

OMM

Obesity Management Medications WHEN, HOW, WHY AND WHY NOT

Dr. Giulia Maria Pontesilli

Medicina Interna

Ospedale Santa Maria della Misericordia, Rovigo

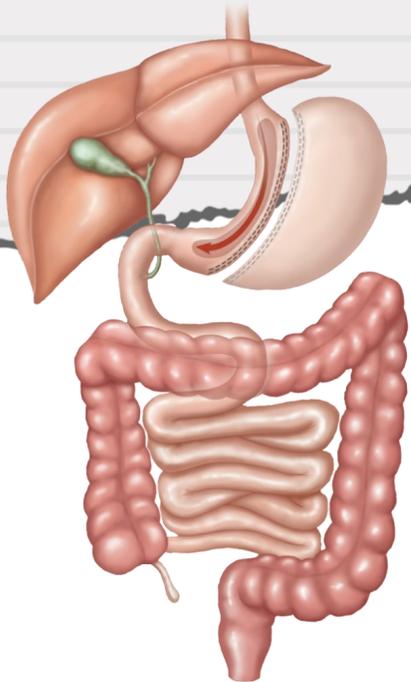
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WHEN?

M.S. ♀ 34 anni

Ipertensione arteriosa, IGT, PCOS

Desidera una gravidanza



BMI 51
(132 Kg, 160 cm)
Peso ideale: 64 kg
EBW: 68 kg

Sleeve gastrectomy
Peso post chirurgico a 18 mesi: 113 kg
- 19 kg
(= 14% BW, 28% EBW)

Perdita di peso insufficiente
(IWL, insufficient weight loss)
Perdita di < 50% del peso in eccesso (EWL) a 18 mesi dall'intervento

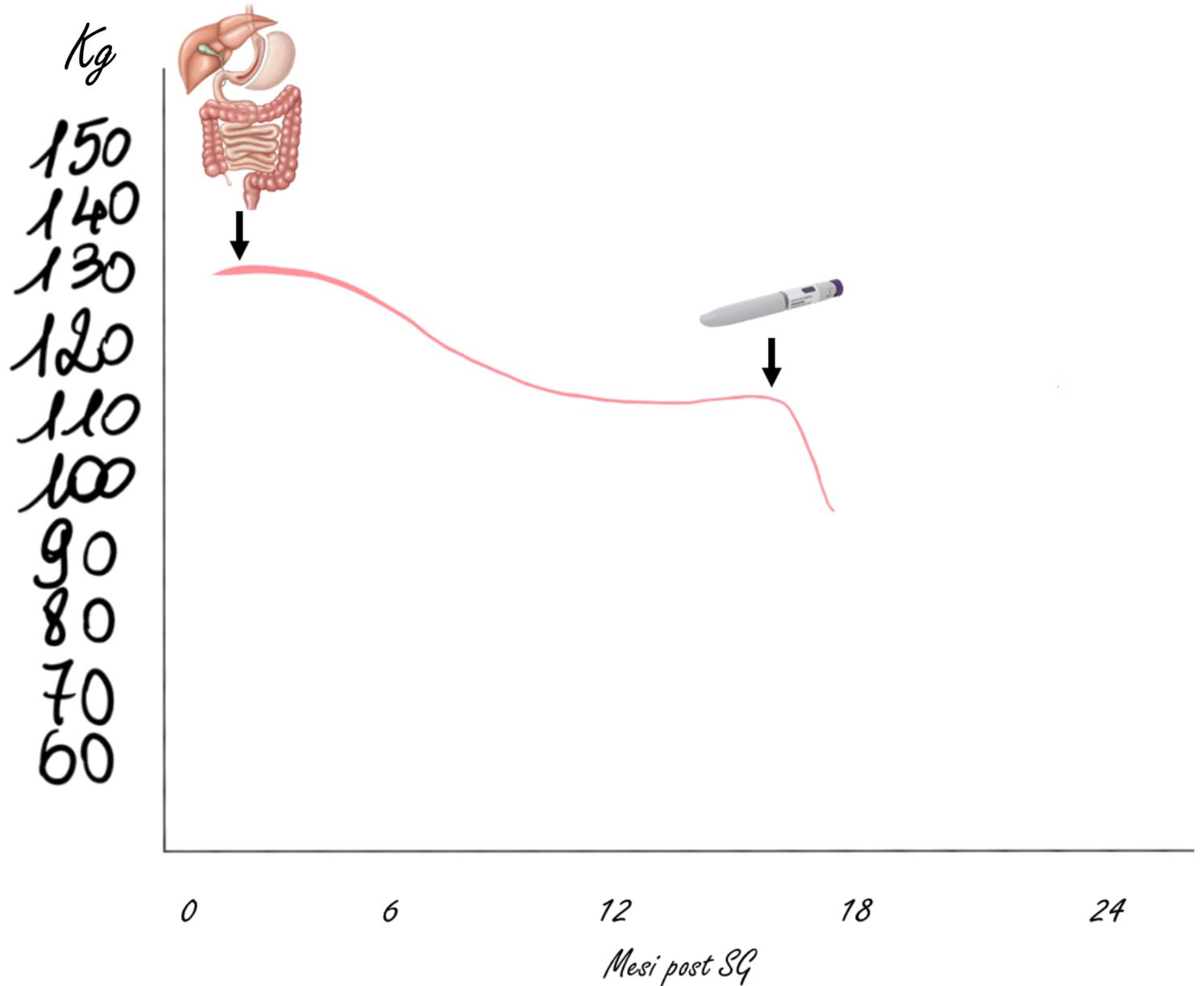
Successo terapeutico
Perdita di almeno il 50% del peso in eccesso (EWL)

POLYCYSTIC OVARIES >12 follicles in the ovary, follicle size (2-9 mm)	1 DIAGNOSED BY: Presence of underdeveloped follicles verified by ultra-sonography
HYPERANDROGENISM Hirsutism, Acne, Androgenic Alopecia	2 DIAGNOSED BY: High circulating levels of testosterone and Androstenedione
MENSTRUAL IRREGULARITY Oligomenorrhea, Amenorrhea	3 DIAGNOSED BY: Clinical History

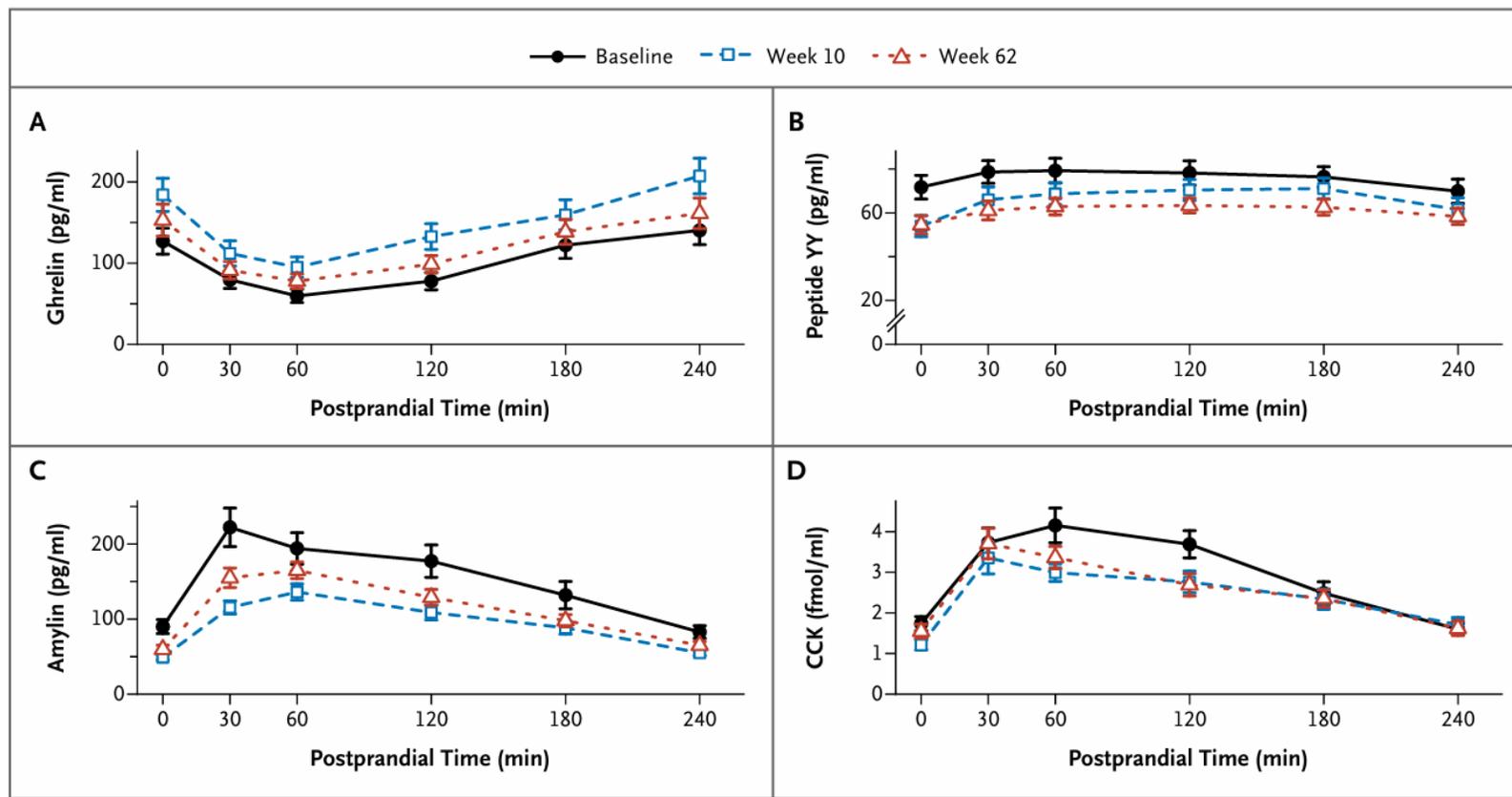
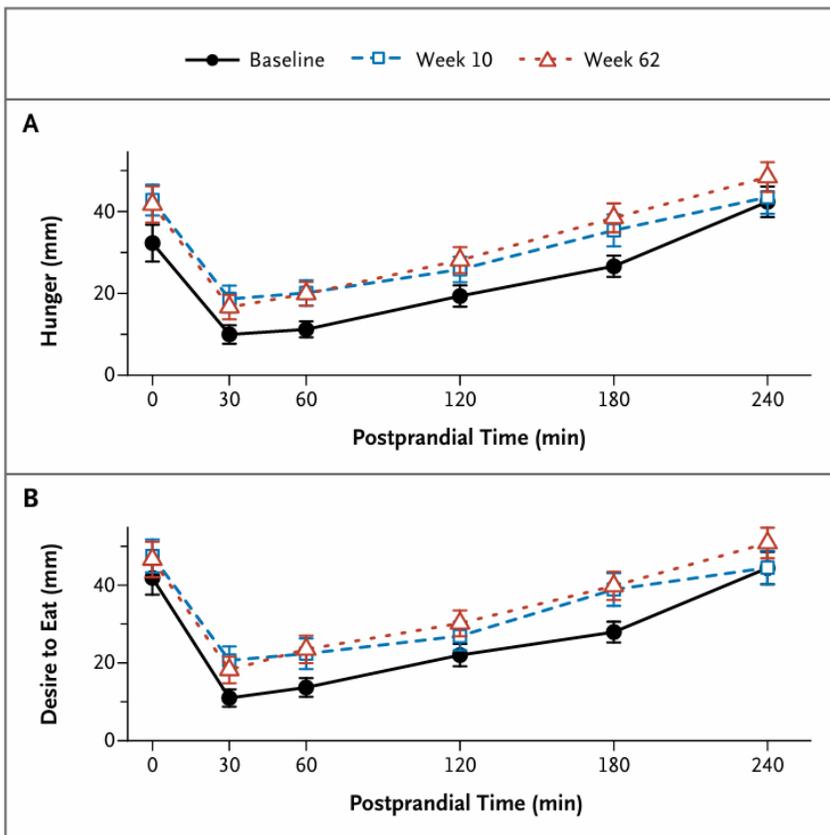
Yu Y, Klem M Lou et al., (2019) Predictors of weight regain after sleeve gastrectomy: an integrative review. Surgery for Obesity and Related Diseases

Nedelcu M et al., (2016) Weight regain after bariatric surgery-how should it be defined? Surg Obes Relat Dis.

Nelle pazienti con PCOS e desiderio di fertilità, tirzepatide è controindicato finché non saranno noti i suoi effetti teratogeni. In caso di utilizzo, è prudente prevedere un periodo di washout e posticipare il concepimento di almeno 2-3 mesi dalla sospensione.



Persistenza a lungo termine degli adattamenti ormonali alla perdita di peso



Ruolo degli Ormoni Intestinali nel Recupero del Peso

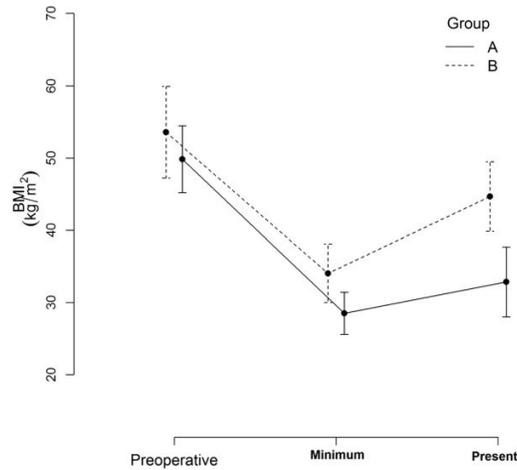


Fig. 1 BMIs in the preoperative period and when the minimum and present weights were reached

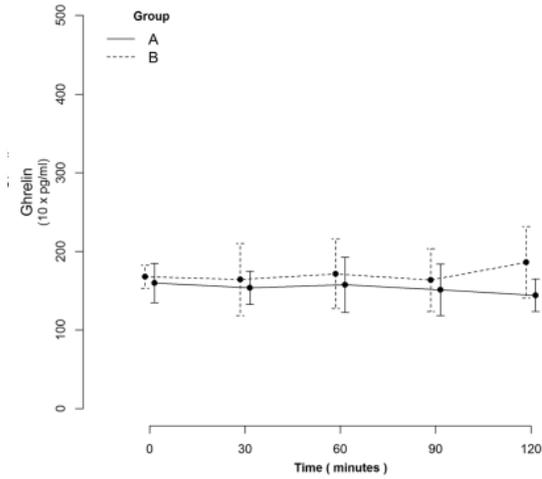


Fig. 2 Ghrelin secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

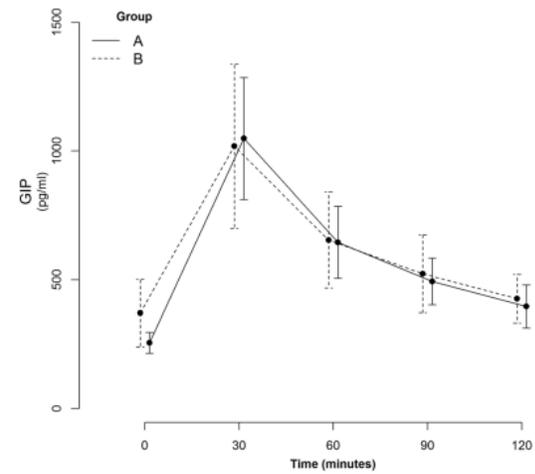


Fig. 3 GIP secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

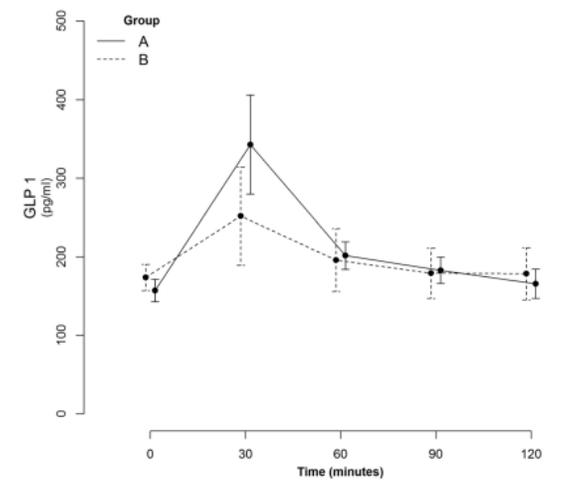


Fig. 4 GLP-1 secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

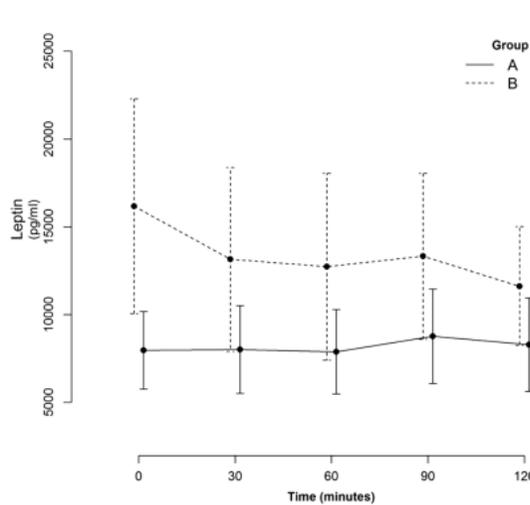


Fig. 5 Leptin secretion levels at baseline and after ingestion of a standard meal

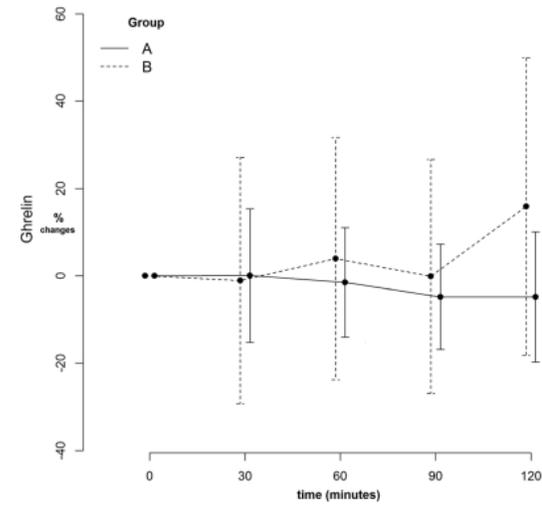


Fig. 2 Ghrelin secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

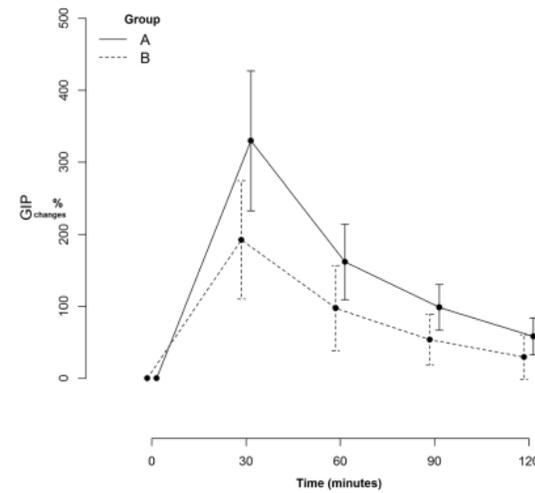


Fig. 3 GIP secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

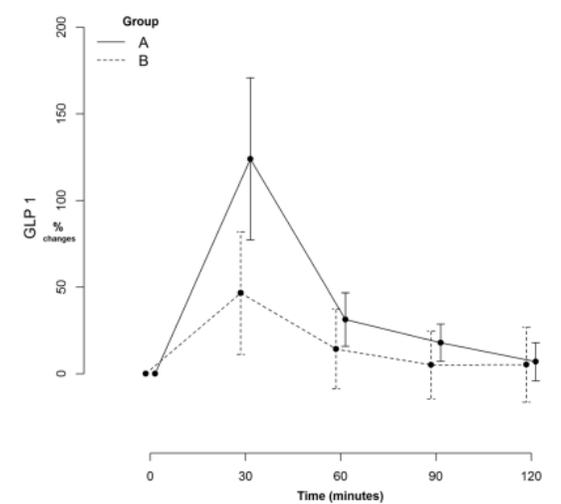


Fig. 4 GLP-1 secretion levels and percentage changes relative to baseline levels after ingestion of a standard meal

Tackling suboptimal clinical response after metabolic bariatric surgery:
Impact of tirzepatide on weight loss and body composition

Fabian Stoll^{a,*}, Tobias Kantowski^a, Jonas Laaser^a, Ulrike Kloiber^a, Gabriel Plitzko^b,
Oliver Mann^b, Jens Aberle^a, Anne Lautenbach^a

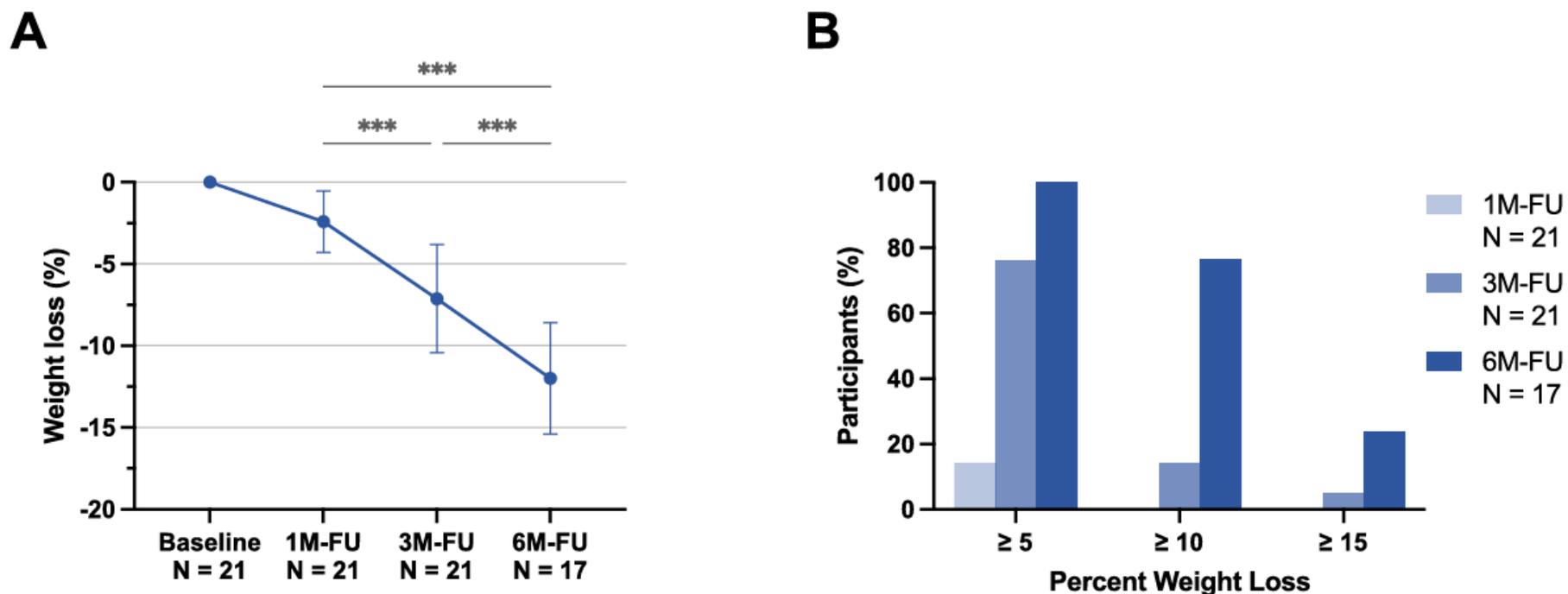
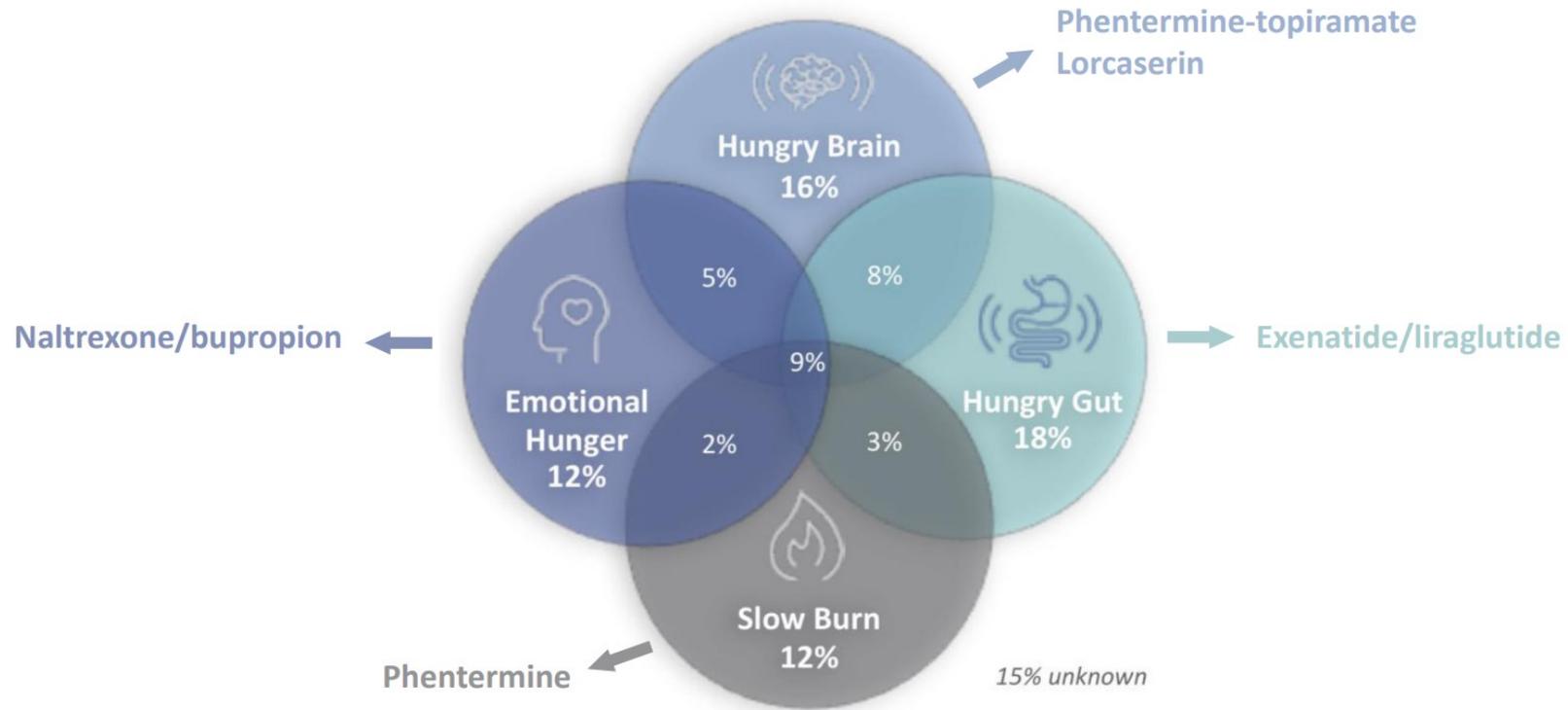


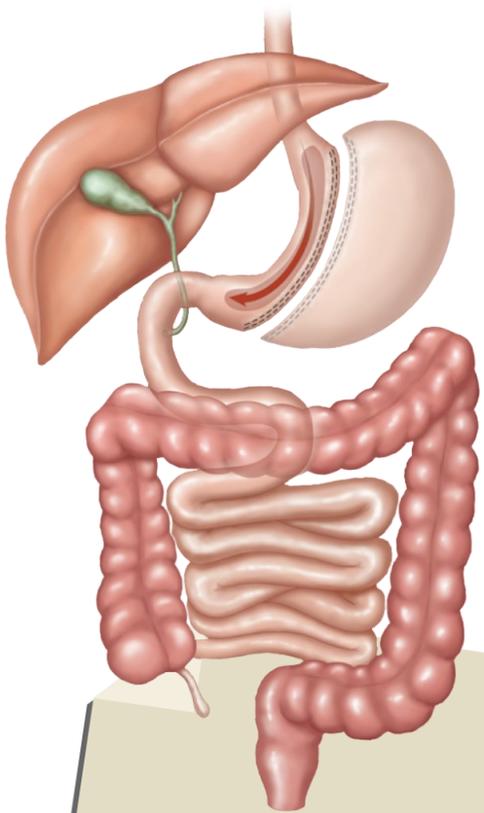
Fig. 1. (A) Weight loss (%) over time and (B) percentages of patients who reached weight loss of at least 5 %, 10 %, 15 %, respectively, following adjunct treatment with tirzepatide for 1, 3 and 6 months. FU, follow-up. N, number of individuals. Results are expressed as means and standard deviation. **, $p < 0.01$. ***, $p < 0.001$.



HOW?

Solo 4 fenotipi di obesità?





*Sleeve gastrectomy
(2017)*

*Peso post chirurgico a 18 mesi: 103 kg
- 25 kg
(= 55% EBW)*

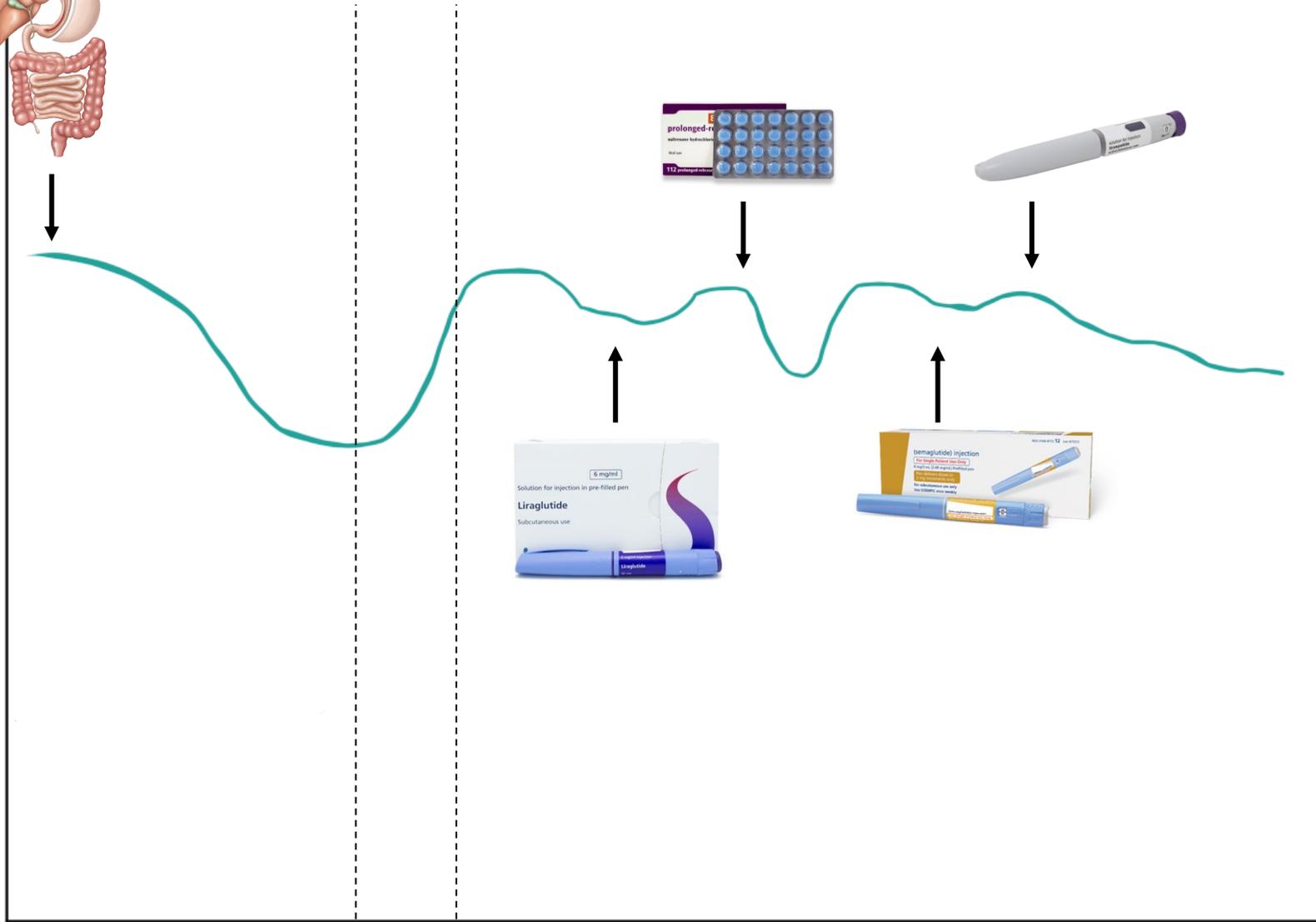
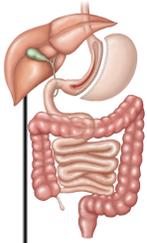
C.M. ♂ 59 anni

Iperensione arteriosa, dislipidemia, OSAS.

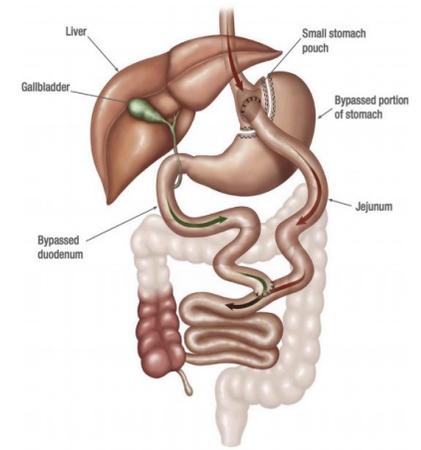
Consumo alcolico

*BMI 43
(128 Kg, 171 cm)
Peso ideale: 73 kg
EBW: 55 kg*

Kg
150
140
130
120
110
100
90
80
70
60

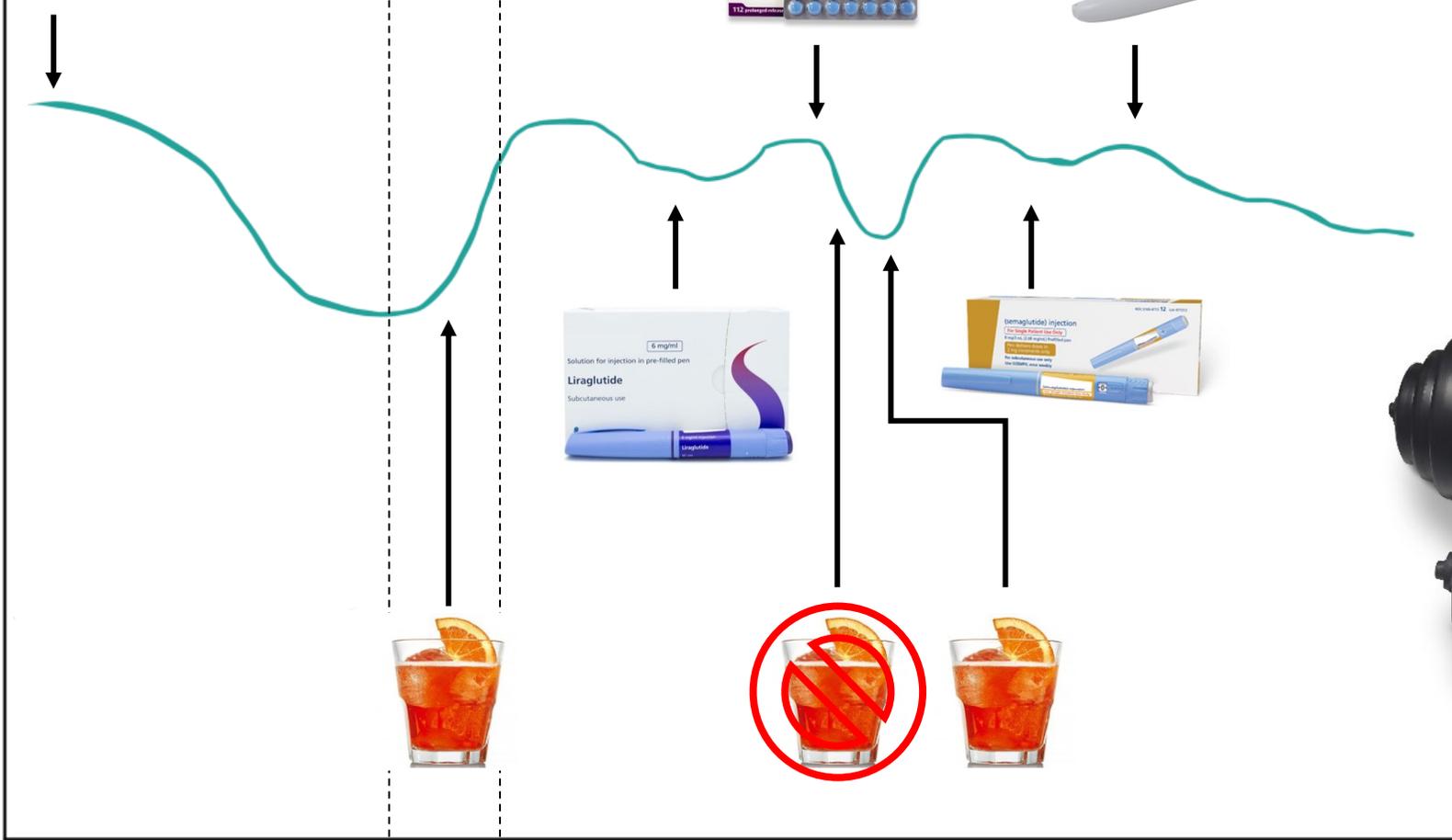
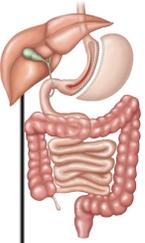


???



Mesi

Kg
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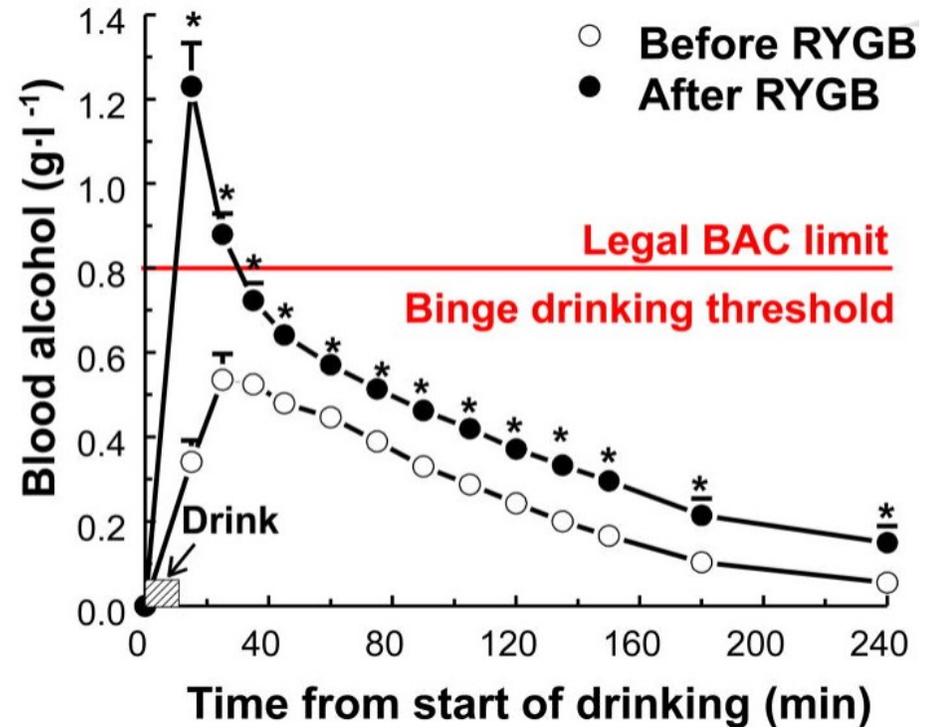
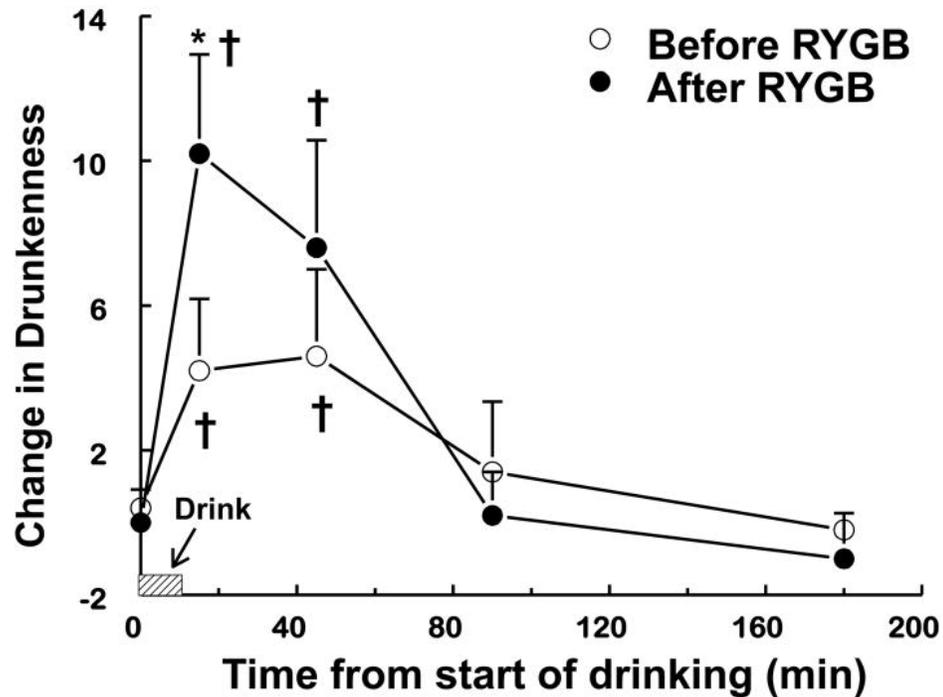


0 6 12 18 24 (5 anni) 0 6 12 18 24 32 38

Mesi



Effetto del RYGB sulla farmacocinetica dell'alcol: ebbrezza doppia a parità di dose



Le persone con obesità hanno generalmente più massa muscolare rispetto a soggetti normopeso, ma con funzionalità ridotta.

L'obesità è associata a maggior massa muscolare assoluta, ma anche a minor forza relativa, mobilità ridotta, e minor qualità muscolare (miosteatosi, fibre lente).

Qualsiasi perdita di peso comporta perdita di massa muscolare, oltre che di grasso.

La perdita muscolare contribuisce in modo significativo alla riduzione del metabolismo basale (-13 kcal/die per kg muscolo vs -4 kcal/die per kg di grasso).

Dopo una perdita iniziale, il peso tende a stabilizzarsi o a risalire per adattamenti omeostatici (**adattamento metabolico**).

Circa il 60% della riduzione del metabolismo basale è dovuto alla perdita di tessuti,

il restante 40% a maggiore efficienza energetica (**termogenesi adattativa**).

Organi come fegato, cuore e reni hanno un metabolismo più elevato rispetto al muscolo scheletrico e perdono massa con il dimagrimento.

La perdita di peso migliora la sensibilità insulinica di muscolo, fegato e tessuto adiposo, anche in presenza di una modesta perdita di massa magra.

L'insulina sopprime la proteolisi muscolare → protegge la massa magra. La resistenza insulinica favorisce la perdita muscolare e la sarcopenia.

Il miglioramento dell'insulino-sensibilità con il calo ponderale può favorire adattamenti positivi nella massa e funzione muscolare.

Farmaci GLP-1 RA e agonisti GLP-1/GIP migliorano l'insulino-sensibilità indirettamente tramite la perdita di peso e direttamente tramite azione insulinotropica.

La proporzione della perdita di massa magra è simile tra dieta, farmaci e chirurgia (ma la quantità totale di peso perso è maggiore con chirurgia e farmaci).

L'adattamento metabolico

REE = Resting Energy Expenditure (kcal/day)

RMR = Resting Metabolic Rate (kcal/day)

Rappresenta il 60-70% della spesa energetica, determinata principalmente dalla composizione corporea

Direttamente proporzionale alla FFM (fat free mass).

L'**adattamento metabolico** è una riduzione sproporzionata del RMR rispetto alla perdita di peso e di FFM.



	Before	After	Delta%
Weight (kg)	127.6 ± 26.0	89.0 ± 21.2***	-29.8 ± 10.6
FFM (kg)	69.8 ± 16.8	59.7 ± 13.2***	-13.7 ± 9.9
FM (kg)	54.7 ± 15.1	29.5 ± 12.6***	-44.5 ± 22.8
REE (kcal)	1980 ± 483	1410 ± 312***	-27.3 ± 12.9
REE per weight unit (kcal/kg)	15.5 ± 2.3	16.9 ± 12.3	+10.7 ± 85.1
REE per FFM unit (kcal/kg)	28.6 ± 4.7	23.9 ± 4.3***	-14.9 ± 16.2

Paired Student's *t* test before vs after: **P* < 0.05; ***P* < 0.01; ****P* < 0.001

FFM, fat-free mass; FM, fat mass; REE, resting energy expenditure

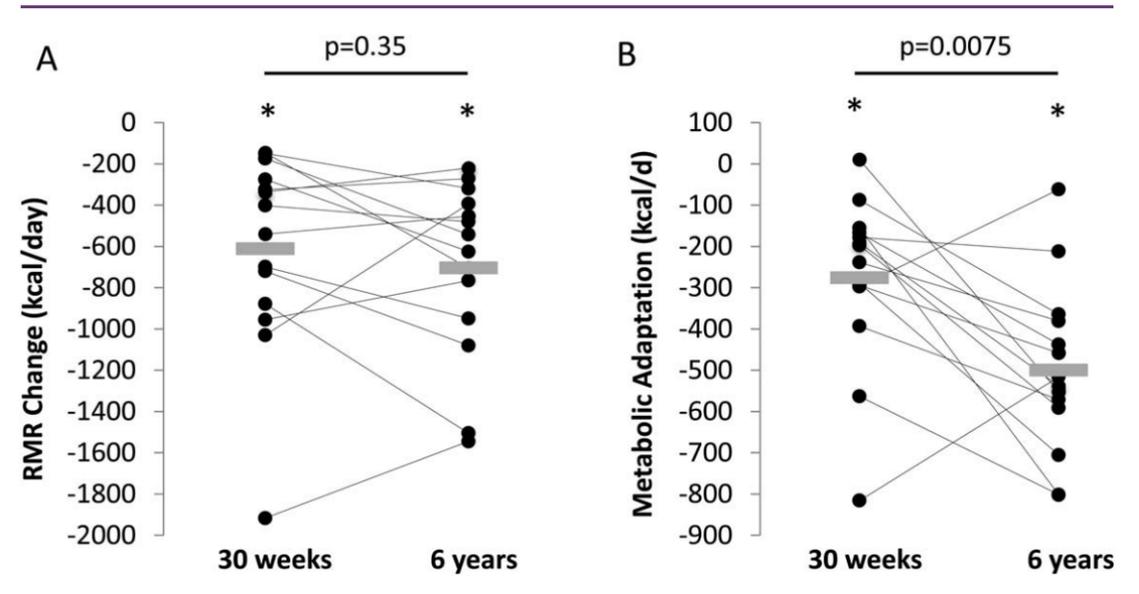
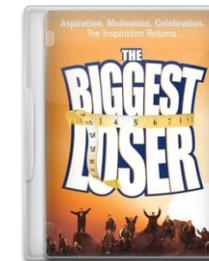


Figure 4 Individual (•) and mean (gray rectangles) changes in (A) resting metabolic rate and (B) metabolic adaptation at the end of "The Biggest Loser" 30-week weight loss competition and after 6 years. Horizontal bars and corresponding *P* values indicate comparisons between 30 weeks and 6 years. **P* < 0.001 compared with baseline.



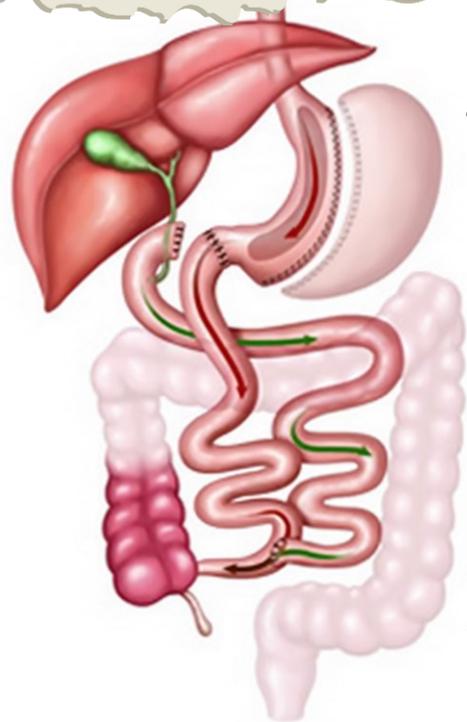


*WHY
NOT?*

B.G. ♀ 36 anni

«Metabolicamente sana»

*Binge eating ritenuto compensato
in terapia farmacologica*



*Diversione biliopancreatica
nel 2004, 110 kg*

*Calo ponderale
fino a 70 kg.*

Follow-up scadente.

↓
*Recupero ponderale fino a
100 kg in 20 anni.*

... 56 anni nel 2024

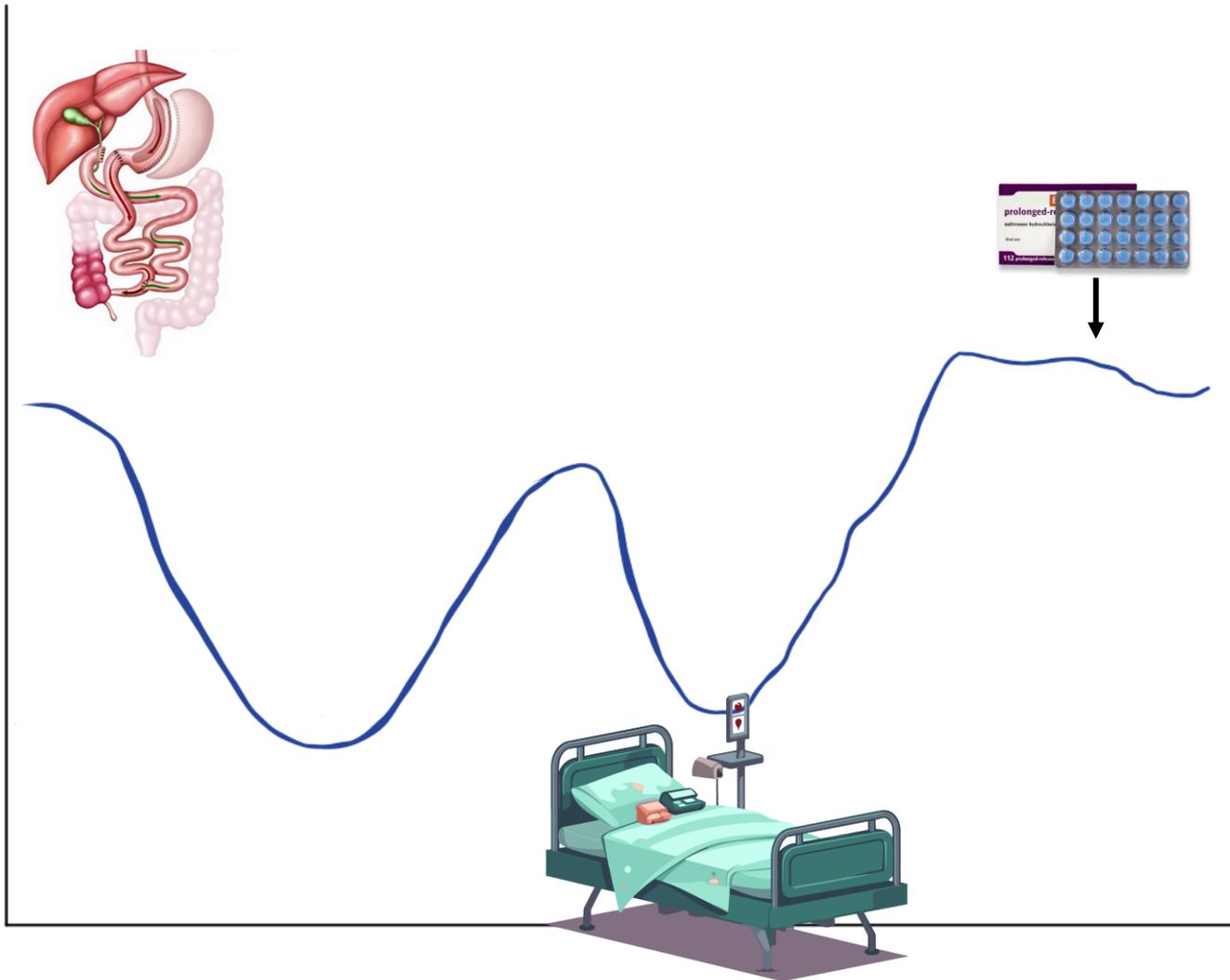
*Ricovero in Medicina per diarrea profusa, calo ponderale di 30 kg (70 kg).
Inoltre: anemia carenziale, ipovitaminosi D, ipoalbuminemia, malnutrizione calorico-
proteica, edentulia, crolli vertebrali. Non deambula.*

*Diagnosi presuntiva di SIBO e intolleranza al glutine non celiaca.
Trattata con ripresa degli integratori specifici, dieta priva di glutine, ciclo di
metronidazolo seguito da probiotici.*

*Presa in carico presso
l'Ambulatorio Internistico Obesità,
follow-up ogni 3-6 mesi*

*Binge eating in labile compenso, paziente in terapia con
duloxetina e trazodone, fame scarsamente controllata e con
forte componente emotiva.*

Kg
150
140
130
120
110
100
90
80
70
60



What Is a Panic Attack?

Unlike an anxiety attack, a panic attack doesn't build gradually. It often strikes unexpectedly. Panic attacks disrupt and leave the sufferer with a feeling of lack of contact with the world.

Symptoms include:

- Chest pain
- Lightheadedness
- Feeling dizzy
- Numbness
- Shaking
- Shortness of breath
- Racing heartbeat
- Nausea
- Chills
- Hot flashes



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WHY?

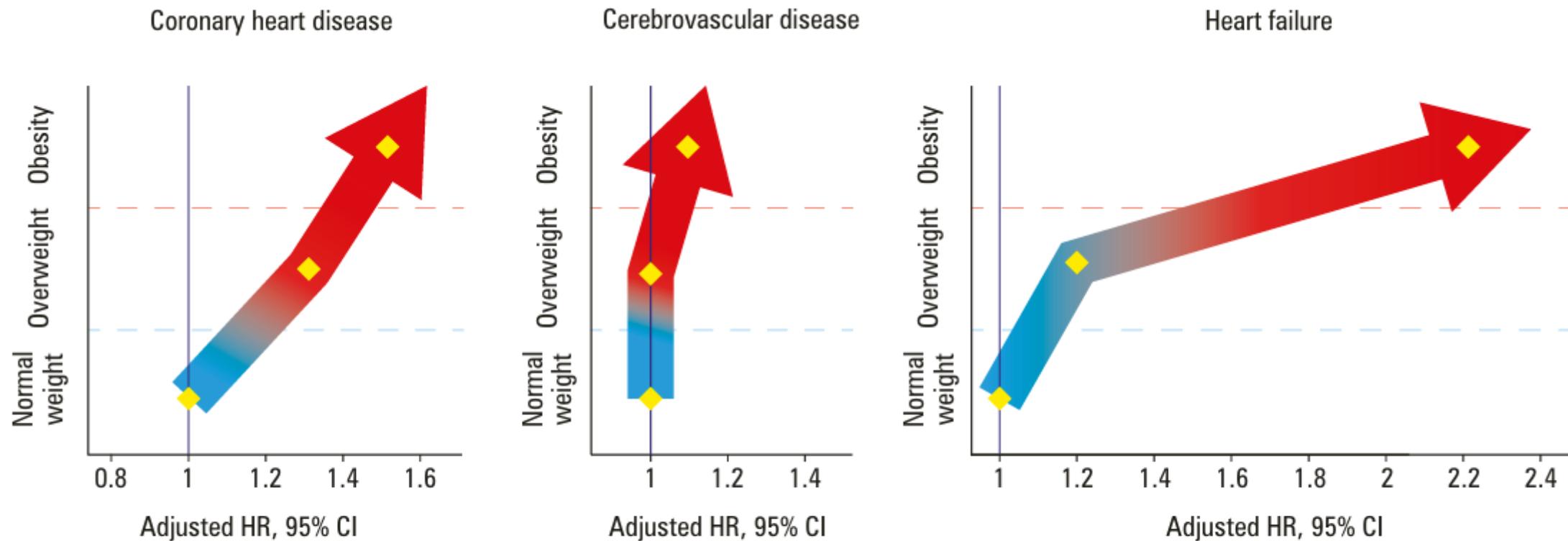


FIGURE 1 Incident cardiovascular events in metabolically healthy obese individuals (no diabetes, hypertension, or hyperlipidemia). Based on Caleyachetty et al⁷⁵

Abbreviations: HR, hazard ratio

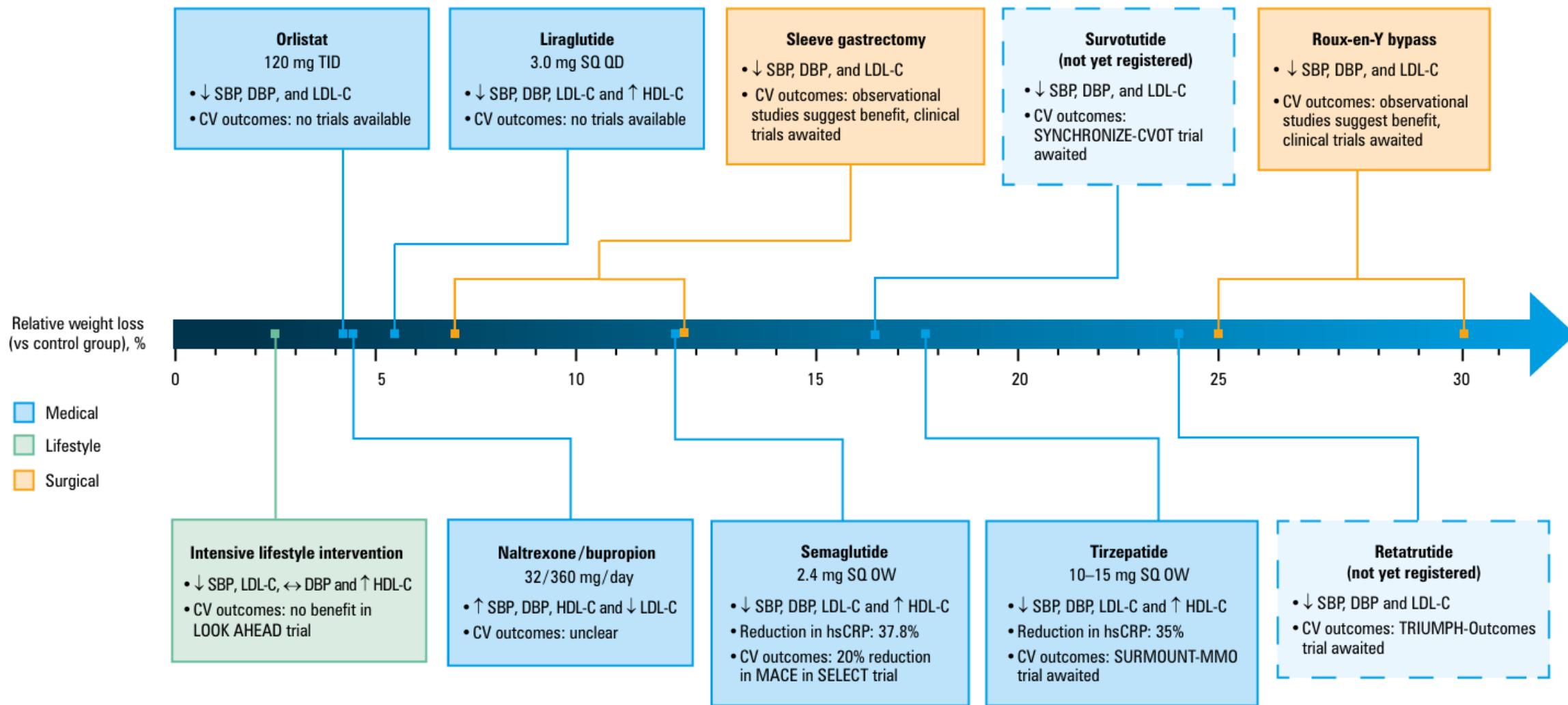


FIGURE 3 Comparative effectiveness of lifestyle, pharmacological, and surgical interventions on weight management and cardiovascular outcomes. Based on Usman et al⁶⁹
 Abbreviations: CV, cardiovascular; CVOT, cardiovascular outcomes trial; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular event (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke); OD, once daily; OW, once a week; SBP, systolic blood pressure; SQ, subcutaneous; TID, three times a day

Trial	Intervention	Patients enrolled	Design	Event rate	HR	Discontinuation rate	Primary outcome	Results
LOOK AHEAD ²¹	ILI	5145	Superiority	1.83 events per 100 person-years (ILI) vs 1.92 (control)	HR, 0.95 (95% CI, 0.83–1.09; <i>P</i> = 0.51)	Not specified	MACE	No significant reduction in CV events; terminated early for futility
SCOUT ²³	Sibutramine	10744	Superiority	11.4% (sibutramine) vs 10% (placebo)	HR, 1.16 (95% CI, 1.03–1.31; <i>P</i> = 0.02)	30%	MACE + resuscitated cardiac arrest	Increased risk of nonfatal MI and stroke; led to market withdrawal
CRESCENDO ³²	Rimonabant	18695	Superiority	3.9% (rimonabant) vs 4% (placebo)	HR, 0.97 (95% CI, 0.84–1.12; <i>P</i> = 0.68)	10%	MACE + CV hospitalization	No significant CV benefit; increased psychiatric adverse events; terminated early
LIGHT ³²	Naltrexone/bupropion	8910	Noninferiority	2% (naltrexone/bupropion) vs 2.3% (placebo) ^a	HR, 0.88; adjusted 99.7% CI, 0.57–1.34 ^a	28.1%	MACE + angina hospitalization	Terminated due to data integrity concerns
CONVENE ³⁸	Naltrexone/bupropion	About 8800	Noninferiority	ND	ND	ND	MACE	Terminated early
CAMELLIA-TIMI ²⁴	Lorcaserin	12000	Noninferiority	2% (lorcaserin) vs 2.1% (placebo)	HR, 0.99 (95% CI, 0.85–1.14)	5%	MACE + type 2 diabetes	Demonstrated noninferiority for CV safety; later withdrawn due to cancer risk concerns
SELECT ¹⁰	Semaglutide 2.4 mg	17604	Superiority	6.5% (semaglutide) vs 8% (placebo)	HR, 0.8 (95% CI, 0.73–0.87; <i>P</i> < 0.001)	16.6%	MACE	Significant 20% reduction in MACEs, superior to placebo
SURMOUNT-MMO ^b	Tirzepatide 15 mg	15374	Superiority	Ongoing	Ongoing	Ongoing	MACE	Ongoing study; results pending 2027 ^b

a Interim analysis after 50% of planned events

b Based on ClinicalTrials.gov (ClinicalTrials.gov identifier: NCT05556512)

Abbreviations: ILI, intensive lifestyle intervention; MI, myocardial infarction; ND, no data (trial terminated); others, see **FIGURES 1** and **3**

Grazie



AULSS 5 Polesana
Ospedale Santa Maria della Misericordia di Rovigo



giulia.pontesilli@aulss5.veneto.it



[@giuliamariapontesilli.md](https://www.instagram.com/giuliamariapontesilli.md)



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