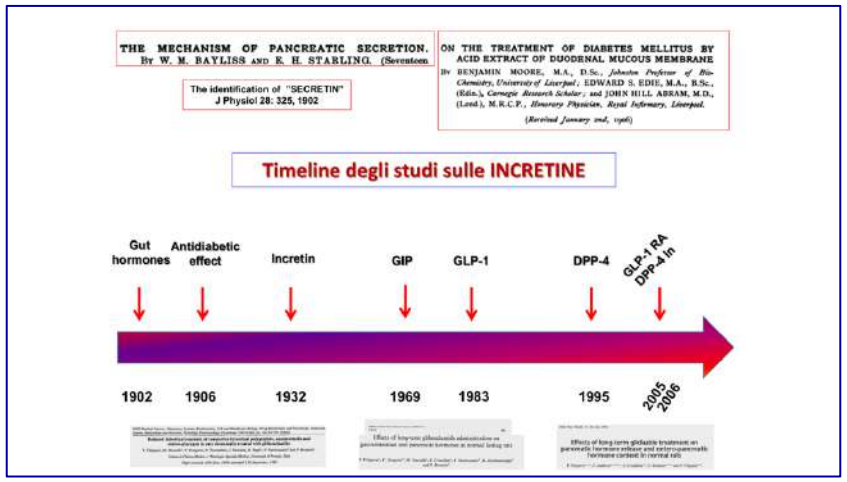
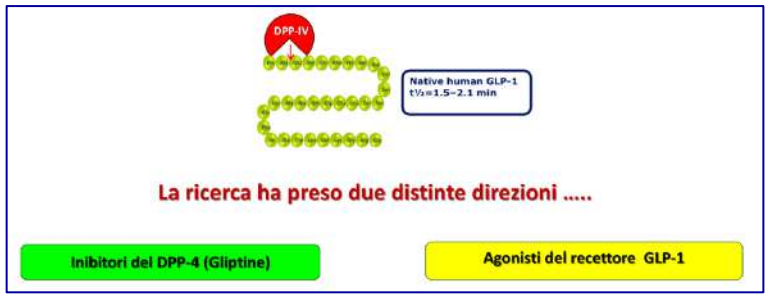


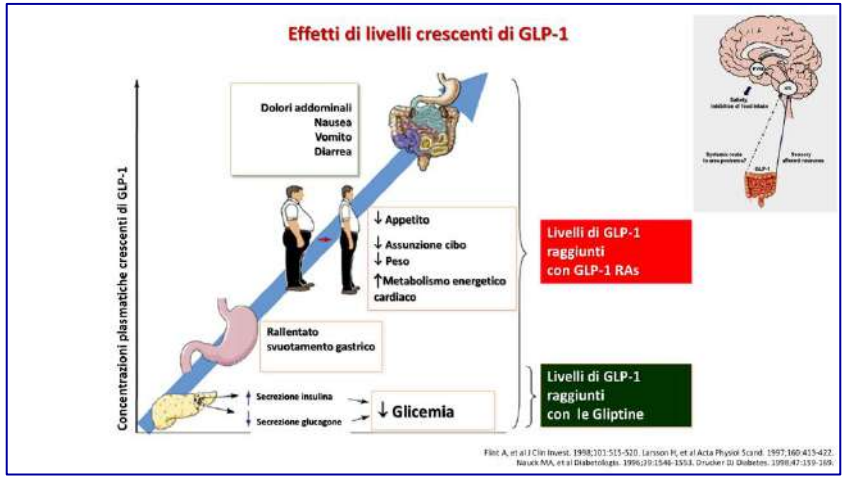
Terapia con incretine: serve un cambio di alimentazione?

Franco Gregorio

Responsabile UOS Diabetologia - Jesi







GLP-1RAs

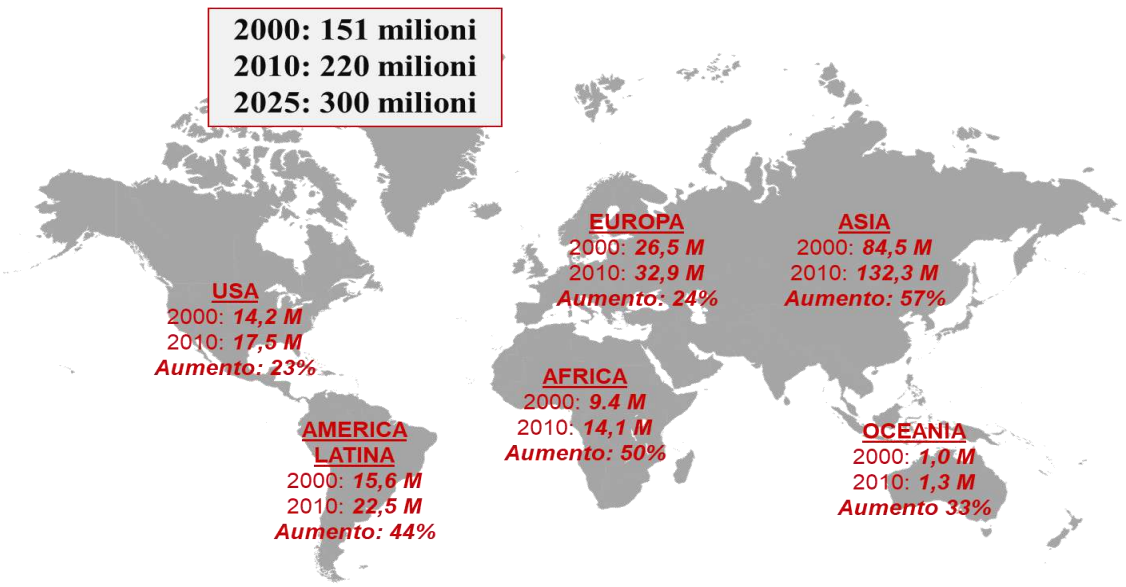
Diabetes mellitus

Overweight/Obesity

Gliptine

Il Diabete Tipo 2: i numeri

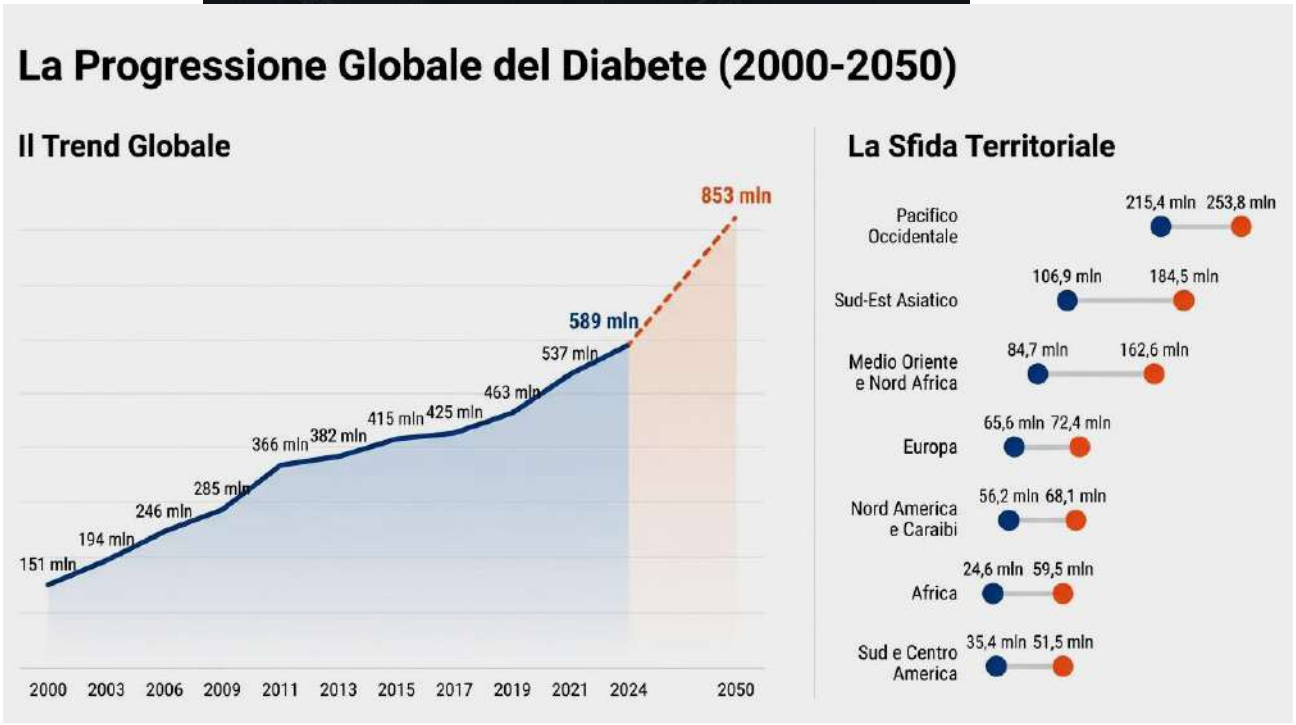
"Non-insulin dependent diabetes mellitus: the gathering storm !"



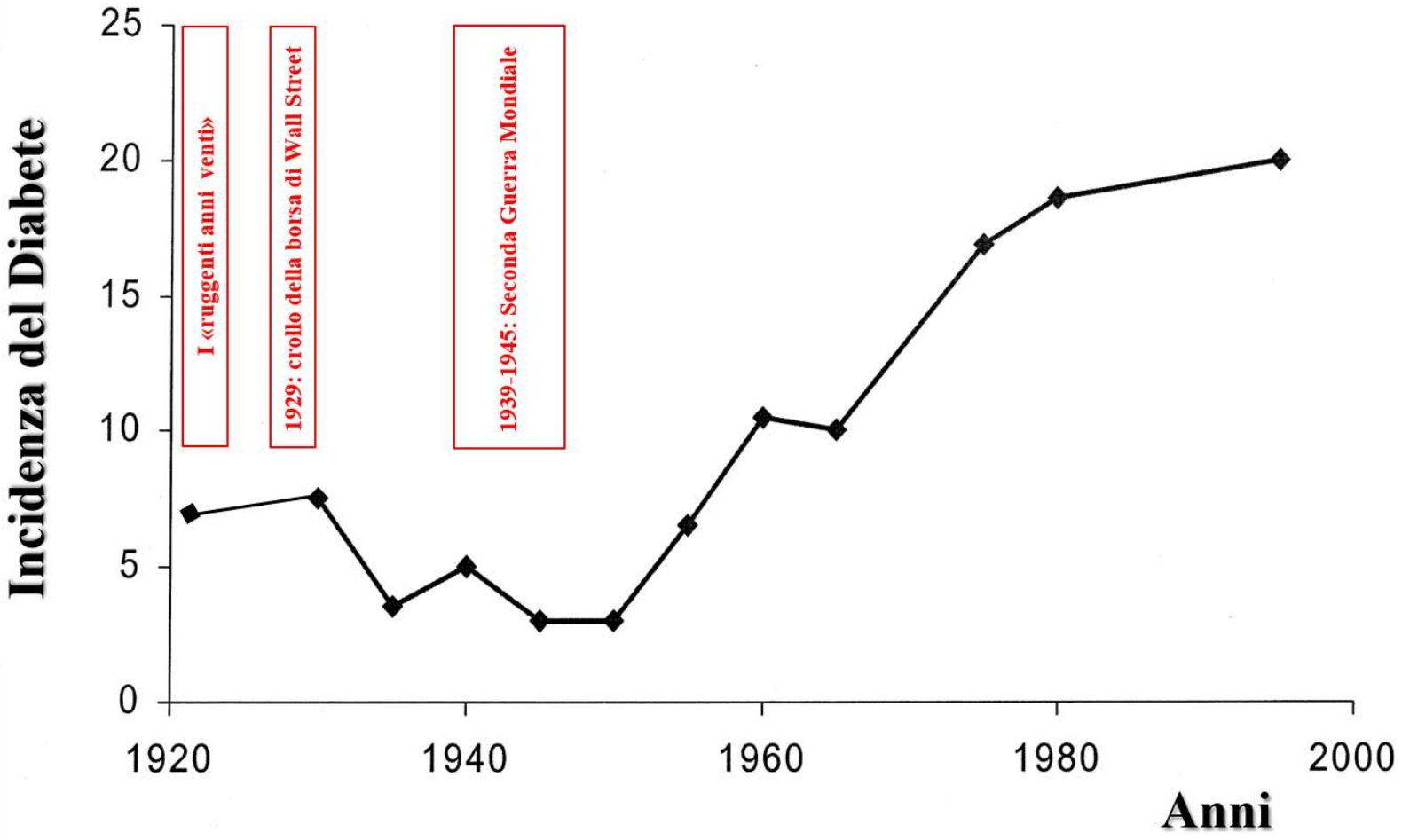
O'Rahilly S. B.M.J. 314, 955-959, **1997**



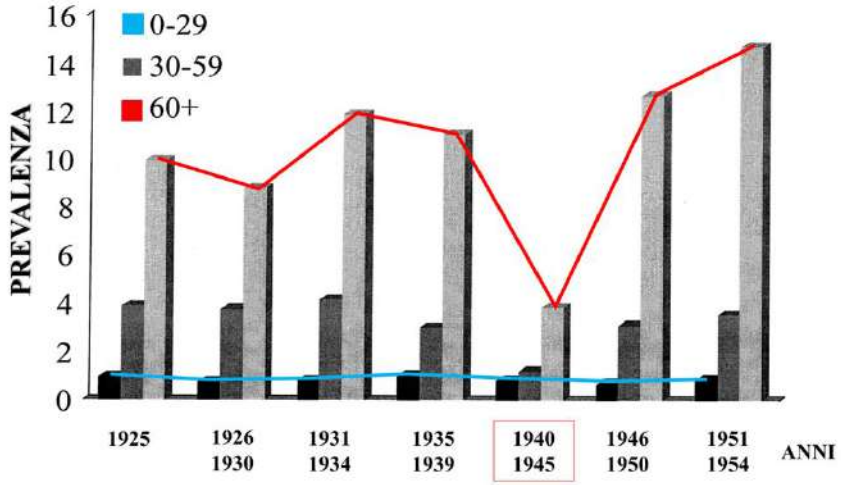
Mappatura della prevalenza e proiezioni al 2050
(Dati IDF Atlas 2024/2025)



I benefici effetti …….. della Guerra !!!

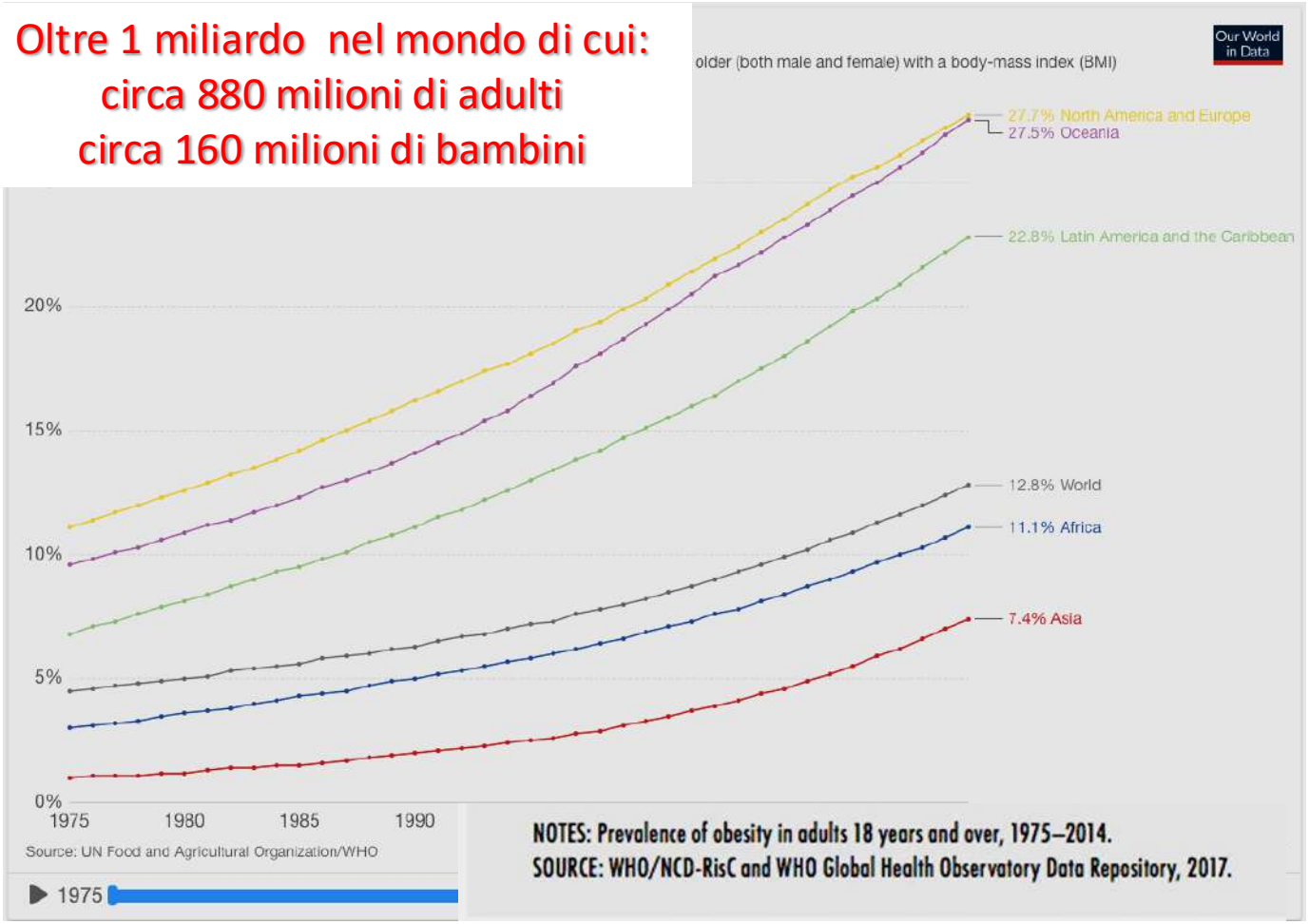


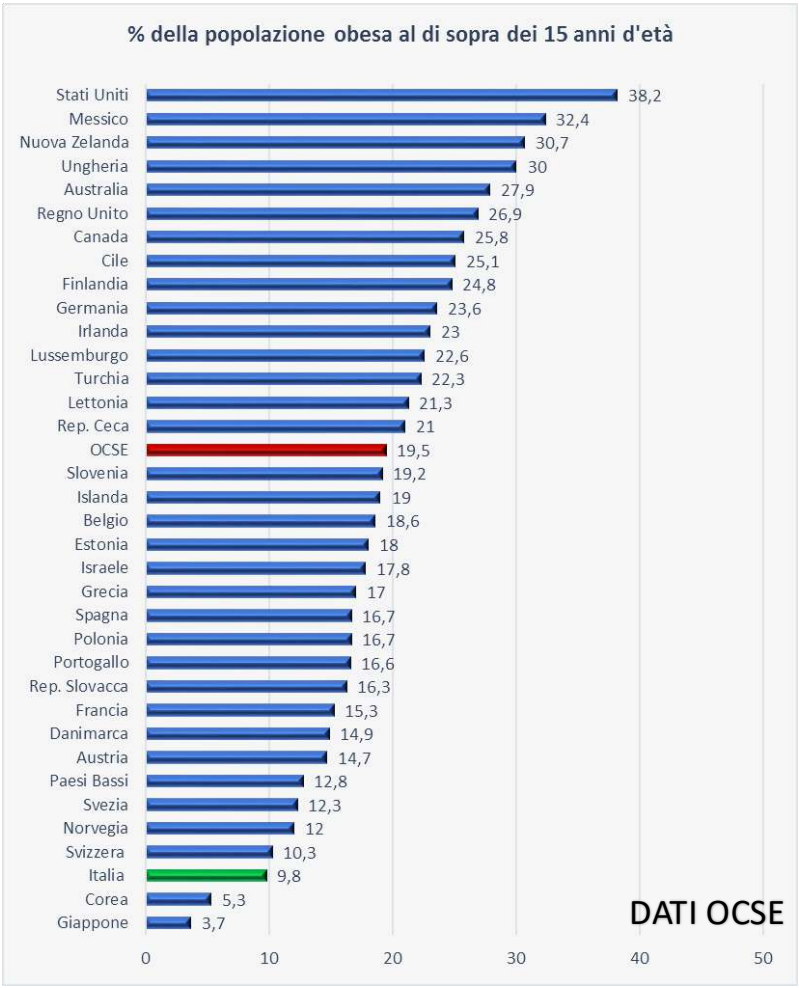
…ma solo nel Diabete di Tipo 2



L'Obesità: i numeri

Oltre 1 miliardo nel mondo di cui:
circa 880 milioni di adulti
circa 160 milioni di bambini

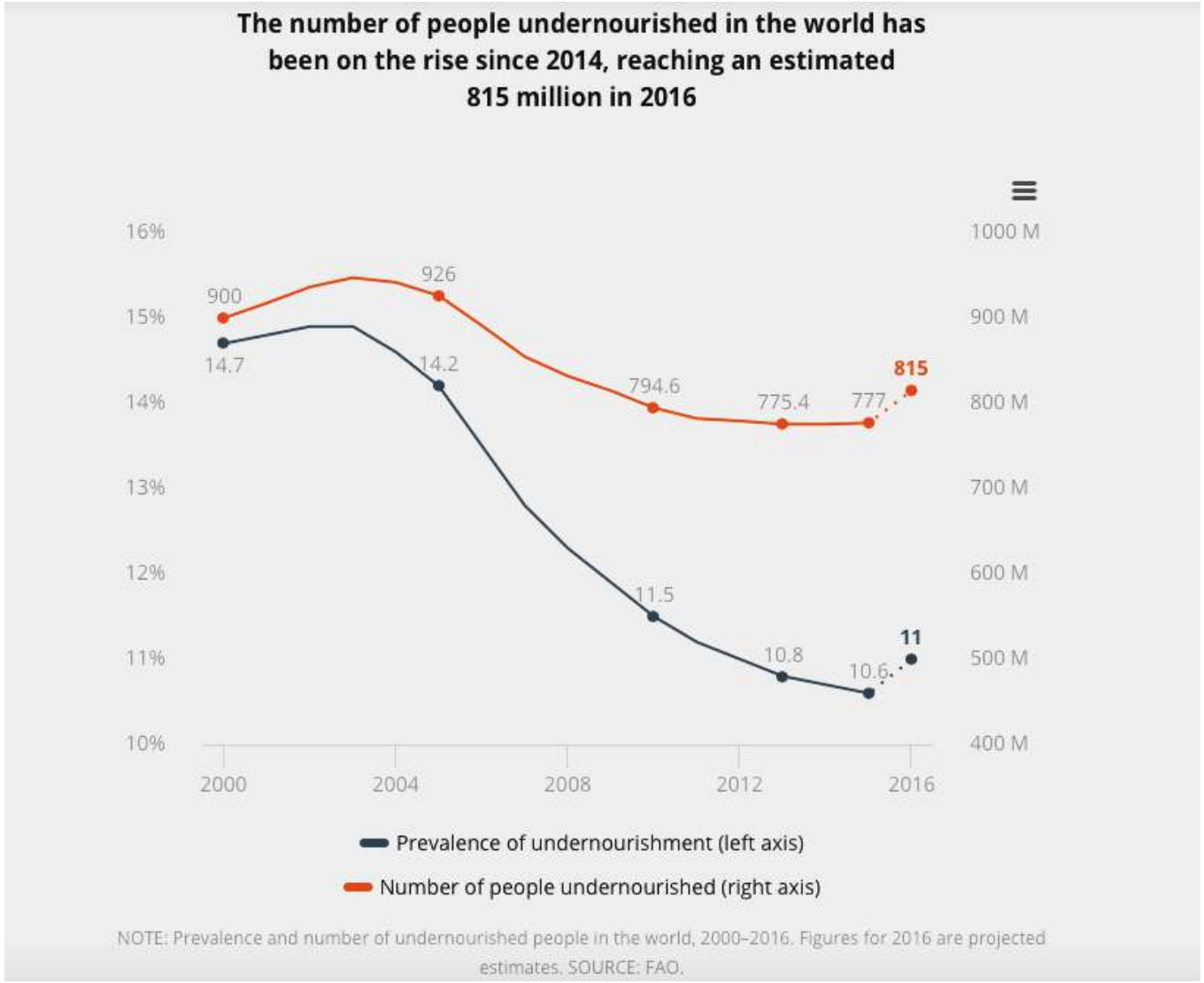




Nel 2024 si sono registrati 3,7 milioni di decessi correlati all'obesità pari al 12% di tutti i decessi dovuti a malattie non trasmissibili (WHO)

Anche nello scenario più ottimistico attualmente previsto la produzione di terapie a base di GLP-1 potrebbe coprire solo circa 100 milioni di persone, meno del 10% delle persone che attualmente convivono con l'obesità.

La FAO avverte: la fame nel mondo è tornata ad aumentare



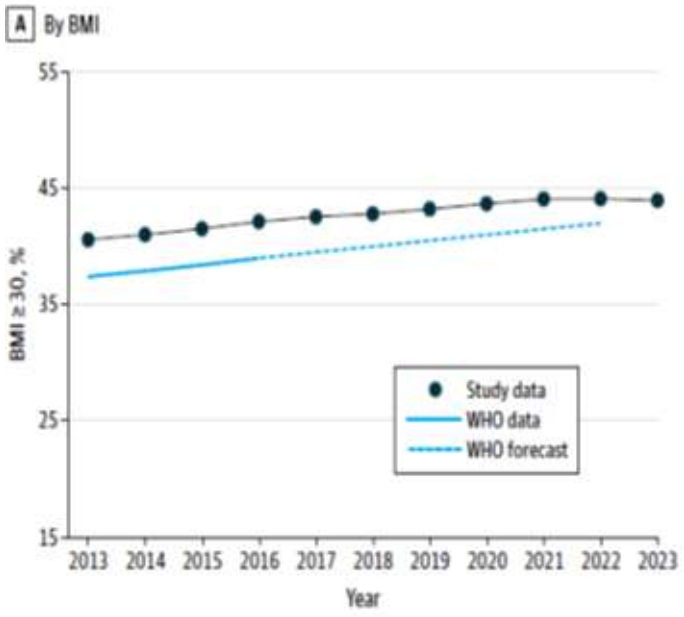


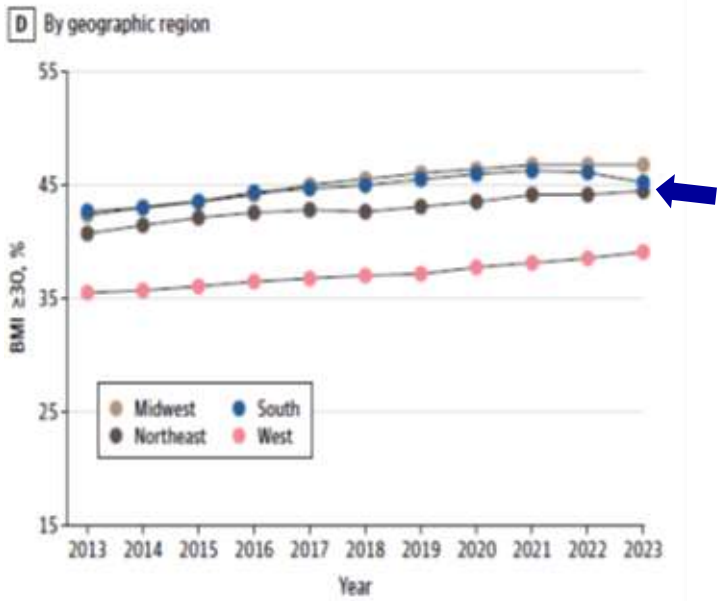


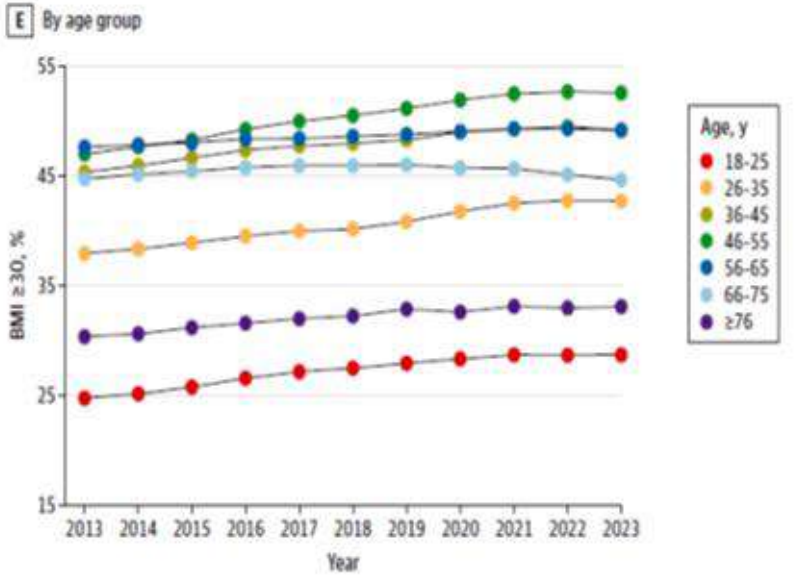


Changes in Adult Obesity Trends in the US

JAMA Health Forum. 2024;5(12):e243685.







- These findings suggest that BMI and obesity prevalence in the US decreased in 2023 for the first time in more than a decade.
- The most notable decrease was in the South (among individuals aged 66 to 75 years) which had the highest observed per capita GLP-1RA dispensing rate.

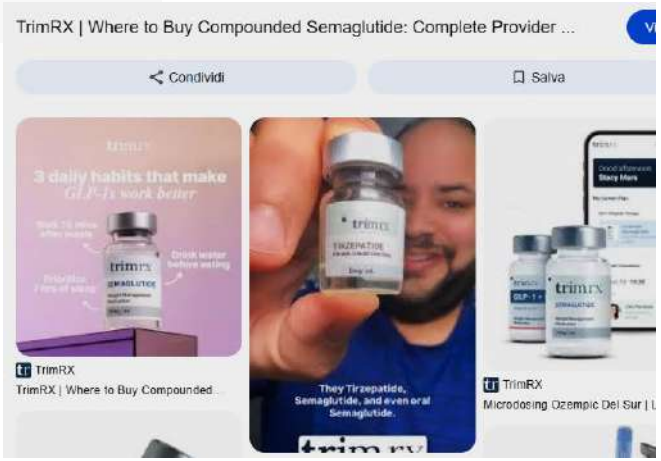


FDA alerts health care providers, compounders and patients of dosing errors associated with compounded injectable semaglutide products

An official website of the United States governme

FDA U.S. FOOD & DRUG ADMINISTRATION

10/01/2026



La Food and Drug Administration (FDA) ha richiamato medici e pazienti sui rischi associati alle versioni non approvate degli agonisti del recettore GLP-1 utilizzati anche per la perdita di peso, comprese le preparazioni di semaglutide e tirzepatide realizzate mediante compounding negli Stati Uniti.

Al 31 maggio 2026, la FDA aveva ricevuto 990 segnalazioni di eventi avversi associate a semaglutide preparato mediante compounding e oltre 730 relative a tirzepatide. L'Agenzia precisa che le segnalazioni non consentono sempre di stabilire un rapporto causale con il medicinale e potrebbero sottostimare il fenomeno, poiché non tutte le farmacie statunitensi che effettuano queste preparazioni sono tenute a trasmettere gli eventi avversi.

Il richiamo riguarda anche sostanze come retatrutide e cagrilintide, che negli Stati Uniti non sono ancora approvati dalla FDA.

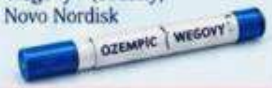
Patients are already using peptides.
Physicians are often the last to know.



GLP-1 Mean Weight Reduction

CURRENT APPROVED THERAPIES

ESTABLISHED AND EXPANDED INDICATIONS WITH NEW DATA PRESENTED AT EASD 2026

MEDICINE (Brand / Developer)	MECHANISM	KEY CLINICAL TRIALS (Phase)	POPULATION	KEY RESULTS (from EASD 2026 and recent pivotal data)	STATUS
SEMAGLUTIDE (Ozempic® (T2D) Wegovy® (obesity) Novo Nordisk 	GLP-1 receptor agonist	SUSTAIN (T2D) STEP (obesity) OCTANE (real-world)	Type 2 diabetes Obesity / overweight (with or without T2D)	**Weight loss: 10–16%** (Wegovy 68 weeks) HbA1c: **~1.0–1.8%** (T2D) **Cardiovascular risk reduction** (proven)	**APPROVED** T2D, obesity, weight management. Expanded data presented at EASD 2026.
TIRZEPATIDE Mounjaro® / Zepbound®) Eli Lilly 	Dual GIP/GLP-1 receptor agonist	SURPASS (T2D) SURMOUNT (obesity) SURPASS-CVOT	Type 2 diabetes Obesity / overweight High cardiovascular risk	**Weight loss: 15–22%** (SURMOUNT, 72 weeks) HbA1c: **~2.0–2.4%** (T2D) **Non-inferior for MACE-3 vs dulaglutide** (HR 0.92, 95.3% CI 0.83–1.01)	**APPROVED** T2D, obesity, weight management.
ORFORGLIPRON Eli Lilly 	Oral non-peptide GLP-1 receptor agonist	**ACHIEVE** (Phase 3) ACHIEVE-4 vs insulin glargine	Type 2 diabetes (oral option) Overweight / obesity	**Non-inferior glycaemic control** vs insulin glargine (no injections) **Weight loss: ~7–14%** (dose dependent) **MACE-4 HR 0.84; MACE-3 HR 0.77** (CIs crossed 1) – encouraging signals	**APPROVED (2026)** T2D. Regulatory submission anticipated in multiple regions.



Orforglipron (commercializzato con il nome di **Foundayo**).
Approvazione EMA 15 ottobre 2026

PIPELINE / INVESTIGATIONAL THERAPIES

PROMISING NEW AGENTS WITH KEY TRIAL DATA PRESENTED AT EASD 2026

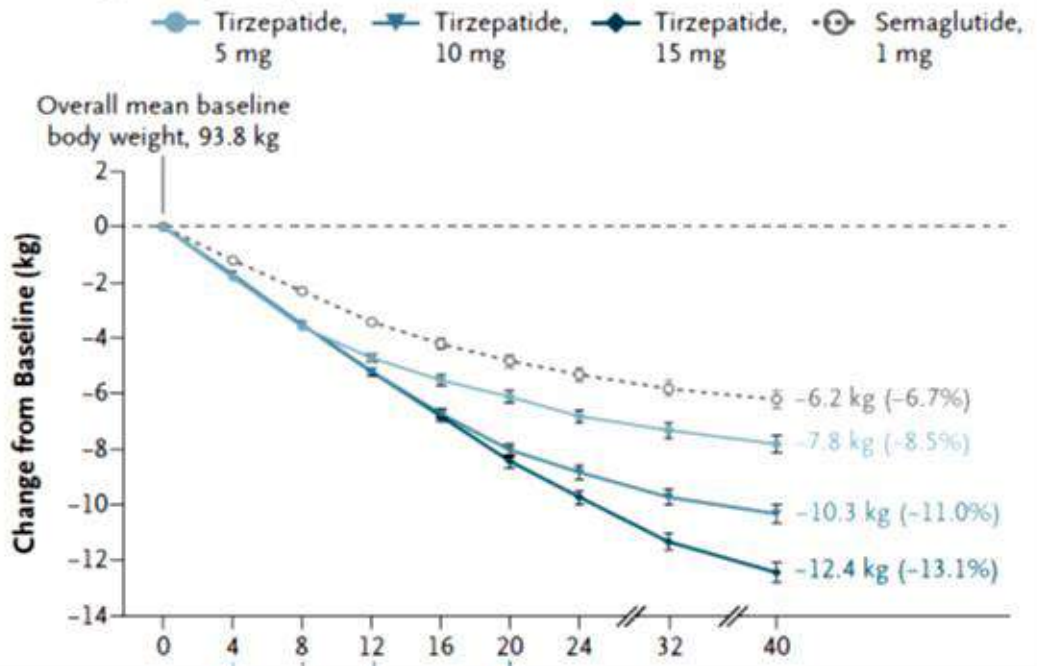
MEDICINE (Developer)	MECHANISM	KEY CLINICAL TRIAL (Phase)	POPULATION	KEY RESULTS (from EASD 2026)	STATUS
RETATRUTIDE Eli Lilly 	**Triple agonist** (GIP + GLP-1 + glucagon receptor)	**TRIUMPH-2** (Phase 3)	Obesity/overweight with type 2 diabetes	**Weight loss: 20.8%** (22.5 kg) at 80 weeks HbA1c: **~1.6%** Largest weight loss among investigational agents	**PHASE 3** Investigational Not yet approved
ELORATZP Eli Lilly 	**Eloralintide + tirzepatide** (Amylin + GIP/GLP-1 pathway)	Phase 2	Obesity/overweight with type 2 diabetes	**Weight loss: 23.3%** at 48 weeks (vs 14.8% with tirzepatide) HbA1c: **~2.9%** vs **~2.4%**	**PHASE 3** Planned Investigational
CAGRISEMA Novo Nordisk 	**Cagrilintide + semaglutide** (Amylin analogue + GLP-1 receptor agonist)	**REIMAGINE** (Phase 3)	Type 2 diabetes and separate obesity studies	**~14%** weight loss (T2D) with reductions in visceral, hepatic and pancreatic fat **22.4%** weight loss at 52 weeks (obesity study)	**PHASE 3** Ongoing Investigational
SURVODUTIDE (Boehringer Ingelheim 	Dual glucagon receptor + GLP-1 receptor agonist (once-weekly subcutaneous)	**SYNCHRONIZE-1** (Phase 3) 725 participants	Adults with obesity without diabetes	**Week 76 mean weight change:** **–12.2%** (3.6 mg) | **–13.0%** (6.0 mg) vs **–5.4%** (placebo) ≥5% weight loss: **72.6%** | **71.9%** | **46.3%** Most common adverse events: gastrointestinal, generally mild-to-moderate	**PHASE 3** Investigational

Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes

SURPASS-2

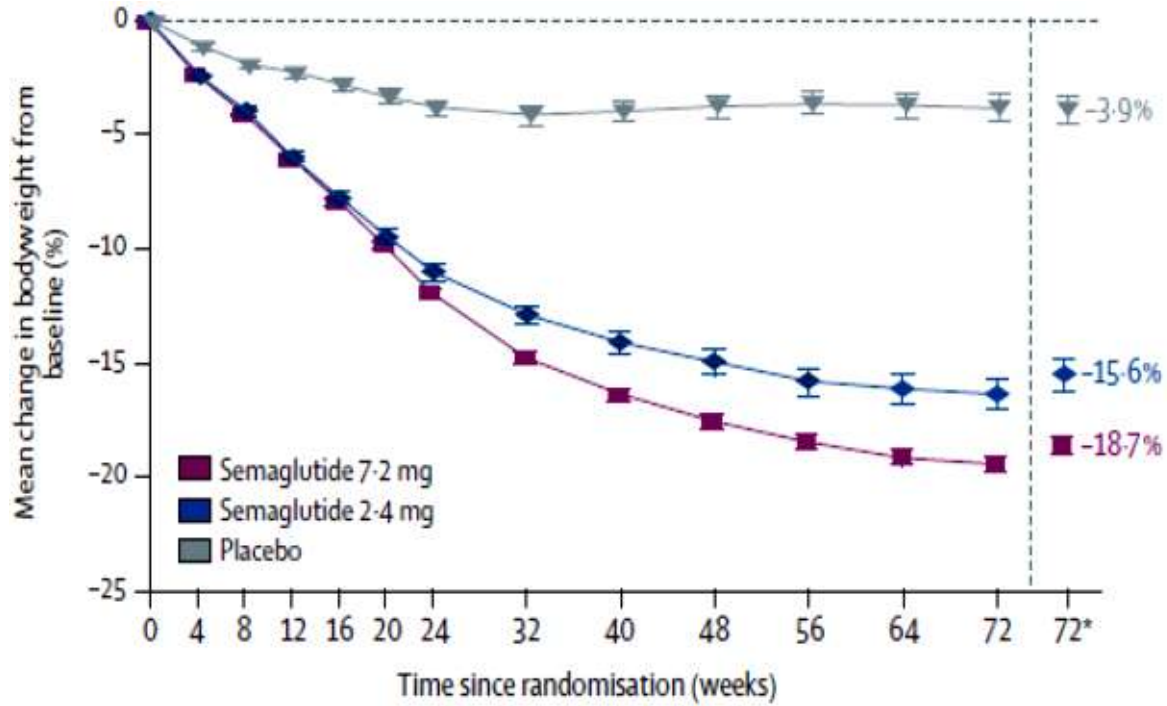
NEJM.ORG AUGUST 5, 2021

B Change in Body Weight from Wk 0 to Wk 40



Once-weekly semaglutide 7·2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial

Lancet Diabetes Endocrinol 2025



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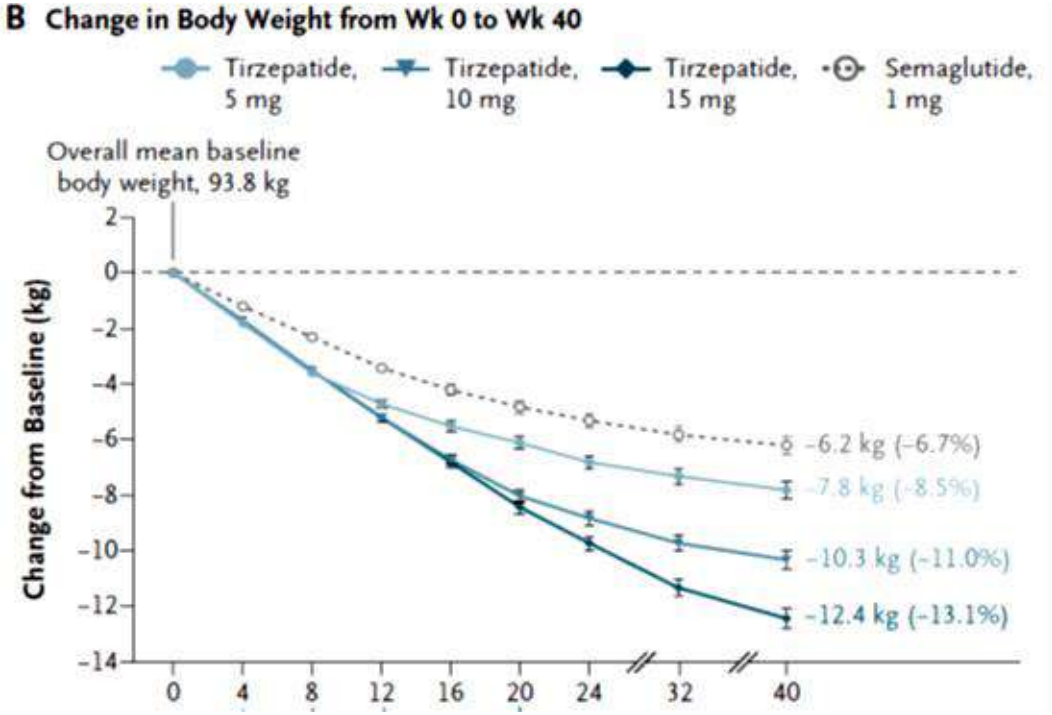

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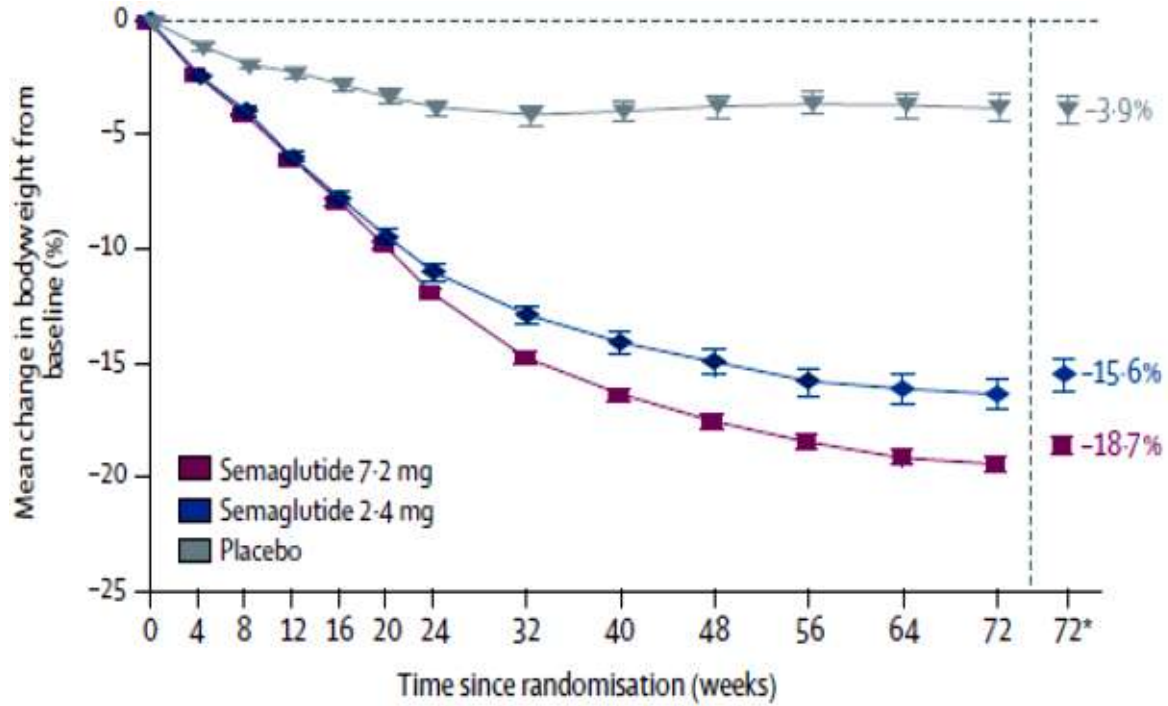


Efficacy and Safety of GLP-1 Receptor Agonists, Dual Agonists, and Retatrutide for Weight Loss in Adults With Overweight or Obesity: A Bayesian NMA

Obesity, November 2025

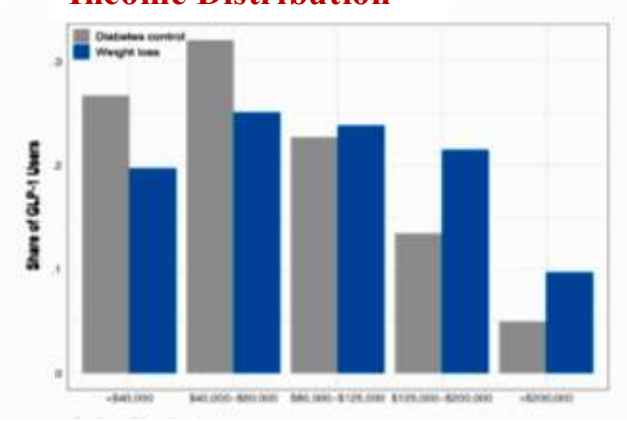
Conclusion: Retatrutide offers superior weight loss efficacy but with a higher AE risk.... Personalized treatment selection based on patient characteristics is recommended.

Il dosaggio massimo (12 mg-studio, TRIUMPH 1) ha prodotto una riduzione di peso del 28% a 80 settimane ma con 28% nausea, 33%diarrea, 15% vomito

The No-Hunger Games: How GLP-1 Medication Adoption Is Changing Consumer Food Demand

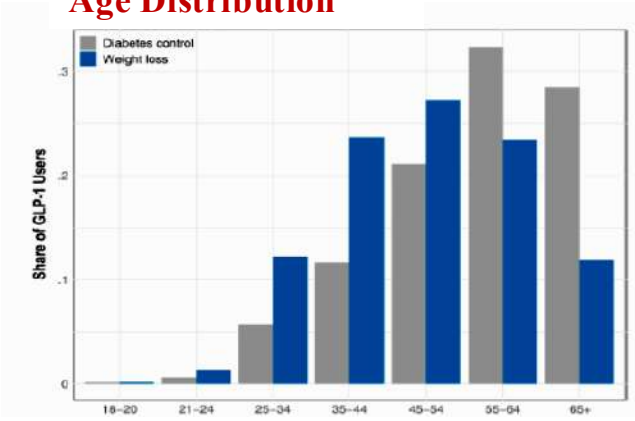
Journal of Marketing Research
2026, Vol. 63(3) 427-444

Income Distribution



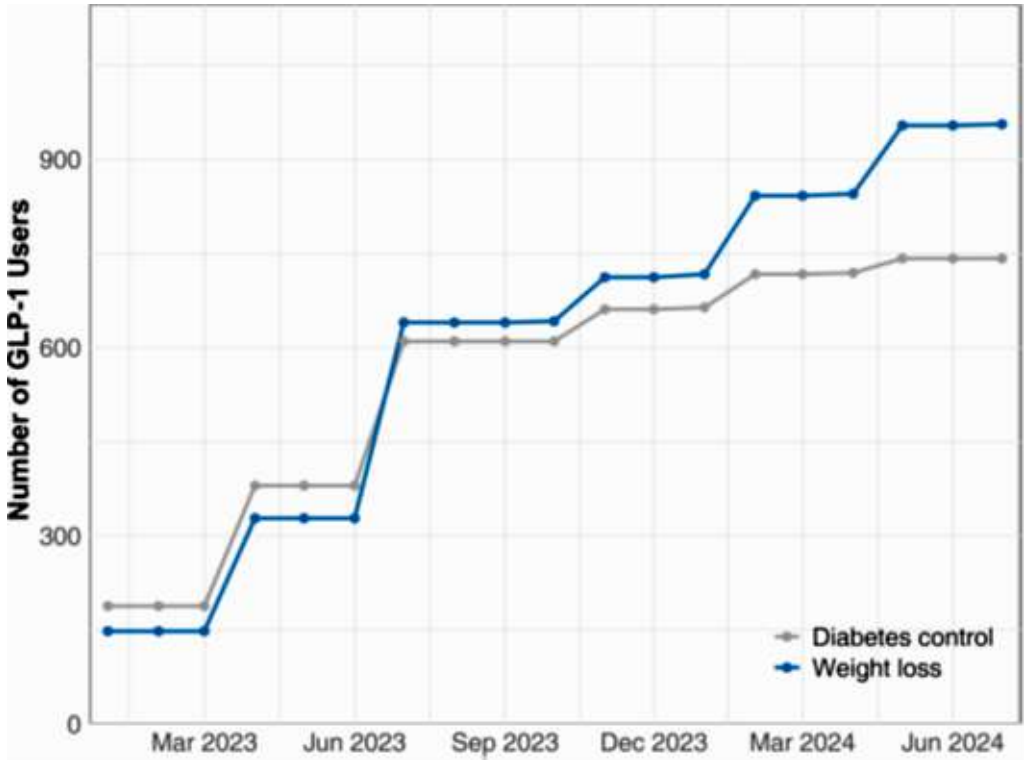
Weight-loss users are concentrated in higher-income households. In contrast, diabetes control users are more evenly distributed across income brackets.

Age Distribution

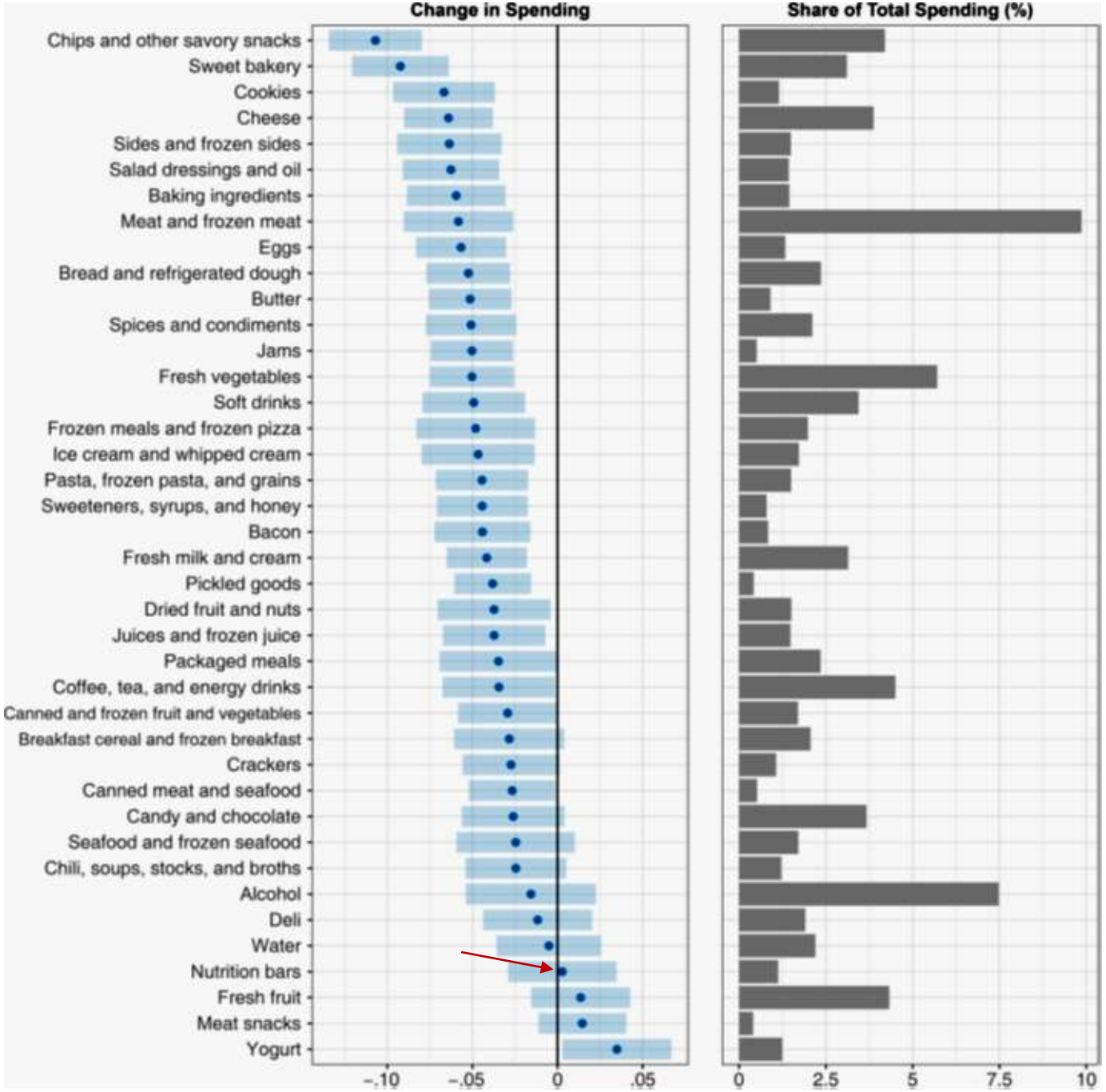


Consistent with the higher prevalence of diabetes among older individuals, GLP-1 users for diabetes control are predominantly concentrated in the over 55 age groups.

Reason for Use



Usage of GLP-1 drugs for weight loss surpasses usage for diabetes control by July 2023, and the gap between weight-loss usage and diabetes control usage widens over subsequent survey waves.



The largest spending reductions are primarily concentrated in high-calorie, high-sugar, and high-fat categories: the three categories with the largest declines in spending are chips and savory snacks (−10.1%), sweet bakery (−8.8%), and cookies (−6.5%).

Only four categories show estimated increases in spending: nutrition bars, fresh fruit, meat snacks (e.g., meat sticks), and yogurt, with yogurt showing the highest positive point estimate.

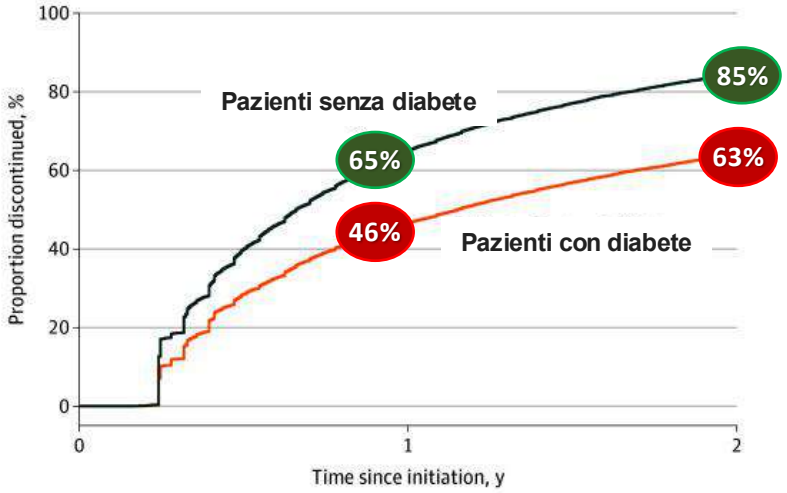
The patterns are similar across both diabetes users and weight-loss users

After discontinuation spending generally reverts toward preadoption levels across nearly all product categories. The notable exception is again candy and chocolates, where spending increases to 11.4% above preadoption levels after medication discontinuation.

Discontinuation and Reinitiation of Dual-Labeled GLP-1 Receptor Agonists Among US Adults With Overweight or Obesity

JAMA Network Open. 2025;

A Time to discontinuation of GLP-1 RA

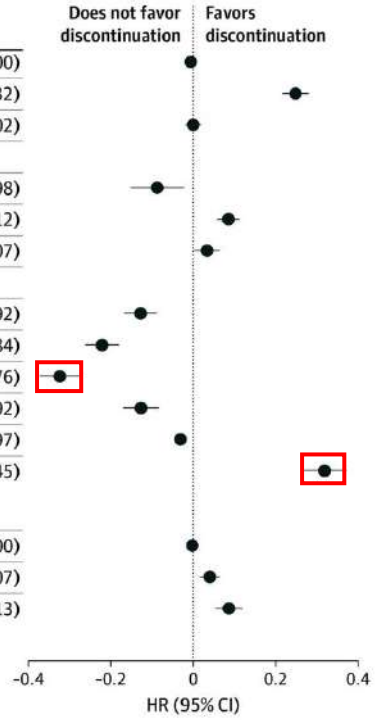


No. at risk

Patients with type 2 diabetes	76 524	36 709	10 774
Patients without type 2 diabetes	48 950	15 696	2750

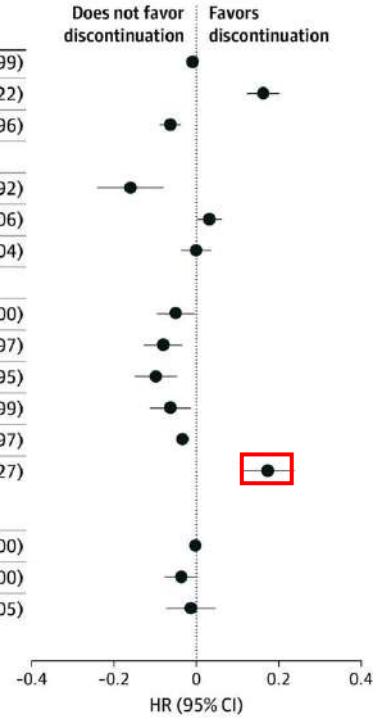
A Patients with type 2 diabetes

Covariate	HR (95% CI)
Age	0.99 (0.99-1.00)
Age ≥65 y	1.28 (1.24-1.32)
Male	1.00 (0.98-1.02)
Race and ethnicity	
Asian	0.92 (0.86-0.98)
Black	1.09 (1.06-1.12)
Other[a]	1.03 (1.00-1.07)
Income, $	
30 001-50 000	0.88 (0.85-0.92)
50 001-80 000	0.80 (0.77-0.84)
>80 000	0.72 (0.69-0.76)
Unknown	0.88 (0.84-0.92)
Weight loss (per 1%)	0.97 (0.97-0.97)
Gastrointestinal adverse events with treatment	1.38 (1.31-1.45)
Baseline BMI	1.00 (1.00-1.00)
CKD	1.04 (1.02-1.07)
Heart failure	1.09 (1.06-1.13)



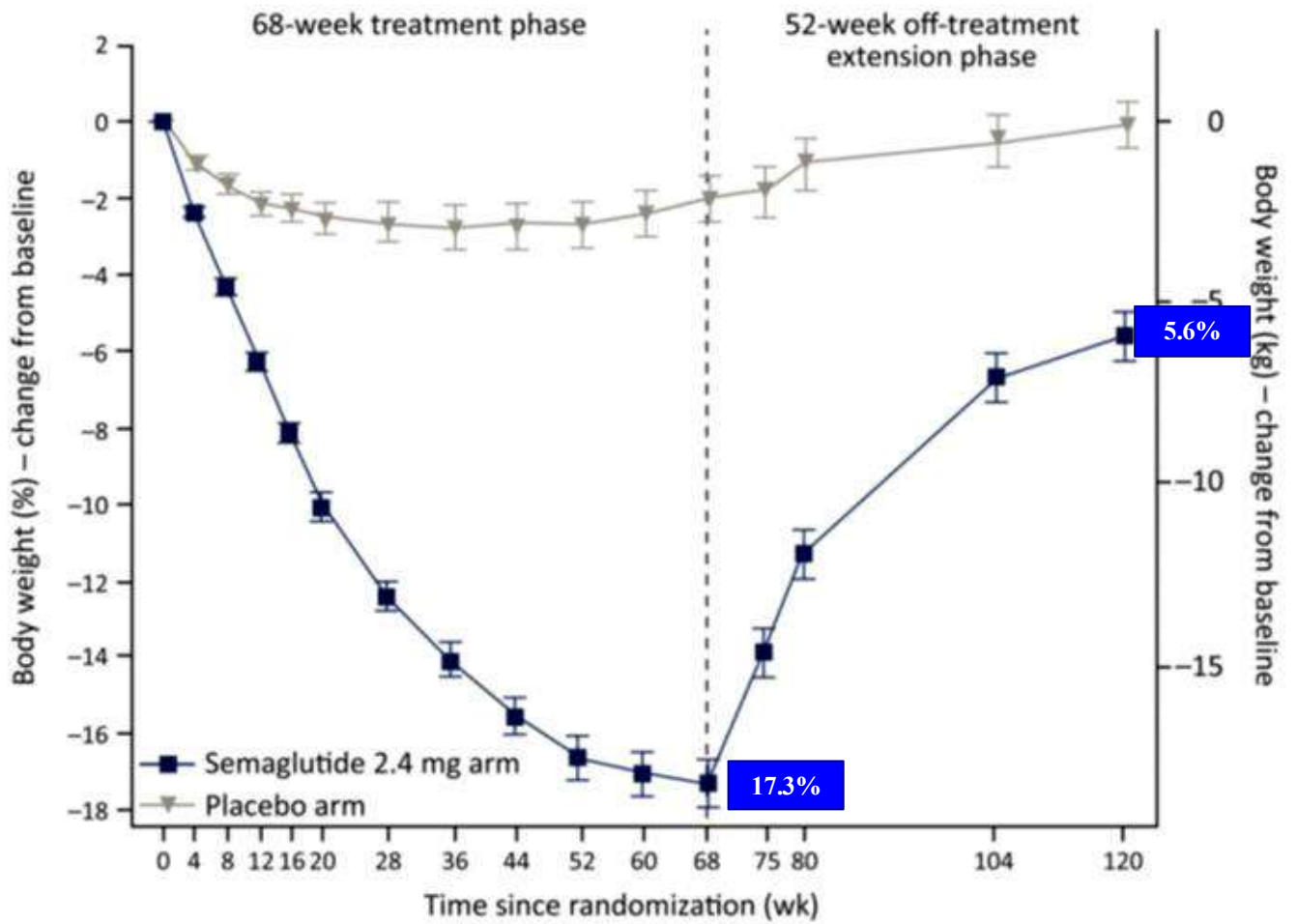
B Patients without type 2 diabetes

Covariate	HR (95% CI)
Age	0.99 (0.99-0.99)
Age ≥65 y	1.18 (1.13-1.22)
Male	0.94 (0.92-0.96)
Race and ethnicity	
Asian	0.85 (0.79-0.92)
Black	1.03 (1.00-1.06)
Other[a]	1.00 (0.96-1.04)
Income, $	
30 001-50 000	0.95 (0.91-1.00)
50 001-80 000	0.92 (0.88-0.97)
>80 000	0.91 (0.86-0.95)
Unknown	0.94 (0.89-0.99)
Weight loss (per 1%)	0.97 (0.97-0.97)
Gastrointestinal adverse events with treatment	1.19 (1.12-1.27)
Baseline BMI	1.00 (1.00-1.00)
CKD	0.96 (0.93-1.00)
Heart failure	0.99 (0.93-1.05)



Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension

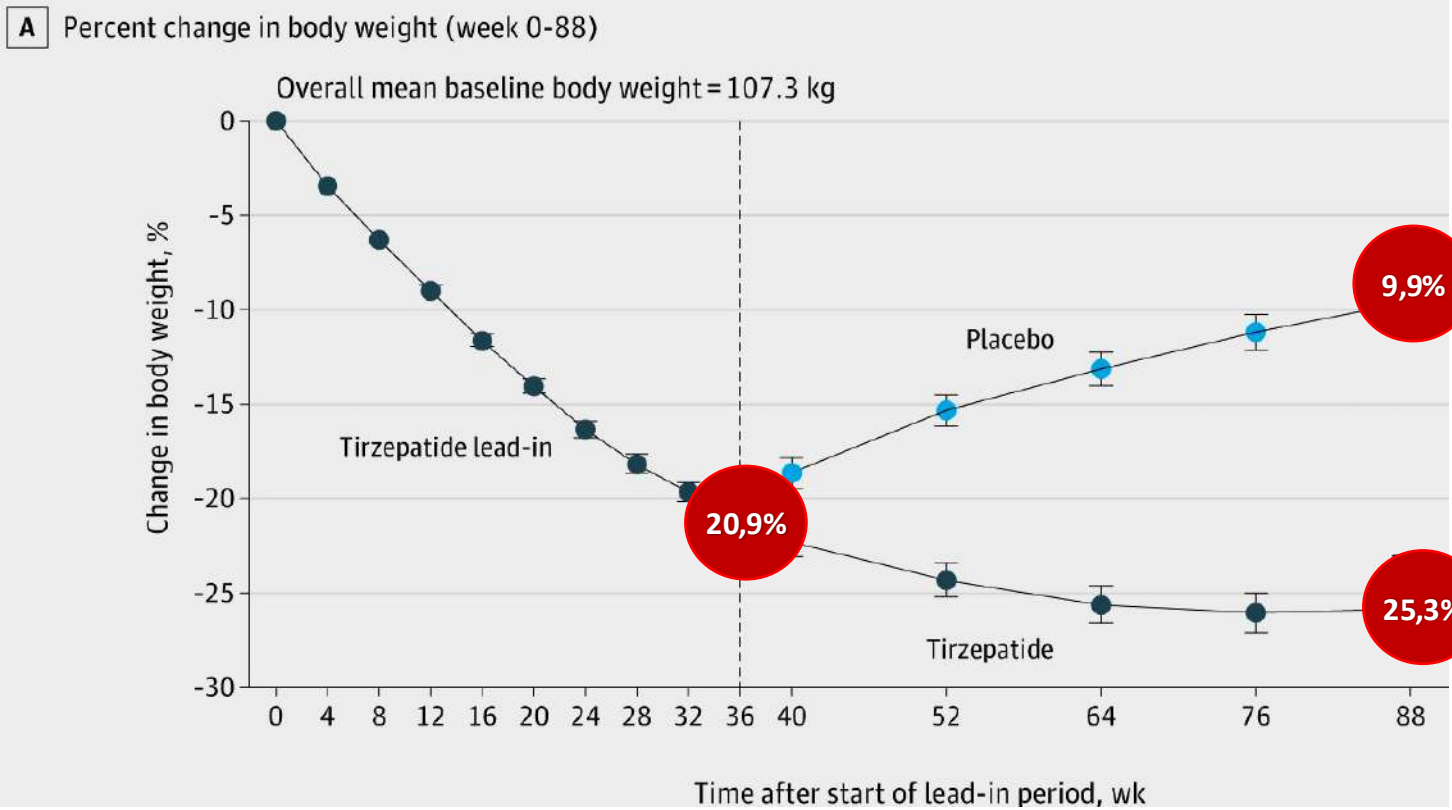
Diabetes Obes Metab. 2022



Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity

The SURMOUNT-4 Randomized Clinical Trial

JAMA
Published Online: December 11, 2023



Weight regain after cessation of medication for weight management: systematic review and meta-analysis

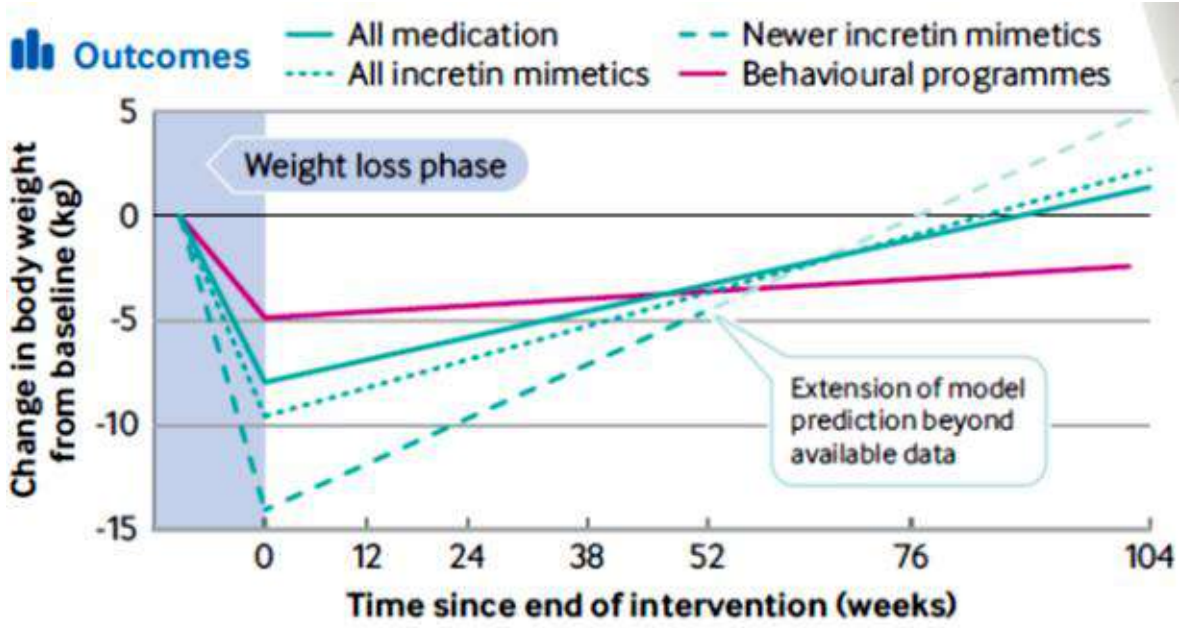
the bmj | BMJ 2026;

Summary People return to their baseline weight within 1.7 years on average after stopping treatment with any weight management medication, and just 1.5 years after using semaglutide or tirzepatide

Study design Systematic review and meta-analysis | Trials (randomised, non-randomised, single arm) and cohort studies (prospective or retrospective)

Data sources 37 studies | 9341 participants ≥18 years old with overweight or obesity

Intervention	Control
Pharmacological interventions currently or previously licensed for weight loss	Non-pharmacological weight loss interventions or placebos



WHAT IS ALREADY KNOWN ON THIS TOPIC

The development of highly effective weight management medications (WMMs) has transformed the treatment of obesity

Real world observations estimate that around 50% of people with obesity discontinue WMMs within 12 months

A previous systematic review quantified and compared the rate of weight regain with behavioural weight management programmes (BWMPs)

WHAT THIS STUDY ADDS

People on average regain weight at a rate of 0.4 kg/month after cessation of WMMs, leading to a projected return to baseline weight after 1.7 years

Although weight loss resulted in improvements in HbA_{1c}, fasting glucose, total cholesterol, triglycerides, systolic and diastolic blood pressure, all markers returned to baseline within 1.4 years of treatment cessation

The rate of weight regain after the cessation of WMMs was faster than after the cessation of BWMPs, independent of the amount of weight lost during treatment

World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults doi:10.1001/jama.2025.24288

l'OMS definisce l'obesità una *malattia cronica e recidivante*, importante causa di morbilità, mortalità e oneri economici

L'OMS raccomanda di abbinare la farmacoterapia alla terapia comportamentale intensiva (Intensive Behavioral Therapy, IBT): "*for individual who are prescribed GLP-1 receptor agonists or GLP-1/GIP dual agonists, counseling on behavioral, nutritional and lifestyle changes should be provided as first step to amplify and support optimal health outcomes*."

I 4 punti fondamentali da gestire attraverso modifiche dell'alimentazione sono:

- Prevenire/Ridurre gli effetti indesiderati GI (soprattutto nella fase di up-titration)
- Monitorare/Mitigare le possibili conseguenze nutrizionali derivante dal deficit di apporto alimentare
- Preservare la massa magra (contrastando il rischio di sarcopenia)
- Contrastare la ripresa ponderale alla sospensione

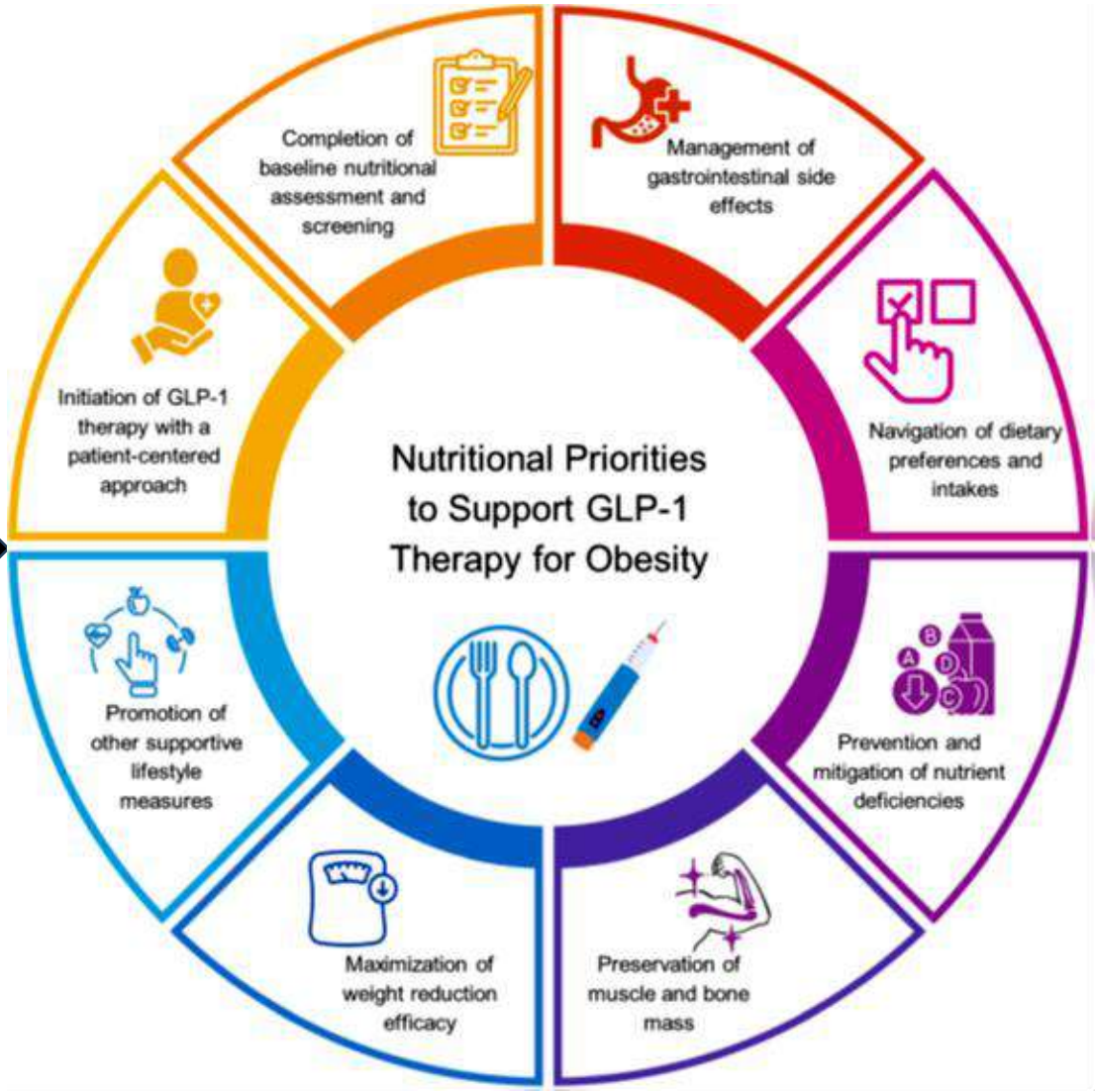
Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society

Obesity (Silver Spring). 2025;33:1475-1503.

Although authoritative health and medical entities recommend comprehensive lifestyle modification as part of the treatment plan for obesity, the use of such therapies before or to support GLP-1 use is not widespread in practice…

As GLP-1s are becoming more commonly prescribed for obesity by providers across multiple disciplines, there is growing concern for the continued lack of formal medical training in nutrition…and competencies to provide nutrition counseling.

For example, one study found that 90% of cardiologists receive minimal or no nutrition education during fellowship [113]—despite the critical role of diet in cardiovascular health.



Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society

Obesity (Silver Spring). 2025;33:1475-1503.



Initiation of GLP-1 use with a patient-centered approach

The approach to initiating pharmacologic therapy for obesity should be individualized, with a focus on overall physical health, mental health, and well-being rather than body weight alone.

Because many individuals request GLP-1s due to a focus on body weight, other key components in the obesity management… must be considered and discussed before initiating these therapies

Decisions about how quickly or slowly to titrate therapy or restrict calories should be guided by an individual's needs.

Completion of baseline nutritional assessment and screening

This includes, for example, any GI symptoms or disorders…

Current dietary habits should be assessed, including frequency of fast foods, frozen meals, take-out foods, sweet and savory snacks, processed meats, and sugar sweetened beverages…. Cultural and household food preferences, are helpful to understand…

Clinicians should ask about positive and negative emotional triggers for off-plan, loss of control, or late-night eating…individuals should be screened for signs of eating disorders: effects of GLP-1s on these disorders are not well established…

Many people who reduce their weight on GLP-1s experience improved mood, including fewer depressive symptoms.. The role of GLP-1s in the setting of antidepressant medications, which could have both synergistic and opposing benefits and side effects, requires more study.

Individuals should be assessed for risk of sarcopenia and osteopenia, seen in individuals who are older, sedentary, chronically ill, malnourished..

Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society

Obesity (Silver Spring). 2025;33:1475-1503.



Management of GastroIntestinal side effects

Side effect	Semaglutide 2.4 mg group (%)	Placebo group (%)	Tirzepatide 15 mg group (%)	Placebo group (%)
Nausea	44	16	28	8
Diarrhea	30	16	23	8
Vomiting	24	6	13	2
Constipation	24	11	11	5
Abdominal pain	20	10	10	5
Headache	14	10	-	-
Fatigue	11	5	7	3
Dyspepsia	9	3	10	4
Dizziness	8	4	4	2
Abdominal distension	7	5	4	2
Eructation	7	<1	5	1
Hypoglycemia[b]	6	2	-	-
Flatulence	6	4	4	2
Gastroenteritis	6	4	-	-
Gastroesophageal reflux	5	3	5	2
Gastritis	4	1	-	-
Hair loss	3	1	5	1

Comparative gastrointestinal adverse effects of GLP-1 receptor agonists and multi-target analogs in type 2 diabetes: a Bayesian network meta-analysis

frontiers | Frontiers in Pharmacology
19 September 2025

TABLE 1 Gastrointestinal adverse reaction rankings in type 2 diabetic patients receiving GLP-1 receptor agonists.

Medicine	Nausea		Diarrhea		Vomiting		Dyspepsia		Costipation	
	SURCA	Rank	SURCA	Rank	SURCA	Rank	SURCA	Rank	SURCA	Rank
Dulaglutide	26.4	7	56.2	4	22.3	7	33.6	5	56.1	3
Exenatide	41.5	6	32.6	6	52.8	5	31.4	6	43.1	6
Liraglutide	46.5	5	41.0	5	38.6	6	46.9	4	65.1	2
Lixisenatide	74.2	3	15.1	7	86.6	1	84.8	2	48.9	5
Loxenatide	46.9	4	88.1	2	73.1	2	—	—	—	—
Placebo	1.4	8	1.5	8	0.9	8	1.0	7	5.5	7
Semaglutide	77.4	2	73.3	3	65.7	3	64.3	3	79.5	1
Tirzepatide	85.8	1	92.2	1	60.1	4	88.1	1	51.9	4

Note: SURCA, cumulative adverse reaction rate below.

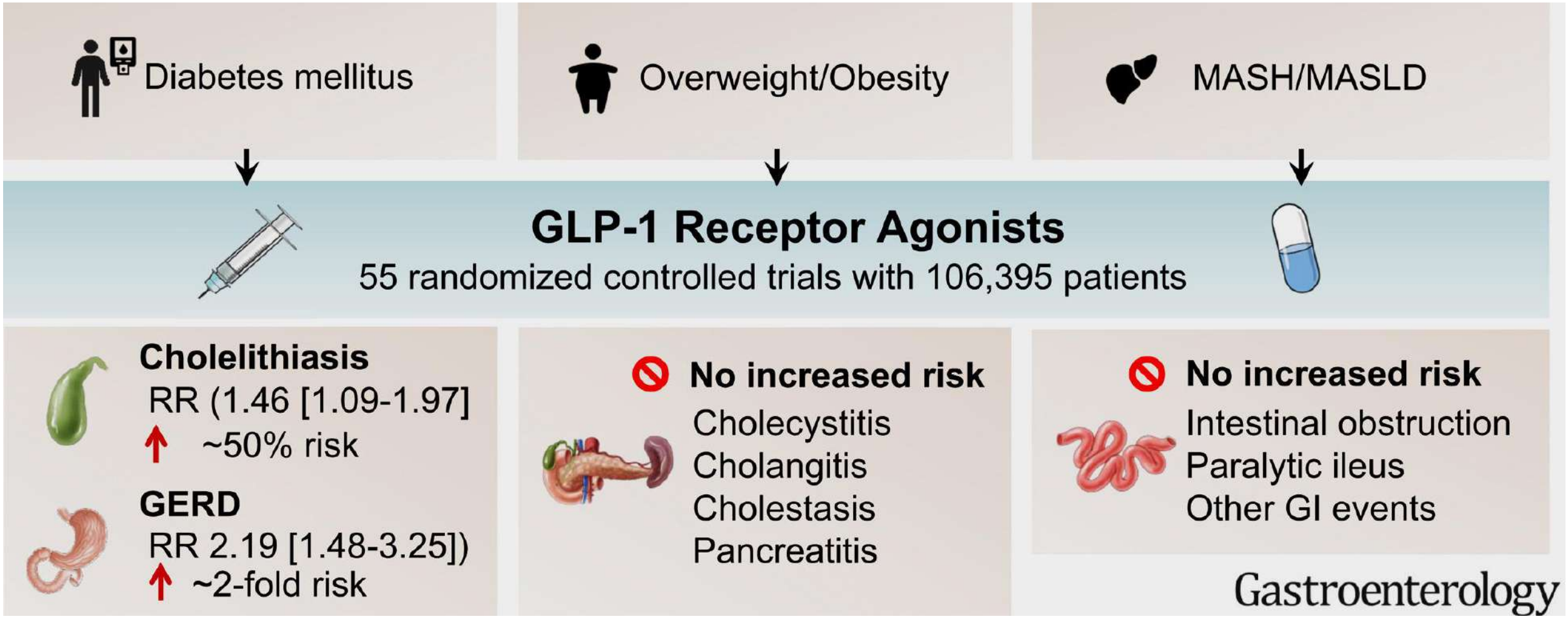
Semaglutide had the highest risk of inducing constipation

Tirzepatide had the highest risk of inducing nausea and diarrhea

SURCA: Surface Under Ranking Curve Adverse events

Glucagon-Like Peptide-1 Receptor Agonists and Gastrointestinal Adverse Events: A Systematic Review and Meta-Analysis

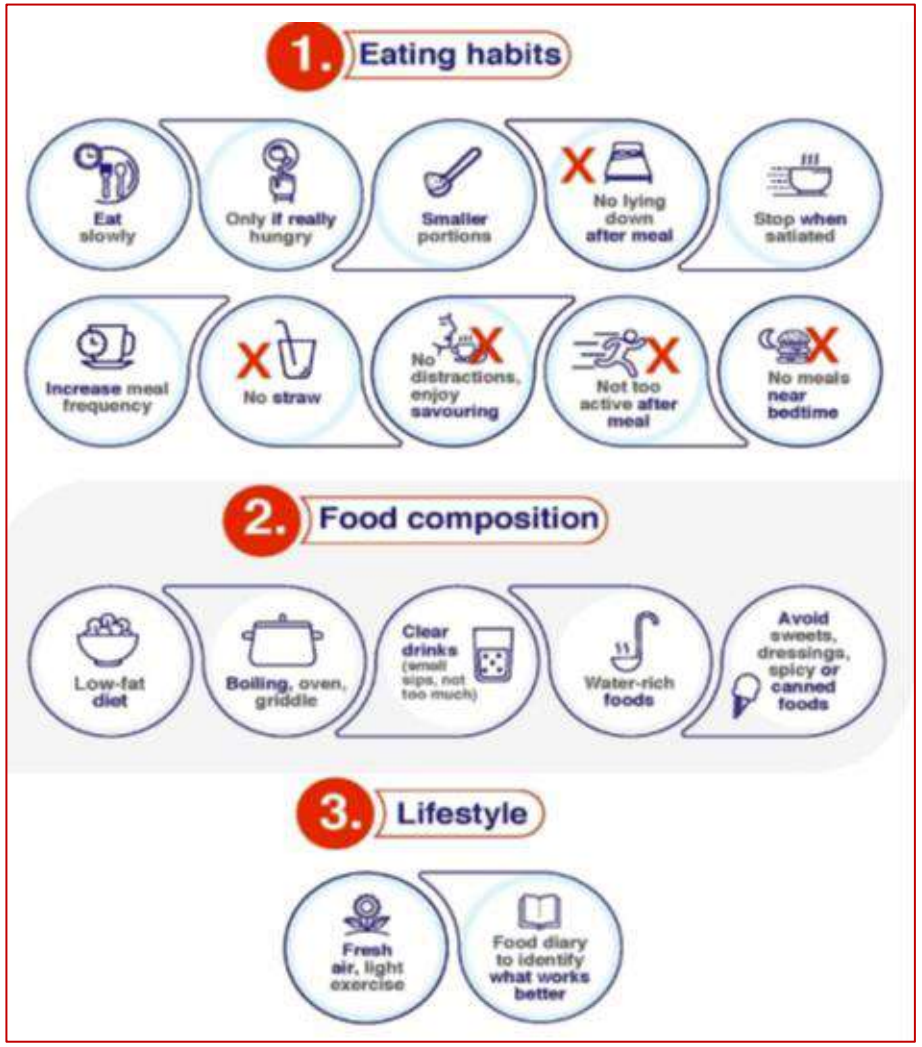
Gastroenterology 2025



GLP-1RAs are associated with an increased risk of cholelithiasis and GERD (gastroesophageal reflux disease), but do not appear to increase the risk of other gastrointestinal or biliary adverse events.

Perspective
Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus
J. Clin. Med. 2023,

1) Minimizing occurrence/severity of GI AEs when starting GLP-1 RA: general recommendations



Observe the guidelines of the data sheet regarding posology and method of administration
Improve eating habits Eat slowly Eat only if you are really hungry Eat smaller portions Avoid lying down after having a meal Stop eating in case of feeling of fullness Increase meal frequency Avoid drinking using a straw Eat without distractions and enjoy savouring the food Try not to be too active after eating Avoid eating too close to bedtime
Adapt food composition to your requirements Choose easy-to-digest food, low fat diets (focus on bland foods) Use oven, cooking griddle or boiling Increase fluid intake, especially clear, fresh drinks (in small sips), but no so much as to make you feel too full Healthy food that contain water (soups, liquid yogurt, gelatin, and others) Avoid sweet meals Avoid dressings, spicy foods, canned food, sauces that are not home-cooked
Get some fresh air and do some light exercise
Keep a food diary, as it may be useful to identify foods or meal timings that make it worse

Prima

Pasti Frazionati

Frazionare l'apporto in pasti piccoli e frequenti (3-6 al giorno).

Durante

Masticazione Lenta

Mangiare lentamente, masticare in modo prolungato. Regola clinica: fermarsi al primissimo segnale di sazietà.

Dopo

Prevenzione Reflusso

Vietato sdraiarsi immediatamente. Attendere 2-3 ore prima del riposo orizzontale.

Protocollo Idratazione

Bere a piccoli sorsi rigorosamente
Divieto assoluto di bevande gassate e uso della cannuccia per evitare l'ingestione di aria.

Da Evitare (Triggers)



Cibi ad alto contenuto di grassi, fritti, eccessivamente dolci o molto piccanti. Evitare l'esposizione a odori forti durante la preparazione dei cibi (potenti catalizzatori di nausea e reflusso).

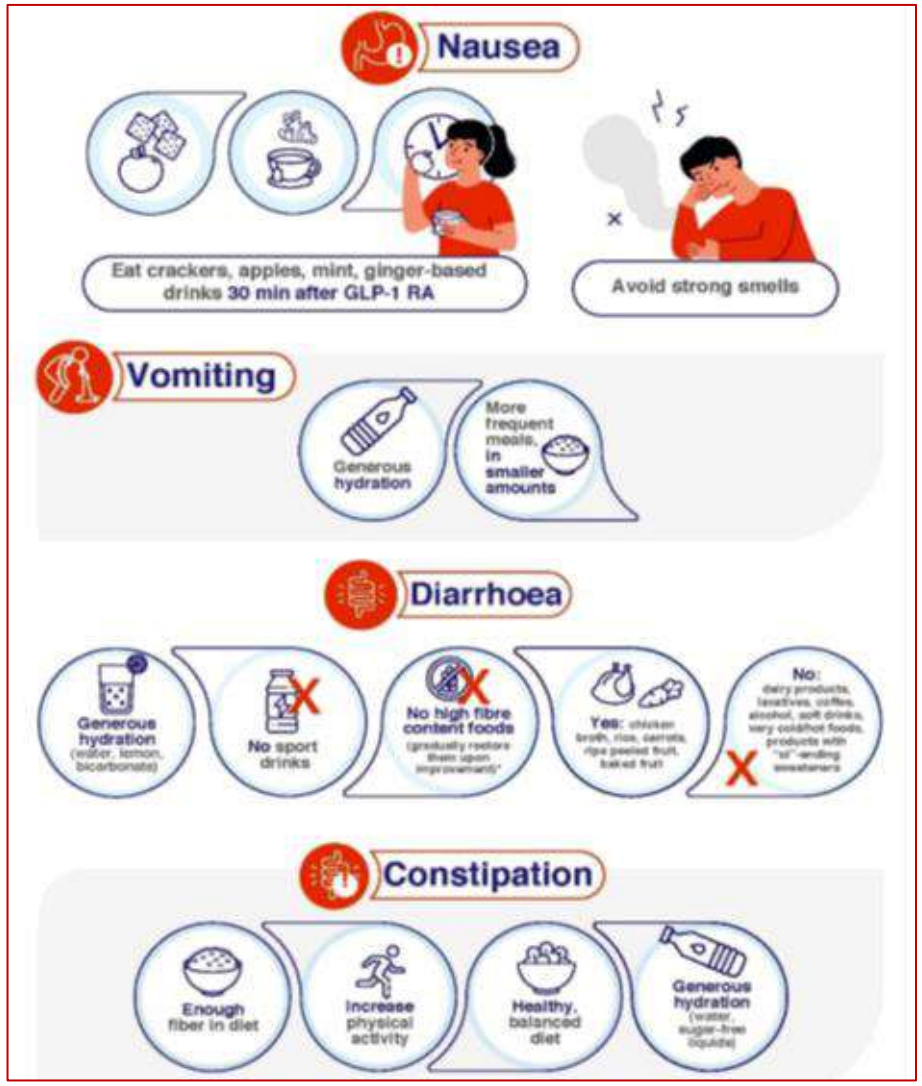
Da Adottare (Rimedi)



Utilizzare radice di zenzero o menta (anche come tisane) come antiemetici naturali per contrastare attivamente la nausea, distanziati di 30 minuti

Perspective
Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus
J. Clin. Med. 2023,.

2) Additional specific guidelines for each separate GI AE



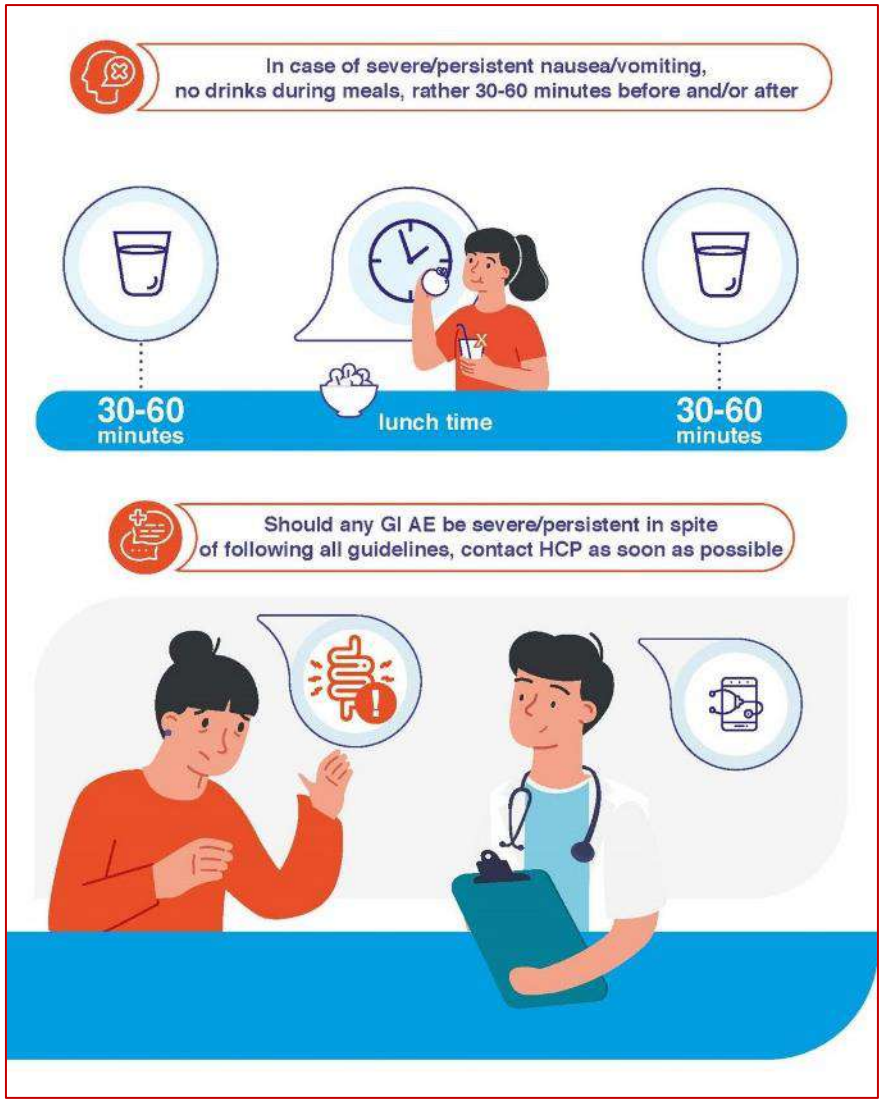
Additional recommendations for patients with nausea
Provided that 30 min have passed since the last GLP-1 RA dose, eat foods able to ease the symptoms of nausea, such as crackers, apples, mint, ginger root or ginger-based drinks
Avoid strong smells
Additional recommendations for patients with vomiting
Be particularly careful with hydration
Eat smaller amounts of food in more frequent meals
Additional recommendations for patients with diarrhoea
Generous hydration, for example with water, lemon and a teaspoon of bicarbonate
Avoid isotonic drinks intended to be used in the context of sport activities
Avoid dairy products, laxative juices or meals, coffee, alcoholic drinks, soft drinks, very cold or very hot foods, products with sweeteners ending in "ol" (sorbitol, mannitol, xylitol, maltitol), including candy and gum
Avoid (or temporarily reduce your intake of) foods with high fibre content * such as grain and seed products, such as grain cereals, nuts, seeds, rice, barley, whole grain bread or baked goods vegetables such as artichokes, asparagus, beans, cabbage, cauliflower, garlic and garlic salts, lentils, mushrooms, onions, sugar snap, snow peas skinned fruits, apples, apricots, blackberries, cherries, mango, nectarines, pears, plums
Eat chicken broth, rice, carrots, very ripe fruit without skin
Additional recommendations for patients with constipation
Ensure the amount of fibre in your diet is adequate
Increase physical activity
Ensure your diet is healthy and balanced
Drink generous amounts of water (or other sugar-free liquids)

Perspective

Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus

J. Clin. Med. 2023,.

3) Additional specific guidelines for unusually severe/persistent GI AEs



Additional recommendations when GLP-1 RA are unusually severe or/and persistent
In case of persistence of nausea and/or vomiting, avoid drinks during meals, rather have them between 30 and 60 min before and/or after meals
If nausea, vomiting, diarrhoea and/or constipation persist in spite of following all the guidelines depicted above, inform HCP as soon as possible

La perdita di peso durante la terapia con GLP-1RAs è in gran parte indipendente dagli eventi avversi gastrointestinali

Journal of Clinical Medicine BMJ Open Diab Res Care 2020; MDPI

Perspective

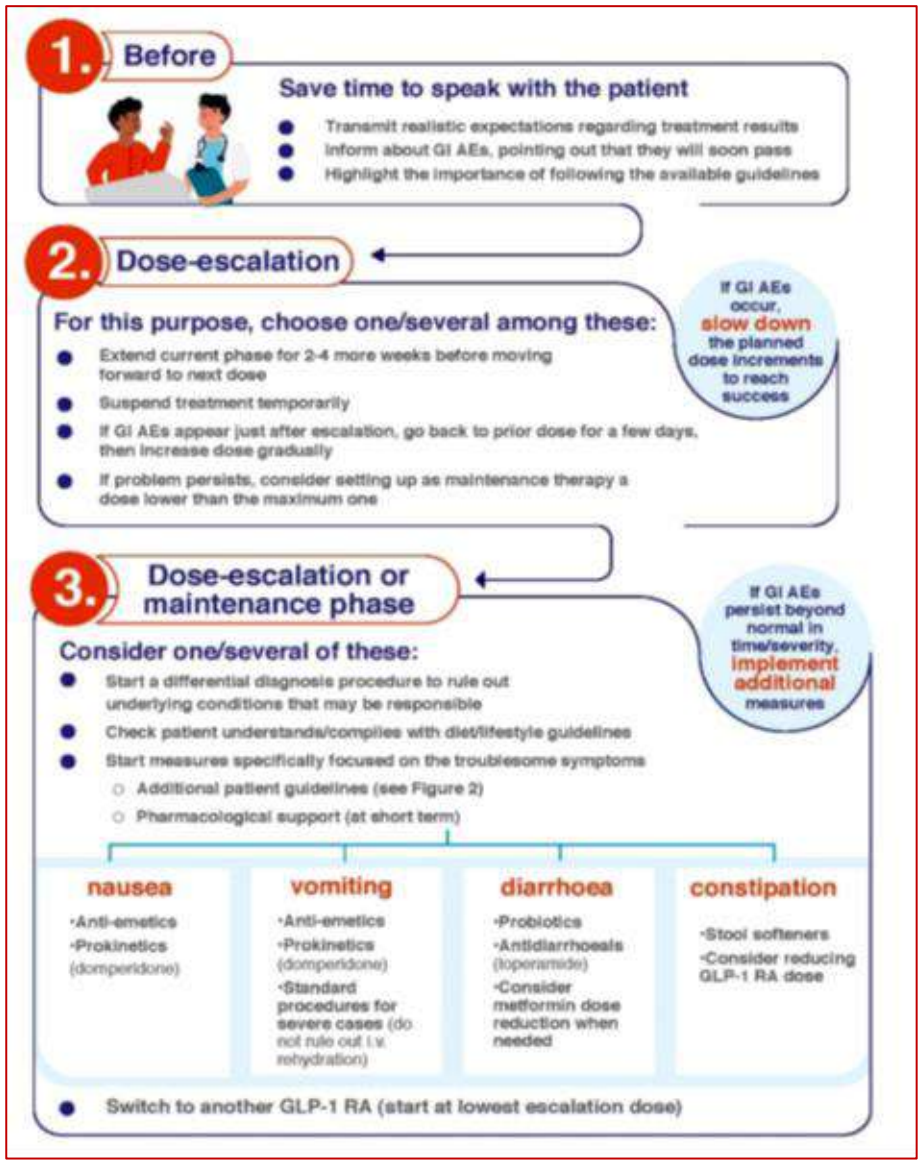
Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus

Perspective

Clinical Recommendations to Manage Gastrointestinal Adverse Events in Patients Treated with Glp-1 Receptor Agonists: A Multidisciplinary Expert Consensus

J. Clin. Med. 2023,.

4) Minimizing occurrence/severity of GI AEs when starting GLP-1: the role of Healthcare Professionals



- Switching to another GLP-1 RA may be considered. Although reported data from trials and real-world series do not show definitive differences between GLP-1 RAs in terms of tolerability (Table 1), there are studies claiming that the tolerability profile may vary between different compounds [1,33,39]. In fact, the switching strategy has already been proposed in the context of the treatment of people with T2D [40,41]. It is advisable to start the new GLP-1 RA at its lowest escalation dose. If the patient is on treatment with semaglutide, switching the route of administration, i.e., from s.c. to oral semaglutide or vice versa, may be an option [42].

- In the case of persistent tolerability limitations set a dose lower than the maximum one recommended by the technical data sheet as a maintenance dose.

Comparison of cardiometabolic benefits and tolerability in patients on sustained low doses of semaglutide or tirzepatide

Biology Methods and Protocols, 2026.

On the other hand…. it must be remarked that pivotal trials have repeatedly shown that the beneficial effects on weight loss and glycemic control can be achieved with no need to reach the recommended maintenance doses

- Start symptomatic treatment focused on the specific GI AE

Nutritional priorities to support GLP-1 therapy for obesity: A joint Advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the Obesity Medicine Association, and The Obesity Society

Obesity (Silver Spring). 2025;33:1475-1503.

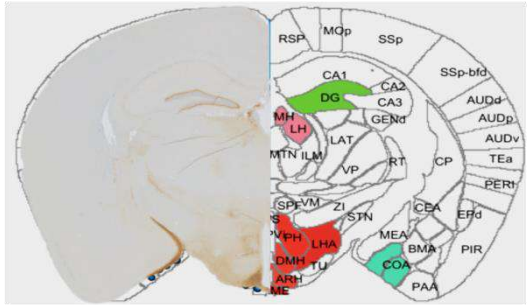


Navigation of dietary preferences and intakes

GLP-1s reduce "food noise", emotional eating, external eating (eating that responds to external triggers, irrespective of satiety), and fewer binge eating episodes…and sweet cravings.

In addition to lower energy intake, many individuals report changes (increases and decreases) in preferences for specific foods.

At times, frustration or even a loss of quality of life from the reduced pleasure obtained from food (or other aspects of life) may result in changes in effect and potentially medication discontinuation



- GLP-1R identified in 50+ regions including the mitral cell layer of the **olfactory bulb**; temporal cortex; caudal **hippocampus**; lateral septum; **amygdala; nucleus accumbens**; ventral pallium; nucleus basalis Meynert; bed nucleus of the stria terminalis; preoptic area; **paraventricular**, supraoptic, **arcuate,** and **dorsomedial nuclei** of the hypothalamus; lateral habenula; zona incerta; substantia innominata; posterior thalamic nuclei; ventral tegmental area; dorsal tegmental, posterodorsal tegmental, and interpeduncular nuclei; substantia nigra, central gray; raphe nuclei; parabrachial nuclei; locus ceruleus, nucleus of the **solitary tract; area postrema**; **dorsal nucleus of the vagus**; lateral reticular nucleus; and spinal cord.
- Therefore GLP-1 not only functions as a satiety factor but also acts as a neurotransmitter or neuromodulator.

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Obesity (Silver Spring). 2025;33:1475-1503.



- Prevention and mitigation of nutrient deficiencies

Nutrition Strategies for Next-Generation Incretin Therapies: A Systematic Scoping Review of the Current Evidence

Obesity Reviews, 2026;

Semaglutide and tirzepatide have demonstrated weight-loss efficacy comparable to bariatric surgery, with mean reductions of up to 20.9% in body weight

Retrospective data indicate the onset of nutritional deficiencies in 12.7% of patients during the first 6 months and in 22.4% of patients within 12 months

Available data indicate reductions in caloric intake of 16%-39% during incretin therapies, yet few studies have examined diet quality, protein intake, or micronutrient adequacy

Very-low-and low-energy intakes (≤ 800 and 1200 kcal/day, respectively)…. may increase the risk of inadequate protein intake, dietary quality, and micronutrient deficiencies



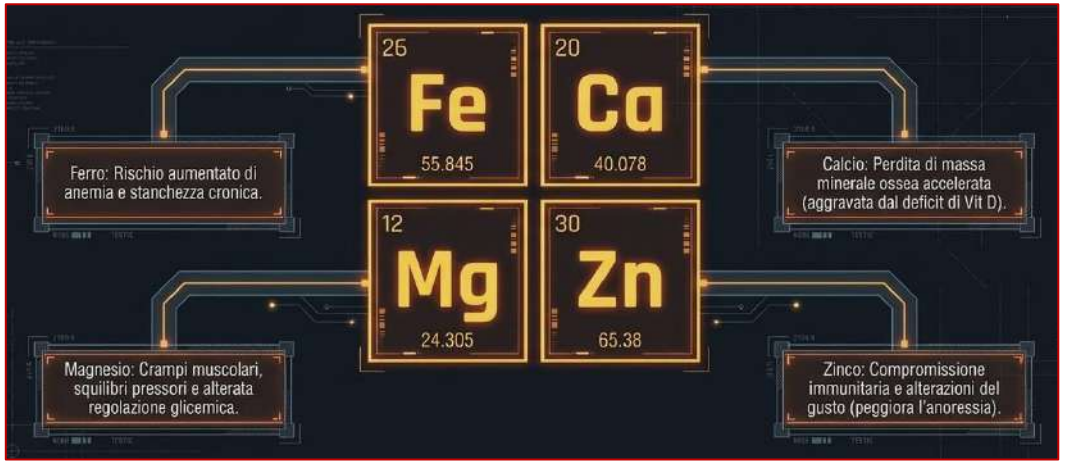
Fra le vitamine, la B_{12} e il Folato sono quelle più ridotte.



La triade critica è rappresentata dai deficit di Vit D, Potassio e Colina con una ineguatezza di oltre il 90% rispetto all'assunzione raccomandata.



I minerali più soggetti a deficit sono il Fe, il Ca, il Mg e lo Zn con una ineguatezza intorno al 50% rispetto all'assunzione raccomandata.



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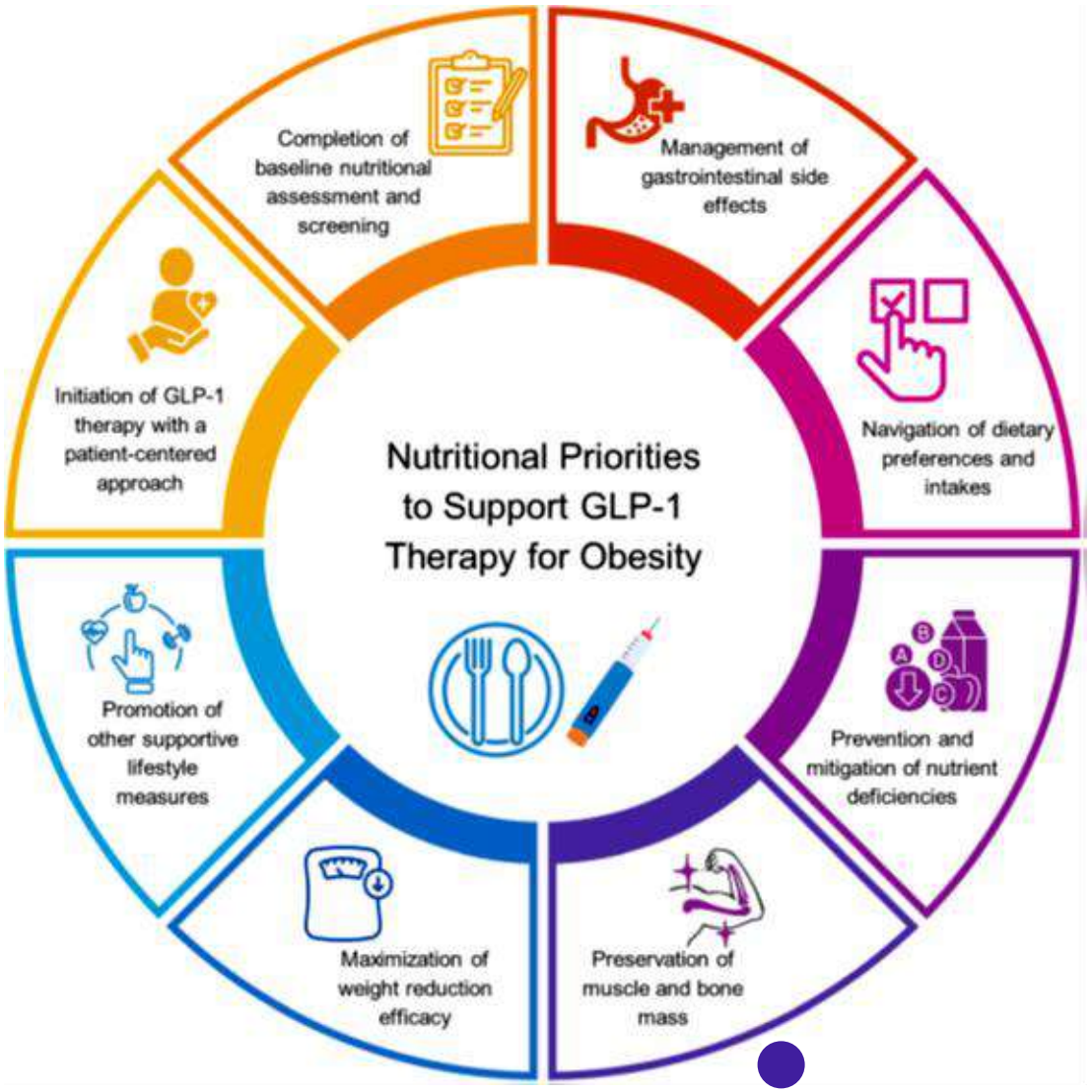

- Preservation of muscle and bone mass

Nutrition Strategies for Next-Generation Incretin Therapies: A Systematic Scoping Review of the Current Evidence

Obesity Reviews, 2026;

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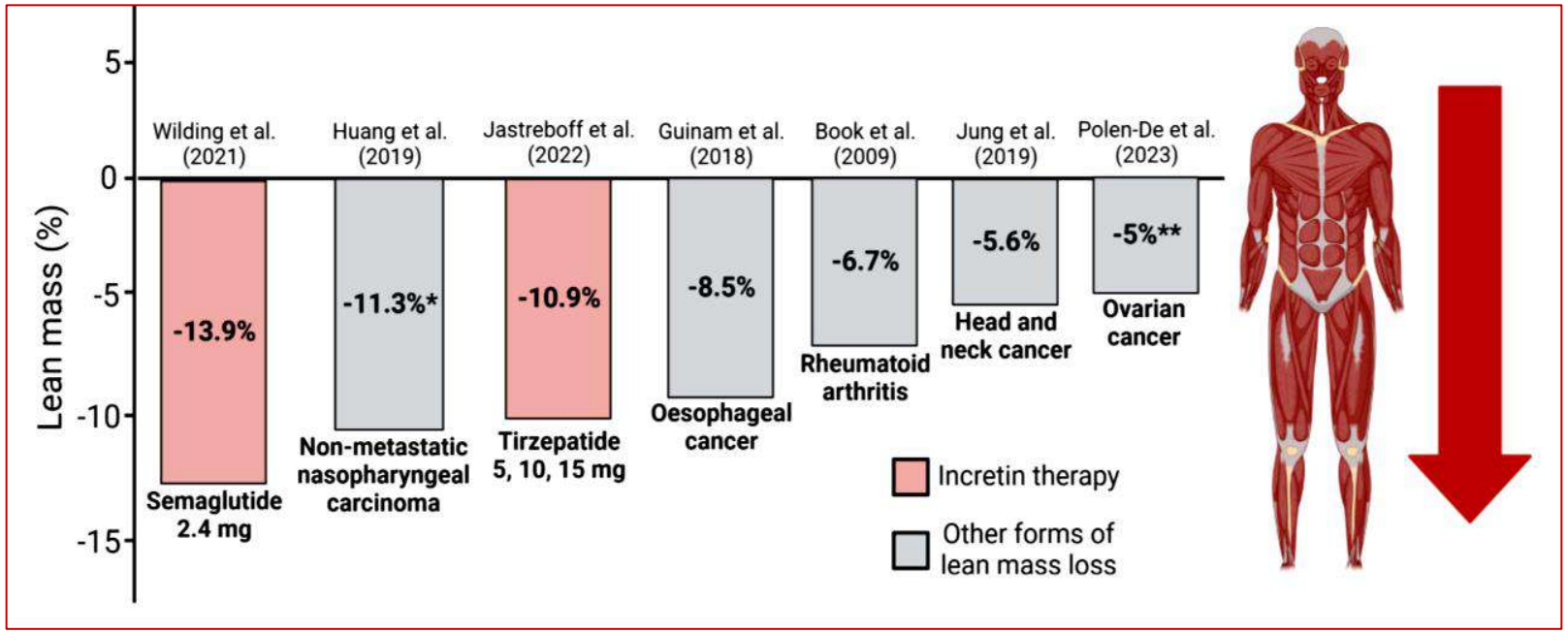
Very-low-and low-energy intakes (≤ 800 and 1200 kcal/day, respectively)…. may increase the risk of inadequate protein intake, dietary quality, and micronutrient deficiencies

This is particularly concerning given *that lean body mass can constitute up to 40% of total weight lost during treatment*

IL RISCHIO SOMMERSO: OBESITA' SARCOPENICA E PERDITA OSSEA

Sarcopenia: Le donne perdono il 10-15% del peso come massa magra; gli uomini fino al 20-25%. Aumenta il rischio di **declino funzionale** negli anziani.

Osteoporosi: Aumento documentato del turnover osseo e perdita di densità minerale ossea (BMD). Rischio elevato di fratture



Apitegromab for lean mass preservation during tirzepatide-induced weight loss: a randomized, double-blind, placebo-controlled phase 2 trial 08 June 2026

Apitegromab is an investigational, fully human monoclonal antibody that selectively inhibits myostatin activation and is, thereby, capable of increasing muscle mass.
In summary ….selective targeting of myostatin by apitegromab was well tolerated and effective in preserving lean mass when combined with tirzepatide

Il Protocollo M.E.A.L.

World Health Organization Guideline on the Use and Indications of Glucagon-Like Peptide-1 Therapies for the Treatment of Obesity in Adults doi:10.1001/jama.2025.24288

M — Maintain Muscle



Consumare **20-30g** di **proteine** come prima cosa ad ogni pasto (pesce, pollame, uova, legumi).
Utilizzare shake e supplementi proteici se l'appetito è gravemente compromesso dal farmaco.

E — Energize (Enrgizza & Bilancia)



Inserire **spuntini** ad altissima **densità** energetica (noci, yogurt greco).
Privilegiare carboidrati **carboidrati a digestione lenta** (avena) e **grassi sani** protettivi (avocado, olio d'oliva).

A — Avoid (Evita gli effetti avversi)



Nausea: cibi secchi integrali, zenzero, no fritti.
Pirosi: evitare spezie e decubito post-pasto (2-3h).
Stipsi: massimizzare l'introito di fibre solubili e insolubili.

L — Liquids (Idratazione Strategica)





Bere 2-3 Litri (8-12 bicchieri) al giorno.
Privilegiare acqua e cibi idratanti (zuppe, cetrioli).
Evitare le calorie liquide e gli zuccheri semplici.

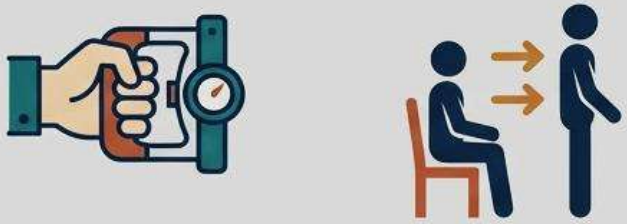
Non prescrivere la perdita di peso senza prescrivere la conservazione del muscolo

Istituto Nazionale di Endocrinologia e Nutrizione Clinica

Sarcopenia: Le donne perdono il 10-15% del peso come massa magra; gli uomini fino al 20-25%. Aumenta il rischio di **declino funzionale** negli anziani.

Osteoporosi: Aumento documentato del turnover osseo e perdita di densità minerale ossea (BMD). Rischio elevato di fratture

La Valutazione (Monitorare la Funzione)



Non affidarsi solo al BMI. La sarcopenia è un rischio reale, specie nei pazienti anziani.

Test suggeriti: Handgrip strength (forza di presa aggiustata) e test Sit-to-stand 5x.

Uso di DXA o BIA dove disponibile per monitorare la composizione corporea.

Il Protocollo di Difesa

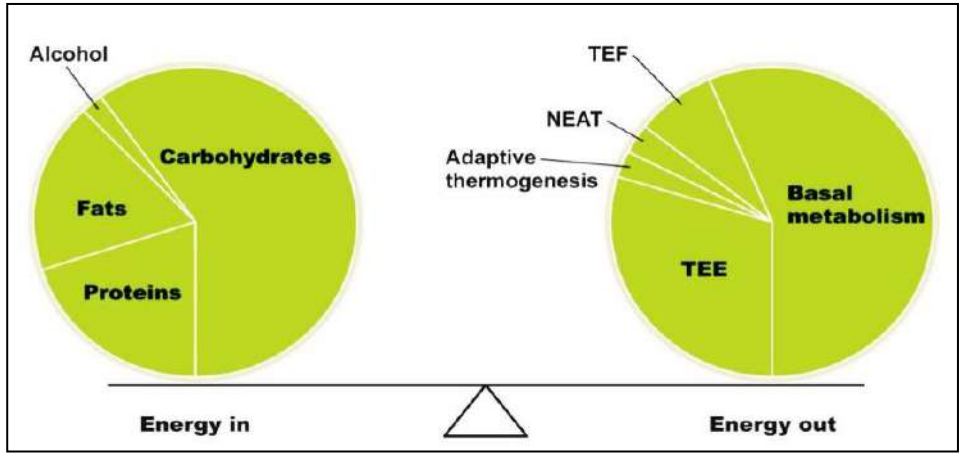


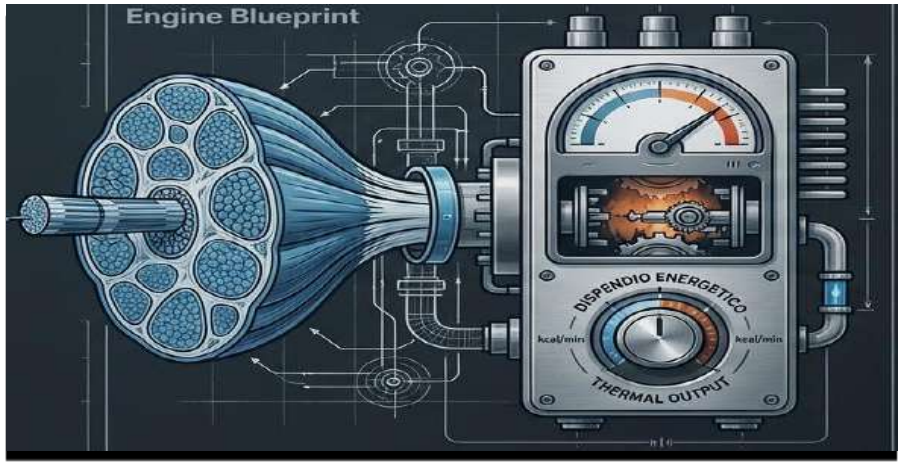
Le proteine da sole non bastano senza lo stimolo meccanico né per il muscolo né per l'osso

Implementare un Allenamento di Resistenza Progressivo.

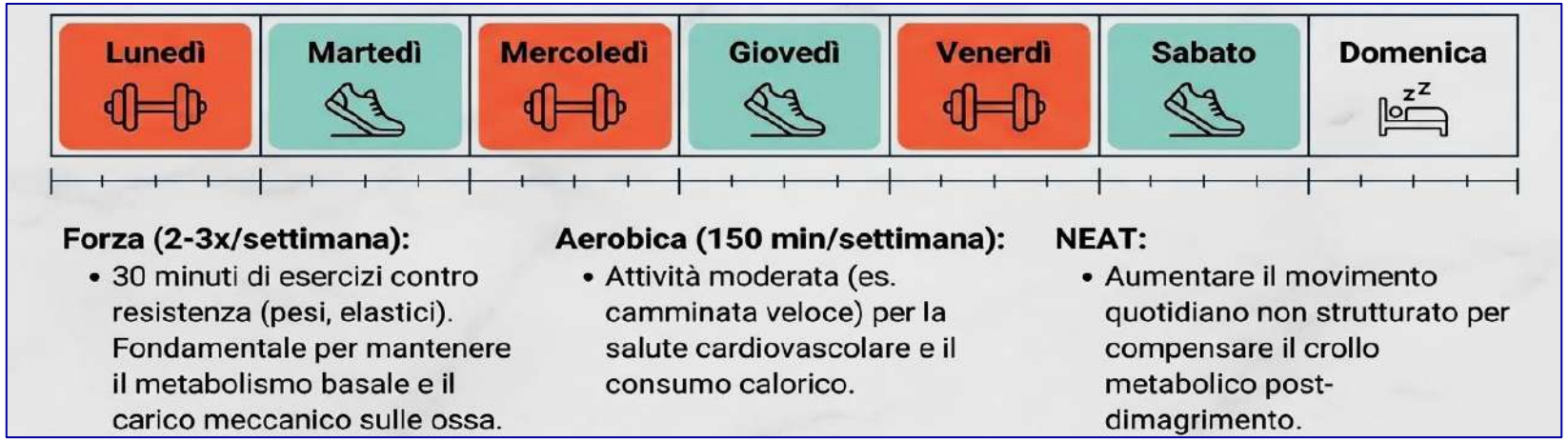
Combinare con esercizio aerobico in base alla tolleranza individuale.

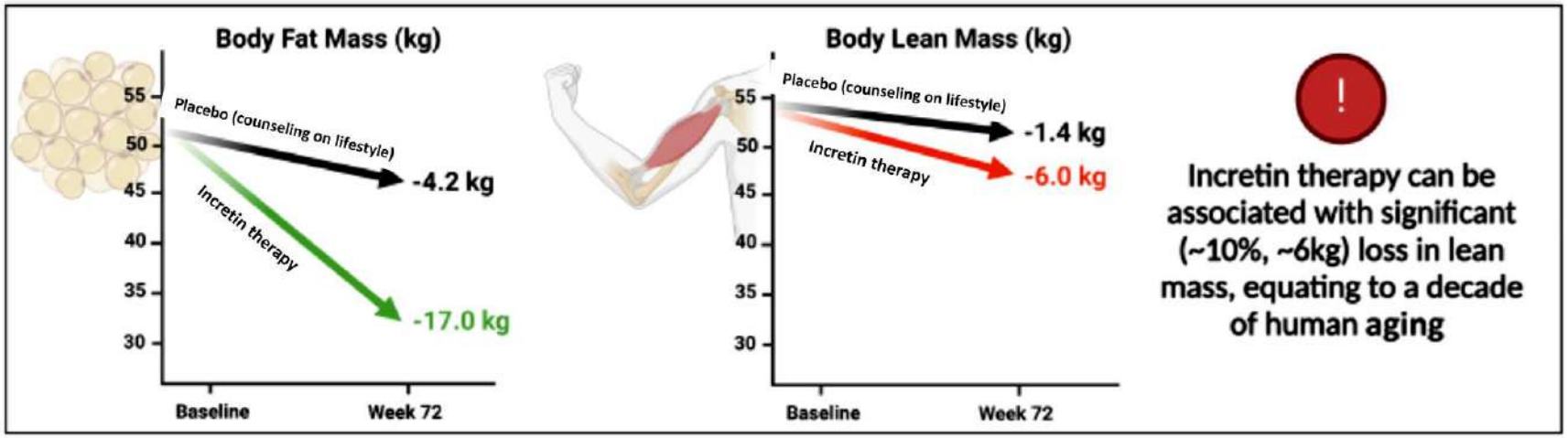
L’attività fisica: prescrizione non negoziabile





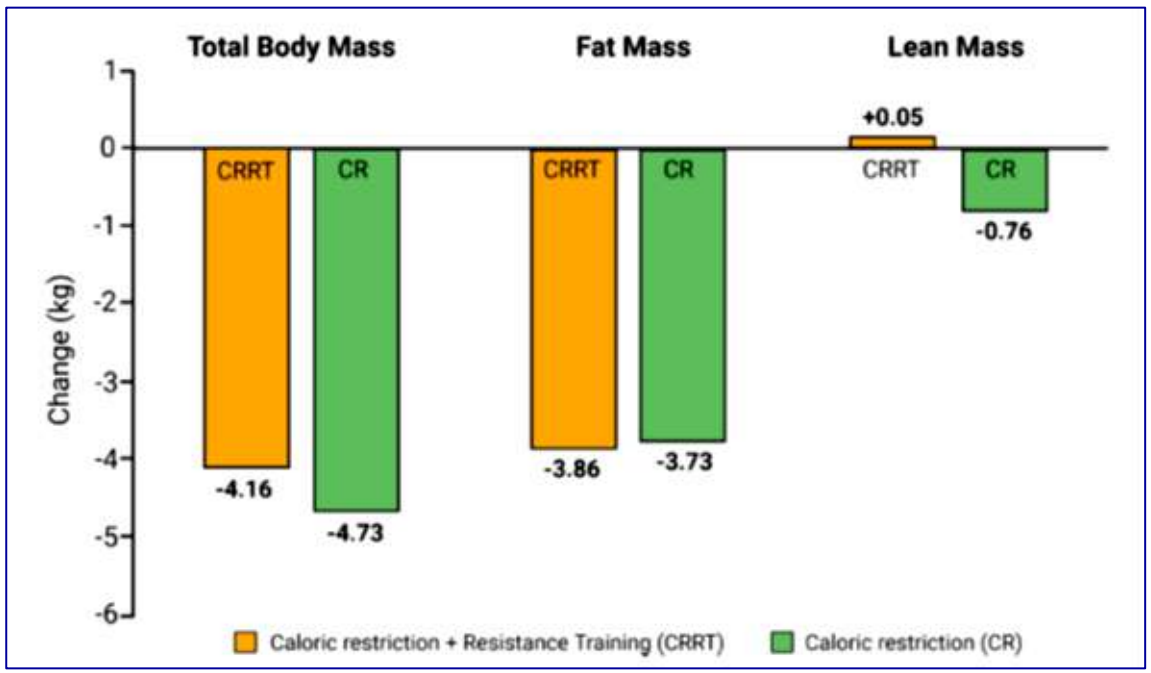
- Il muscolo è il principale determinante del Metabolismo Basale.
- La diminuzione della massa muscolare produce una riduzione del MB che va da 1,2% fino a crolli del 5,6%.
- Ciò contribuisce al rebound adiposo post-terapia
- Una riduzione del 5% del MB equivale a circa 4,7 kg di massa grassa in un anno.



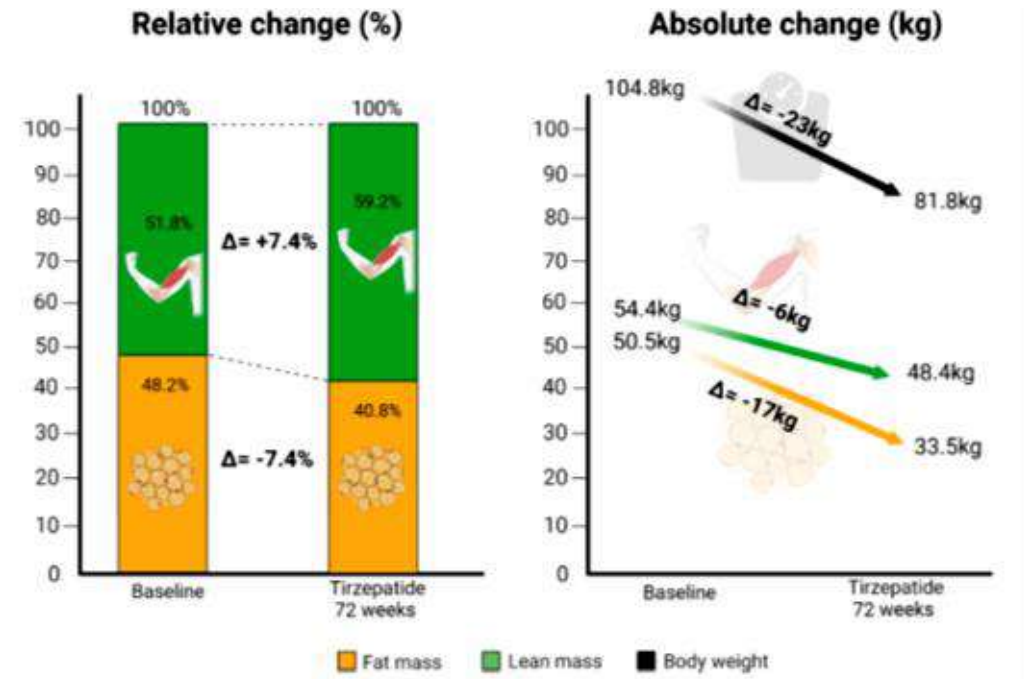


Incretin-Based Weight Loss Pharmacotherapy: Can Resistance Exercise Optimize Changes in Body Composition?

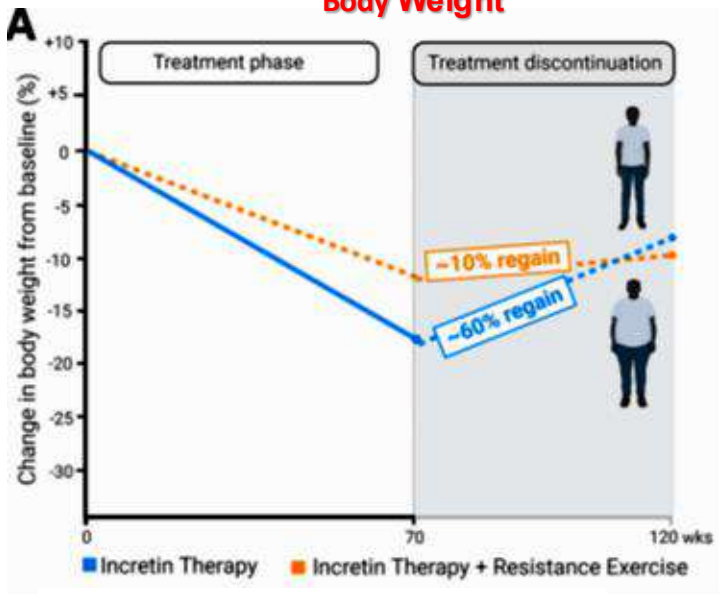
Diabetes Care 2024;47:1718–1730 | https://doi.org/10.2337/dci23-0100



Despite an increase in the percent LM, absolute LM decreased by 6 kg



Body Weight



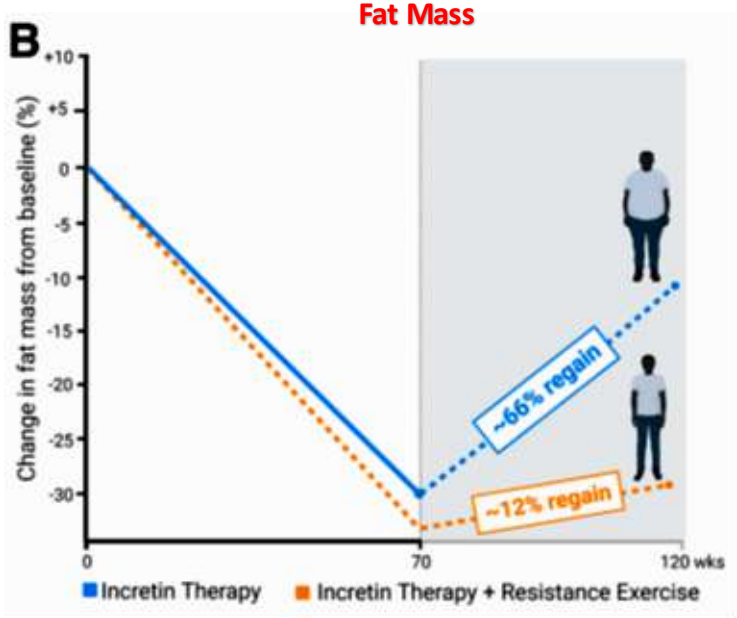
Pooled data from available literature

Hypothesized outcomes

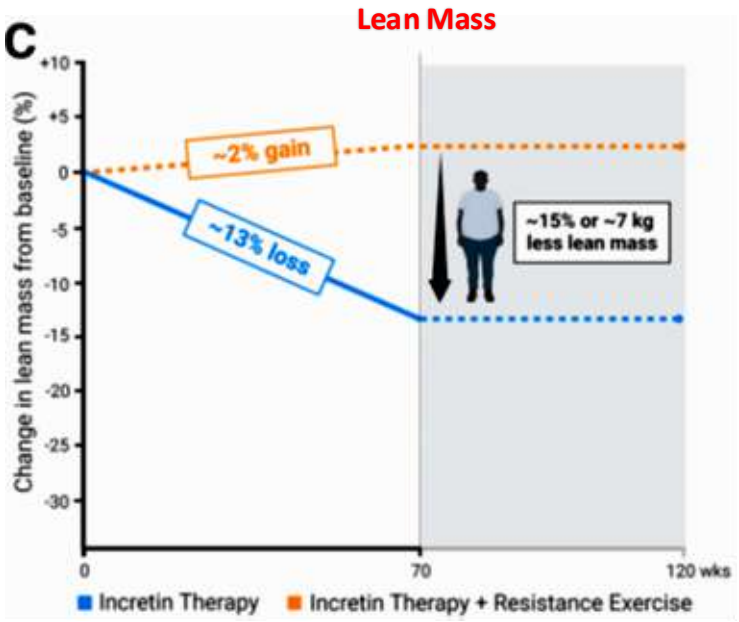
Incretin-Based Weight Loss Pharmacotherapy: Can Resistance Exercise Optimize Changes in Body Composition?

Diabetes Care 2024;47:1718–1730 | https://doi.org/10.2337/dci23-0100

Fat Mass



Lean Mass



CONCLUSIONS

- Incretin therapy induces an average LM loss of ~13%……
- LM is highly metabolically active, so its retention during incretin therapy may mean that less fat is regained after treatment cessation.
- Resistance Exercise should prevent loss of LM associated with incretin therapy, with less fat rebound after treatment discontinuation.

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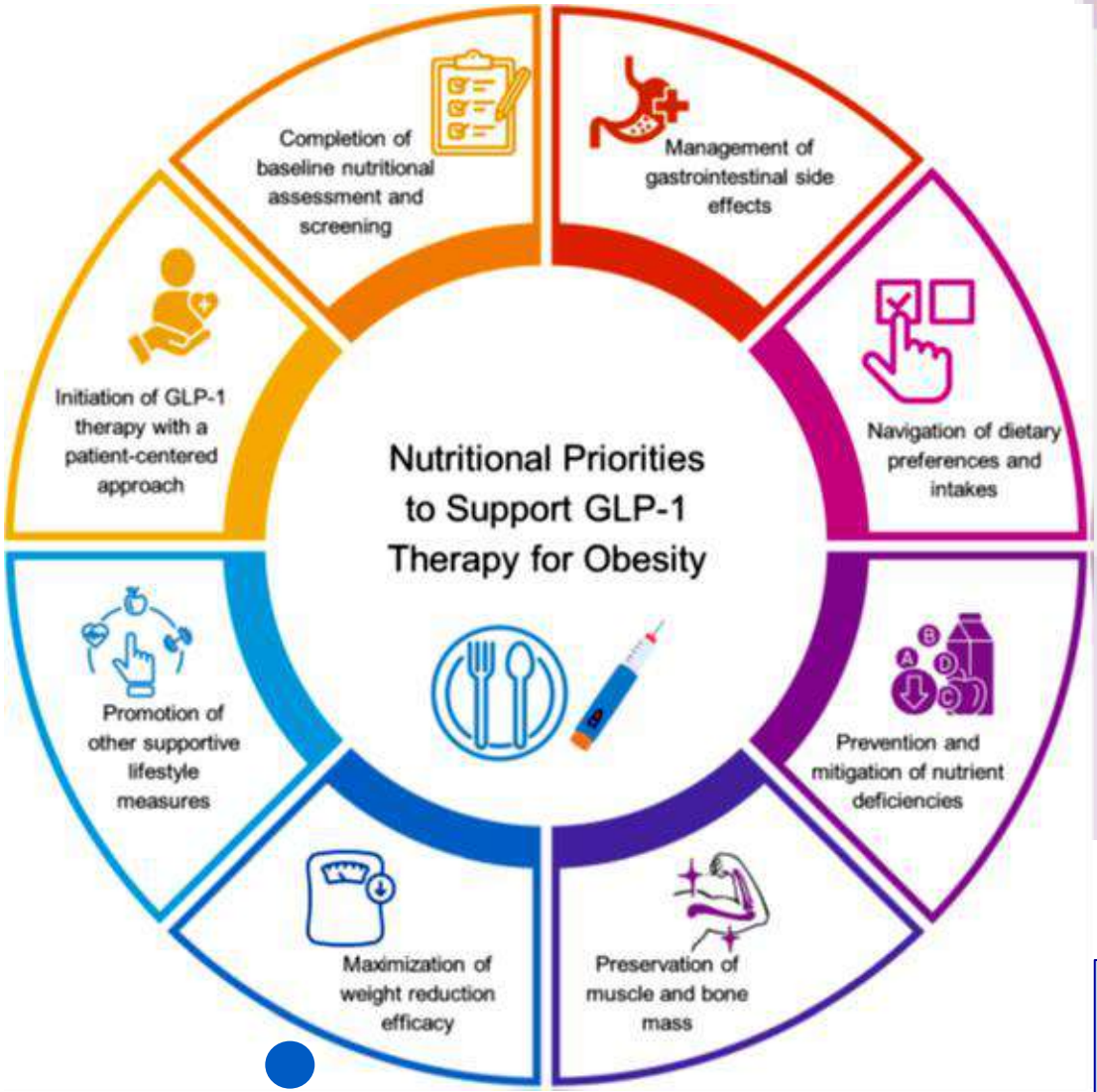


- Maximization of weight reduction

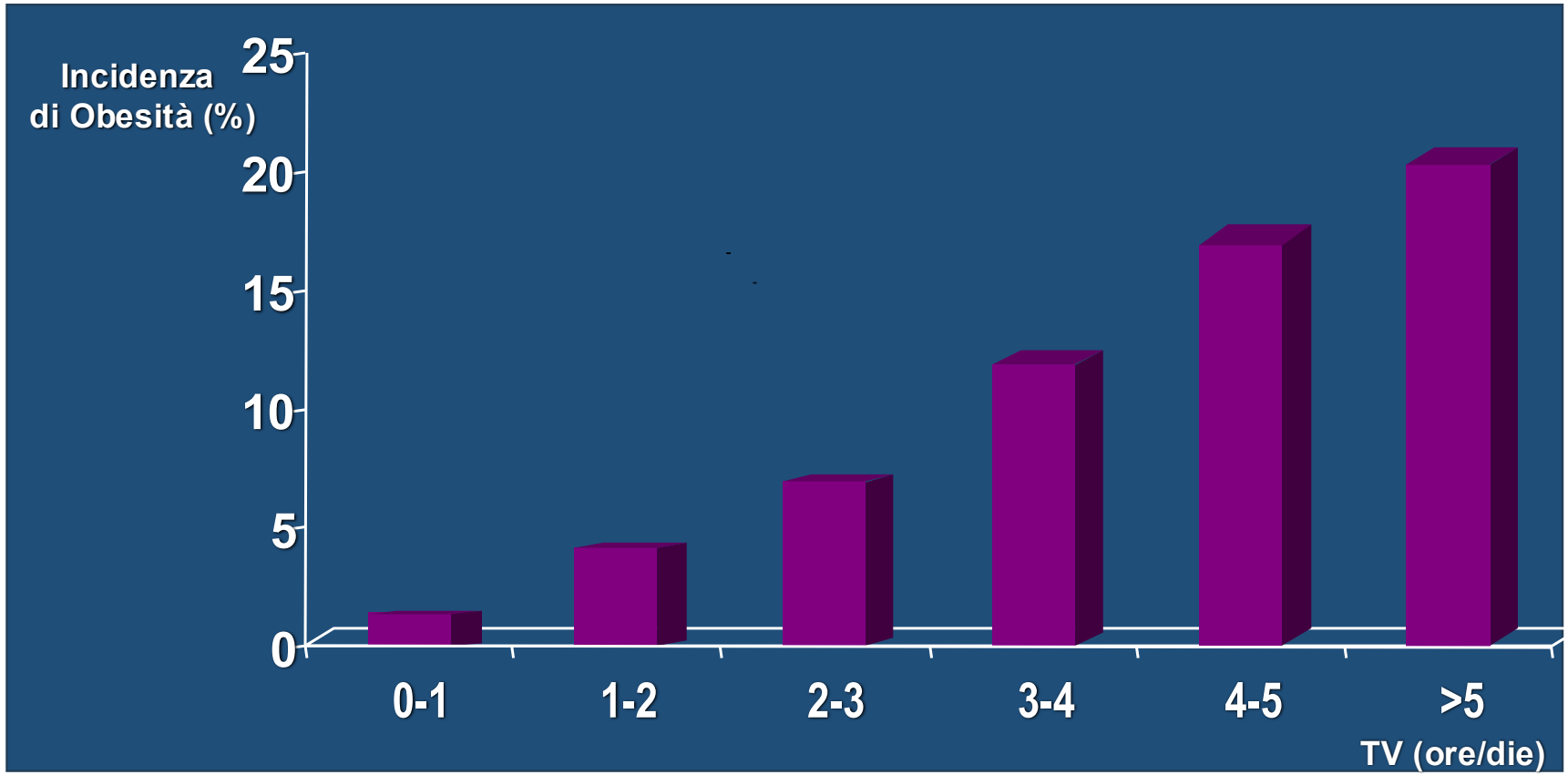
Factors to encourage	Factors to minimize/avoid
Food groups	
Fruits (e.g., berries, apples, citrus fruits, banana, grapes, avocado)	Refined carbohydrates (processed grains, flours, added sugar
Vegetables (e.g., broccoli, leafy greens, tomatoes, carrots, peas, squashes)	Sugar-sweetened beverages
Whole grains (e.g., oats, quinoa, brown rice, and whole-grain breads, cereals, and pastas)	Red and processed meats
Dairy (e.g., yogurt, milk, cheese)	Most fast foods
Lean proteins (e.g., poultry, fish/seafood) and eggs	Sweets and savory snacks
Nuts and seeds (e.g., almonds, peanuts, chia seeds, sesame seeds, hemp seeds)	
Plant fats/oils (e.g., olive, canola, avocado oils)	
Ginger or peppermint tea	
Eating habits[b]	
Regular, small meals at consistent times	Emotional, mindless, or nighttime eating
Flexibility with food choices	Long periods without meals (i.e., becoming overly hungry)
Enjoy portion-controlled treats	Consumption of large meals
Ensure adequate fluids	

…….Additional behaviors generally associated with long-term weight maintenance include regular physical activity (≥60 min/day), ……..limiting screen time (<10 h/week)…

Rapporto fra ore di Televisione e Obesità







RIASSUMENDO

1°

Matrice di Risposta agli Effetti Collaterali GI

	Cosa Fare ✅	Cosa Evitare ❌
Nausea	Pasti piccoli e freddi, zenzero, cibi secchi (cracker, avena).	Odori forti, cibi fritti/grassi, bere durante i pasti.
Sazietà Precoce	"Proteine prima di tutto" (Protein first), consistenze morbide.	Saltare i pasti, cibi ad alto volume ma poveri di nutrienti.
Diarrea	Idratazione abbondante (acqua, elettroliti), brodi, riso.	Alimenti ricchi di fibre insolubili o zuccheri semplici.
Stipsi	Fibra solubile (psillio, prugne), movimento, liquidi.	Aumentare troppo in fretta l'introito di fibre senza liquidi.

2°



Nutritional, functional, and psychological considerations for incretin-based therapies in adults—an EASO, EFAD, and ECPO Consensus Statement

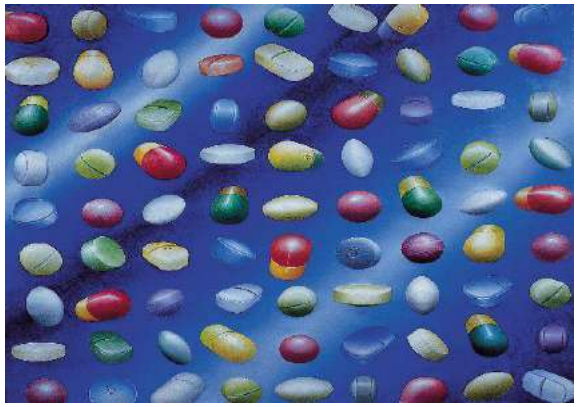
thelancet.com/diabetes-endocrinology Published online July 8, 2026

European Federation of the Associations of Dietitians (EFAD)
European Association for the Study of Obesity (EASO)
European Coalition for People Living with Obesity (ECPO)

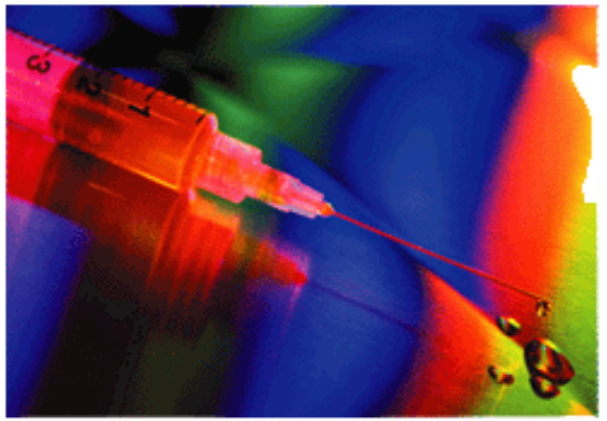
3°

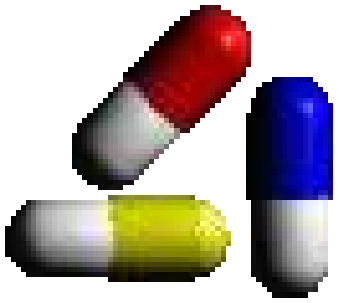


CONCLUSIONE:
certamente i GLP-1RAs aiutano
a contrastare le principali conseguenze dell'obesità ma ……









Il desiderio di prendere medicine
è forse la più grande differenza
fra l'uomo e l'animale

Sir William Osler, 1882
The Priciples and Practice of Medicine

