CONGRESSO CONGIUNTO SID-AMD-SIEDP-SIE-AME- ANIED-OSDI

"DIABETE ED OBESITA': SI PUO' INVERTIRE LA ROTTA?
Cosa abbiamo guadagnato e cosa abbiamo perso"

Genova (GE), 15 e 16 dicembre 2023

Obesità nel DM2 due malattie, ciascuna richiede trattamento ottimale: Tirzepatide ed i risultati dei trials SURMOUNT

Andrea Natali

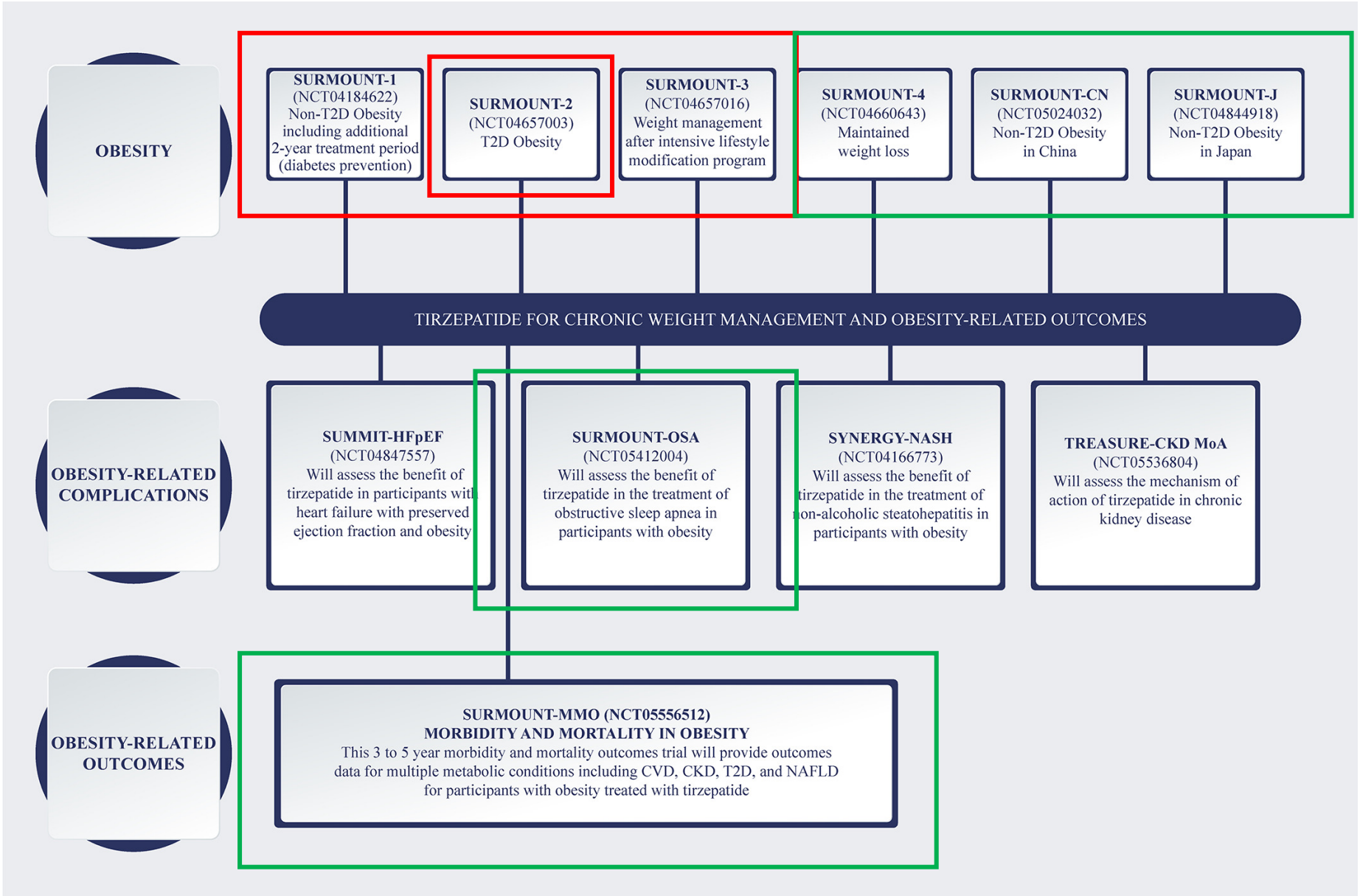
Conflitto di interesse

Dichiaro di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- *Boehringer Ingelheim*
- *Eli Lilly*
- *Servier*
- *Nestlè*

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

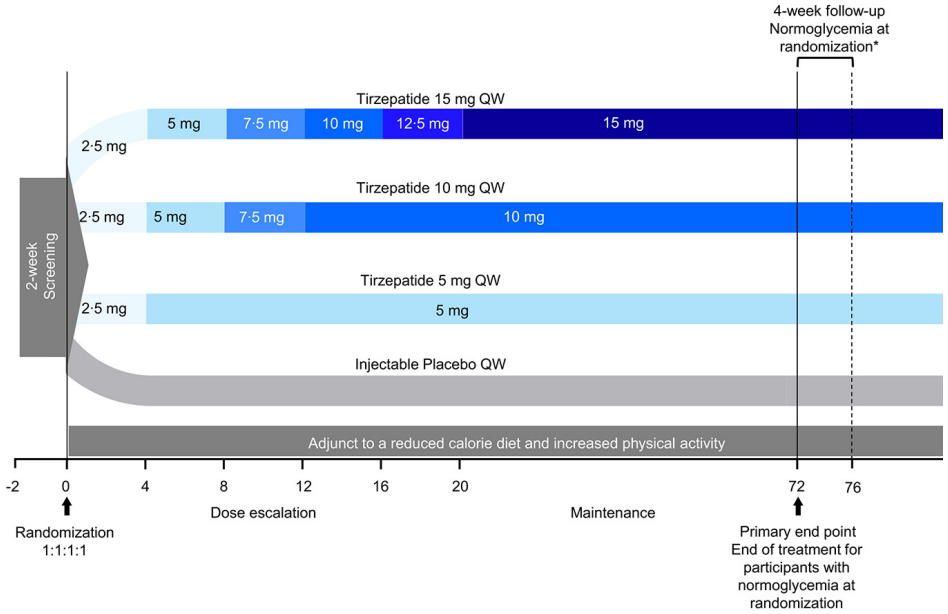
SURMONT Programme



SURMONT 1-3 Study design

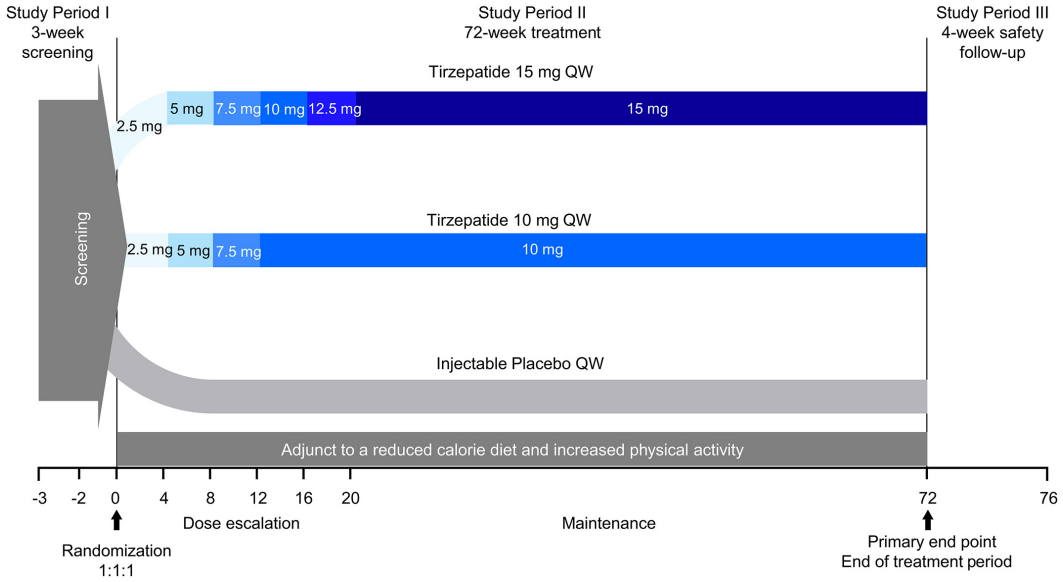
SURMONT 1
Obese no T2D

N=2,539



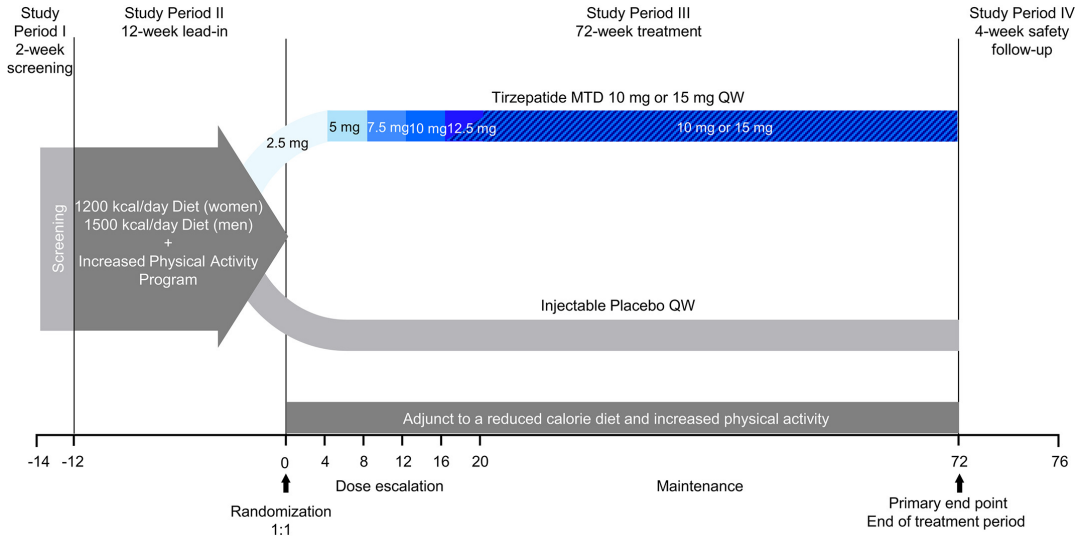
SURMONT-2
Obese T2D

N=938

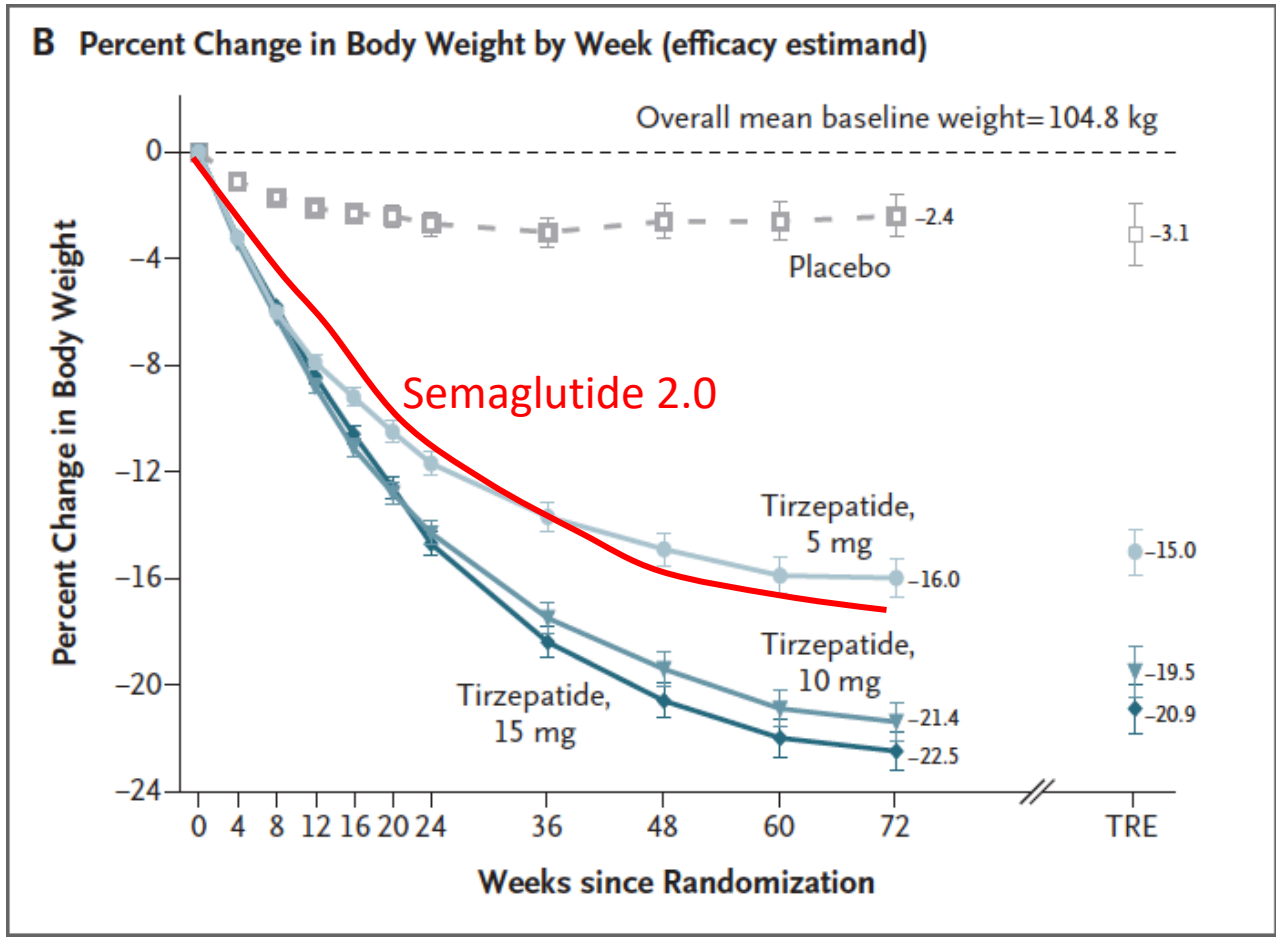


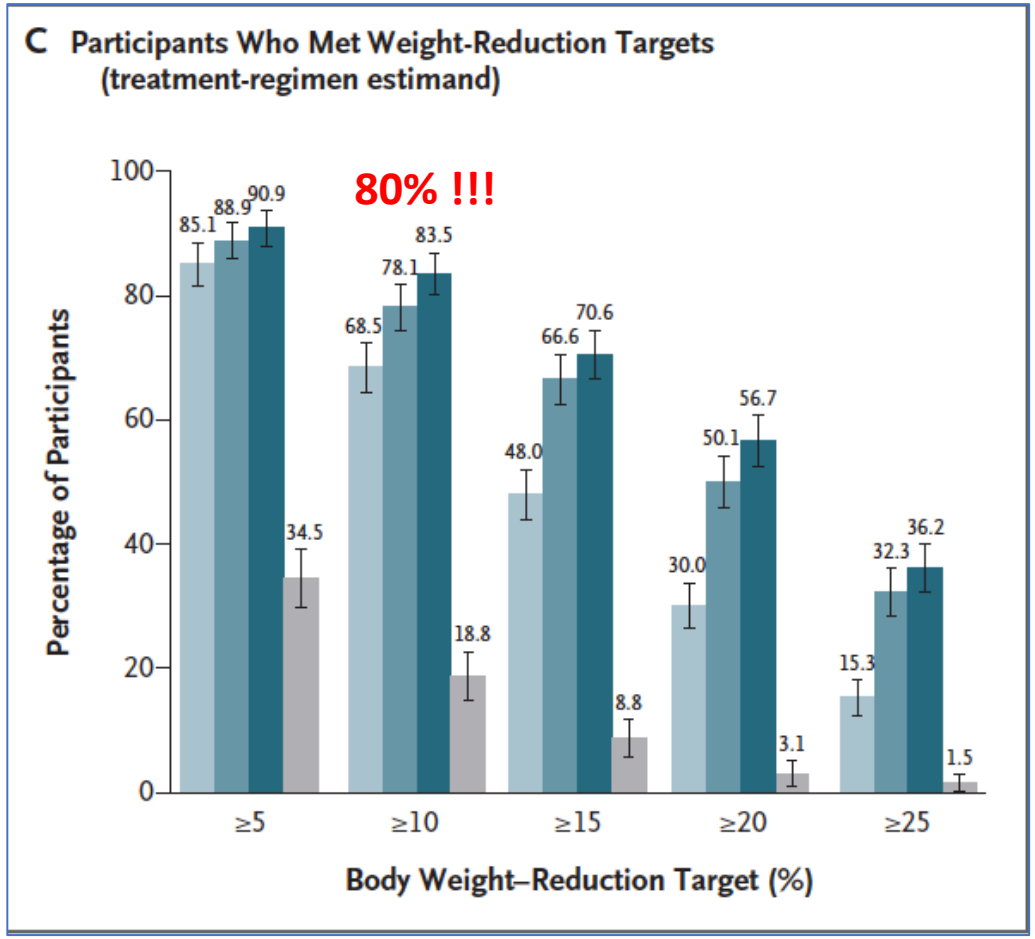
SURMONT-3
Obese no T2D

N=579



SURMONT-1 - Results





Physical function score: Doubled

PAS: - 6 mmHg
TH: -20 mg/dl
HDL: +9 mg/dl

Discontinuation for GI AE: 6 %

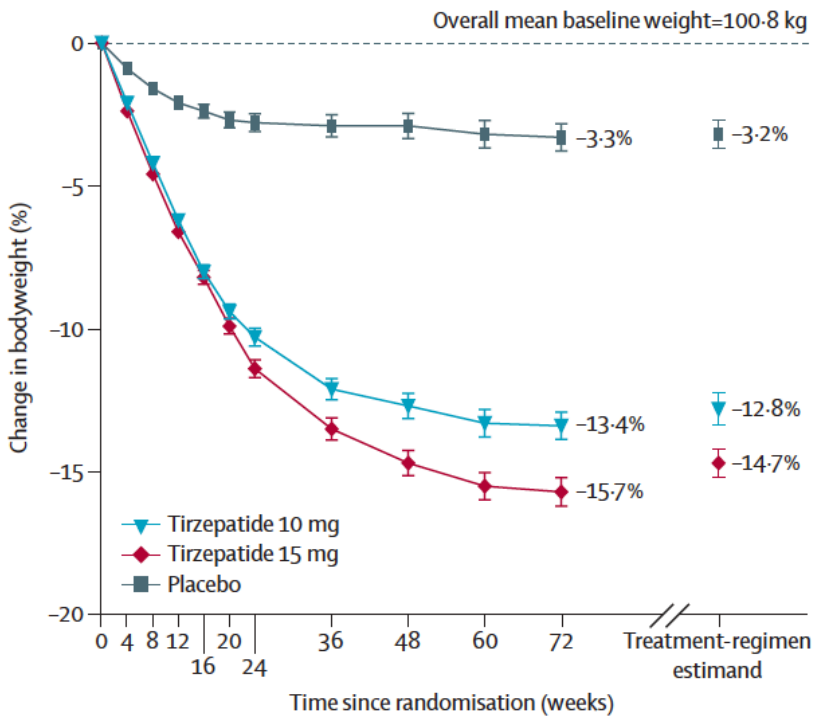
Jastreboff AM *NEJM* 2022

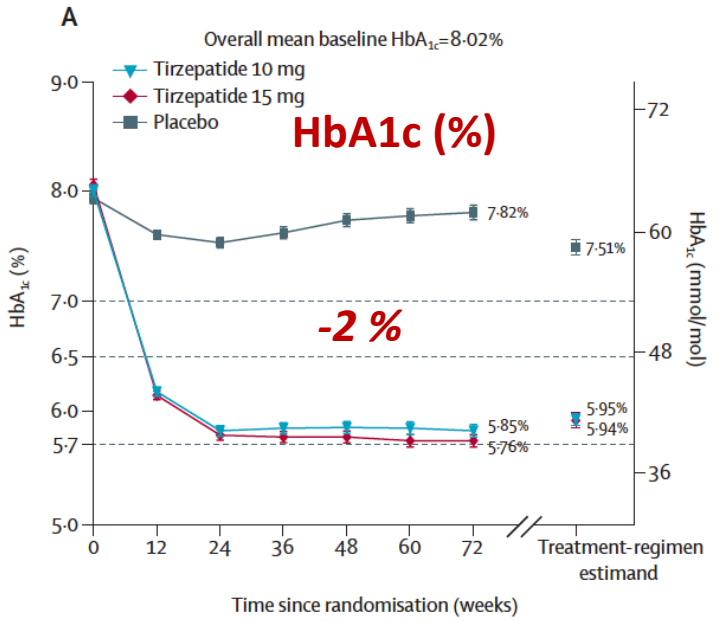
SURMONT-2 - Results

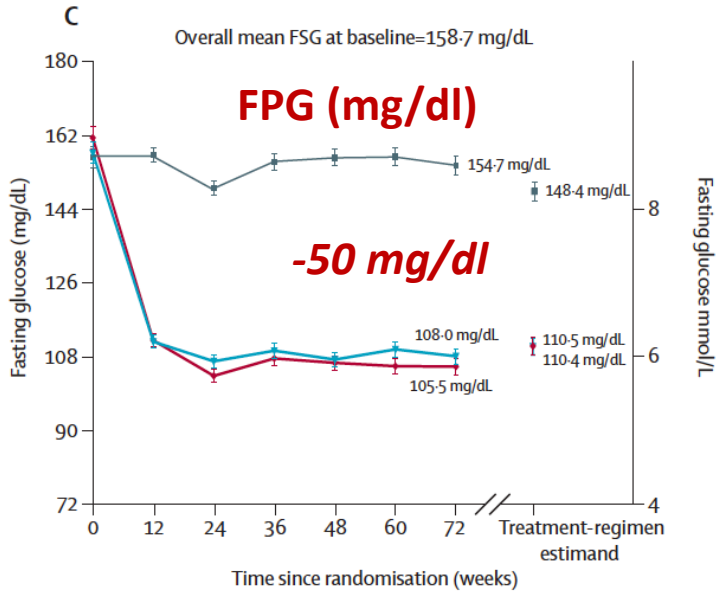
BMI: ≥27 kg/m2
HbA1c: 7-10%

AGE:	55+/-10	yrs
Female:	50	%
BMI:	36+/-6	kg/m²
HbA1c	8+/-1	%
Treatment		
	Diet only	6 %
	MonoT	55%
	2 drugs	32%
	3 drugs	7%
Metf.	90 %	
SU	20 %	
SGLT-2	20%	
Other	5 %	

Body weight loss (%)







Discontinuation for GI AE **TIRZ 10: 4 %**
TIRZ 15: 7 %

Garwey WT, *Lancet* 2023

SURMONT-2 (7 points PG profile)

BMI: ≥27 kg/m2
HbA1c: 7-10%

AGE:	55+/-10	yrs
Female:	50	%
BMI:	36+/-6	kg/m²
HbA1c	8+/-1	%
Treatment		
	Diet only	6 %
	MonoT	55%
	2 drugs	32%
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SU	20 %	
SGLT-2	20%	
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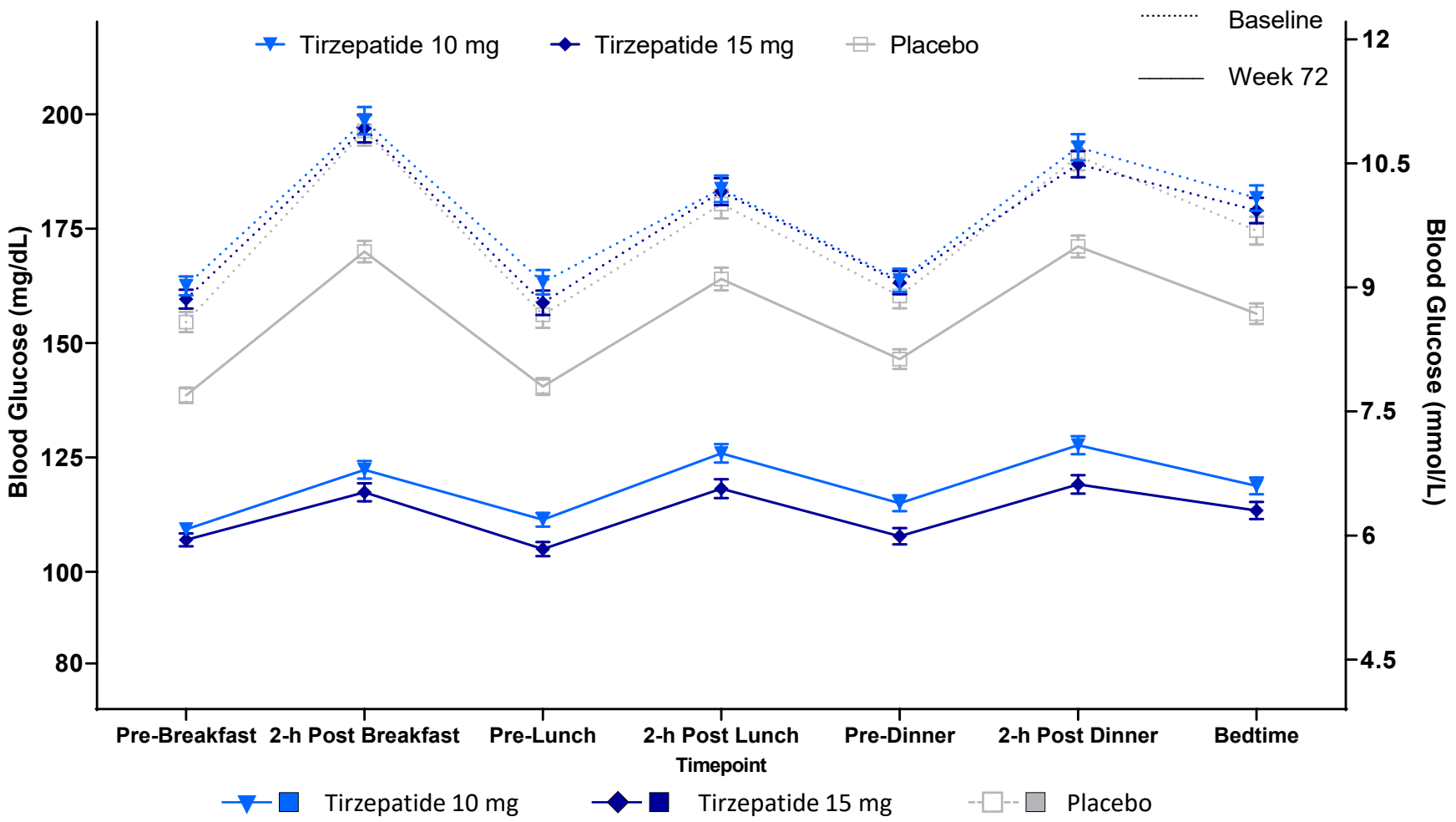
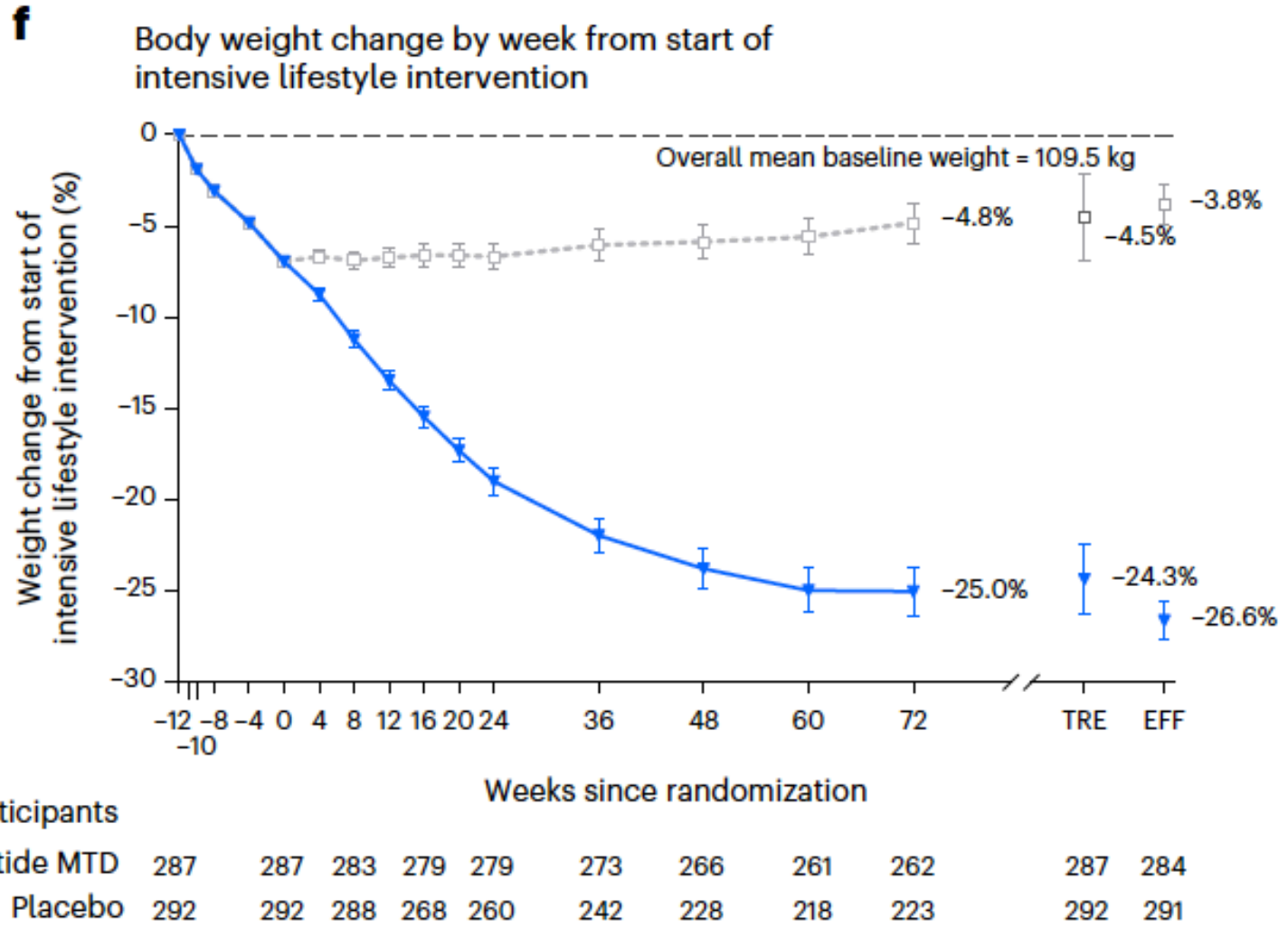


Discontinuation for GI AE **TIRZ 10: 4 %**
TIRZ 15: 7 %

Garwey WT, *Lancet* 2023

SURMONT-3 (TZP after LS intervention)



Wadden TA, *Nature Medicine* 2023

Estimated pooled treatments diffrence

Triglycerides (mg/dl)
−28.0 (−32.3, −23.4)

HDL-C (mg/dl)
11.4 (8.2, 14.7)

SBP (mmHg)
−9.2 (−11.2, −7.2)

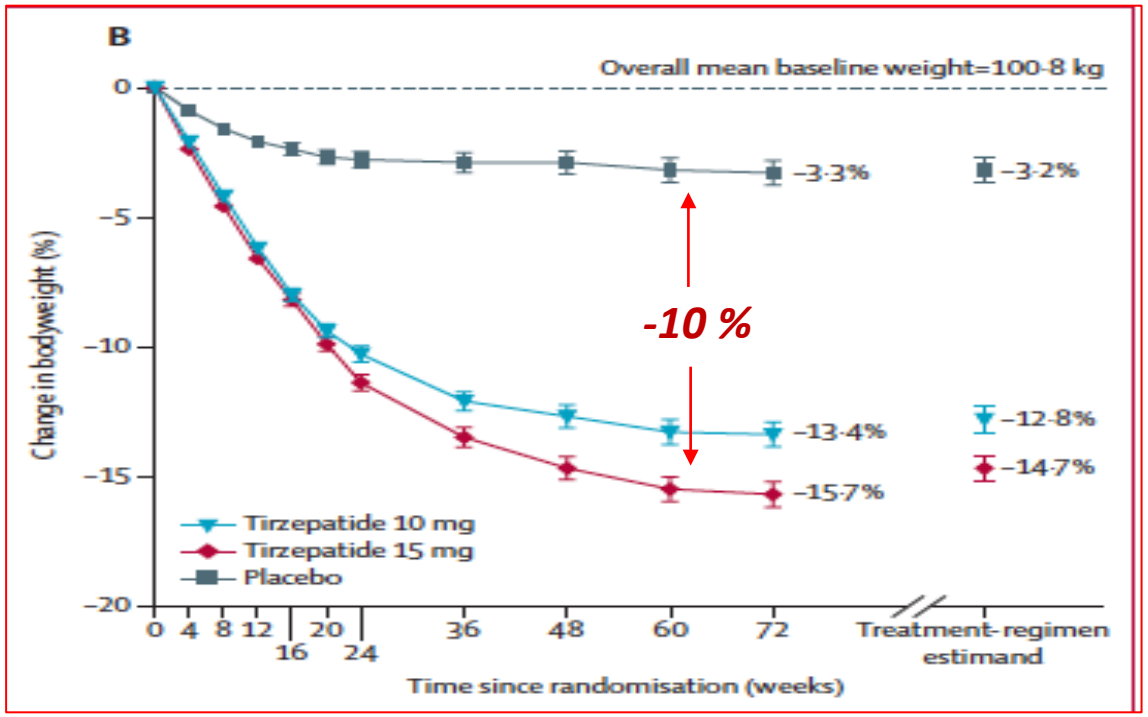
Fast. Glucose (mg/dl)
−11.2 *(−13.5, −8.8)*

HbA1c (%)
−0.5 *(−0.5, −0.4)*

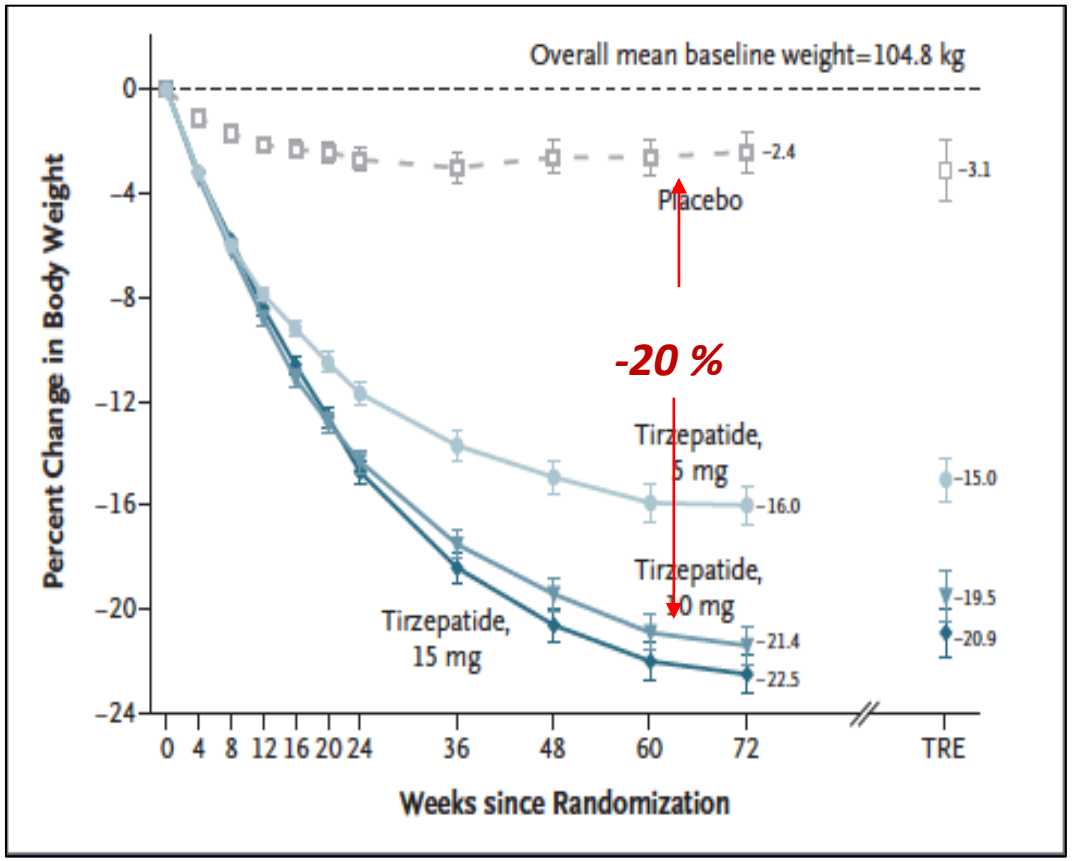
Discontinuation for GI AE: 10 %

In T2D Tirzepatide is less effective on weight loss

SURMONT-2 (T2D, BMI 36)



SURMONT-1 (No T2D, BMI 37)



Equal LS intervention

SURMONT-1 e 2

- Regular lifestyle counseling sessions, delivered by a dietitian or a qualified health care professional

- Deficit of 500 calories per day

- At least 150 minutes of PA per week.

SURMONT-2

To minimise the risk of hypoglycaemia, participants taking sulfonylureas at randomisation had their dose halved (or stopped if already on the lowest dose).

No insulin.

Domanda

E’ vero che i pazienti con diabete hanno difficoltà a perdere peso ?

T2D are resistant to WL

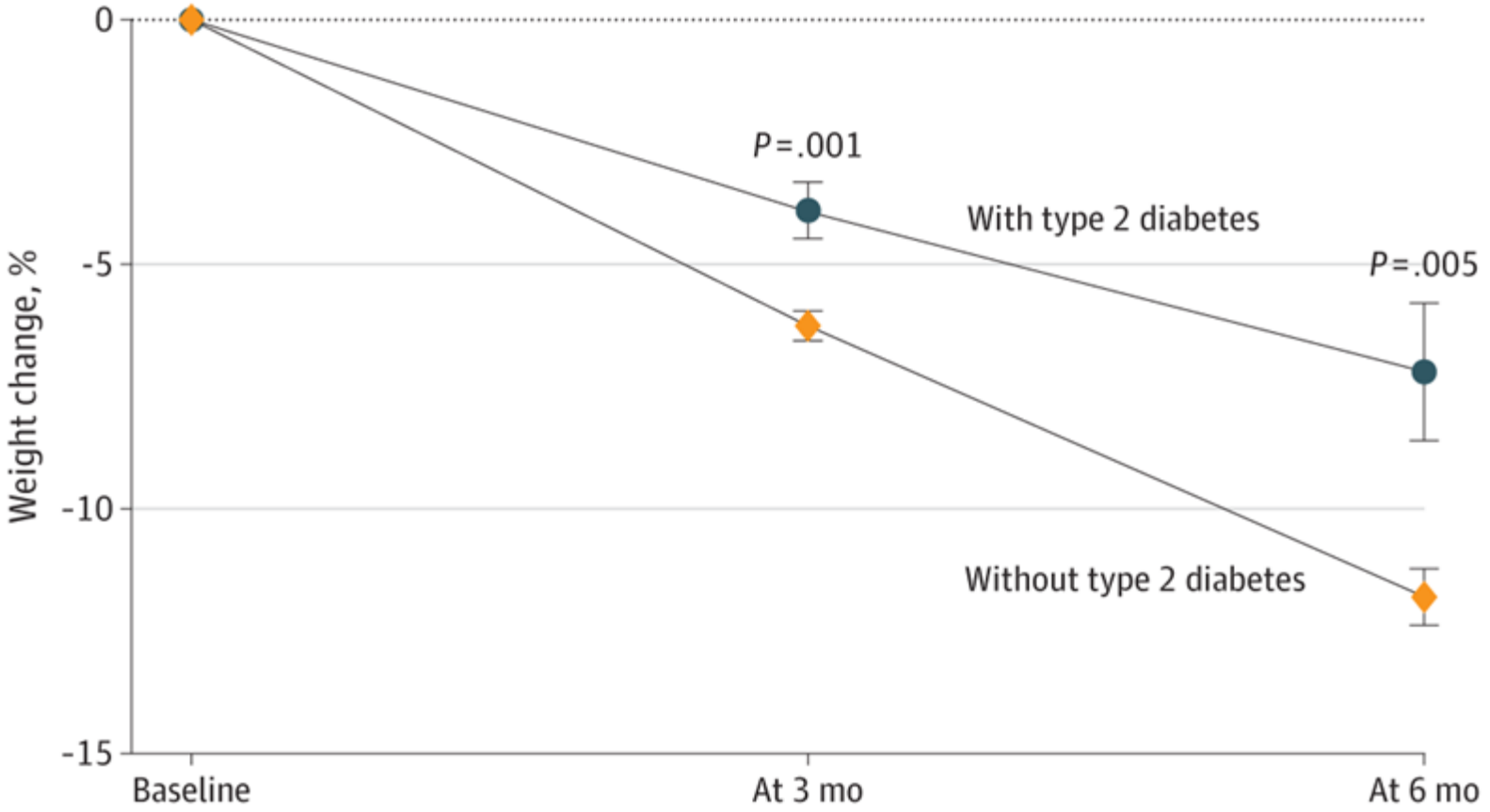
Table 1. Weight Change and Effect on A1C From Weight-Loss Interventions in People With Type 2 Diabetes Compared to Weight Change from Similar Interventions in People Without Diabetes

Interventions	Weight Change in Subjects With Type 2 Diabetes (lb)		12-Month A1C Change (%)	12-Month Weight Change in Subjects Without Diabetes (lb)
	6-month	12-month		
Weight-loss diet (n = 532)	–5.3	–5.7	–0.4	–10.1 to –16.7
Orlistat, 120 mg three times a day (n = 574)	–11	–11.2	–0.8	–18
Sibutramine, 15–20 mg (n = 152)	–16.5	–15.8	–0.4	–18
Rimonabant, 20 mg (n = 355)*	–13	–13.2	–0.6	–18.7

**New drug that blocks endocannabinoid receptors, thus reducing appetite and the brain's craving for flavorful foods and nicotine. Adapted from ref. 16*

Diabetes Spectr 2007;20(3):133–

Real world (Semaglutide)



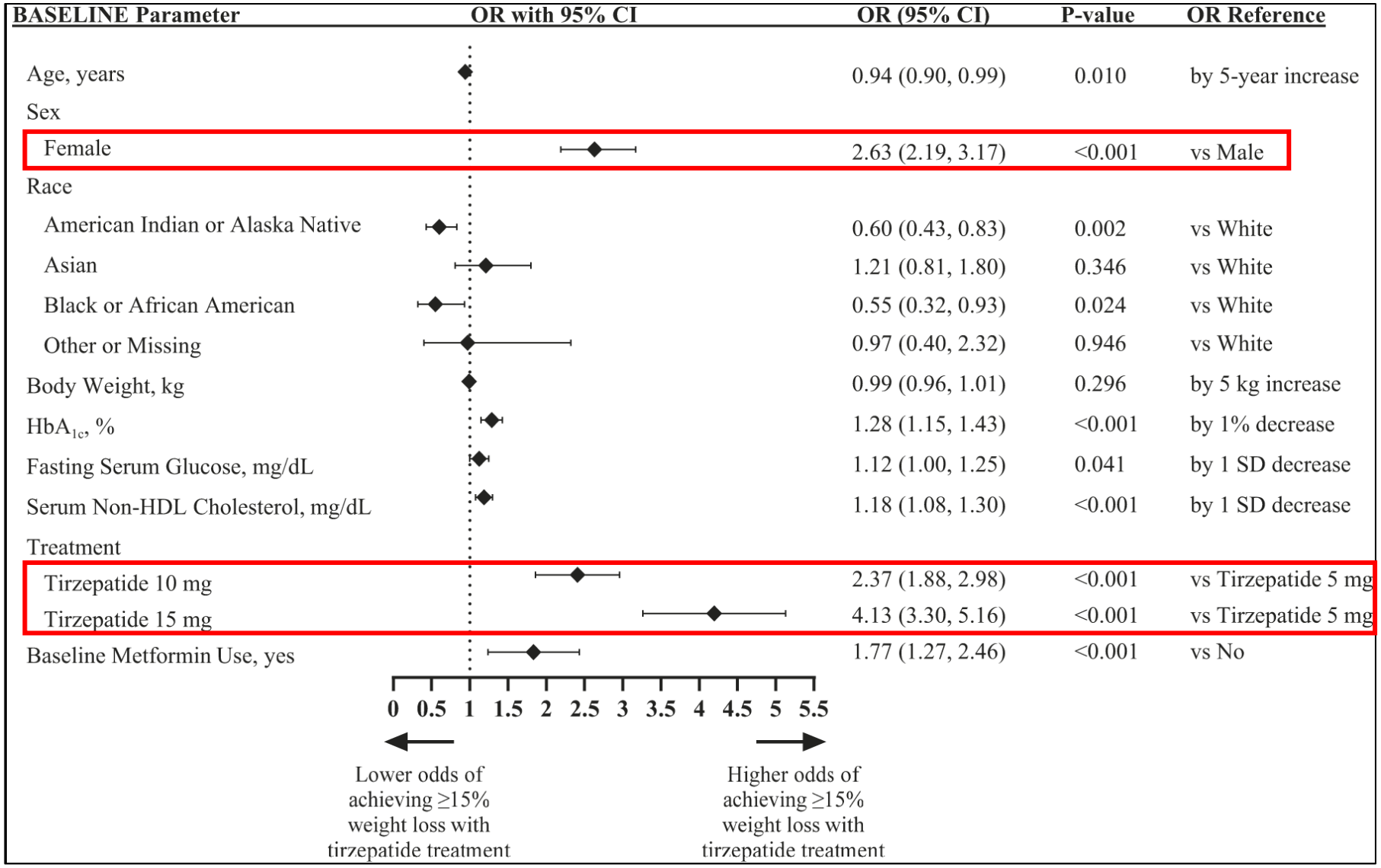
No. at risk			
With type 2 diabetes	28	20
Without type 2 diabetes	147	82

JAMA Netw Open. 2022;5(9):e2231982.

Domanda

Perché ?

Predittori di WL >15% in T2D (SURPASS 1-4)



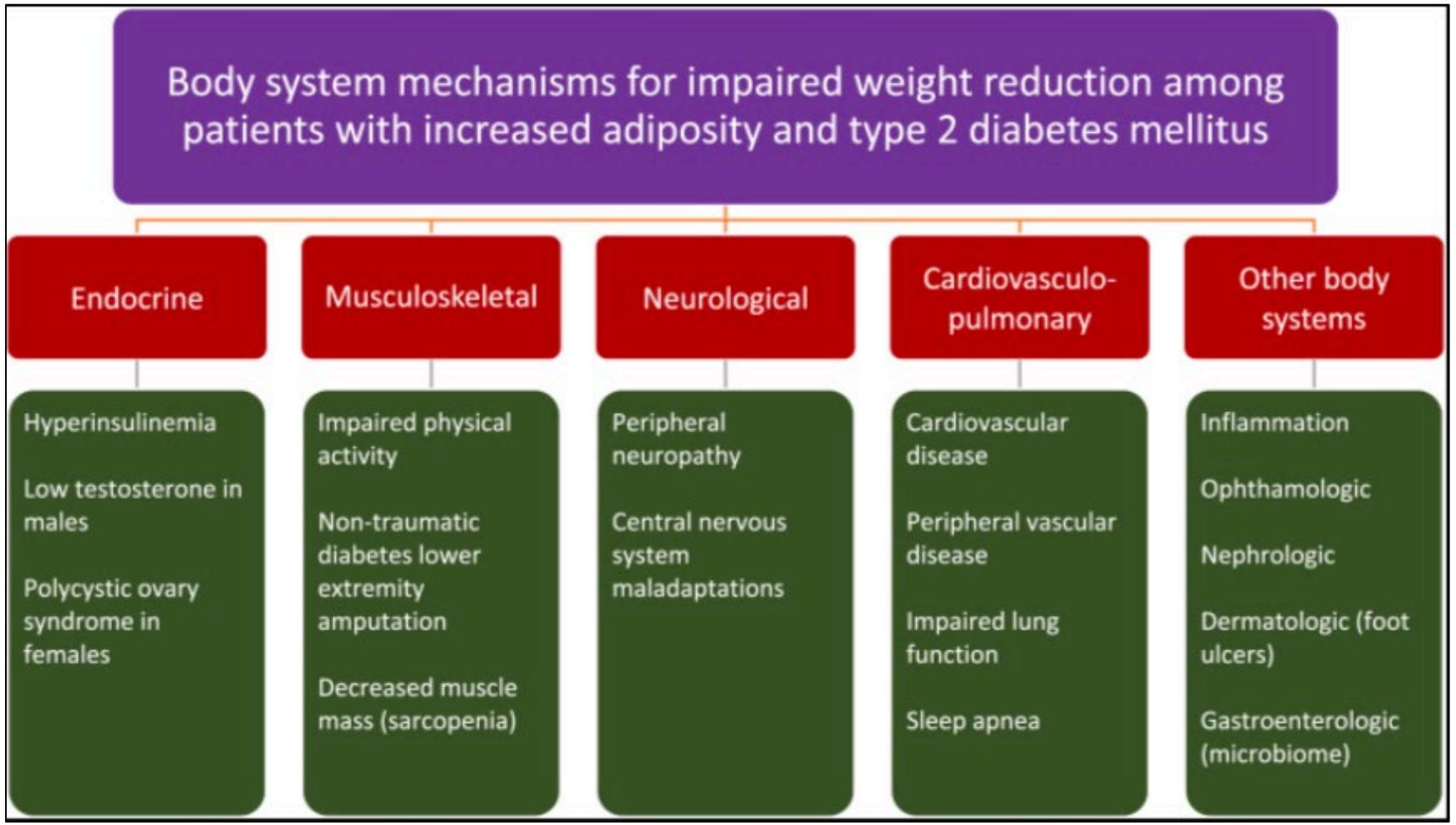
Female %

SURMOUNT-1
67%

SURMOUNT-2
51%

Diabetes Care 2023;46:2292–2299

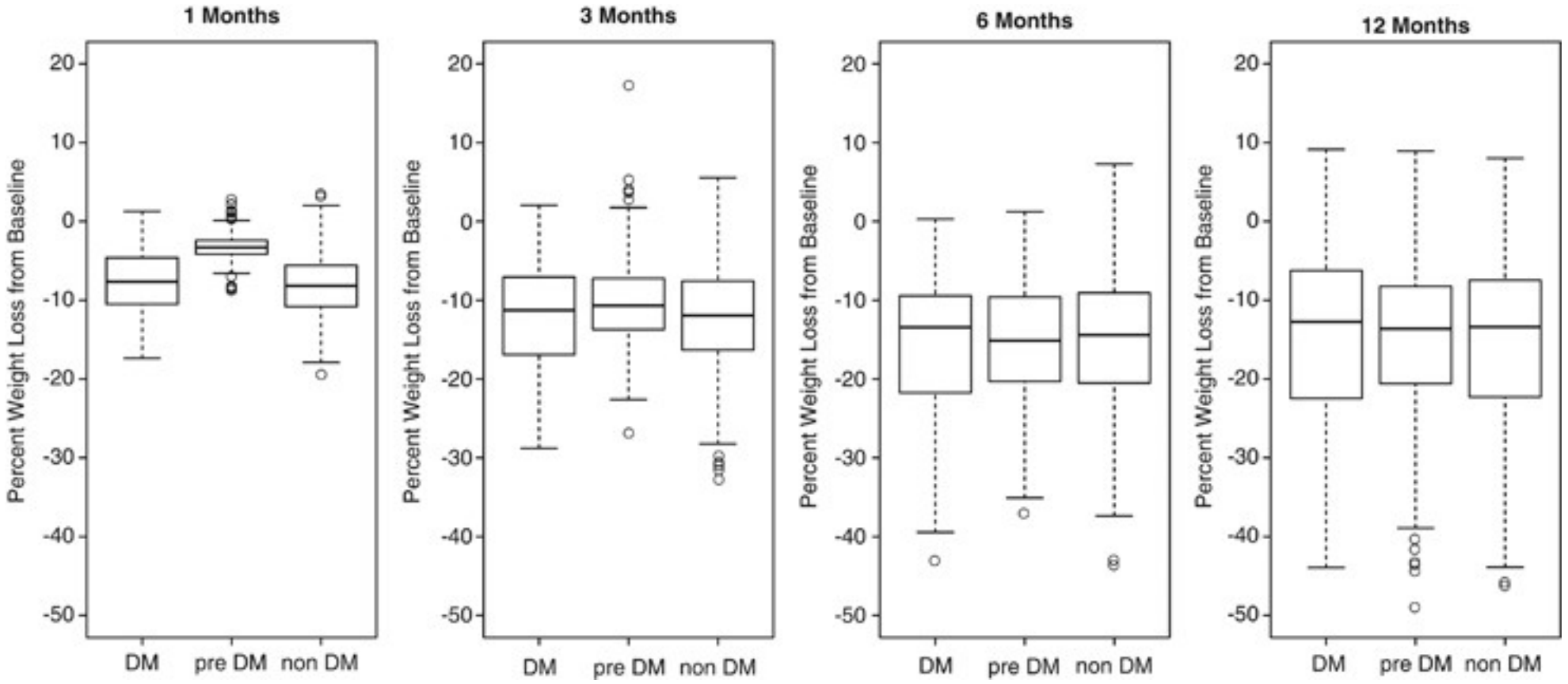
Diabete e Resistenza alla perdita di peso



Compliance ?

Ho perso peso, ho glicemie ottime quindi ….. finalmente posso mangiare

Liquid formula

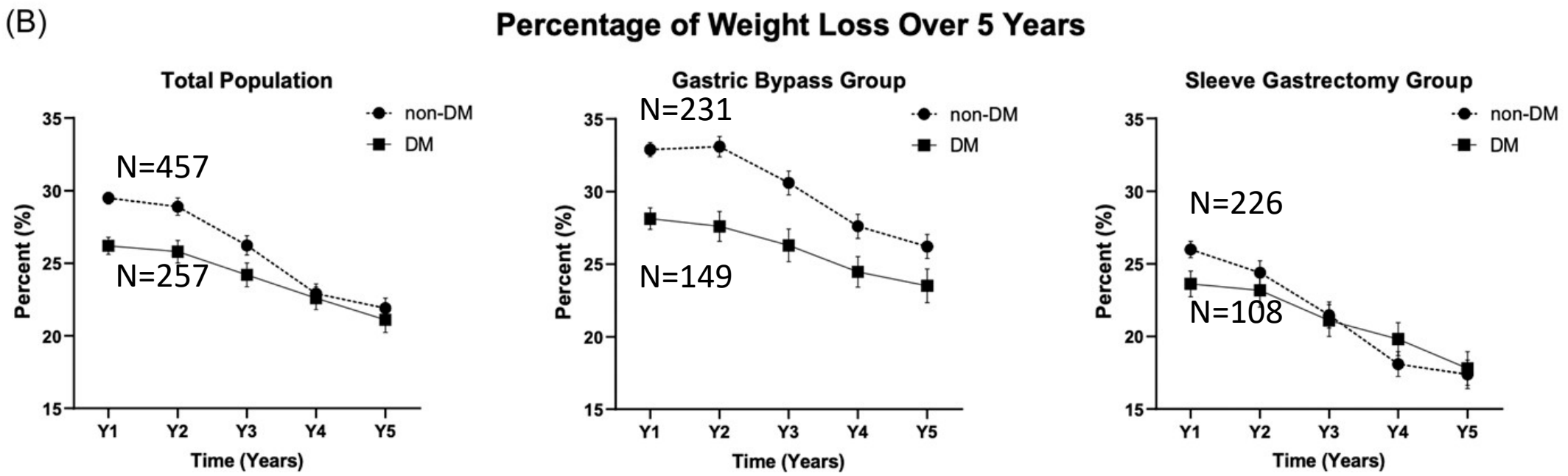


1143 normoglycemic
583 patients with pre-DM
367 patients with T2DM

•Z Li, *Nutrition & Diabetes* **volume 4**, page e105 (2014)

Bariatric surgery

Michigan Bariatric Surgery Cohort (MI-BASiC)

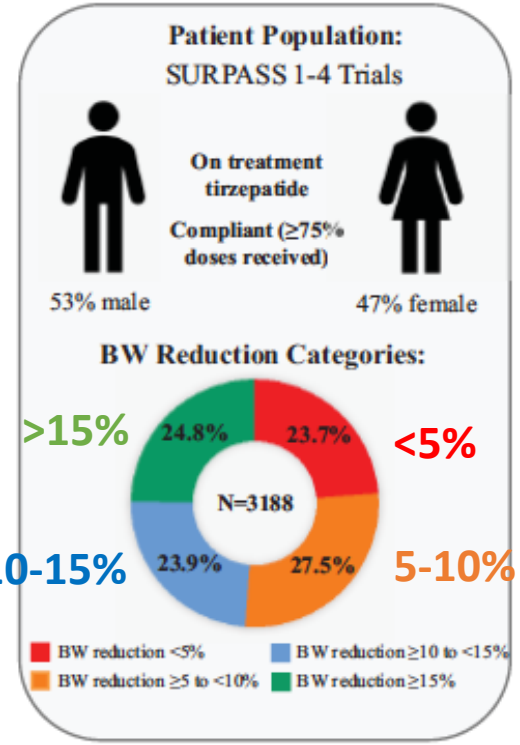


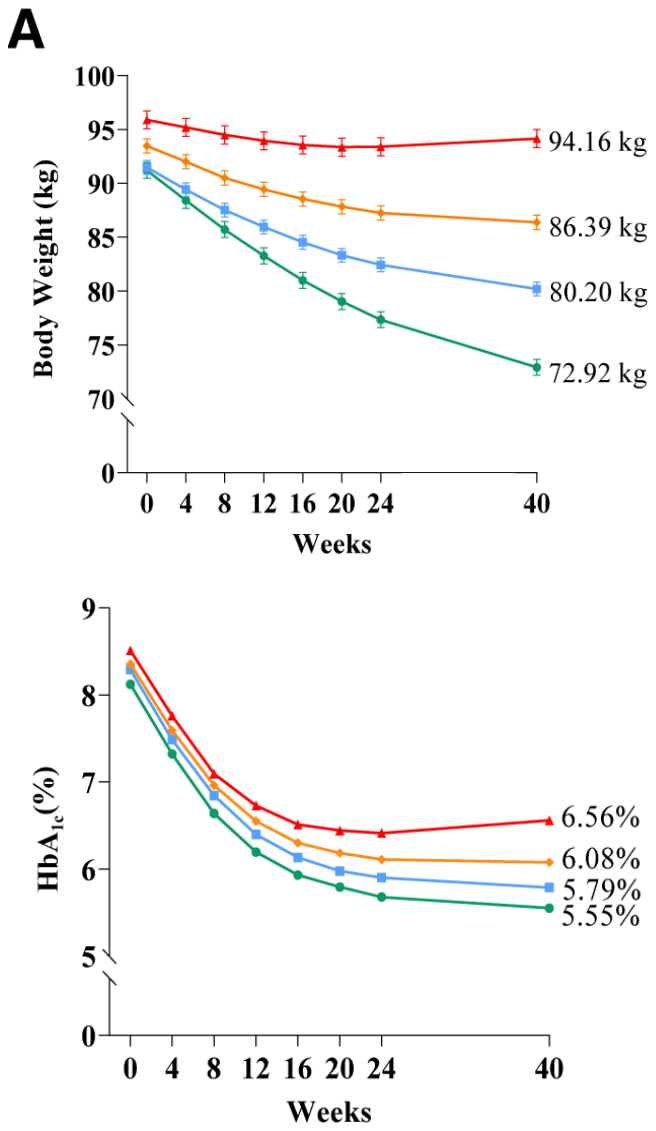
Luo Y *Clin Endocrinol* 2023

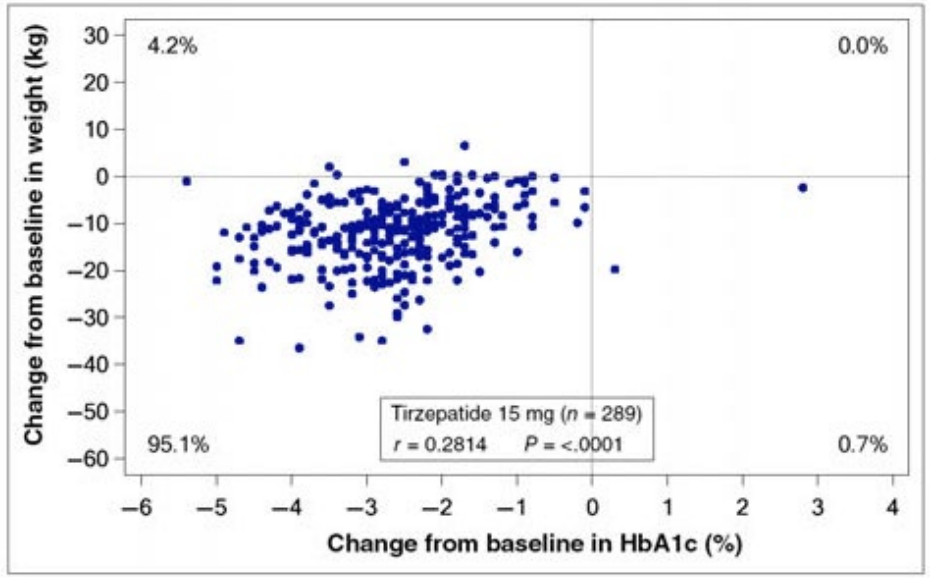
Domanda

Conseguenze ?

Dissociazione tra HbA1c e FRCV in T2D (SURPASS)



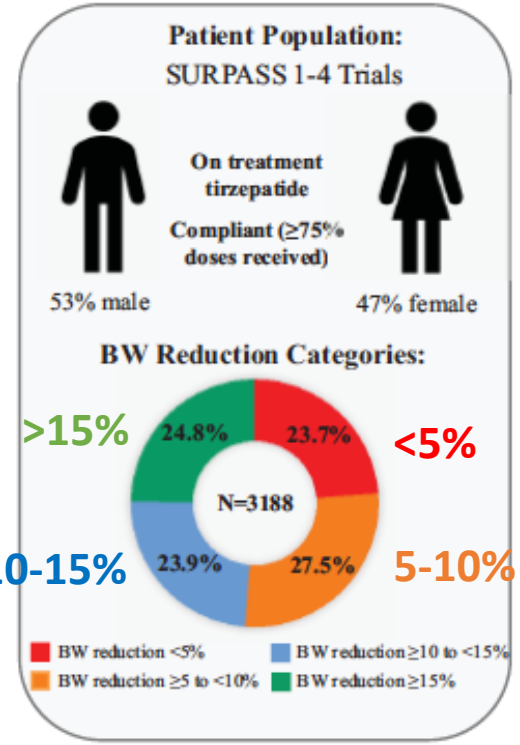


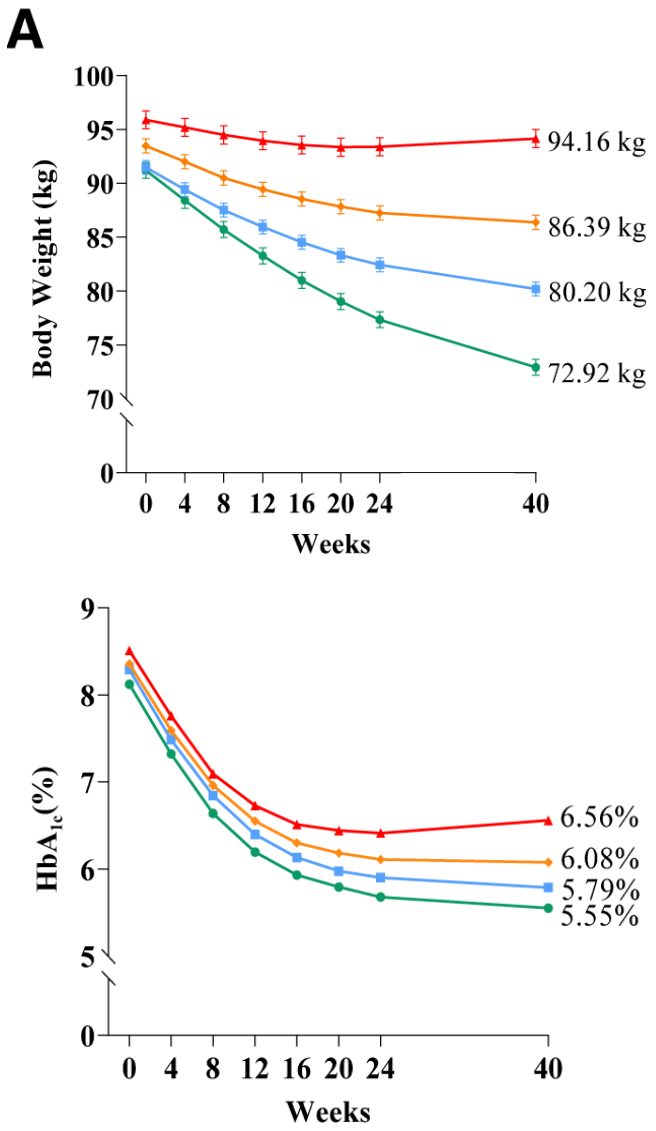


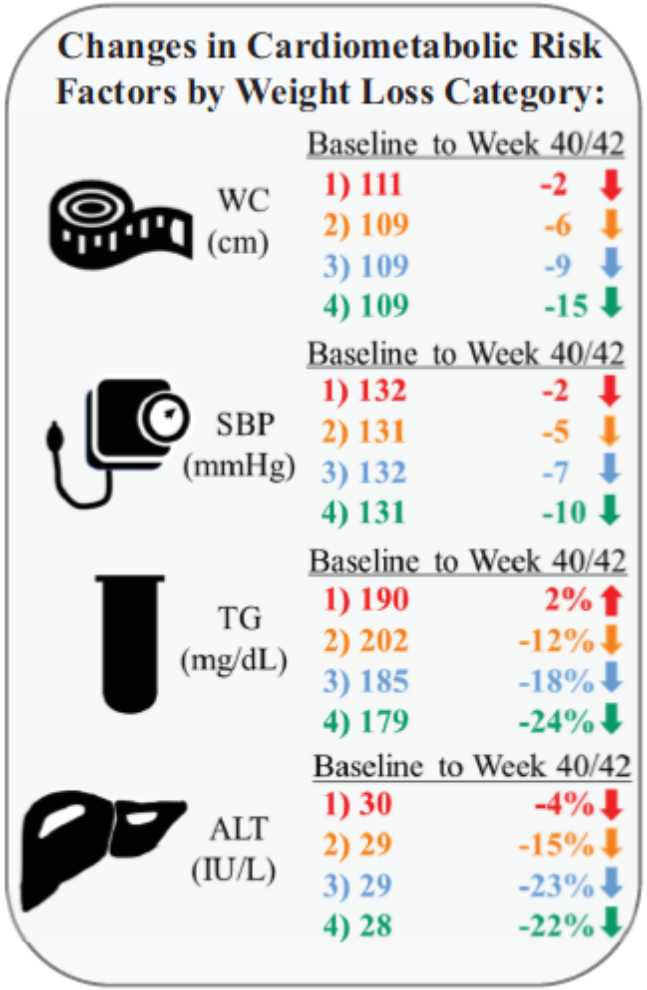
Pedersen SD Diabetes Obes Metab. 2023

Diabetes Care 2023;46:2292–2299

Dissociazione tra HbA1c e FRCV in T2D (SURPASS)







Diabetes Care 2023;46:2292–2299

Conclusioni

1) **Tirzepatide è molto efficace nelle 2 malattie**

2) **I pazienti con diabete di tipo 2 sono resistenti al calo ponderale**
   - **Hanno più comorbidità ?**
   - **Hanno minore compliance ?**

3) **La variabilità del calo ponderale influenza i fattori di rischio CV e, verosimilmente, la qualita di vita, ma non il miglioramento del controllo metabolico (effetto diretto del farmaco sulla ßcellula).**