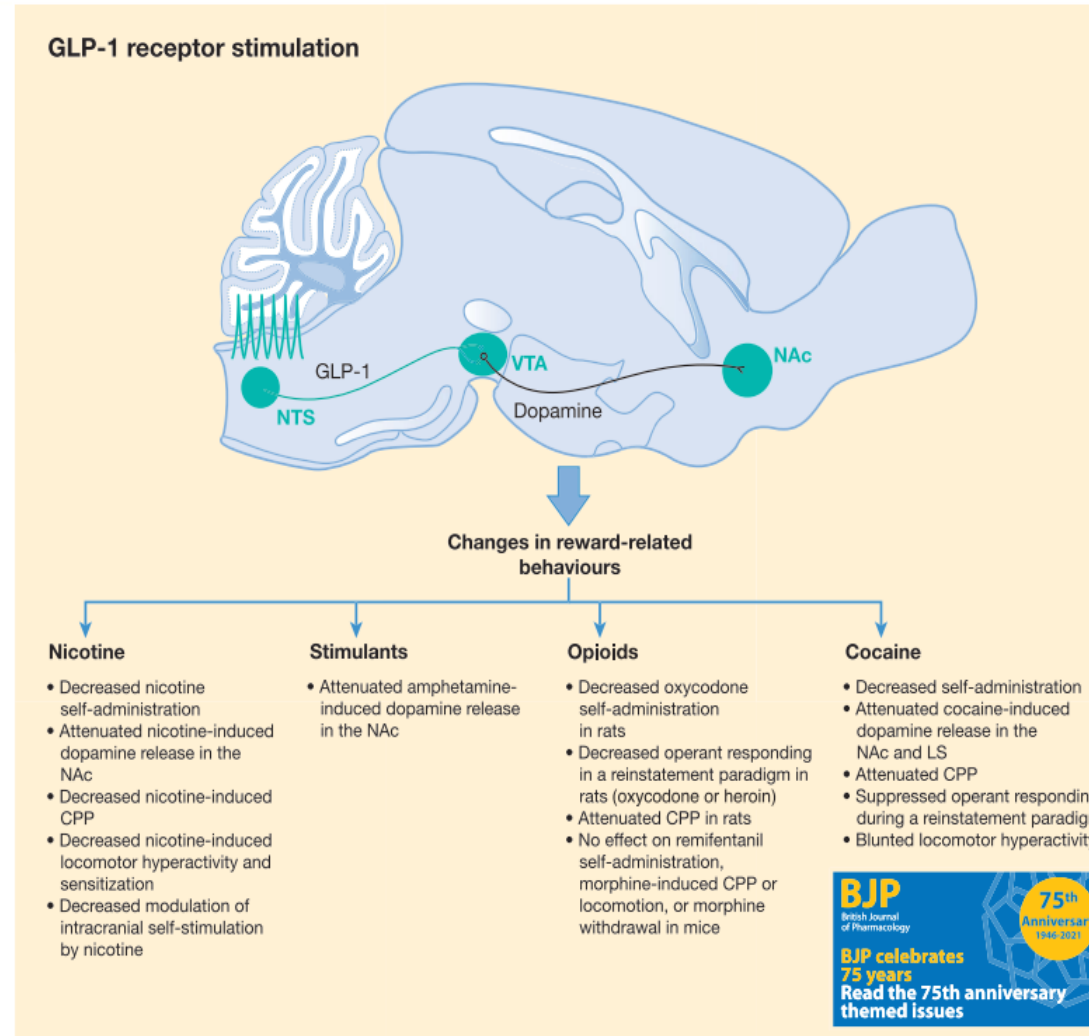


## company announcement

### **Evoke phase 3 trials did not demonstrate a statistically significant reduction in Alzheimer's disease progression**

**Bagsværd, Denmark, 24 November 2025** – Novo Nordisk today announced the top-line results from the 2-year primary analysis of evoke and evoke+ phase 3 trials in early-stage symptomatic Alzheimer’s disease. The two trials were randomised, double-blinded, enrolled a total of 3808 adults and evaluated the efficacy and safety of oral semaglutide compared to placebo on top of standard of care. The decision to pursue an Alzheimer’s disease indication with semaglutide was based on real-world evidence studies, pre-clinical models as well as post-hoc analyses from diabetes and obesity trials.

# IL RUOLO DEL GLP1 NELLE AREE CHE CONTROLLANO LA GRATIFICAZIONE



Klausen MK et al. BJP 2021

Congresso Nazionale SINPE 2025

CLINICAL NUTRITION: shaping a better future of health care

# FARMACI INCRETINICI ED ADDICTION

nature communications



Article

<https://doi.org/10.1038/s41467-024-48780-6>

## Associations of semaglutide with incidence and recurrence of alcohol use disorder in real-world population

Received: 8 November 2023

William Wang<sup>1</sup>, Nora D. Volkow<sup>2</sup>✉, Nathan A. Berger<sup>1</sup>, Pamela B. Davis<sup>3</sup>, David C. Kaelber<sup>4</sup> & Rong Xu<sup>5</sup>✉

Molecular Psychiatry

[www.nature.com/mp](http://www.nature.com/mp)

IMMEDIATE COMMUNICATION **OPEN**



Association of semaglutide with reduced incidence and relapse of cannabis use disorder in real-world populations: a retrospective cohort study

William Wang<sup>1</sup>, Nora D. Volkow<sup>2</sup>✉, Nathan A. Berger<sup>1</sup>, Pamela B. Davis<sup>3</sup>, David C. Kaelber<sup>4</sup> and Rong Xu<sup>5</sup>✉

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ORIGINAL RESEARCH

Annals of Internal Medicine

## Association of Semaglutide With Tobacco Use Disorder in Patients With Type 2 Diabetes

Target Trial Emulation Using Real-World Data

William Wang; Nora D. Volkow, MD; Nathan A. Berger, MD; Pamela B. Davis, MD, PhD; David C. Kaelber, MD, PhD, MPH; and Rong Xu, PhD

JAMA Network | **Open**



Research Letter | Psychiatry

## Semaglutide and Opioid Overdose Risk in Patients With Type 2 Diabetes and Opioid Use Disorder

William Wang; Nora D. Volkow, MD; QuangQiu Wang, MS; Nathan A. Berger, MD; Pamela B. Davis, MD, PhD; David C. Kaelber, MD, PhD, MPH; Rong Xu, PhD

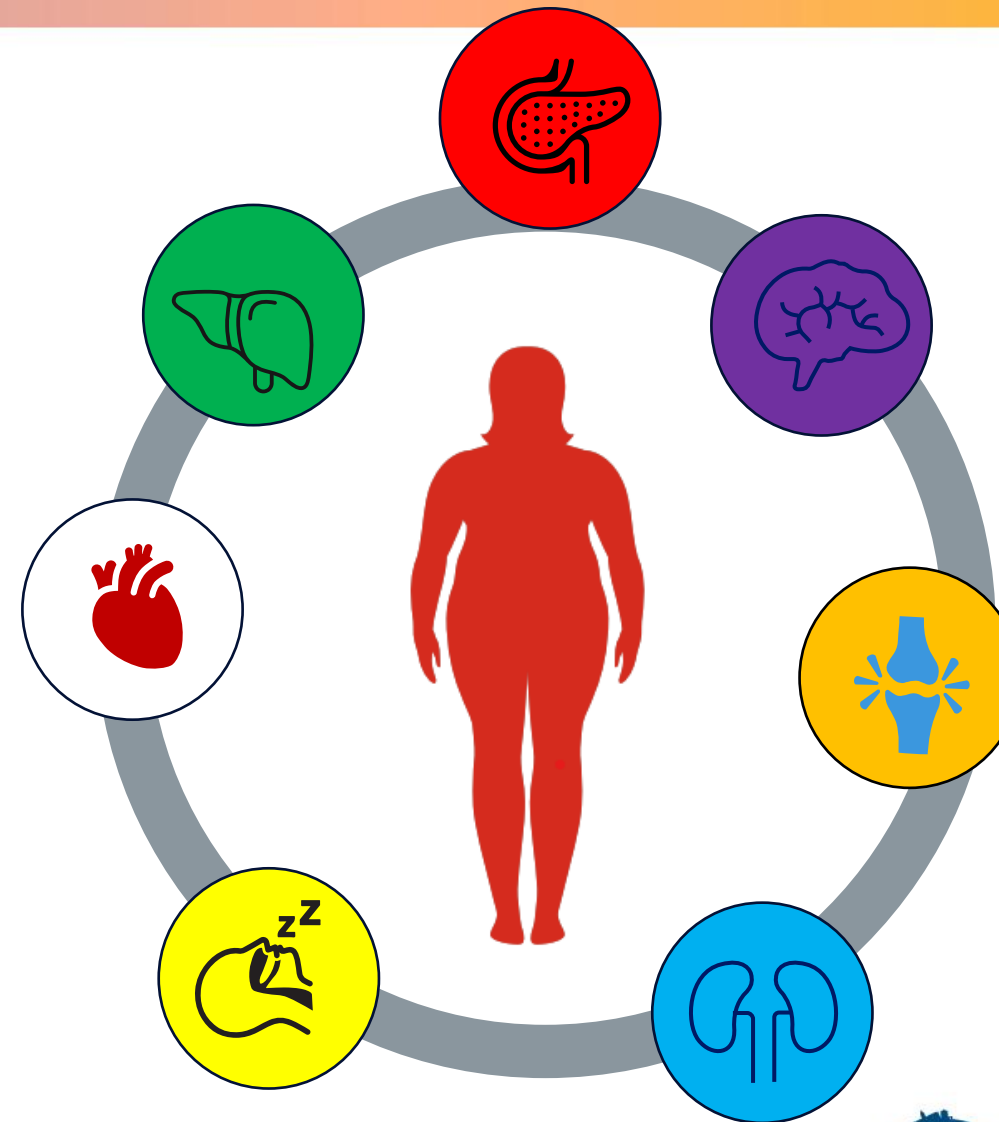
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# CONCLUSIONI

- I FARMACI INCRETINICI MIGLIORANO IL CONTROLLO GLICEMICO IN PAZIENTI CON OBESITA' E T2D, RIDUCONO L'INCIDENZA DI T2D IN PAZIENTI SIA CON PREDIABETE CHE CON NORMOGLICEMIA
- I FARMACI INCRETINICI RIDUCONO LA MASH SENZA PEGGIORARE LA FIBROSI EPATICA E RIDUCONO LA FIBROSI SENZA PEGGIORARE LA MASH
- I FARMACI INCRETINICI MIGLIORANO LA FUNZIONALITA' RENALE
- **SEMAGLUTIDE RIDUCE I MACE IN PREVENZIONE SECONDARIA IN PAZ CON OBESITA' SENZA DIABETE**
- I FARMACI INCRETINICI MIGLIORANO GLI OUTCOME SULLO SCOMPENSO IN PAZIENTI CON HFPEF
- TIRZEPATIDE MIGLIORA LE OSAS SIA IN PORTATORI DI CPAP CHE IN NON PORTATORI DI CPAP
- SEMAGLUTIDE MIGLIORA LA SINTOMATOLOGIA DOLOROSA ASSOCIATA ALL'OSTEOARTRITE
- I FARMACI INCRETINICI SEMBRANO MIGLIORARE GLI ASPETTI COGNITIVI
- I FARMACI INCRETINICI SEMBRANO RIDURRE L'USO DI SOSTANZE DOTATE DI CAPACITA' ADDITIVA



**Grazie per l'attenzione**

**27 - 29 novembre 2025**

**Padova Congress**  
Via Carlo Goldoni 8, Cancellò C - Padova

