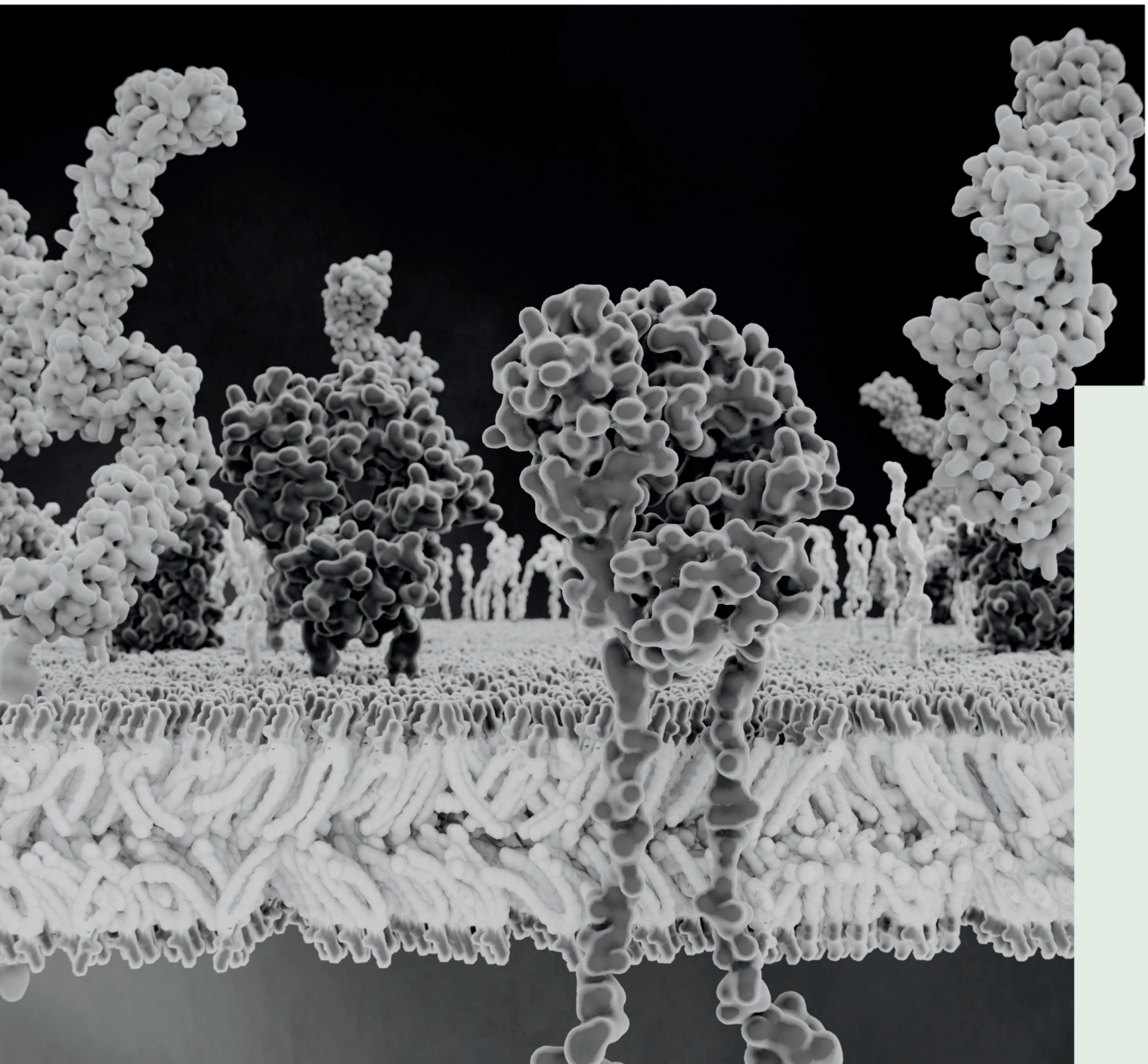
GLOBAL PREBIOTIC ASSOCIATION

GLUCAGON-LIKE PEPTIDE-1 (GLP-1)

WHITE PAPER

PREPARED BY THE GLOBAL PREBIOTIC ASSOCIATION



BACKGROUND

THE GLOBAL OBESITY EPIDEMIC AND DIETARY FIBER

Obesity is a multifactorial disease characterized not only by excessive body fat, but also by chronic inflammation, insulin resistance, and oxidative stress (Gasmi et al., 2021). These metabolic disruptions significantly increase the risk of cardiovascular disease (CVD), type 2 diabetes (T2D), hyperlipidemia, and premature mortality. Contributing factors such as a sedentary lifestyle, poor nutrition, and genetic variations further predispose individuals to obesity and reflect its multi-faceted nature (Abad-Jiménez & Vezza, 2025). With a rising prevalence, obesity has become a global health epidemic, affecting 890 million adults and 160 million children and adolescents worldwide in 2022, as reported by the World Health Organization (WHO) (WHO, 2025). The same report highlighted that 2.5 billion adults and 390 million children and adolescents were overweight (WHO, 2025).

Among the key contributors to this epidemic is the westernized diet, which is typically characterized by high consumption of calorie-dense foods rich in refined sugars, saturated fats, and omega-6-rich oils, often combined with overeating and frequent snacking. Common examples include processed meats, fried foods, soft drinks, high-fat dairy products, and various pre-packaged snacks. In contrast, the western diet is notably low in unprocessed fruits and vegetables, whole grains, grass-fed animal products, fish, nuts, and seeds. As a result, it provides insufficient dietary fiber, vitamins, essential minerals, and plant-derived compounds, including antioxidants, which can be detrimental to long-term health (Malesza et al., 2021).

Dietary fiber, in particular, is a critical yet under-consumed component of the average western diet. Most Americans consume only 11.8–19.8 grams per day, well below the recommended daily intake of 25–35 grams (Fatima et al., 2023). Similarly, adults in European countries report average intakes of 16-29 grams per day (Seljak et al., 2021). According to the European Food Safety Authority (EFSA), a minimum of 25 grams of dietary fiber per day is necessary to maintain regular laxation, while higher intakes are associated with a reduced risk of T2D and coronary heart disease (EFSA, 2010).

This white paper provides the scientific rationale supporting the Global Prebiotic Association's (GPA) previously published best practices for glucagon-like peptide-1 (GLP-1)-related claims.

GLP-1: A KEY PLAYER IN APPETITE AND METABOLIC REGULATION

In brief, endogenous GLP-1 is a peptide hormone secreted in response to nutrient intake and plays a central role in appetite and metabolic regulation. GLP-1 is produced in enteroendocrine L-cells of the intestinal mucosa, pancreatic α-cells, and specific neurons in the brainstem. After consuming a meal, GLP-1 acts on the GLP-1 receptors which are expressed not only in pancreatic β-cells, but across multiple tissues including the lung, heart, kidney, liver, various cell types of the gastrointestinal tract, salivary glands, and in neurons throughout the central and peripheral nervous systems. Naturally occurring GLP-1 has a short half-life due to rapid enzymatic inactivation by dipeptidyl peptidase (DPP-4), producing inactive metabolites. To overcome this limitation, GLP-1 receptor agonists were developed with structural modifications that confer resistance to DPP-4 degradation and prolong their half-life (Holst 2008). Through these pathways, GLP-1 slows gastric emptying, promotes satiety, and regulates glucose metabolism (Barać & Roganović, 2025; Coskun et al., 2018).

APPETITE REGULATION IN RESPONSE TO FEEDING: INTRODUCING GLP-1

Following a meal, appetite regulation is governed by a complex interplay of mechanical and chemical signals that communicate satiation to the central nervous system. The distension of the stomach wall activates mechanoreceptors that transmit satiety signals to the brain via the vagus nerve (Brierley & Lartigue, 2022). Simultaneously, the presence of macronutrients such as fats, fiber, proteins, and carbohydrates in the gastrointestinal tract individually triggers the release of various gut-derived hormones that act as chemical messengers to regulate appetite (Alsalim et al., 2023; Bodnaruc et al., 2016). Among the most critical of these hormones is GLP-1, an incretin that plays a central role in promoting satiety and reducing food intake (Kabahizi et al., 2022).

The effects of GLP-1 on appetite regulation are mediated through the gut-brain axis, a bi-directional communication network linking the gastrointestinal tract with the central nervous system (Kaelberer et al., 2018). GLP-1 is secreted from intestinal epithelial endocrine L-cells, which are most abundant in the distal ileum and colon, in response to nutrient ingestion. Once released, GLP-1 influences feeding behavior through several mechanisms. It slows gastric emptying, thereby prolonging the feeling of fullness and reducing the rate of glucose absorption. Peripherally, GLP-1 activates receptors on vagal afferent neurons, which transmit signals to the nucleus of the solitary tract (NTS) in the brainstem. These signals are then projected to higher brain centers, including the hypothalamus, a key brain region that coordinates energy balance, satiety and appetite control. In addition, GLP-1 can cross the blood-brain barrier and directly activate GLP-1 receptors in the hypothalamus and other brain regions. This central signaling not only suppresses hunger but diminishes the reward aspects of food, collectively leading to reduced caloric intake and enhanced satiety (Drucker et al., 2018).

THE GUT MICROBIOME AND SATIETY SIGNALING

The gut microbiome refers to the community of microorganisms that colonize the gastrointestinal tract (termed the gut microbiota) along with their collective genomes. The gut microbiome includes around 1,000 microbial species and almost 10 million genes. In a balanced gut microbiota, Firmicutes, Bacteroidetes, and Actinobacteria are highly abundant, along with smaller populations of Proteobacteria and Verrucomicrobia. In contrast, in a state of gut dysbiosis, such as that found in T2D and obesity, the gut microbiota composition is marked by reduced levels of beneficial bacteria from the genus Bifidobacterium and the phylum Firmicutes, alongside increased levels of gram-negative bacteria like Bacteroidetes and Proteobacteria (Zeng et al., 2024). Similarly, growing evidence highlights a strong association between the gut microbiota and obesity pathogenesis, with recent studies showing that an 'obesogenic' microbiome shares distinct compositional features, including decreased short-chain fatty acid (SCFA) production, increased energy harvest from food, elevated production of lipopolysaccharides (LPS), and increased proinflammatory cytokines and adipokines (Abad-Jiménez & Vezza, 2025; Zabolotneva et al., 2024; Duan et al., 2021).

The gut microbiome plays a pivotal role in regulating host energy homeostasis by obtaining energy from food, influencing gut hormones, and producing metabolites that regulate host metabolism (Corbin et al., 2023). The gut microbiota produces a variety of metabolites, including SCFAs derived from the fermentation of dietary fibers, secondary bile acids (BAs) produced through bacterial dihydroxylation of primary BAs, and LPSs. These metabolites can influence the secretion of incretins, including GLP-1 (Zeng et al., 2024). As such, SCFAs are key mediators of GLP-1 secretion from enteroendocrine L-cells, and thus, contribute to the metabolic benefits of GLP-1 in obesity (Tolhurst et al., 2012).

GLP-1 secretion increases in the post-prandial state and plays a key role in energy balance by activating hypothalamic receptors to promote satiety and reduce appetite and caloric intake. GLP-1 also inhibits hepatic glucose production via pancreatic alpha-cells, enhances insulin secretion in pancreatic beta-cells, upregulates genes associated with glucose transport and glucokinase, and slows gastric emptying (Guney-Coskun & Basaranoglu, 2024; Ismail et al., 2025).

OBESITY AND GLP-1 RECEPTOR AGONISTS

Obesity is characterized by increased body fat, inflammation, and insulin resistance, and it significantly increases the risk of adiposity-associated diseases, including CVD and T2D (Ghusn & Hurtado, 2024; Gasmi et al., 2021). Anti-obesity medications such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have grown in popularity due to their ability to achieve weight loss outcomes while being less invasive than bariatric procedures. These medications are indicated for individuals with a body mass index (BMI) of ≥ 30.0 kg/m2 or a BMI of 27.0 – 29.9 kg/m2 with weight-related co-morbidities (Ghusn & Hurtado, 2024). Collectively, these factors underscore the growing reliance on pharmacological interventions for obesity and T2D management and highlight the importance of considering the landscape of current strategies.

CURRENT STRATEGIES

Bariatric surgeries, such as Roux-en-Y gastric bypass (RYGB), have been used as a frontline approach to manage obesity by restricting food intake and promoting long-term weight loss. However, these surgeries are associated with high costs and numerous complications (Ibrahim et al., 2025). Recently, treatment with GLP-1 RA medications have garnered significant interest for their ability to increase satiety, slow digestion, and improve insulin resistance. Examples of GLP-1 RA medications include Exenatide (Bydureon®, Byeta®), Liraglutide (Victoza®, Saxenda®), Semaglutide (Ozempic®, Rybelsus®, Wegoxy®), Lixisenatide (Lyxumia®), and Dulaglutaide (Trulicity®) (Ismail et al., 2025). Most of these GLP-1 RA medications are intended for use by adults for treating T2D and anti-obesity effects; however, some have demonstrated the ability to also improve cardiovascular and renal outcomes (Kristensen et al., 2019).

DIETARY, LIFESTYLE, AND OTHER CONSIDERATIONS FOR GLP-1 RA USERS

When using GLP-1 RA medications, optimizing nutritional intakes, dietary patterns, and lifestyle factors is critical to help prevent nutrient deficiencies, maintain lean body mass, and minimize potential side effects associated with these medications (Richardson et al., 2025). Despite these considerations, a substantial proportion of individuals receiving GLP-1 RA medications fail to meet adequate daily intakes of essential macronutrients and micronutrients.

DIETARY, LIFESTYLE, AND OTHER CONSIDERATIONS FOR GLP-1 RA USERS (CONT.)

However, nutritional inadequacies remain a concern among GLP-1 users. In a cross-sectional study of GLP-1 RA users in the United States, data from online surveys and 3-day food records revealed that users do not meet recommended intakes of dietary fiber, calcium, iron, magnesium, potassium, choline, or vitamins A, C, D and E, all falling below the Dietary Reference Intakes. Furthermore, self-reported MyPlate data on food servings and 3-day food records suggest that low fiber intake is largely due to inadequate consumption of fruits, vegetables, and whole grains, accompanied by excessive intake of refined grains (Johnson et al., 2025).

For patients on GLP-1 RA medications, it is important to meet dietary fiber intakes while simultaneously increasing fluid intakes to alleviate gastrointestinal symptoms associated with these medications such as constipation or diarrhea (Almandoz et al., 2024). The 2020-2025 Dietary Guidelines for Americans recommends a protein intake of 0.8 g/kg/day; however, Almandoz et al. (2024) suggest up to 1.5 g/kg/day for patients undergoing substantial weight loss to prevent significant loss of muscle mass (Richardson et al., 2025). Carbohydrates typically contribute 45-65% of total daily energy intake in heathy adults, and very low carbohydrate diets are not recommended as they may lead to dehydration, electrolyte imbalance, and reduced fiber intake from fruits, vegetables, and whole grains (Almandoz et al., 2024). According to EFSA (2010), the average carbohydrate intake among adults in European countries ranges from 38% to 56% of total energy intake (EFSA, 2010). Regarding dietary fats, current recommendations emphasize the incorporation of omega-3 polyunsaturated fatty acids (PUFAs) from sources such as flaxseed, omega-6 PUFAs from nuts and seeds, and monounsaturated fats from foods like olive oil. The Mediterranean diet exemplifies this balanced model and has been associated with lower risk of cardiovascular disease and reduced mortality (Almandoz et al., 2024). According to the EFSA Panel on Nutrition, Novel Foods and Food Allergens, most European populations continue to exceed recommended intakes of saturated fats, sodium, and added sugars, while falling short in dietary fiber and potassium consumption (EFSA, 2022). For individuals using anti-obesity medications, it is particularly important to avoid high-fat, fried, greasy, and high-sugar foods, as well as late-night eating, to optimize treatment outcomes and minimize adverse effects (Richardson et al., 2025; Wadden et al, 2023).

A recent study by Dilley et al. (2025) assessed food consumption and preferences among current, previous, prospective, and non-users of GLP-1 RA medications to evaluate medication-related effects on eating behaviour. Current GLP-1 RA users reported lower caloric intake than other groups. Both current and previous users demonstrated 50% reduction in consumption of processed foods, sugar-sweetened beverages, refined grains, and beef, accompanied by increased intake of fruits, leafy greens, and water. Notably, despite these changes, participants continued to express cravings for the foods they were limiting (Dilley et al., 2025).

SAFETY CONCERNS AND SIDE EFFECTS OF GLP-1 THERAPY

The most common side effects of GLP-1 RA therapies (e.g., semaglutide, tirzepatide, and liraglutide) are gastrointestinal-related, including upper-gastrointestinal side effects such as nausea and vomiting, and lower-gastrointestinal side effects such as diarrhea and constipation, which are generally mild to moderate in severity (Wharton et al., 2021; Ghusn & Hurtado, 2024). Additional side effects such as reduced appetite, dyspepsia, and abdominal pain have contributed to treatment discontinuation in clinical trials, including those involving semaglutide (Kushner et al., 2025). Semaglutide has also been linked to an increased incidence of gallbladder-related disorders, particularly cholelithiasis (Kushner et al., 2025). Furthermore, both liraglutide and semaglutide carry higher risks of pancreatitis, bowel obstruction, and gastroparesis compared with bupropion naltrexone (Sodhi et al., 2023). Rare but serious adverse events, such as acute kidney injury, retained gastric contents with aspiration, and possible neuropsychiatric effects and sarcopenia, have also been reported and warrant further investigation (Drucker et al., 2024).

A growing concern associated with GLP-1 RA use is the potential loss of lean mass that can accompany weight reduction. Lean mass encompasses total body weight excluding fat, including muscles, bones, organs, and skin. Because muscle tissue plays a central role in energy metabolism, glucose regulation, and inflammation control, its loss can have significant long-term metabolic implications (Neeland et al., 2024; Prado et al., 2024). Research suggests that 20-50% of total weight loss achieved on GLP-1 RAs and sodium-glucose cotransporter-2 (SGLT2) inhibitors may be attributed to reductions in lean mass, largely due to decreased caloric and protein intake (Sargeant et al., 2019; Stefanakis et al., 2024). Given that a substantial percentage of weight loss on GLP-1 RAs is fat-free mass, effective strategies to preserve muscle are critical. Resistance training enhances muscle mass, strength, and physical function while stimulating muscle protein synthesis, which increases the body's demand for dietary protein. As such, adequate protein intake not only supports muscle growth but also promotes satiety, reduces food intake, and facilitates weight loss (Chavez et al., 2025).

In addition to protein intake, prebiotic fibers, such as oligo-fructose-enriched inulin, have demonstrated anti-inflammatory effects in individuals with T2D, including reductions in interleukin-6, tumor necrosis factor-alpha, and plasma lipopolysaccharide, suggesting a potential role in attenuating inflammation (Dehghan et al., 2014). SCFAs produced by fiber fermentation, specifically butyrate, may also regulate human myotube metabolism, suggesting a possible role in protein synthesis (Tingstad et al., 2025). Interestingly, a prebiotic supplement containing inulin and FOS administered to older adults improved frailty-related outcomes, including exhaustion and handgrip strength, highlighting the potential influence of prebiotics on the gut-microbiota-muscle-brain axis (Buiges et al., 2026).

SAFETY CONCERNS AND SIDE EFFECTS OF GLP-1 THERAPY (CONT.)

With reduced food intake, micronutrient and macronutrient deficiencies are common, and malnutrition is often overlooked in patients with overweight and obesity. A study by Butsch et al. (2025) suggests that over 20% of patients starting GLP-1 RA treatment were diagnosed with a nutritional deficiency within one year. Therefore, supplementation with micronutrients is an important consideration to prevent deficiencies. Common deficiencies in individuals with obesity are vitamin D, vitamin B12, folate, thiamine, iron, and zinc. Insufficient intakes have also been reported for magnesium, calcium, and vitamins A, E, and C (Almandoz et al., 2024). Beyond preventing deficiencies, certain nutrients may provide additional supportive effects. For example, zinc supplementation among individuals with obesity has been shown to support body composition, reduce high sensitivity C-reactive protein, modulate apelin levels, improve markers of insulin resistance, and influence appetite (Khorsandi et al., 2019). Similarly, magnesium supplementation has been shown to improve glycemic indices among overweight subjects, and vitamin D supplementation has been associated with reductions in body fat mass (Mooren et al., 2011; Salehpour et al., 2012).

Additionally, GLP-1 RA therapies may show reduced efficacy in some individuals due to GLP-1 resistance, a condition potentially influenced by gut microbiota dysbiosis. In such cases, discontinuation of therapy is recommended. However, early termination of GLP-1 RA treatment, whether due to intolerance or reduced efficacy, limits long-term therapeutic benefits and poses a barrier to sustained success with these medications (Zeng et al., 2024). Incorporating prebiotics after GLP-1 RA use may provide additional support for satiety, weight management, gut health, and overall metabolic outcomes. For example, research by Li et al. (2010) and Guérin-Deremaux et al. (2011) demonstrated that resistant dextrin may support weight loss, promote satiety, and improve factors associated with metabolic syndrome in overweight and obese individuals. Similarly, Hobden et al. (2021) found that consuming 14 g/day of resistant dextrin over a 4-week period enhanced satiety, suggesting a potential mechanism of action through the modulation of the gut microbiota. Additionally, prebiotics should not be used in replacement, as a treatment, or in the prevention of disease. Overall, further research is needed to understand the effects of prebiotic consumption in individuals who have discontinued GLP-1 therapy.

Overall, maintaining adequate protein and fiber intake is critical to support muscle mass, satiety, and gastrointestinal health, while nutritional supplementation may be necessary to prevent micronutrient deficiencies. Adequate fiber type intake and progressive dietary adjustments also may help support digestive tolerance during GLP-1 RA therapy. These strategies are particularly important during substantial weight loss or reduced food intake and can help mitigate some of the metabolic and safety concerns associated with GLP-1 RA therapy.

PREBIOTICS AND RELATIONSHIP TO GLP-1

Prebiotics in general are linked to GLP-1 through their ability to modulate the gut microbiota and enhance the production of SCFAs, including acetate, propionate, and butyrate, during fermentation in the large intestine. These SCFAs stimulate the secretion of satiety hormones such as GLP-1 and peptide YY (PYY), while also conferring additional health benefits, including promotion of beneficial gut bacteria, suppression of pathogenic bacteria, modulation of gut barrier permeability, and support of immune function (Gezer & Okburan, 2021).

PREBIOTICS AND GLP-1 REGULATION

The gut microbiome plays a central role in modulating intestinal hormone signaling, including the secretion of GLP-1. This connection highlights a strong link between diet quality, microbial composition, and appetite regulation. One of the most studied dietary factors influencing this relationship is prebiotics, which are non-digestible food components that feed the gut microbiota, resulting in health benefits to the host (Deehan et al., 2024). Through microbial fermentation in the colon, prebiotics contribute to SCFA production. These metabolites contribute to enhanced glucose and lipid metabolism and stimulated satiety hormones, including GLP-1. Common examples of prebiotics include fructans (such as fructo-oligosaccharides (FOS), oligofructose, and inulin), galactans (such as galacto-oligosaccharides (GOS)), resistant starch (RS) types 2 and 3 (RS2 and RS3), non-starch polysaccharides (such as beta-glucans), and several emerging compounds with similar functional properties (Gezer & Okburan, 2021).

The relationship between prebiotics and GLP-1 in the context of metabolic health lies in the ability of prebiotics to enhance SCFA production. Prebiotics are resistant to digestion in the human small intestine due to the absence of appropriate enzymes capable of breaking them down, allowing them to reach the large intestine, where they are fermented by the gut microbiota through carbohydrate-active enzymes. This fermentation produces SCFAs, which are partly utilized by the microbiota and act as key signaling molecules. SCFAs bind to G-protein-coupled receptor 41 (GPR41) and 43 (GPR43), highly expressed in enteroendocrine L-cells, thereby stimulating the release of anorexigenic hormones, including GLP-1 (Brown et al., 2003; Zeng et al., 2024).

PREBIOTICS AND GLP-1 REGULATION (CONT.)

The effect of prebiotics in stimulating GLP-1 secretion has been demonstrated in both preclinical and clinical studies. In preclinical studies, Makki et al. (2023) showed that mice fed a Western diet enriched with oligofructose exhibited increased gut bacteria and produced 6α-hydroxylated bile acids, which activate G protein-coupled bile acid receptor 1 (GBPAR1) and stimulate GLP-1 receptor activity. Similarly, Hira et al. (2018) reported that male rats supplemented with resistant maltodextrin or FOS had elevated GLP-1 production, with no significant difference between treatments. Zhou et al. (2008) demonstrated that RS2 supplementation in murine models enhanced GLP-1 and PYY secretion, promoted fermentation, SCFA production, and improved glucose tolerance. Cani et al. (2005) also reported that oligofructose supplementation increased GLP-1 levels in the colon. Interestingly, Xiao et al. (2022) showed that the synbiotic combinations of Lactobacillus paracasei LC-37 with isomaltooligosaccharide (IMO) and Bifidobacterium animals MN-Gup with GOS enhanced GLP-1 secretion in vitro, surpassing the effects of the respective probiotics alone.

In humans, evidence suggests that prebiotics may support GLP-1 secretion and other satiety-related markers. Hamilton and Bomhof (2023) showed that oligofructose-enriched inulin supplementation after exercise led to reduced perceived hunger, increased plasma GLP-1 and PYY, and reduced acyl-ghrelin, supporting the satiating potential of prebiotics. Similarly, Chu et al. (2025) reported that fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) in combination with metformin may reduce postprandial glycemic indices and increase GLP-1 secretion in prediabetic individuals, with these effects being potentially a result of gut microbiome modulation. Ye et al. (2015) demonstrated that resistant maltodextrin stimulated the production GLP-1 and PYY and affected perceptions of hunger and appetite among healthy subjects. Similarly, a randomized, double-blind, placebo controlled, crossover trial in healthy, normal-weight subjects showed that consumption of 40 g of high amylose RS2 compared to an energy-matched control starch, with three identical diets per day, significantly increased active GLP-1 levels at 30 minutes during a meal tolerance test and serum acetate levels after 4 weeks (Zhang et al., 2019). This compares to rodent models that have demonstrated circulating GLP-1 levels sustained in a day-long manner following RS2 supplementation (Zhou et al., 2008). In addition, RS2 reduced visceral and subcutaneous fat mass, and beneficially modulated gut hormones and gut microbiota composition (Zhang et al., 2019). Calikoglu et al. (2021) reported that prebiotic-probiotic supplementation (yogurt with inulin and oligofructose) led to increased GLP-1 and PYY compared to probiotic supplementation alone in patients who had undergone RYGB surgery. Paradoxically, there was an increase in anthropometric markers and appetite in the early post-operative period among participants supplementing with the prebiotic, when theoretically the latter was anticipated. This underscores important gaps in the literature and how further research is needed in this population, as factors related to RYGB may interfere with achieving the anticipated improvements in anthropometric outcomes.

STRATEGIES FOR USING PREBIOTICS IN CONJUNCTION WITH GLP-1 RAS

Prebiotics have several applications and may provide benefits when taken orally alongside GLP-1 therapies. They can help promote stool consistency and frequency, support blood glucose control, and modulate immune responses (Kellow et al., 2013). Meanwhile, up to 50% of GLP-1 RA users experience gastrointestinal-related adverse events, including nausea, vomiting, diarrhea, eructation, and constipation, which can negatively impact patient compliance and quality of life (Despain & Hoffman, 2024). These adverse events are dose-dependent and most frequently occur during initial treatment phases (Kim & Yoo, 2025). A review by Ghusn & Hurtado (2024) evaluated studies on GLP-1 RA medications, including three pivotal trials of liraglutide, semaglutide and tirzepatide, to assess tolerability, side effects, and associated risks. The review highlighted the prevalence of adverse events per medication, with 80.3% of participants receiving liraglutide experiencing adverse events, 89.7% with semaglutide, and 78.9–81.8% with tirzepatide, with gastrointestinal being the most common.

Studies suggest that certain prebiotics may help improve gastrointestinal disturbances such as diarrhea and constipation in healthy individuals (Bush et al., 2023; Schoemaker et al., 2022). While these effects have not yet been specifically demonstrated in GLP-1 RA users, the evidence point to a potential role for prebiotics in alleviating similar gastrointestinal side effects commonly associated with GLP-1 RA therapies. Bush et al. (2023) demonstrated that supplementation with 3.5 g/day of potato-based RS2 significantly reduced diarrhea- and constipation-related bowel movements compared with placebo. Similarly, Schoemaker et al. (2022) reported that daily supplementation with 11 g of GOS significantly increased stool frequency in individuals with self-reported constipation (≤3 stools per week) and modulated gut microbiota, with significant increases in Anaerostipes hadrus and dose-dependent elevation in fecal Bifidobacterium. Also, Silk et al. (2009) and Vulevic et al. (2018) demonstrated less bloating and abdominal pain in adults with irritable bowel syndrome (IBS) or those with a higher probability of functional bowel disorder who were on a GOS supplementation for at least two weeks. Basturk et al. (2016) found that supplementation with a synbiotic containing Bifidobacterium lactis B94 with inulin improved some gastrointestinal related symptoms in children with IBS, including belching, abdominal fullness, bloating, constipation, and mucus in stools. These benefits were more pronounced than those observed with prebiotic supplementation alone. However, research remains limited regarding the effects of prebiotics on other symptoms such as nausea and vomiting. In addition to prebiotics, other strategies may alleviate GLP-1 RA-related side effects. According to Gorgojo-Martínez et al. (2022), nausea can be eased by consuming light foods such as crackers or apples, drinking mint or ginger beverages shortly after dosing, and avoiding strong odors. Vomiting may be minimized through adequate hydration and smaller, more frequent meals. To manage diarrhea, recommendations include maintaining hydration, avoiding laxatives, coffee, alcohol, and sugar alcohols, and temporarily reducing high-fiber intake until symptoms subside. For constipation, strategies include adequate fiber and fluid intake, regular physical activity, and a balanced diet.

MICROBIOME MODULATION: A POTENTIAL MECHANISM FOR ENHANCING SATIETY AND PROMOTING WEIGHT LOSS

By modulating the gut microbiome, prebiotics represent a novel dietary strategy with potential benefits for metabolic outcomes, particularly in obesity and related conditions. Importantly, nutritional supplements such as prebiotics cannot claim to treat or prevent diseases such as obesity. Nonetheless, increasing evidence support their positive effects on the gut microbiome and various key metabolic markers. For example, Li et al. (2024) demonstrated that RS2 supplementation significantly improved body weight, fat mass, waist circumference, and glycemic indices in overweight or obese patients. Following RS supplementation, significant increases were observed in beneficial gut bacteria, including Bifidobacterium adolescentis, Bifidobacterium longum, and Ruminococcus bromii, which are involved in the metabolism of energy, lipids, and carnitine. This study highlighted the importance of adequate resistant starch intake for improving the metabolic profile of overweight and obese individuals. Similarly, Hiel et al. (2020) reported that 16 g/day of inulin led to reduced body weight, diastolic blood pressure (DBP), insulin levels, and aspartate aminotransferase compared to placebo in obese individuals. These effects were accompanied by microbiota changes, including increased Bifidobacterium and Catenibacterium and decreased Desulfovibrio and Clostridium sensu stricto, linked to improvements in anthropometric outcomes. Zhang et al. (2024) demonstrated that a synbiotic mixture containing GOS significantly improved glycemic indices, including hemoglobin A1C (HbA1c), serum insulin, homeostatic model assessment of insulin resistance (HOMA-IR), while also increasing the relative abundance of Bifidobacterium compared to the probiotic blend alone in T2D patients. Notably, GLP-1 levels were significantly increased in both groups after the interventions. Another study (Vulevic et al. 2013) reported that supplementation with a GOS mixture in overweight adults increased fecal bifidobacteria and secretory immunoglobulin A (IgA), lowered plasma C-reactive protein, calprotectin, insulin, total cholesterol (TC), triglycerides (TG), the ratio of TC to high-density lipoprotein cholesterol (HDL), highlighting the role of GOS in reducing risk factors associated with metabolic syndrome. Lastly, a study by Sergeev et al. (2020) found that supplementation with a synbiotic containing GOS and probiotics led to improvements in body composition, increased abundance of Bifidobacterium and Lactobacillus, and reduced blood glucose over time, which was associated with increasing Lactobacillus among other positive health effects in overweight and obese individuals. Notably, these individuals were also enrolled in a weight loss program and followed dietary modifications.

Overall, evidence indicates that prebiotic supplementation can enhance GLP-1 and PYY secretion while reducing acyl-ghrelin, leading to improved hunger control and satiety following exercise or RYGB surgery. Prebiotics alone, without concurrent GLP-1 therapy, have also been shown to improve glycemic indices among individuals with prediabetes and T2D. Additionally, prebiotic intake can positively impact anthropometric markers including body weight, fat mass, waist circumference, and other markers like DBP, insulin levels, and among overweight or obese individuals. These benefits were observed after supplementation with RS, inulin, and GOS.

PRACTICAL IMPLICATIONS AND FUTURE DIRECTIONS

Gaps remain in the literature regarding nutrition, diet, and lifestyle education for individuals using GLP-1 medications. Health professionals working with these patients emphasize the importance of personalizing dietary recommendations to align with individual needs and lifestyles (Dispain & Hoffman, 2024).

For individuals receiving anti-obesity medications, the recommended daily fiber intake is 21-25 g for women and 30-38 g for men, ideally from whole grains, vegetables, nuts, and seeds (Almandoz et al., 2024). When dietary intake is insufficient, supplementation may be appropriate, with gradual increases and adequate fluid intake to minimize constipation. The World Gastroenterology Organization Global Guidelines (WGO) recommend increasing dietary fiber gradually over several weeks, rather than days, to a target dose of 20-30 grams daily, allowing the body to adjust (WGO, 2018). Although intake targets for specific prebiotics such as FOS, GOS, and inulin vary across the literature, emerging evidence suggests potential benefits when these prebiotics are combined with nutrition counselling. For example, Mayengbam et al. (2025) reported that patients with metabolic dysfunction-associated steatotic liver disease receiving oligofructose-enriched inulin alongside weight loss counselling experienced significantly reduced hunger and desire to eat compared with those receiving counselling alone. Furthermore, tolerance to prebiotic fibers can differ between individuals; therefore, careful selection and dosing are key to maximize benefits while minimizing potential gastrointestinal discomfort (Mysonhimer & Holscher, 2022). Further investigation into the fermentation rates and digestive tolerance of various prebiotic types could provide valuable insights for future clinical applications.

Another gap in the literature is that, although emerging evidence suggests prebiotics can enhance GLP-1 secretion and promote satiety, these effects may not extend to individuals with metabolic conditions such as obesity or T2D. For example, Birkeland et al. (2021) assessed inulin-type fructans in patients with T2D and observed no significant improvements in post-prandial GLP-1, GLP-2, or glycemic indices; post-prandial GLP-1 levels were even reduced compared with controls. Similarly, Medawar et al. (2023) reported that inulin supplementation in individuals with obesity failed to increase GLP-1 or other satiety-related biochemical markers, although notable shifts in gut microbiome composition were observed.

These findings highlight the need for further investigation of prebiotic interventions in populations with metabolic dysfunction. Future research should explore whether specific prebiotic fibers are superior to others in promoting GLP-1 secretion, and whether co-administration with GLP-1 RA medications enhance satiety and mitigate treatment-related side effects. The delivery vehicle also warrants attention: while most studies have incorporated fiber into dosage formats such as beverages, Emilien et al. (2020) found that soluble fiber dextrin delivered in a food matrix did not affect GLP-1 or satiety markers in healthy adults, suggesting that formulation may influence efficacy.

CLAIM ENVIRONMENT SURROUNDING PREBIOTICS AND GLP-1 WITHIN THE MAJOR REGULATORY DOMAINS

The regulatory environment for claims linking prebiotics and GLP-1 therapies require a cautious approach. Current evidence on the safety and efficacy of prebiotic supplementation in individuals using GLP-1 RA medications is limited; therefore, only broad, well-established claims are advisable. This principle applies across categories, including foods, natural health products/dietary supplements, and nutraceuticals containing prebiotic ingredients. Key regulatory considerations include:

- **Avoid positioning prebiotics as substitutes for, or enhancers of, GLP-1 RA medications, as this may classify the product as a pharmaceutical/drug.**
- **Do not reference specific GLP-1 medications (e.g., Ozempic) in prebiotic-related claims.**
- **Refrain from using the term "GLP-1" in claims unless necessary.**
- **Focus on well-substantiated health benefits and claims regarding prebiotics' role in gastrointestinal health, regularity, and related outcomes.**
- **Acknowledge that prebiotics may offer complementary benefits when taken alongside GLP-1 therapies, while advising consultation with a health care professional before use.**
- **Recommend gradual introduction of prebiotics with adequate fluid intake to minimize gastrointestinal side effects.**

CONCLUSIONS

In conclusion, prebiotics exert many of their health benefits through the production of SCFAs, which support gut function and promote GLP-1 secretion. GLP-1 plays a central role in metabolic regulation by influencing glucose and lipid metabolism, delaying gastric emptying, and, most notably, reducing appetite and inducing satiety. Accordingly, GLP-1–based therapies have become widely used for T2D and obesity management, though they are often associated with gastrointestinal side effects, such as diarrhea and constipation, symptoms that prebiotic consumption may help mitigate. Although preclinical studies demonstrate that prebiotics stimulate GLP-1 secretion and modulate the gut microbiome, findings in obese populations remain mixed, underscoring the need for further clinical research. For patients receiving GLP-1 therapies, maintaining adequate daily fiber intake is essential alongside sufficient protein intake. Nutritional supplementation should be considered when portion sizes are reduced or dietary sources are insufficient with adequate hydration to help manage potential side effects associated with GLP-1 RAs. Importantly, prebiotics should not be positioned as substitutes for GLP-1-based medications but may serve as complementary interventions. From a regulatory perspective, caution is warranted when framing claims, and explicit reference to GLP-1 or branded products should be avoided.

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