Medication to Maintenance: A Guide to Sustaining Weight Loss Beyond GLP-1 Therapy with Natural incretin analogues

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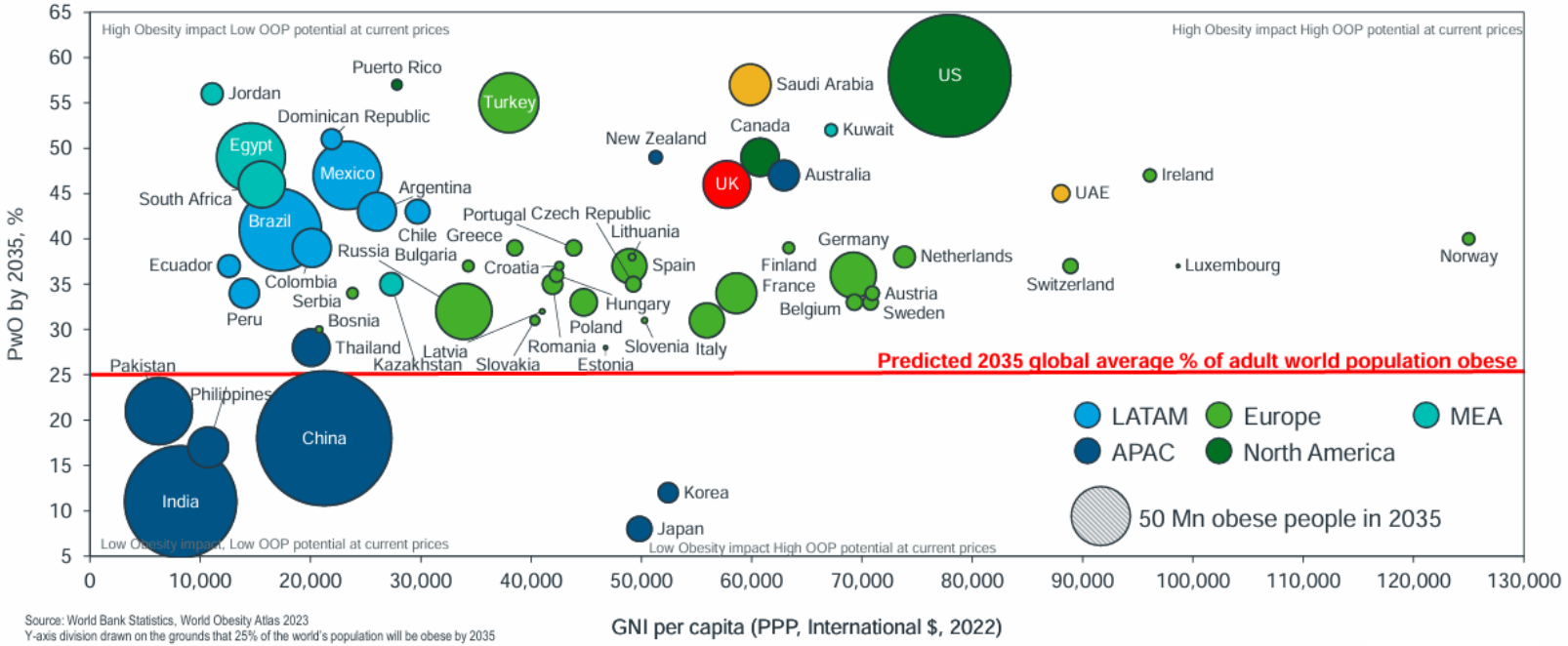
The Obesity crisis

The world is at a population health crossroad-countries must act now to address the next decade of the Obesity crisis

*Majority of world's obese population predicted to be in **lower and middle income** countries by 2035; UK predicted to have among highest European levels of obesity by 2035-if we maintain status quo*



Source: World Bank Statistics, World Obesity Atlas 2023
Y-axis division drawn on the grounds that 25% of the world's population will be obese by 2035
$50k GNI/capita approaches the level at which spending out of pocket for a year's Wegovy (UK prices) is approximately 5% of annual income
IQVIA Quarterly Pharmaceutical Market Outlook Webinar – June 2024

Key Obesity Data for England (2023–2024)

Adult Prevalence: 64.5% of adults (18+) are overweight or obese, up from 64.0% the previous year.

Obesity Rate: 26.5% of adults are classified as living with obesity.

Gender Differences: 69.7% of men are overweight/obese compared to 59.2% of women. However, 26.9% of women are living with obesity compared to 26.2% of men.

NHS Digital. *Health Survey for England 2024.*

Redefining obesity as a chronic disease

The Global Lancet Commission on Obesity and draft FDA guidance on Obesity trials recognise obesity as a CHRONIC DISEASE

The clinical consensus is that Obesity is a treatable disease and treatment prevents downstream health problems

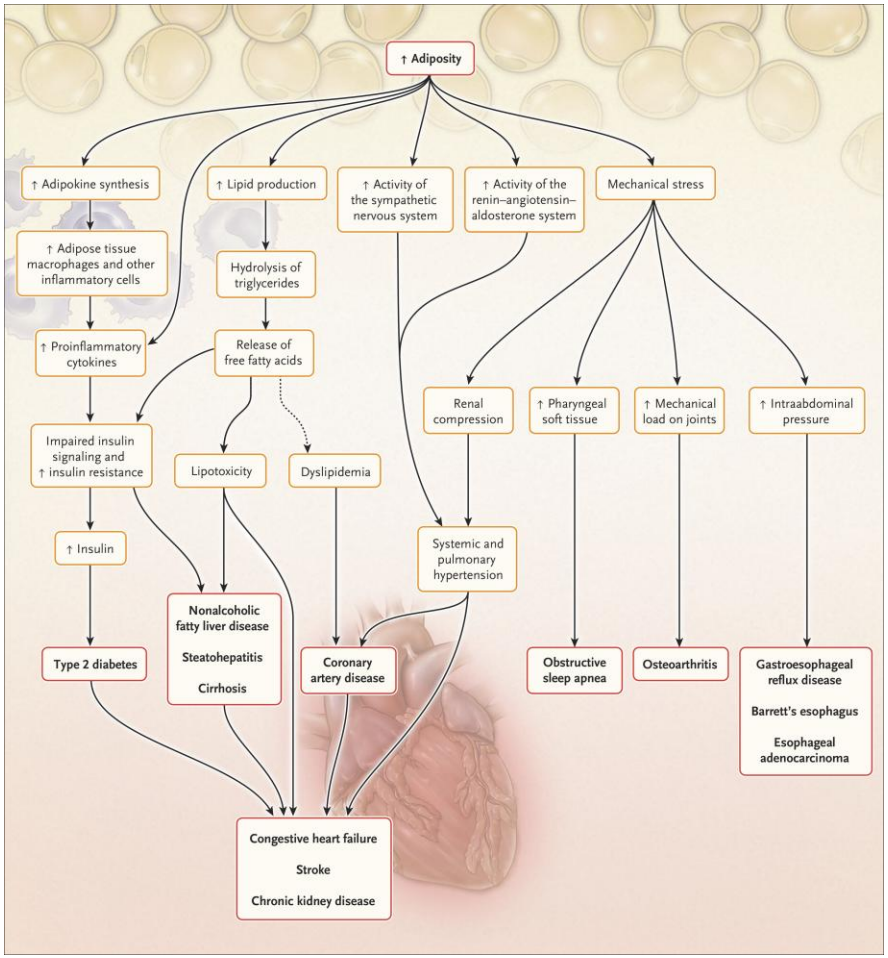
Lancet Commission on Obesity (global)

- Initiated 2019 (prior to advent of new AOMs), global group of 56 experts, with endorsement from 75 medical organisations working in obesity
- Published Commission on Definition and diagnostic criteria of clinical obesity 14/01/2025
- Key recommendation is a distinction between:
  - Obesity as a risk factor (termed preclinical obesity)
  - Obesity as a standalone disease (clinical obesity)
- Proposes removing focus on BMI alone to define obesity and create a broader base of multiple indicators, measuring obesity-caused organ dysfunction and illness
- Proposals would need to be adopted by regulators, payers, clinicians
- Proposals could complicate collection of data on and quantification of people with clinical obesity

Draft FDA Guidance on Obesity

- First new guidance (currently draft) on obesity since 2007
- **Moves description of obesity from "chronic, relapsing health risk" to "chronic disease"**
  - Fewer mentions of importance of lifestyle interventions than previous guidance
  - Less stringent recommendations for paediatric trials
  - Continued BMI based definition of obesity and for assessment of primary efficacy endpoint
  - However, recommends body composition tracked for subsets and inclusion of subset of type II diabetes patients in trials
  - Trials need to reflect the age, sex race and ethnicity of the obese patients in clinical practice for US population
  - Safety trials to have a minimum of 3,000 subjects on investigational drug

Impacts of Adiposity



Haslam, D.W. and James, W.P.T. (2005) *Obesity*. **The Lancet**, 366(9492), pp.1197–1209

Potential benefits of weight reduction

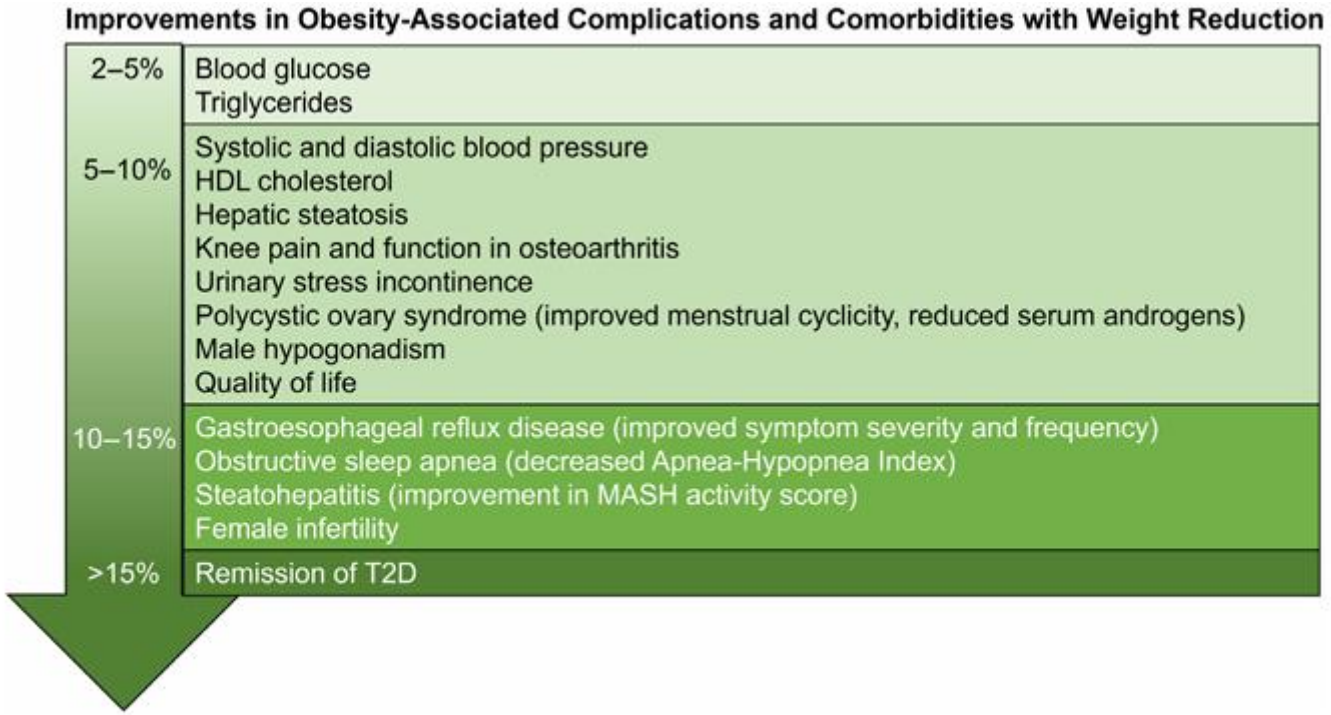


FIGURE 1 Potential benefits of weight reduction in obesity. Garvey et al. [5], Lingvay et al. [6], Ryan and Yockey [7], and Wing et al. [8]. MASH, metabolic dysfunction-associated steatohepatitis (formerly nonalcoholic steatohepatitis [NASH]); T2D, type 2 diabetes.

Wing, R.R. et al. (2011) *Benefits of modest weight loss*. **Diabetes Care**, 34(7), pp.1481–1486.

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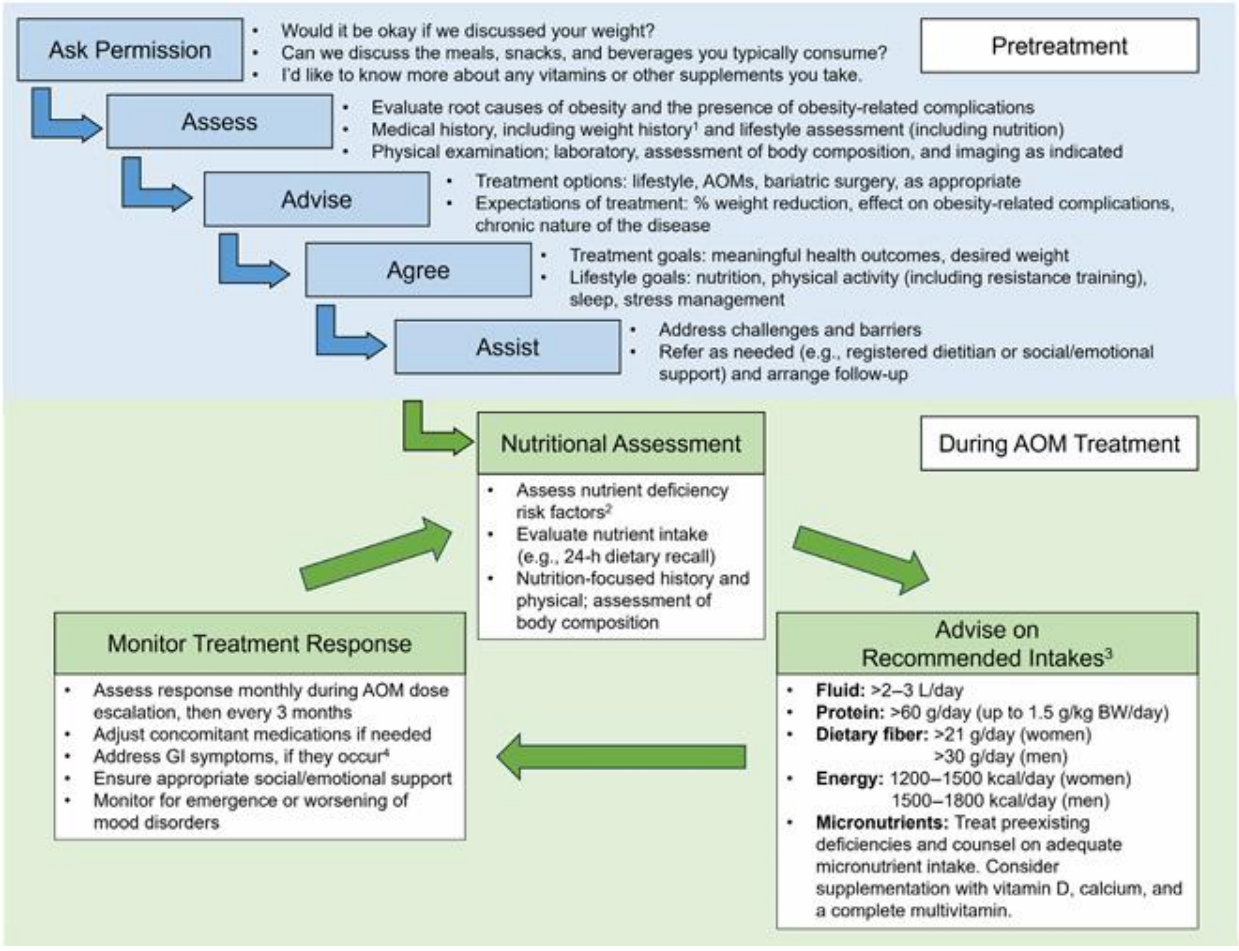
Typical obesity treatment pathway



Theories around obesity

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Energy Balance Model

- Calories in vs. calories out
- Role of diet, physical activity, metabolism
- Limitation: oversimplified view

Genetic Theories

- Heredity and twin studies
- Key genes: FTO, MC4R
- Set-point theory, thrifty gene hypothesis

Neuroendocrine Theories

- Hormones: leptin, ghrelin, insulin, cortisol
- Hypothalamic and reward pathways
- Dysregulation → >appetite, <satiety

Behavioural Theories

- Sedentary lifestyle and screen time
- Ultra-processed foods, portion sizes
- Sleep disruption, circadian rhythm changes

Psychological Theories

- Emotional eating and stress
- Food addiction model
- Links with depression, anxiety, binge eating disorder

Environmental/Social Theories

- Obesogenic environment (urban design, food deserts)
- Family and peer influences
- Socioeconomic status and education

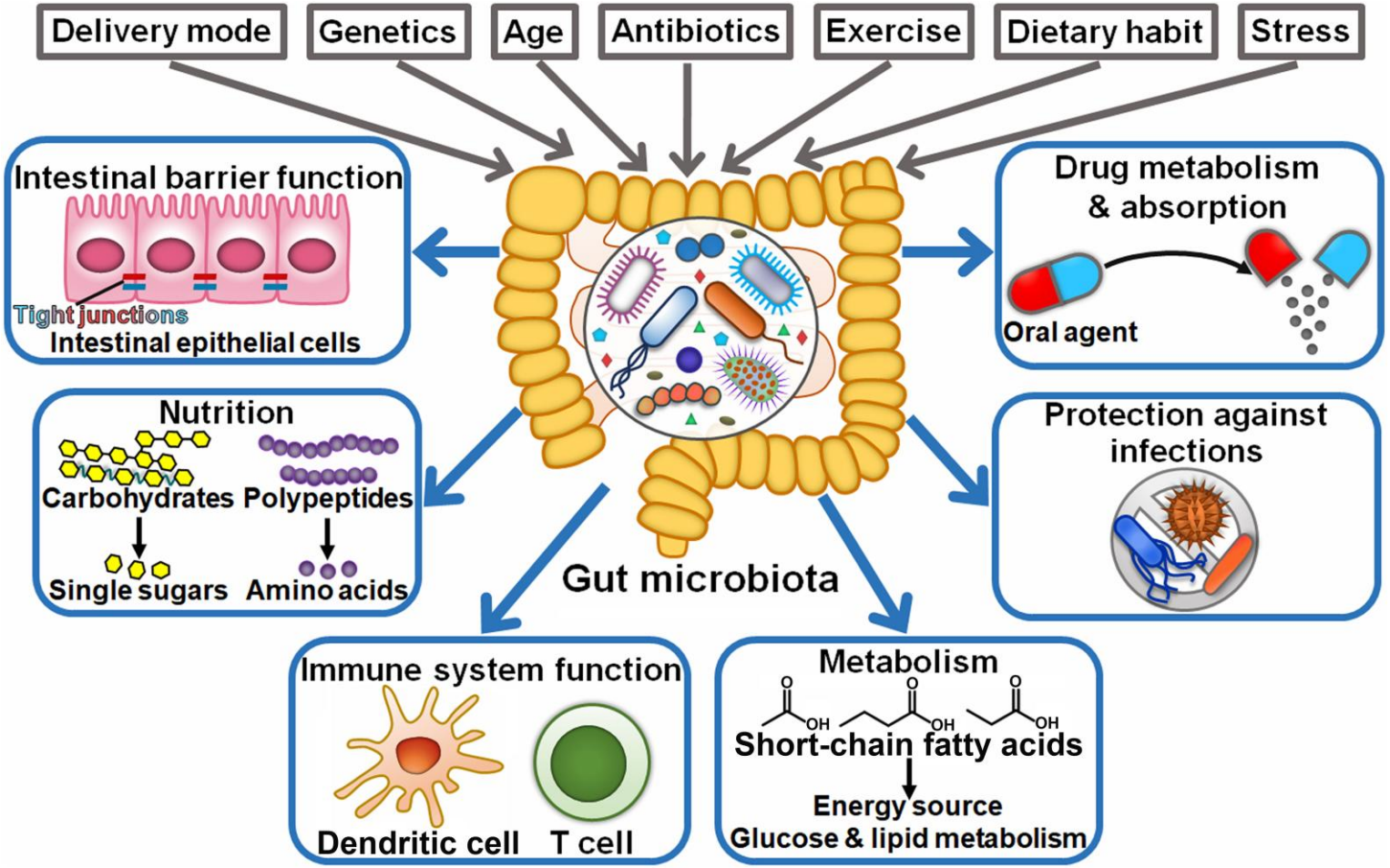
Microbiome and Emerging Theories

- Gut microbiota and energy extraction
- Endocrine disruptors ("obesogens")
- Epigenetic influences

Multifactorial Nature

- **Interaction of biology, psychology, and environment**
- **No single cause**
- **Holistic, individualized care is needed**

Obesity a multifactorial disease



- Hruby, A. and Hu, F.B. (2015) *The epidemiology of obesity: a big picture*. **Pharmacoeconomics**, 33(7), pp.673–689.

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Implications for Healthcare Professionals

- Obesity is complex and multifactorial
- Multiple overlapping theories
- Call for evidence-based, compassionate care

- Avoid weight stigma
- Tailor interventions
- Prevention and public health strategies

The Obesogenic diet

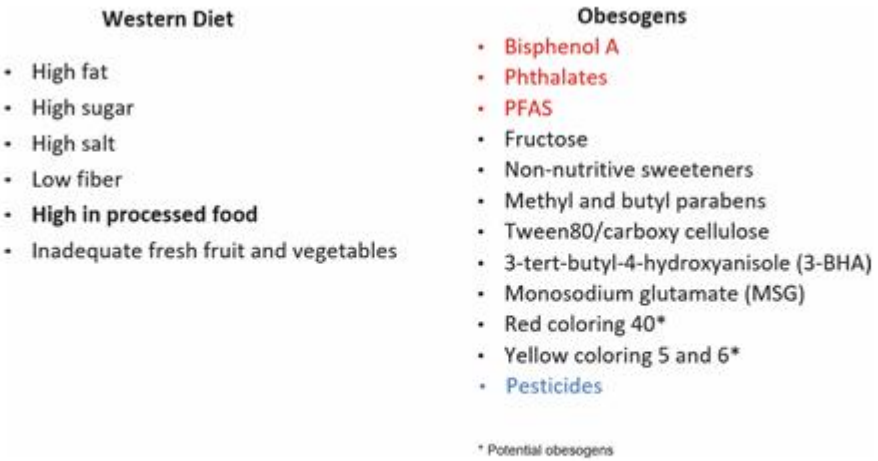


Fig. 3 The Western ultra-processed food diet is obesogenic. The Western Diet (left panel) per se is obesogenic. In addition (right panel), chemicals in food packaging, such as can linings, can contain obesogens (red) which can leach into the food. Many food additives, preservatives, emulsifiers, and antioxidants are obesogens. Many fruits and vegetables are sprayed with pesticides, and some residues remain on them. Potential obesogens are those with only in vitro data.].

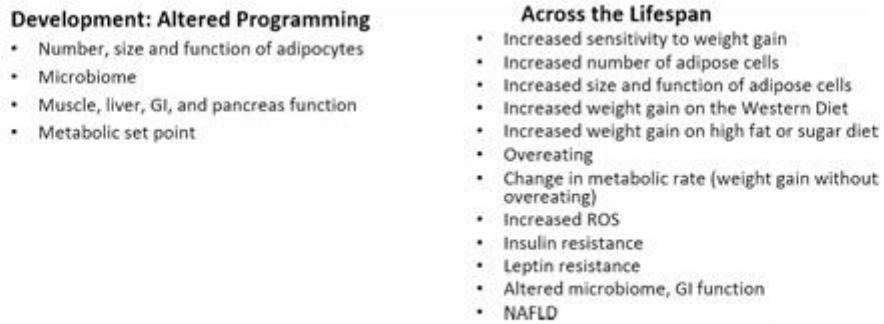


Fig. 4 Integrating obesogen actions. Obesogens act during development to alter the programming of multiple tissues and processes that lead to increased sensitivity/susceptibility to weight gain across the lifespan

Heindel, J.J., Blumberg, B., Cave, M. et al. (2017) *Metabolism disrupting chemicals and metabolic disorders*. Endocrine Reviews, 38(6), pp.589–619.

Advanced Glycation End Products (AGEs) and obesity

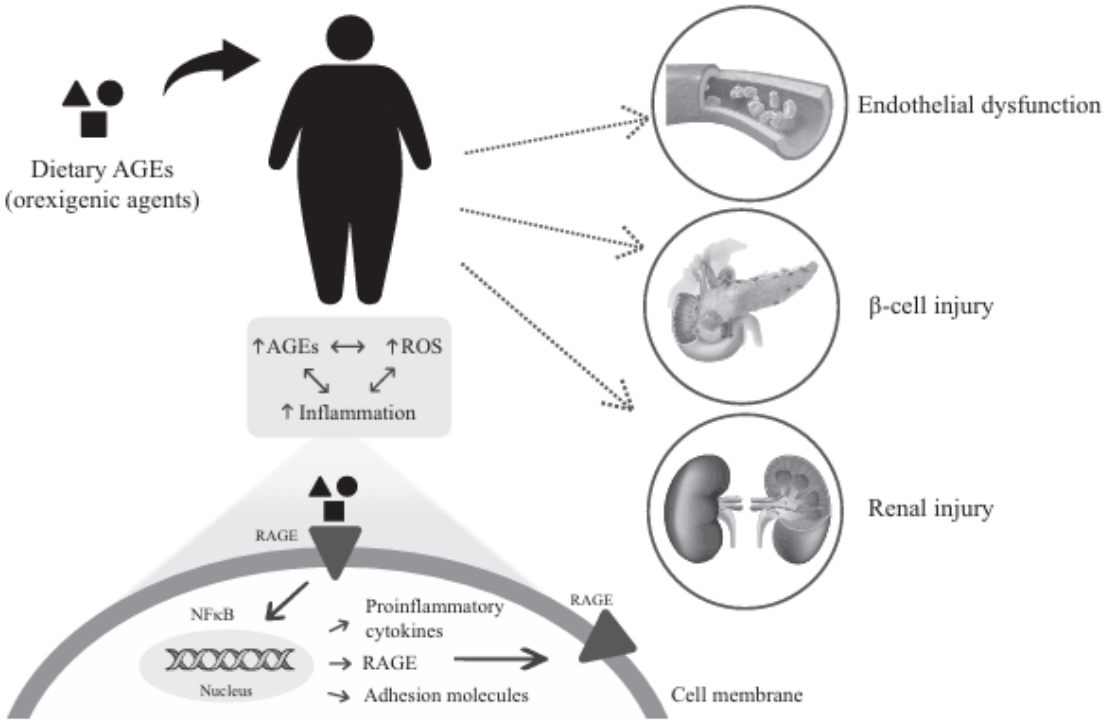


Figure 3 **The effect of dietary AGEs on overweight complications, through the increase in RAGE expression and activation of the NF-κB signaling pathway.** *Abbreviations:* AGEs, advanced glycation end products; NFκB, nuclear factor kappa B; RAGE, receptor for advanced glycation end product; ROS, reactive oxygen species

Uribarri, J. et al. (2010) *Advanced glycation end products in foods and a practical guide to their reduction in the diet*. Journal of the American Dietetic Association, 110(6), pp.911–916.

AGEs and obesity

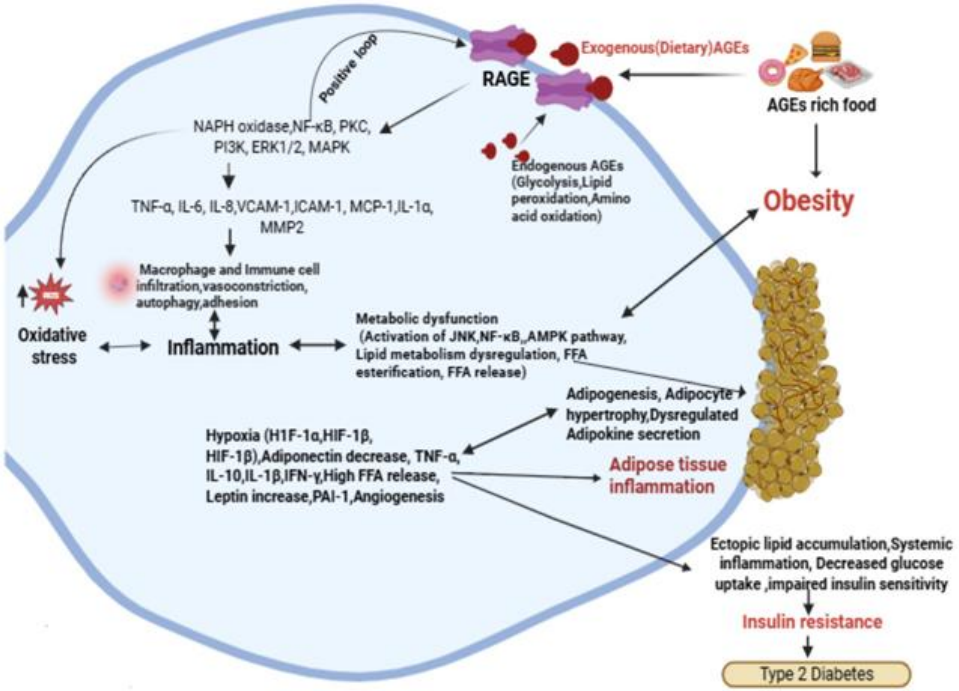


Fig. 3 Interplay of Advanced glycation end products (AGEs), Inflammation and Obesity. AGEs from diet (exogenous) and cellular metabolism (endogenous) interact with its receptor RAGE, promoting oxidative stress and inflammation. This led to increased adipogenesis, adipocyte hypertrophy and adipose tissue inflammation. Adipocyte tissue macrophages produce TNF-α, IL-6 and IL-8 in response to excess nutrient intake, stress and inflammation. These elevated cytokines further recruit and activate immune cells, exacerbating the inflammatory environment and interfering with insulin signaling pathways, leading to impaired insulin sensitivity and glucose uptake leading to exacerbated obesity. Obesity itself triggers inflammation via metabolic stressors, pro-inflammatory cytokines, and oxidative stress, thereby upregulating RAGE, thus creating a cyclic interplay among obesity, inflammation, and AGE contributing to tissue damage and metabolic dysfunction

Yamagishi, S. and Matsui, T. (2016) *Pathologic role of dietary advanced glycation end products in cardiometabolic disorders*. Nutrients, 8(11), 704.

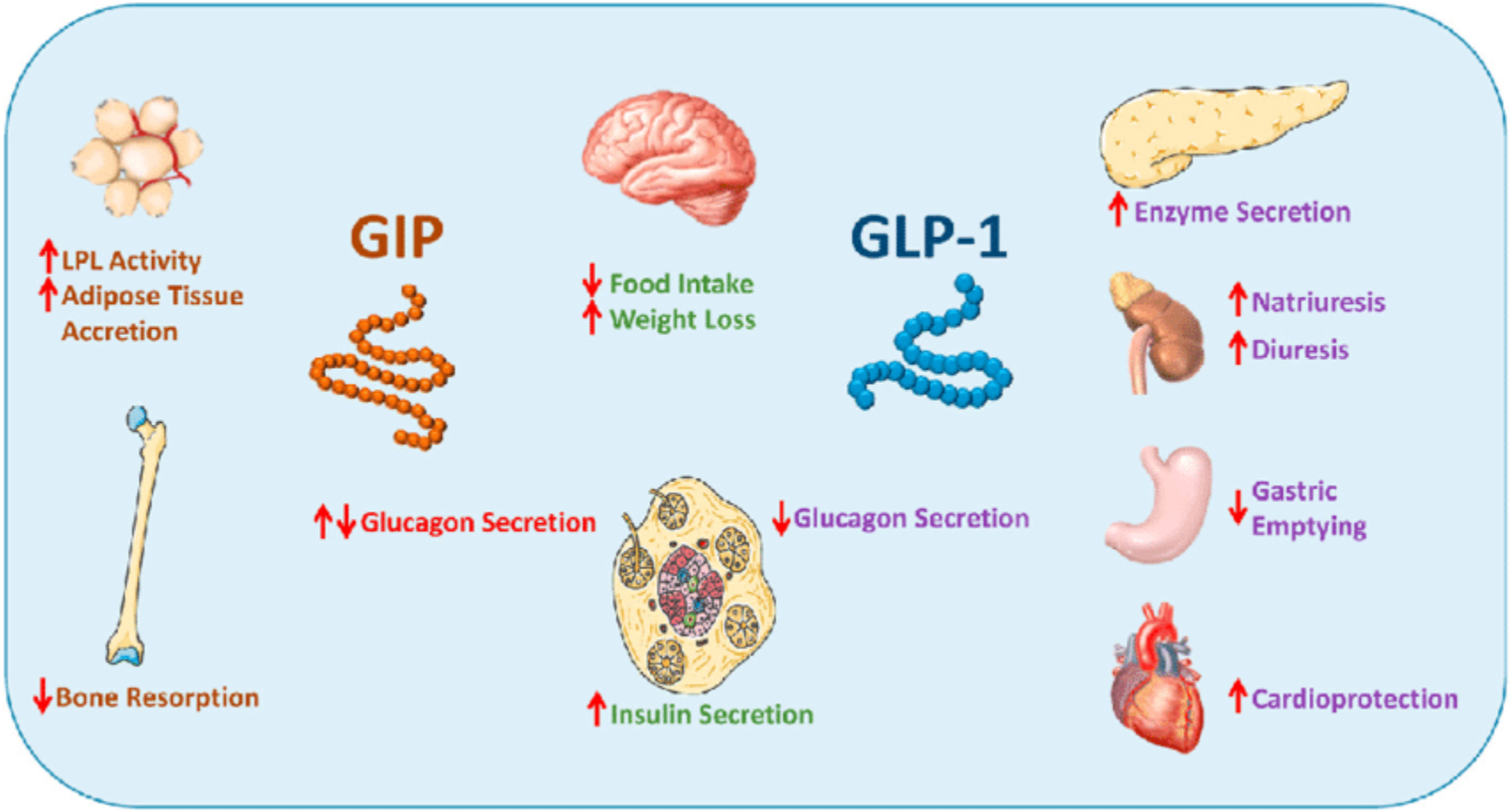
Weight management and incretin medications

- Glucagon-like peptide-1 (GLP-1) is an incretin hormone produced by intestinal L-cells in response to nutrient ingestion.
- It plays a central role in metabolic regulation by enhancing insulin secretion, suppressing glucagon release, delaying gastric emptying and activating satiety pathways in the brain (2). By mimicking or amplifying this signalling pathway, GLP-1 receptor agonists reduce appetite and caloric intake.
- Clinical trials have demonstrated impressive outcomes. Semaglutide patients experienced average weight reductions of nearly 15% over 68 weeks, compared with approximately 2% in the placebo group (3).
- Similarly, tirzepatide, which activates both GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors, has produced weight reductions exceeding 20% of baseline body weight in some studies (4).

1.Müller TD, Finan B, Bloom SR, et al. Glucagon-like peptide-1 (GLP-1). *Mol Metab.* 2019;30:72-130.; 2.Drucker DJ. Mechanisms of action of GLP-1 receptor agonists. *Cell Metab.* 2018;27:740-756.

3.Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med.* 2021;384:989-1002.; 4.Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med.* 2022;387:205-216

GLP-1 and GiP agonists



Nauck, M.A. and Meier, J.J. (2018) *Incretin hormones*. The Lancet Diabetes & Endocrinology, 6(10), pp.799–812

Targeting the glucagon receptor

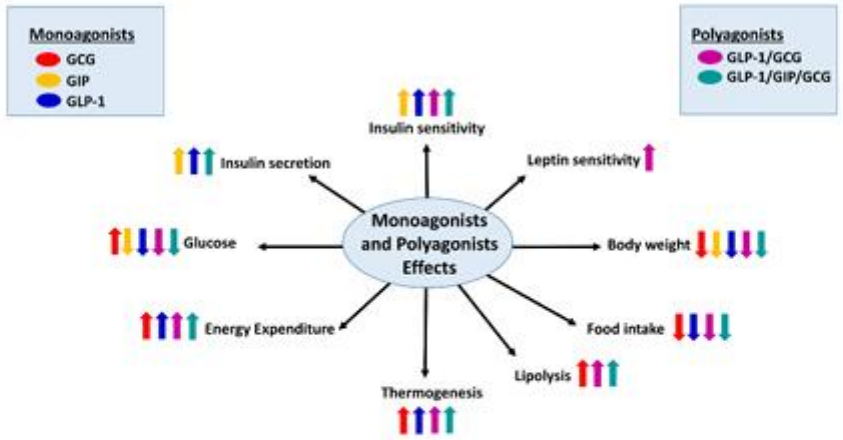


Figure 3. Unimolecular polypharmacy targeting the glucagon receptor: Schematic overview of the effects of polyagonists of glucagon receptor on energy balance regulation. GCG [Glucagon (red)], GIP [glucose insulinotropic peptide (orange)], GLP-1 [Glucagon like peptide-1 (blue)], GLP-1/GCG (purple), and GLP-1/GIP/GCG (green) (right and left panels). Arrows up indicate increase, while arrows down indicate decrease.

Müller, T.D. et al. (2017) *Glucagon receptor agonism for metabolic disease*. Molecular Metabolism, 6(10), pp.1270–1281

Where are we with these drugs?

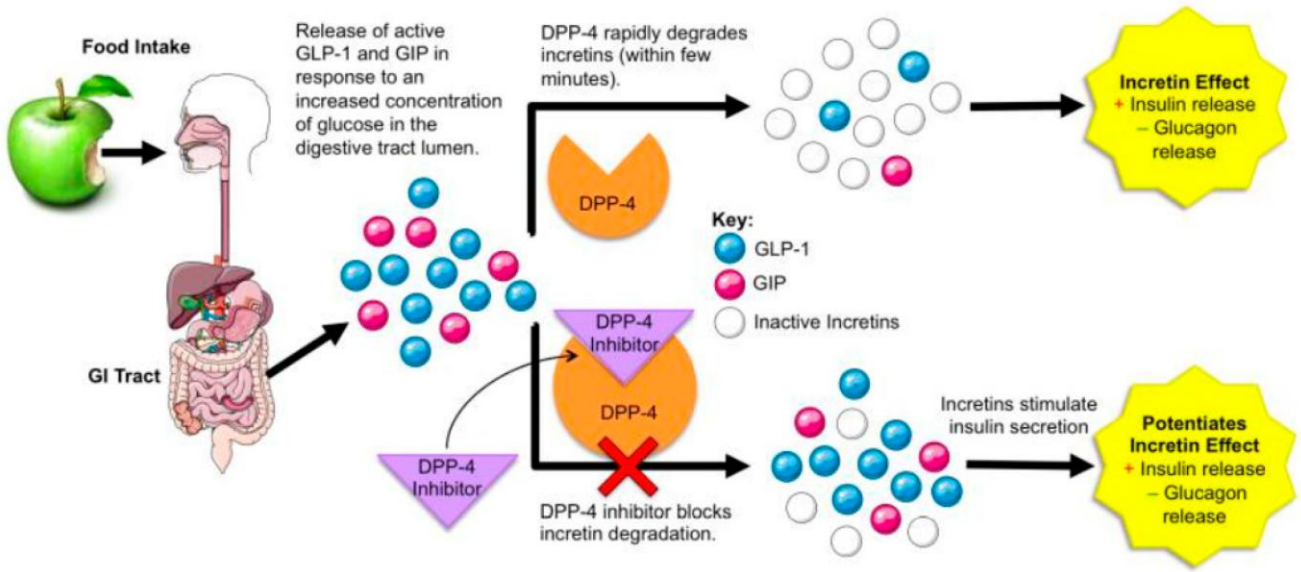
- GLP-1RA medications: semaglutide, liraglutide, tirzepatide (dual GLP-1 and GIP RA) soon to be triple agonists (retatrutide) and others….
- Originally for type 2 diabetes ('incretin' effect with effect on insulin and glucagon secretion)
- Rapidly growing use to support weight management
- Estimates from Kantar survey of 12000 UK households that use increased from 2.3% in March 2024 to 4.1% in 2025[1]

[1] GLP-1 agonists: the next big disruptor in society Kantar 2025

What's coming around the corner

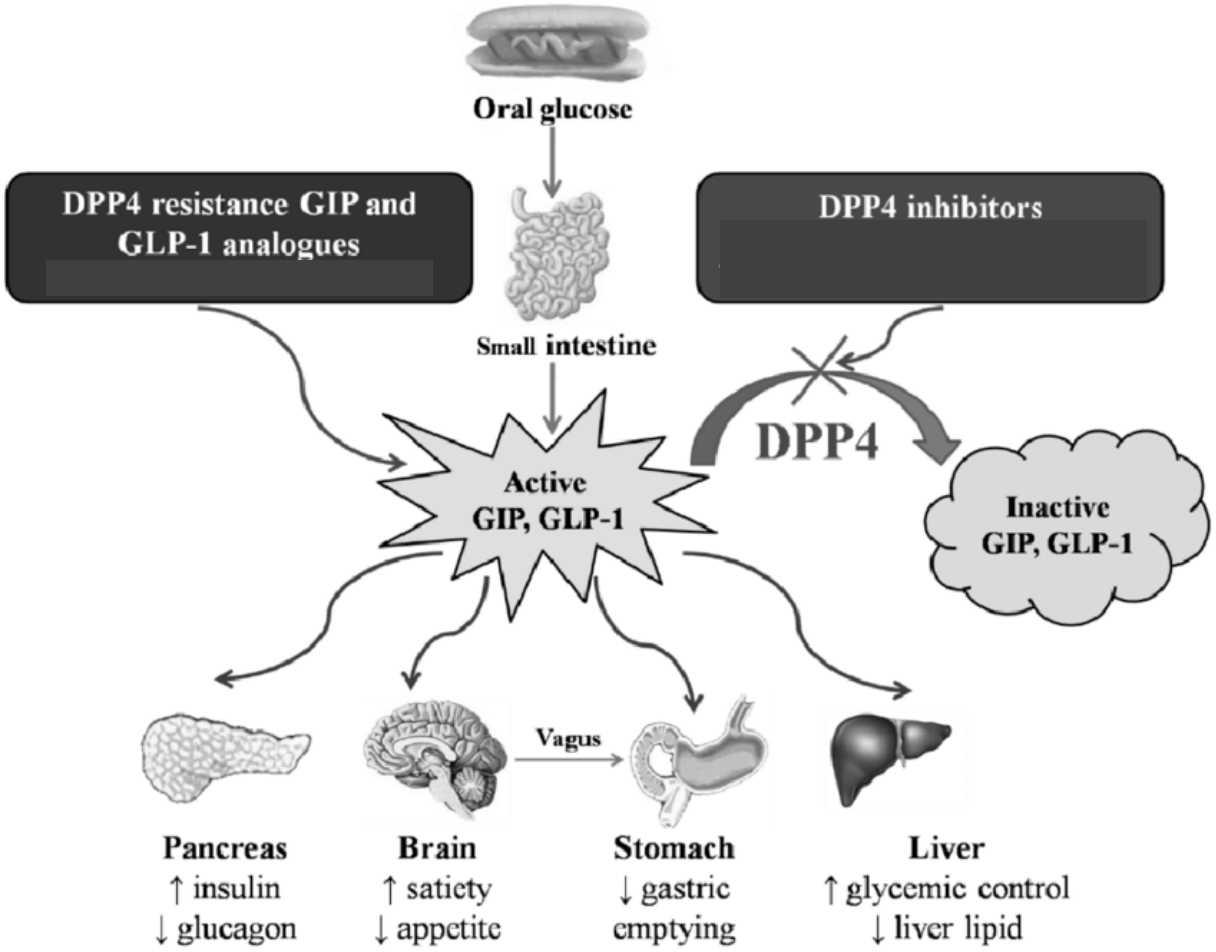
- In adults:
  - Cagrilintide-semaglutide (amylin and GLP1-RA combination) Davies et al., 2025. Phase 3a better HbA1c decrease
  - Mazdutide (GLP1 and glucagon RA) Ji et al., 2025 Phase 3a.
    - Glucagon RA functions through appetite regulation and increased thermogenesis – minimal impact on glycaemia
  - Retatrutide (triple agonist – GLP1, GIP and glucagon RA), up to 100% at least 5% weight loss

DPP-4 antagonists prolong Gip GLP-1 effects



- Aroda, V.R. (2018) *Combination incretin therapy*. Clinical Therapeutics, 40(4), pp.554–570.

DPP-4 and GLP-1 combination



- Mulvihill, E.E. and Drucker, D.J. (2014) *Pharmacology of DPP-4 inhibitors*. Endocrine Reviews, 35(6), pp.992–1019.

Long-Term Safety Considerations of Incretin Therapies

As the number of patients receiving incretin medications continues to grow, emerging data are providing insights into the longer-term physiological consequences associated with these treatments.

The most commonly reported adverse effects involve nausea, vomiting, abdominal discomfort and diarrhoea. These effects are usually transient and tend to occur during the early stages of treatment when doses are escalated (1). However, persistent gastrointestinal symptoms can contribute to treatment discontinuation in some individuals.

Potential associations between incretin therapies and gallbladder disease as well as increased rates of cholelithiasis among patients receiving GLP-1 receptor agonists (2). Early observational studies raised questions regarding a possible association between incretin therapies and pancreatitis (3).

Some patients may experience symptoms consistent with delayed gastric motility or gastroparesis. These effects are usually reversible following treatment cessation, but they highlight the importance of monitoring gastrointestinal symptoms during therapy (4).

1. Nauck MA, Meier JJ. Management of endocrine disease: GLP-1 receptor agonists and adverse effects. *Eur J Endocrinol.* 2019;181:R211-R234.
2. Smits MM, Van Raalte DH. Safety of GLP-1 receptor agonists. *Nat Rev Endocrinol.* 2021;17:72-84.
3. Bethel MA, Patel RA, Merrill P, et al. Cardiovascular safety and pancreatitis risk with GLP-1 receptor agonists. *Lancet Diabetes Endocrinol.* 2018;6:105-113.
4. Camilleri M. Gastrointestinal effects of GLP-1 receptor agonists. *Gastroenterology.* 2020;158:1521-1534.

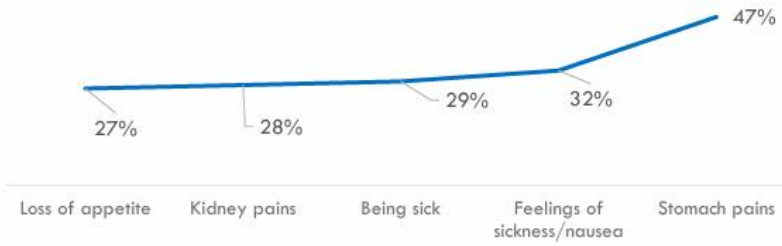
Side effects experienced by users

Have you experienced any side-effects when using GLP-1 drugs or injections such as Ozempic or Wegovy? 2025

Global – Consumers who are currently using GLP-1 drugs or injections

What side effects have you experienced? 2025

Global – Top five answers – Consumers who experienced symptoms



Symptoms when using GLP-1 medication are common and are that severe it can make people consider stop using medication.

These symptoms tend to be severest in those countries where industry experts state that GLP-1 medication is not really used.

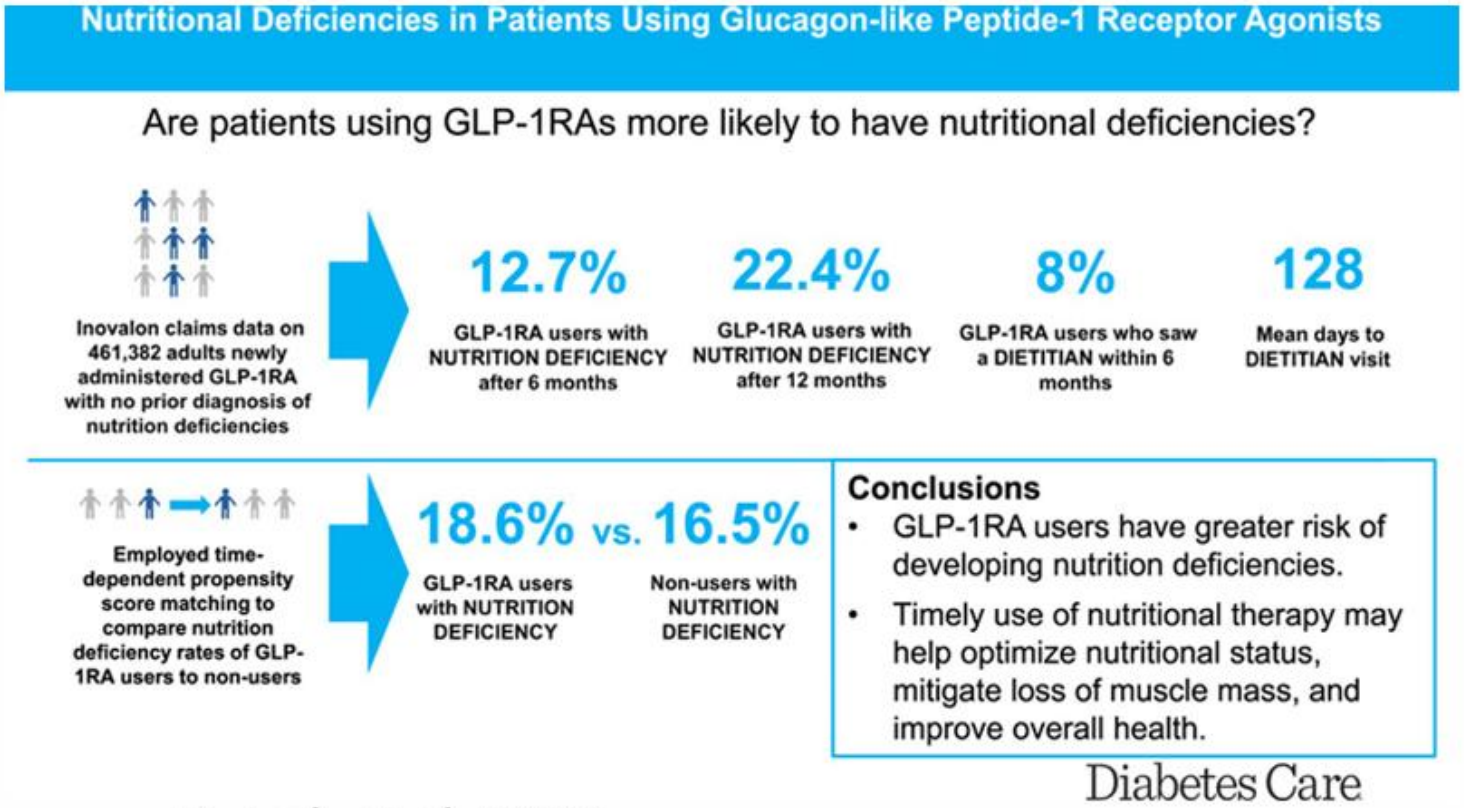
Ex-users of medication report symptoms. Weight gain is the most common symptom, something current users are concerned about.

This is something that will drive demand for products that manage symptoms – including satiety enhancing products.

Incretin-Associated Sarcopenia

- Studies evaluating body composition changes during GLP-1 therapy suggest that approximately 25–40% of total weight loss may involve lean mass, depending on the study population and duration of treatment (1).
- Skeletal muscle is metabolically active tissue that plays a critical role in glucose disposal, insulin sensitivity and resting energy expenditure. When lean body mass decreases, resting metabolic rate often declines.
- This reduction in energy expenditure may increase susceptibility to weight regain once pharmacological appetite suppression is removed.
- Loss of muscle mass can also impair metabolic flexibility-the body's ability to efficiently switch between carbohydrate and fat oxidation depending on nutrient availability. Reduced muscle mass may limit this capacity, contributing to impaired metabolic regulation.
- For these reasons, practitioner-led programmes supporting patients during GLP-1 withdrawal should prioritise strategies that preserve or rebuild lean muscle mass. Exercise and adequate dietary protein intake are particularly important components of this strategy.

- Lundgren JR, et al. Healthy weight loss maintenance with exercise, liraglutide or both combined. *Nat Med.* 2021.



Butsch et al. 2025 https://doi.org/10.1016/j.obpill.2025.100186

Likely deficiencies directly induced by incretin medications

Evidence to suggest that GLP-1 RA significantly decrease gastric pH by 20.7% (95% CI -40.6, -0.8) (1)

Gastric pH is essential for iron and vitamin B12 absorption • Reduced intestinal iron absorption seen with GLP-1RA (2)

Reduced vitamin B12 (3)(may be exaggerated by metformin) (3,4)

1 Quastet al. 2020. https://doi.org/10.2337/dc20-0720
2 Meliset al. 2025 https://doi.org/10.1111/dom.16368
3 Hanks 2024 https://www.medscape.com/viewarticle/five-essential-nutrients patients-glp-1s-2024a1000h6j?form=fpf
4 Rizoset al. 2024 www.doi.org/10.52768/2766-7820/291

Micronutrient Considerations in Weight Loss Management

- Weight loss, particularly when accompanied by reduced caloric intake, can increase the risk of micronutrient deficiencies.
- Several studies examining dietary intake during weight loss interventions have identified reduced consumption of micronutrients such as iron, magnesium, zinc, vitamin B12 and vitamin D (1).
- Vitamin D deficiency is particularly common among individuals with obesity. Adipose tissue can sequester vitamin D, reducing circulating levels. Weight reduction may improve vitamin D status in some individuals, but supplementation is often recommended to achieve optimal levels (2).
- Iron and vitamin B12 are also important considerations. Vitamin B12 deficiency can impair energy metabolism and neurological function, making monitoring important during long-term weight management.
- Magnesium plays an essential role in glucose metabolism and insulin sensitivity. Suboptimal magnesium intake has been associated with increased risk of metabolic syndrome and type 2 diabetes (3).

1. Astrup A, et al. Nutritional deficiencies during weight loss interventions. *Am J Clin Nutr.* 2019;109:1539-1547.
2. Wortsman J, et al. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr.* 2000;72:690-693.
3. Barbagallo M, Dominguez LJ. Magnesium and metabolic syndrome. *World J Diabetes.* 2015;6:273-279.

Weight Regain After GLP-1 Discontinuation

- One of the most important clinical observations associated with incretin therapies is the tendency for weight regain following treatment cessation.
- Individuals who had lost an average of 17.3% of body weight during treatment regained approximately two-thirds of that weight within one year (1).
- An observational analysis published in the *BMJ* reported that many patients discontinue therapy within the first year due to cost, medication supply issues or gastrointestinal side effects (2).
- When treatment is discontinued without structured lifestyle interventions, weight regain often follows.
- These observations emphasise that whilst pharmacological therapies can facilitate weight loss, but long-term success depends on sustainable lifestyle strategies that maintain energy balance once medication is withdrawn.

1. Wilding JPH, et al. Weight regain after semaglutide withdrawal: STEP-1 extension. *Diabetes Obes Metab.* 2022.
2. Bhatt DL, et al. Real-world use and discontinuation patterns of GLP-1 receptor agonists. *BMJ.* 2024.

Biological Drivers of Weight Regain

- Body weight is regulated by complex physiological systems designed to maintain energy balance. When weight is lost, the body activates compensatory responses intended to restore previous energy stores.
- Levels of ghrelin which stimulates appetite, often increase. At the same time, levels of leptin, which normally suppress hunger and promote satiety, tend to decline (1). These hormonal changes increase hunger and reduce feelings of fullness after meals.
- Energy expenditure may also decrease following weight loss. Reductions in resting metabolic rate occur partly because of reduced body mass but also due to adaptive thermogenesis.
- Neural pathways associated with food reward may also become more sensitive following weight loss, increasing the appeal of calorie-dense foods.
- These adaptations can hinder long-term weight maintenance in modern environments where high-calorie foods are readily available.

Bhatt DL, et al. Real-world use and discontinuation patterns of GLP-1 receptor agonists. *BMJ.* 2024.

Exercise and Mitochondrial Function

In the context of GLP-1 therapy discontinuation, exercise plays an especially important role in preserving lean body mass and supporting metabolic stability. Resistance training stimulates muscle protein synthesis and promotes hypertrophy, helping restore muscle mass lost during weight reduction (1).

Maintaining skeletal muscle is essential for preserving resting metabolic rate and preventing metabolic slowdown following weight loss. Exercise also has profound effects on mitochondrial function and cellular energy production through oxidative phosphorylation.

Regular physical activity stimulates mitochondrial biogenesis, increasing both the number and efficiency of mitochondria within skeletal muscle (2). Improved mitochondrial function enhances the body's ability to oxidise fatty acids and utilise glucose efficiently.

Research demonstrates that endurance exercise and resistance training both promote mitochondrial adaptations in skeletal muscle. Increased mitochondrial density improves oxidative capacity and enhances the body's ability to utilise stored energy.

Resistance training two to three times per week can help maintain muscle mass, while regular aerobic activity such as brisk walking, cycling or swimming supports cardiovascular health and metabolic flexibility.

Increasing step counts and reducing sedentary behaviour can help sustain energy expenditure and reinforce metabolic adaptations achieved through structured exercise

Holloszy JO. Biochemical adaptations in muscle. *J Biol Chem.* 1967;242:2278-2282.

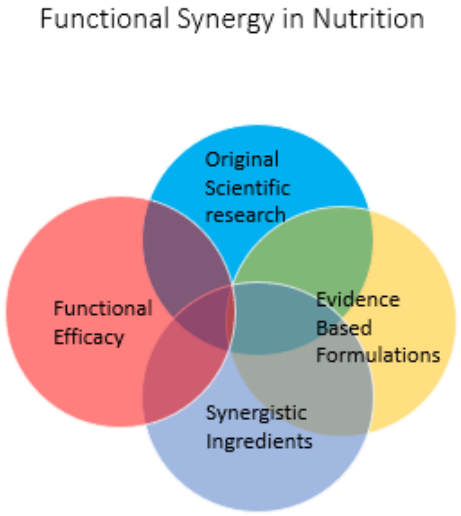
Jakubowicz D, Barnea M, Wainstein J, et al. High caloric intake at breakfast vs dinner. *Obesity.* 2013;21:2504-2512

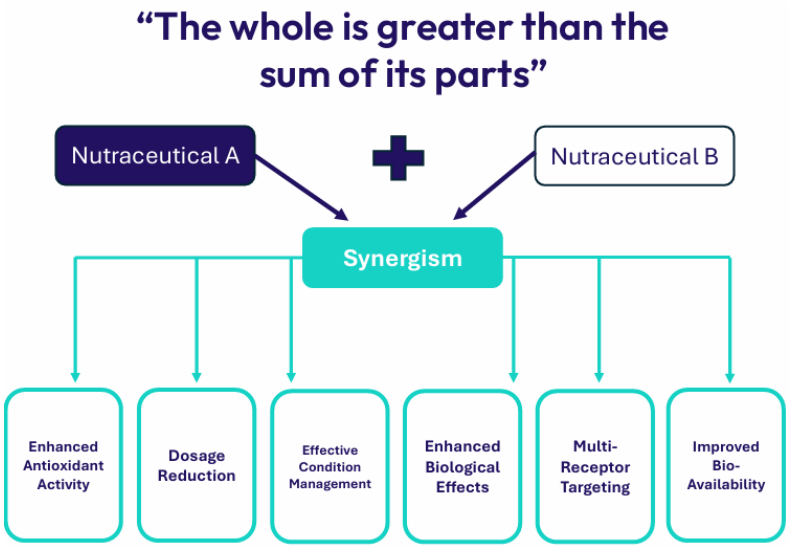
Functional Metabolic Support

- Providing soluble fibre like glucomannan which promotes feelings of fullness and contributes to weight loss when consumed before meals can play an important role (1).
- From a mechanistic perspective, several botanical compounds have demonstrated activity in pathways related to incretin signalling.
- Polyphenols such as those found in green tea, particularly epigallocatechin gallate have been shown to influence glucose metabolism and may enhance incretin signalling pathways (22).
- Similarly, flavonoids such as quercetin and resveratrol, have demonstrated effects on metabolic signalling pathways related to glucose regulation and insulin sensitivity (3).
- Experimental studies have identified DPP-4 inhibitory activity in polyphenols derived from citrus fruits (4). Curcumin has also demonstrated potential effects on metabolic signalling pathways associated with glucose regulation and inflammation (5).
- Although these compounds do not replicate the dramatic potency of pharmaceutical incretin therapies, they may provide supportive metabolic effects when incorporated into dietary strategies.
- The combination of fibre-mediated satiety, micronutrient support and botanical polyphenols such as provided by Go Lean Plus provides a multi-mechanistic approach to appetite regulation and metabolic health.
- Taking the product approximately 15–20 minutes before breakfast, lunch and dinner may enhance satiety and reduce portion sizes during subsequent meals. This approach allows the product to function as a metabolic primer while maintaining nutrient-dense whole-food meals as the foundation of the diet.

1. EFSA Panel on Dietetic Products. Glucomannan and reduction of body weight. *EFSA J.* 2010;8:1798
2. Thielecke F, Boschmann M. Green tea catechins and metabolic health. *Phytochemistry.* 2009;70:11-24.
3. Bruckbauer A, Zemel MB. Polyphenols and metabolic regulation. *Nutrients.* 2014;6:5141-5161.
4. Nongonierma AB, Fitzgerald RJ. DPP-4 inhibitory peptides and polyphenols. *Food Chem.* 2016;197:1153-1163.
5. Panahi Y, et al. Curcumin and metabolic disorders. *Phytother Res.* 2018;32:1648-1660.

Fusion-Functional Synergy in Nutrition

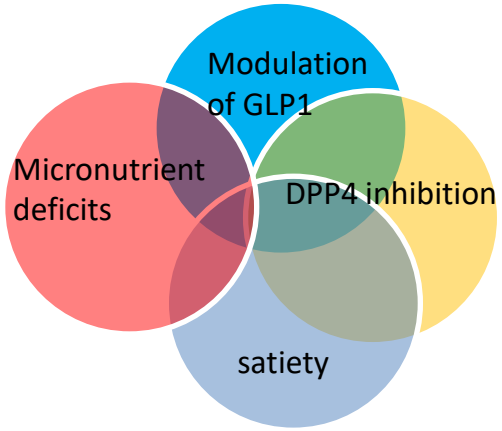




Resolving Common pathologies in weight management

resveratrol; hibiscus; green tea; Glucomannan
berberine; curcumin; cinnamon; mulberry.

Vitamins and minerals



curcumin; resveratrol; cinnamon
maritime pine bark extract; blackcurrant
Mulberry; quercetin; rosemary

Glucomannan
Chromium
Green Tea
Blackcurrant

Dietary modulation of GLP-1

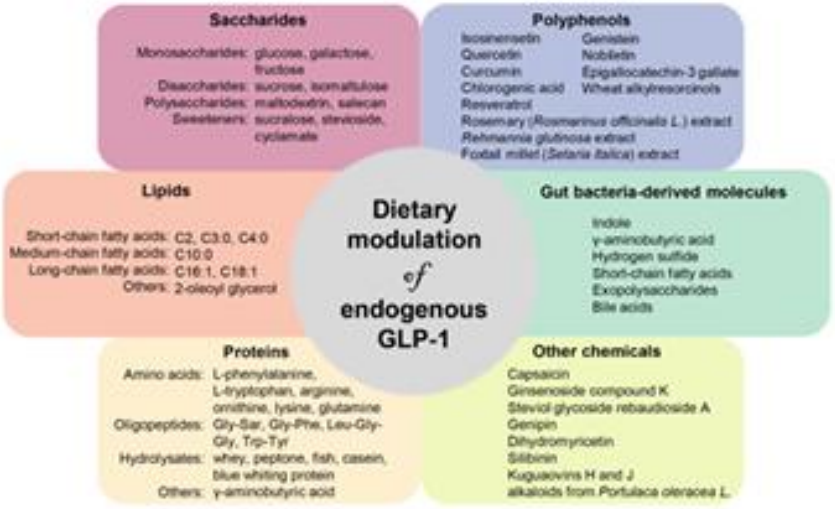


Figure 2 Dietary molecules that modulate endogenous GLP-1 secretion, including saccharides, lipids, proteins, polyphenols, gut bacteria-derived molecules, and other chemicals.

- **Tolhurst, G. et al. (2012) *Short-chain fatty acids stimulate GLP-1 secretion*. Diabetes, 61(2), pp.364–371.**

Anti-obesity effects of polyphenols

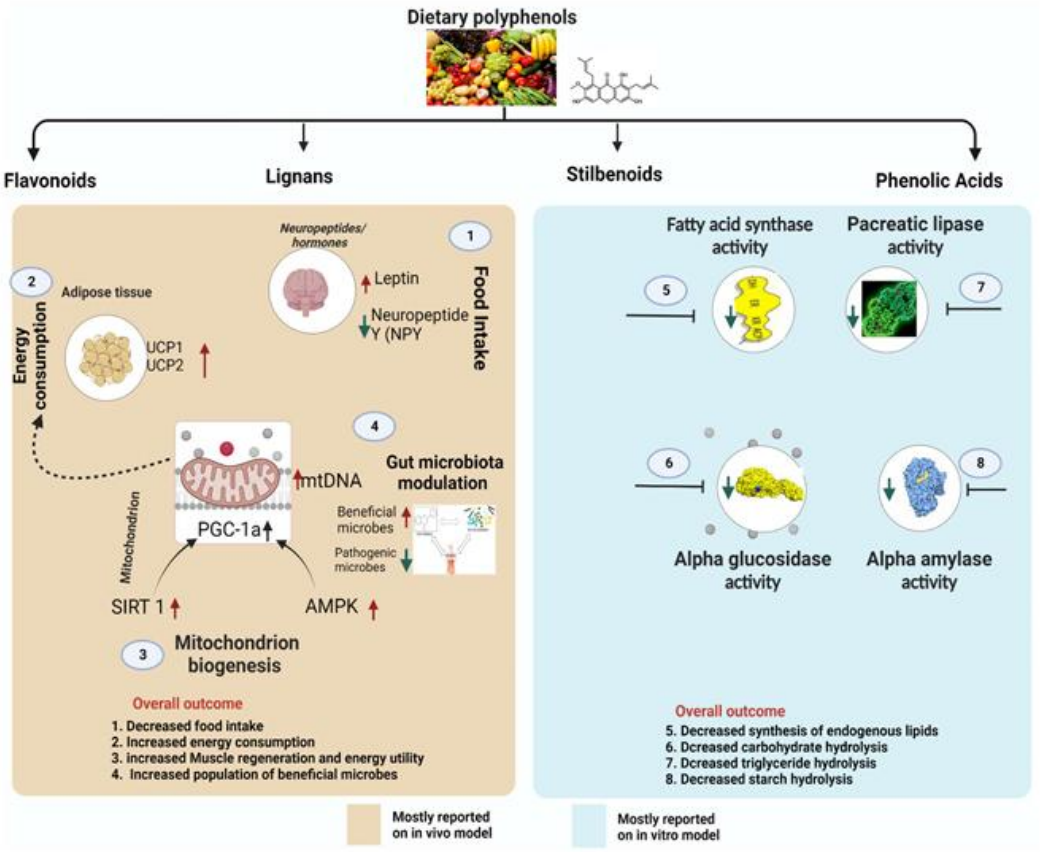
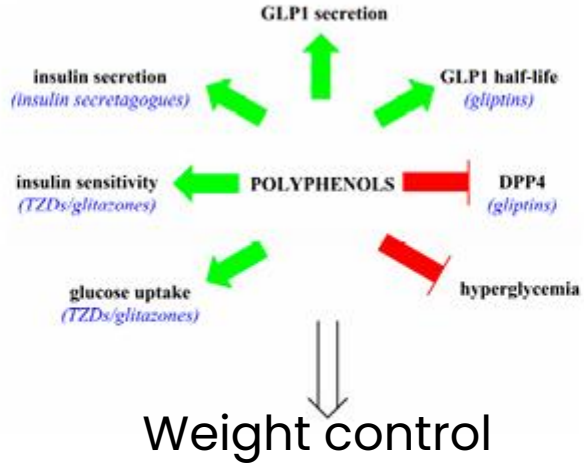


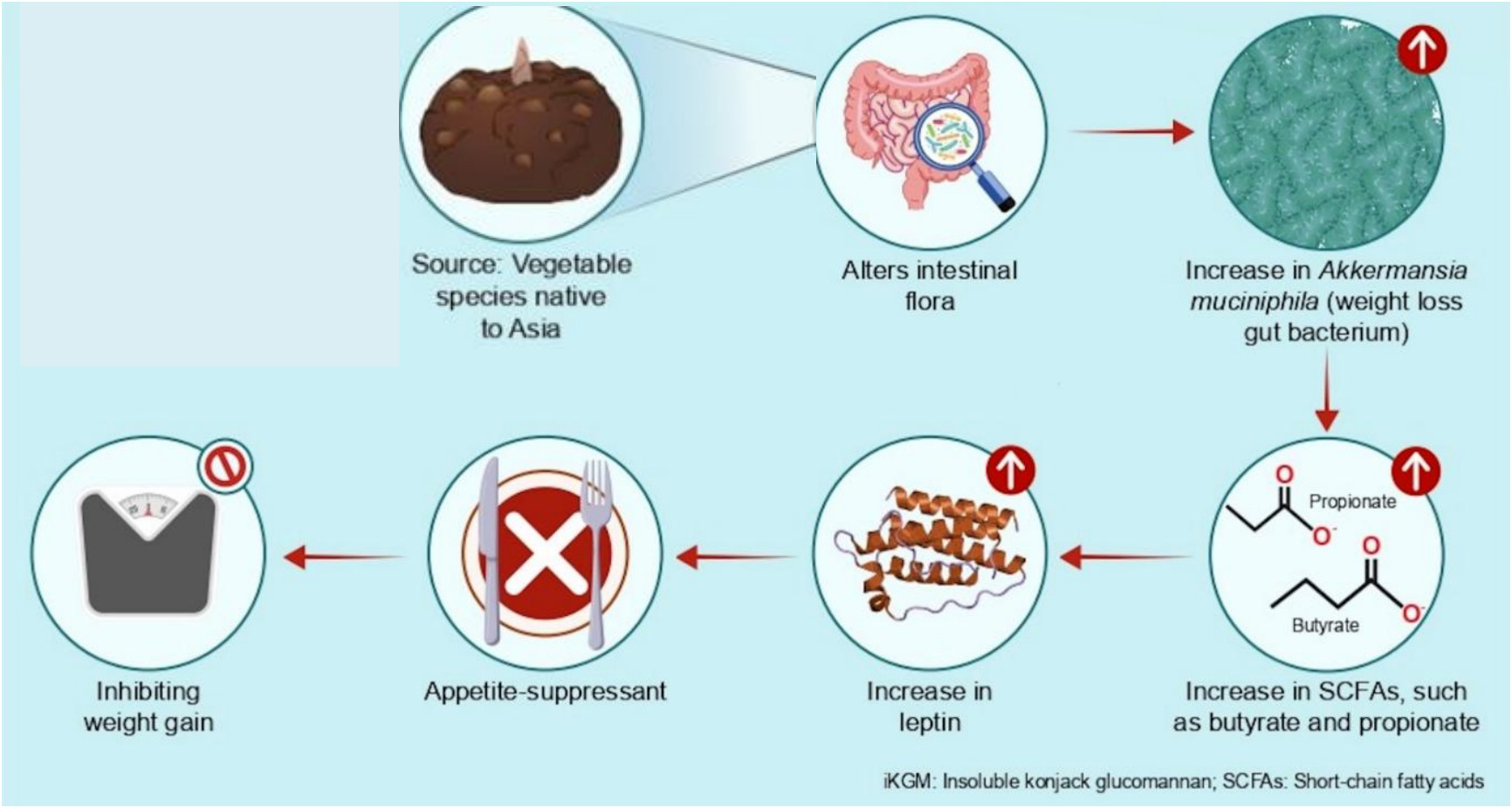
Figure 3. Molecular target and mode of action for antiobesity of polyphenols. ↑, Up-regulation; ↓, down-regulation.

- Hanhineva, K. et al. (2010) *Impact of dietary polyphenols on carbohydrate metabolism*. International Journal of Molecular Sciences, 11(4), pp.1365–1402.

Overall actions of polyphenols



Glucomannan and weight loss



Onakpoya, I. et al. (2014) *Glucomannan for weight loss: systematic review and meta-analysis*. **Journal of Obesity**, 2014, 610908

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Go Lean Plus Formula

Ingredient	Amount per 3 daily servings (8.1g)	% NRV*
Vitamin A	800mcg RE	100 %
Vitamin D	10 mcg	200 %
Vitamin E	12 mg a-TE	100 %
Vitamin K1	47.5mcg	63 %
Vitamin C	40 mg	50 %
Vitamin B1 (Thiamine)	1.1 mg	100 %
Vitamin B2 (Riboflavin)	1.4 mg	100 %
Vitamin B3	16 mg	100 %
Vitamin B6	1.4 mg	100 %
Folic Acid	200mcg	100 %
Vitamin B12	2.5mcg	100 %
Biotin	50mcg	100 %
Vitamin B5	6 mg	100 %
Iron	7 mg	50 %
Zinc	10 mg	100 %
Copper	1 mg	100 %
Manganese	2 mg	100 %
Selenium	55mcg	100 %
Chromium	40mcg	100 %
Iodine	150mcg	100 %
Betaine	20 mg	*
Choline	50 mg	*
Glycine	1512mg	*
Lutein	6mg	*
Zeaxanthin	2mg	*
Resveratrol	10 mg	*
Co-enzyme Q10	5 mg	*
Glucomannan	3g	*
Evera GLP-1 Complex Botanical Fusion™:	Equivalent to 3332 mg of natural botanicals	*

Consisting of standardised extracts of Fenugreek; Quercetin; Berberine; Olive Leaf; Cinnamon; Hibiscus; White Mulberry Leaf; Blackcurrant; Curcumin; Maritime Pine Bark; Pomegranate;

Ingredient Studies

Although all ingredients have been investigated in numerous high-quality clinical studies, the robustness of efficacy is further demonstrated by the outcomes of systematic reviews and meta-analyses

Ingredient	Studies	Participants	Outcomes
Betaine	5	195	Significant reduction in % body fat (BF) and body mass (BM)
Pomegranate extract	28	1624	May yield a beneficial effect on body weight (BW) and Body Mass Index (BMI)
Curcumin extract	39	5666	Significant reduction in BMI, BW and waist circumference (WC)
Resveratrol	28	1265	Significant effect on BMI, WC, BW.
Quercetin	20	1164	Significant reduction in fasting blood glucose (FBG)
Maritime Pine Bark Extract	27	1685	Significant reduction in FBG, BW and cardiometabolic risk factors
Berberine	12	1040	Significant reduction in BMI, and WC
Glucomannan	6	124	Significant reduction in FBG
	7	617	Significant weight difference versus placebo
Green Tea	25	1344	Green Tea combined with a healthy diet and regular physical exercise is beneficial in the management of obese patients
Hibiscus extract	10	453	Administration can improve anthropometry measurement, fat accumulation, increased satiety sensation, while the appetite sensation mainly for fatty, sweet, and salty foods was decreased.
Mulberry leaf extract	12	786	Consumption can provide favourable effects on HbA1C, some lipid profile parameters, and certain inflammatory markers compared to the control group.
Fenugreek extract	19	1306	Supplementation demonstrated significant beneficial effects on HOMA-IR, FPG, HbA1c, LDL-C, TC, HDL-C, and BMI.

References-Appendix 1

Consumer interest in foods and drinks stimulating GLP-1 homones naturally

While attitudes towards medication is polarized, consumers have more favorable opinions towards natural alternatives.

Consumers accept natural alternatives may not be immediately as effective but are safer.

They also feel that there is greater transparency around what is contained within food and drink products.

This market will also be influenced by any future legislation and lobbying around medication.

Circadian pattern of satiety hormones

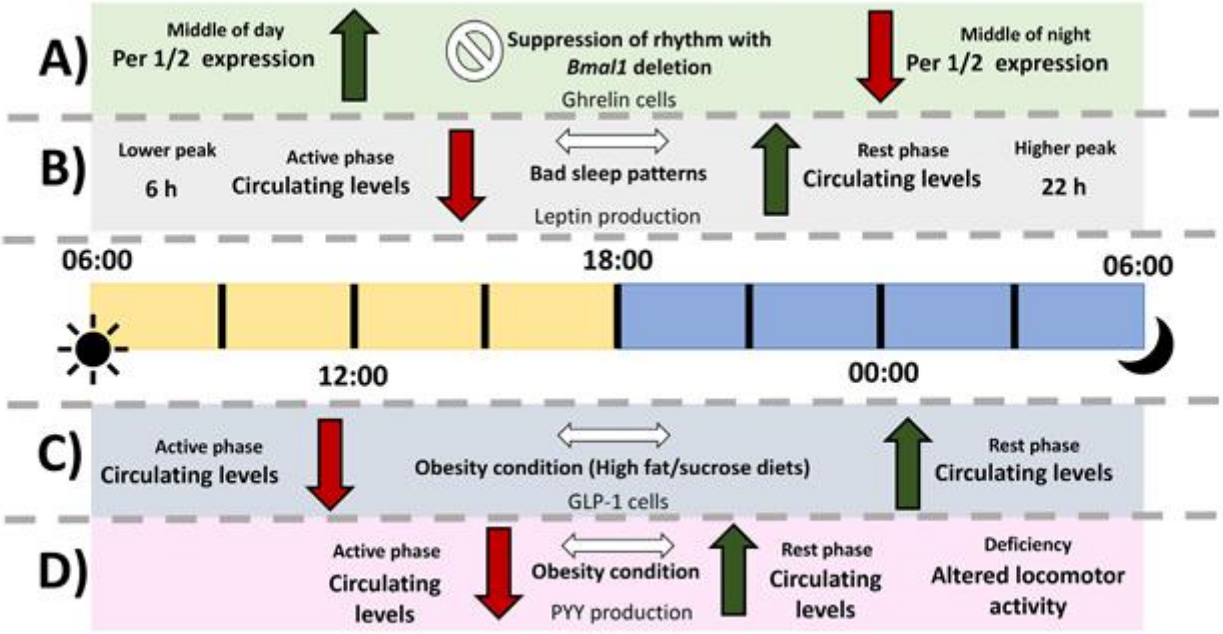

Fig. 1. Circadian pattern of satiety hormones. (A) Circadian behavior of ghrelin producers' cells. (B) Circadian behavior of leptin production. (C) Circadian behavior of GLP-1 producers' cells. (D) Circadian behavior of PYY production.

Kalsbeek, A. et al. (2014) *Circadian control of metabolism by the suprachiasmatic nucleus*. Endocrine Reviews, 35(6), pp. 784–829.

Structured Meal Timing and Appetite Regulation

- During GLP-1 therapy appetite suppression often leads to irregular eating patterns. Many patients report reduced hunger and may skip meals or consume very small portions throughout the day.
- While this may support weight loss during treatment, it can create challenges when medication is discontinued and hunger signals return. Without structured eating patterns, patients may develop erratic meal timing and increased snacking behaviour. Establishing a consistent daily meal structure can help stabilise appetite signals and improve metabolic regulation.
- Research suggests that meal timing influences hormonal patterns that regulate hunger and satiety. Hormones such as insulin, ghrelin and peptide YY respond to predictable eating schedules (1).
- When meals occur at consistent times each day, these hormonal responses become more stable. A structured pattern of three balanced meals per day provides a simple and sustainable framework for many patients.
- Each meal should contain a balance of protein, fibre and healthy fats to support satiety and maintain stable blood glucose levels. Protein intake is particularly important in this context.
- Adequate dietary protein supports muscle protein synthesis and may help preserve lean body mass during weight maintenance.

- Garaulet, M. and Gómez-Abellán, P. (2014) *Timing of food intake and obesity: a novel association*. Physiology & Behavior, 134, pp.44–50.

Stress, Cortisol and Eating Behaviour

- Psychological stress plays a significant role in appetite regulation and eating behaviour. Elevated cortisol levels are associated with increased appetite and greater consumption of high-energy foods (1).
- Stress can also disrupt sleep and impair decision-making related to food choices. These effects may contribute to weight regain following periods of weight loss.
- Breathwork techniques provide a simple and accessible method of regulating stress responses.
- Slow diaphragmatic breathing activates the parasympathetic nervous system and reduces physiological stress markers (2). A commonly recommended technique is **4-6 breathing**, where individuals inhale for four seconds and exhale for six seconds repeatedly for several minutes. This pattern of breathing promotes relaxation and may reduce stress-related eating behaviours.
- Encouraging patients to practise breathing exercises regularly can complement nutritional and exercise interventions during weight-maintenance programmes.

1. Torres SJ, Nowson CA. Relationship between stress and eating behaviour. *Nutrition.* 2007;23:887-894.
2. Zaccaro A, Piarulli A, Laurino M, et al. Breathing techniques and psychophysiological regulation. *Front Hum Neurosci.* 2018;12:353.

Behavioural Coaching and Patient Engagement

- Long-term weight management requires behavioural change alongside physiological interventions. Practitioner support can play an important role in helping patients maintain motivation and develop sustainable habits.
- Goal setting, accountability and regular follow-up consultations can help reinforce lifestyle changes. Educating patients about the biological drivers of weight regain can also improve adherence to interventions.
- When individuals understand that appetite increases after medication cessation are normal physiological responses rather than personal failures, they may be more willing to engage with lifestyle strategies designed to maintain weight loss.
- Mindful eating practices can also be helpful. Encouraging patients to eat slowly, pay attention to satiety signals and avoid distracted eating may help regulate energy intake.

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The framework for support

Practitioners supporting patients during GLP-1 dose reduction may consider implementing a structured transition programme that includes the following components:

1 NUTRITION PLANNING
Establish a consistent three-meal daily structure with balanced macronutrient intake.

2 PRE-MEAL METABOLIC SUPPORT
Use Go Lean Plus before meals to enhance satiety and support appetite regulation.

3 EXERCISE PRESCRIPTION
Encourage resistance training and aerobic activity to preserve lean mass and support mitochondrial function.

4 BEHAVIOURAL COACHING
Provide education about biological drivers of weight regain and support goal-setting.

5 STRESS MANAGEMENT
Introduce breathwork techniques to reduce stress-related eating behaviours.

Implementing these strategies during dose reduction rather than after medication cessation may improve long-term outcomes.

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Thank You

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Appendices

Appendix 1

- Gao, X. et al. (2019) *Betaine supplementation and body composition: a systematic review and meta-analysis*. Nutrients, 11(10), 2482.
- Sahebkar, A. et al. (2017) *Pomegranate supplementation and body weight: a systematic review and meta-analysis*. Critical Reviews in Food Science and Nutrition, 57(8), pp.1751–1758.
- Panahi, Y. et al. (2019) *Curcumin and body weight: a systematic review and meta-analysis*. Phytotherapy Research, 33(2), pp.332–345.
- Mousavi, S.M. et al. (2017) *Resveratrol supplementation and obesity: a meta-analysis*. Clinical Nutrition, 36(5), pp.1346–1354.
- Xu, Y. et al. (2019) *Quercetin and glycaemic control: systematic review*. Phytotherapy Research, 33(7), pp.1812–1820.
- Belcaro, G. et al. (2013) *Pycnogenol® and metabolic syndrome: meta-analysis*. Panminerva Medica, 55(2), pp.217–224.
- Hu, Y. et al. (2012) *Berberine and metabolic parameters: meta-analysis*. Metabolism, 61(12), pp.1750–1757.
- Onakpoya, I. et al. (2014) *Glucomannan for weight loss: systematic review and meta-analysis*. Journal of Obesity, 2014, 610908.
- Hursel, R. et al. (2009) *Green tea catechins and weight loss: meta-analysis*. International Journal of Obesity, 33(9), pp.956–961.
- Serban, C. et al. (2015) *Hibiscus sabdariffa and obesity: systematic review*. Journal of Hypertension, 33(6), pp.1119–1127.
- Naowaboot, J. et al. (2012) *Mulberry leaf extract and metabolic effects*. Evidence-Based Complementary and Alternative Medicine, 2012, 263128.
- Neelakantan, N. et al. (2014) *Fenugreek and glycaemic control: meta-analysis*. Nutrition Journal, 13, 7.

EFSA claims metabolism and weight

- Glucomannan contributes to the reduction of body weight in the context of an energy-restricted diet
- Chromium contributes to normal macronutrient metabolism: to the maintenance of normal blood glucose levels
- Vitamin B6 contributes to normal protein and glycogen metabolism
- Choline contributes to normal lipid metabolism and to the maintenance of normal liver function
- Magnesium contributes to normal protein synthesis
- Zinc contributes to normal carbohydrate metabolism; to normal macronutrient metabolism; to normal metabolism of fatty acids

EFSA claims metabolism and weight

- Cinnamon-Helps to maintenance of a healthy blood sugar level /helps to maintain a normal blood glucose level as part of a healthy lifestyle/contributes to normal glucose level
- Hibiscus-Support gastrointestinal health/Helps to support the digestion/ Contributes to physical well-being“
- Blackcurrant-Traditionally used to facilitate the weight loss in addition to dietetic measures/ Contributes to lose weight in addition to dietetic measures / Helps in weight control/Builds up resistance against stress and unfavourable environmental conditions
- Curcumin-Contributes to the digestive comfort/ Contributes to better fat digestion
- Olive leaf extract-Contributes to maintain a healthy blood sugar level/Can help to maintain a normal function of gastrointestinal tract/Antioxidant.
- Berberine-Normalizes intestinal tract function/Helps to improve blood glucose control

EFSA claims metabolism and weight

- Resveratrol-Helps to control / stabilize body weight
- French Maritime pine bark-helps to maintain good health by protecting cells & tissues through its antioxidant property
- Green Tea-Helps with weight control/Stimulates the lipid degradation/helps to enhance metabolism/contributes to fat oxidation/contributes to metabolism, which in turn helps weight control/helps to reduce the appetite
- Fenugreek-Supports maintenance of normal glucose in blood/helps to maintain a normal blood glucose level as part of a healthy lifestyle/Contributes to normal glucose level
- White mulberry leaf-Can contribute to the maintenance of the carbohydrate metabolism balance of the body