Review

GLP-1 Receptor Agonists for Weight Control: Emerging Insights from Clinical Trials and Future Perspectives

Jiayao Lv [1,†], Shiyi Zhang [1,†], Yizhe Qu [2], Youshen Cao [3], Jiayi Zhang [1], Xiaoshuang Dai [4], and Lin Shi [1,*]

[1] School of Food Engineering and Nutritional Science, Shaanxi Normal University, Xi'an 710062, China
[2] School of Physical Education, Shaanxi Normal University, Xi'an 710062, China
[3] Physical Education Department, Xi'an University of Finance and Economics, Xi'an 710100, China
[4] Xbiome, Scientific Research Building, Room 907, Tsinghua High-Tech Park, Shenzhen 518055, China
* Correspondence: linshi198808@snnu.edu.cn
† These authors contributed equally to this work.
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Abstract: Background: The rising global prevalence of obesity presents a major public health concern. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) emerge as promising therapeutic agents, showing substantial efficacy in weight reduction in clinical settings. Methods: This review synthesizes data from 1565 clinical trials (Phases I–IV) sourced from the Trialtrove database (November 2024), covering nine GLP-1RAs: mono-agonists (beinaglutide, liraglutide, semaglutide, orforglipron), dual agonists (tirzepatide, mazdutide, survodutide, cagrilintide), and the triple agonist retatrutide. We analyzed trial phase distributions and updated current evidence on safety and efficacy across populations, emphasizing both therapeutic promise and current limitations, particularly the scarcity of long-term and comparative effectiveness data as well as associated adverse effects. Future research must prioritize comparative effectiveness, long-term safety, and personalized strategies for GLP-1RAs, addressing evidence gaps in special populations and treatment individualization. Conclusion: This review synthesizes current evidence on the safety and effectiveness of GLP-1RAs in weight management and potential cardiovascular protection. Further trials are imperative to clarify long-term outcomes, individual variability, and specific adverse effects across diverse populations.

Keywords: GLP-1 receptor agonists; clinical trials; weight loss; adverse events; personalized medicine

1. Introduction

Obesity is a global public health issue deeply interconnected to various non-communicable diseases [1]. With the rapid development of the global economy, obesity prevalence has risen at an alarming rate. The World Health Organization estimates that by 2025, approximately 167 million people (adults and children) will face health problems due to overweight or obesity, underscoring its status as a major public health challenge. Lifestyle management is crucial for treating obesity, resulting in an average weight loss of 2% to 9% of initial body weight within a year. However, it often leads to weight regain due to counter-regulatory physiological changes that disrupt metabolism and elevate appetite [2]. Anti-obesity medications address appetite dysregulation related to obesity, offering significant potential for achieving and maintaining weight loss.

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are pioneering agents in the rapidly evolving and highly promising field of nutrient-stimulated hormone-based therapies [3,4]. GLP-1RAs, particularly liraglutide, semaglutide, beinaglutide, were initially introduced for type 2 diabetes (T2D) treatment and have more recently received approval from both the U.S. Food and Drug Administration and the National Medical Products Administration of China for treating obesity [5].

With the understanding of the neurobiology of obesity rapidly expanding, these emerging entero-endocrine and endo-pancreatic agents combined or co-formulated with GLP-1RAs herald a new era of targeted, mechanism-based treatment of obesity. In this aspects, dual GLP-1R/glucose-dependent insulinotropic polypeptide receptor (GIPR) peptide agonists, i.e., tirzepatide, mazdutide, survodutide and cagrilintide, and retatrutide, a novel triple agonist of GIP/GLP-1/glucagon receptors have gain great attentions due to their outstanding weight-loss efficacy and great medication adherences. Moreover, the potential of GLP-1RAs extends beyond weight loss to include

improvements in cardiometabolic parameters. A systematic review and meta-analysis demonstrated that GLP-1RAs improved cardiovascular risk factors such as blood pressure and lipid profiles in obese individuals without diabetes [6].

The present review summarizes clinical trials of GLP-1RAs and polyagonists for weight loss in patients with obesity or overweight: an updated systematic review retrieved from INFORMA Pharmaprojects database (https://clinicalintelligence.citeline.com/) on 12 November 2024. Drugs include monotherapy GLP-1RAs (beinaglutide, liraglutide, semaglutide and orforglipron), dual receptor agonists (tirzepatide, mazdutide, survodutide and cagrilintide), and retatrutide (Table 1). We reviewed the current evidence on their clinical efficacy, pharmacological applications and associated adverse events of each drug, discussed potential challenges, limitations and future developments, allowing for a comprehensive assessment of the efficacy and safety of GLP-1 agonists across diverse populations.

2. Hormones Acted by Agonists for Weight Control

GLP-1, GIP, amylin, and glucagon are key peptide hormones that regulate energy balance, appetite and glucose homeostasis [4,7]. Their coordinated actions form a critical gut-pancreas-brain axis, which has become a major therapeutic target especially for weight management and T2D [8].

Specifically, GLP-1 and GIP are incretin hormones secreted from intestinal L- and K-cells, respectively, in response to nutrient intake. Both enhance glucose-dependent insulin secretion from pancreatic β-cells. GLP-1 suppresses glucagon release, delays gastric emptying, and acts centrally to promote satiety and reduce appetite. GIP also contributes to lipid metabolism and may modulate fat storage, though its role in weight regulation is complex and context-dependent. Amylin is co-secreted with insulin by β-cells in pacraces. It complements incretin action by suppressing glucagon secretion, slowing gastric emptying, and reducing food intake via central nervous system pathways. Besides, glucagon, secreted from pancreatic α-cells regulates insulin by stimulating hepatic glucose production during fasting. While traditionally viewed as a hyperglycemic hormone, its ability to promote energy expenditure makes it a relevant target for weight loss therapies when strategically combined with satiety-enhancing hormones.

Harnessing their synergistic actions offers promising avenues for treating obesity and metabolic diseases. Therapeutically, multi-agonist molecules that simultaneously target receptors for these hormones represent a breakthrough. The interplay between these hormones, particularly in the context of dual or triple agonists, underscores the complexity of their mechanisms and the potential for synergistic therapeutic effects.

3. Clinical Landscape of Clinical Trials

The landscape of 1565 clinical trials for 9 medications conducted between 1999 and 2025, across 71 countries, was clarified (Tables S1–S10). Trials were predominately sponsored by United States, Demark, China and Switzerland (Figure 1). The annual number increased steadily over time (Figure S1). Trials of liraglutide (n = 766, 48.94%) is most dominant, followed by semaglutide (n = 544, 34.76%) and tirzepatide (n = 110, 7.03%). Trials of benaglutide, cagrilintide, retatrutide, survodutide, and mazdutide are relatively limited, accounting for less than 2% of all investigated drugs globally (Figure 1). The majority of clinical trials were conducted in the United States (ranging from 10% to 23%), followed by Europe (ranging from 10% to 14%) and Asia (ranging from 10% to 14%) for all drugs, except for mazdutide and benaglutide (Figure S2, Table S1). A total of 57% trials of mazdutide were conducted in Asia, particularly in China. Trials of benaglutide were conducted exclusively in China.

As to clinical phase, drugs exhibit distinct statuses. Specifically, a majority of trials for benaglutide (73.1%), liraglutide (63.8%), and semaglutide (35.5%) have advanced to phase IV investigations (Figure 2). But half of the registered Phase IV trials are currently in the planning stage, emphasizing long-term safety, efficacy, and expanding approved indications. Retatrutide, cagrilintide, survodutide, and orforglipron are predominantly (>30%) in the phase III investigations worldwide. It is noteworthy that a significant number of trials are in early Phase I investigations, ranging from 9.9% (liraglutide) to 54.2% (survodutide), indicating ongoing research efforts to evaluate their safety profile and therapeutic efficacy. Despite numerous completed trials, particularly for semaglutide and liraglutide, there are a large number of trials were initiated or planned within the past three years, indicating the rapid progress and future potentials of GLP-1RAs.

Moreover, trials of retatrutide, cagrilintide, survodutide, mazdutide, tirzepatide and orforglipron included both adults and elderly people (Figure 2). But semaglutide and liraglutide, two dominant drugs were seldomly tested among elderly patients. Data on safety and efficacy profiles of all medications for children younger than 12 years are extremely insufficient. Obesity during childhood and adolescence have been associated with an increased

risk of mortality from cardiovascular diseases, diabetes and certain types of cancers in adulthood [9]. It is thus an urgent time for framing clinical trials that treats obesity in children.

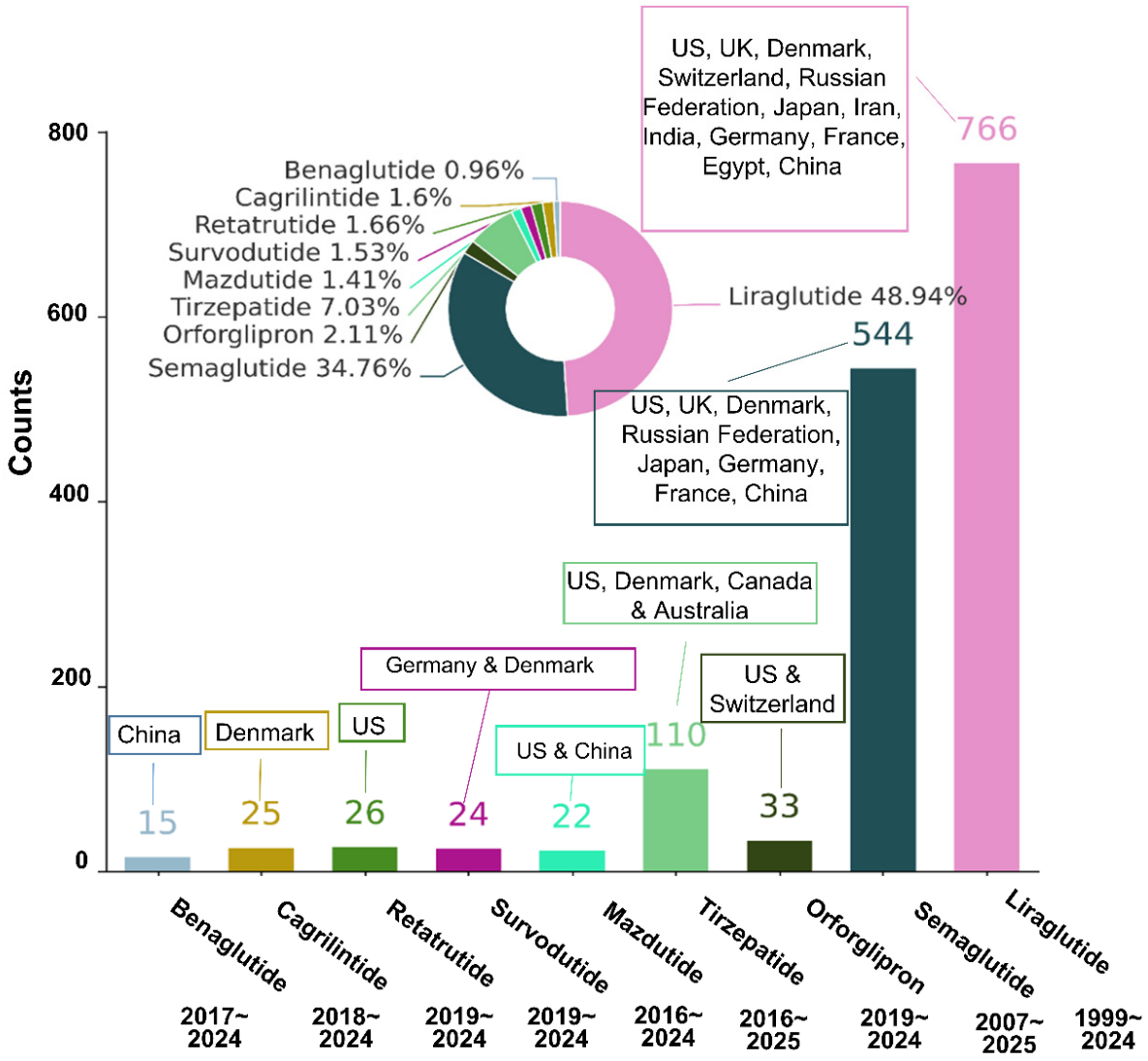

Figure 1. Characterization of clinical trials and sponsoring entities for nutrient-stimulated hormone-based medications. The analysis encompasses GLP-1 receptor agonists (beinaglutide, liraglutide, semaglutide, orforglipron), dual receptor agonists (tirzepatide, mazdutide, survodutide, CagriSema), and the triple receptor agonist retatrutide.

Figure 3 highlights the carious diseases targeted by each drug in clinical settings, showcasing its broad applicability across a diverse area such as metabolic/endocrinology, central nervous system, cardiovascular and autoimmune/inflammation. Among those, obesity and T2D are dominant diseases. Besides, there are ongoing researches about the application of retatrutide on renal disease treatment as well as cagrilintide and survodutide on non-alcoholic fatty liver disease, highlighting the significant potential to enhance therapeutic outcomes and broaden its scope of application.

We also conducted an in-depth analysis of the scenarios where therapy is used either as monotherapy or in combination with other therapeutic strategies. The data indicate that retatrutide, survodutide, mazdutide, and orforglipron are primarily tested as monotherapy, whereas cagrilintide was predominantly tested in combination with other therapies, in particularly with semaglutide (Figure S3). Despite the well-established effects of lifestyle behaviors on obesity and the efficacy of anti-obesity medications, only 6 and 11 trials were observed to investigate the potential interaction between intensive lifestyle modifications and semaglutide and liraglutide, respectively. No studies have been conducted to examine whether behavioral modifications can outperform these medications or enhance therapeutic outcomes, thereby expanding their potential applications.

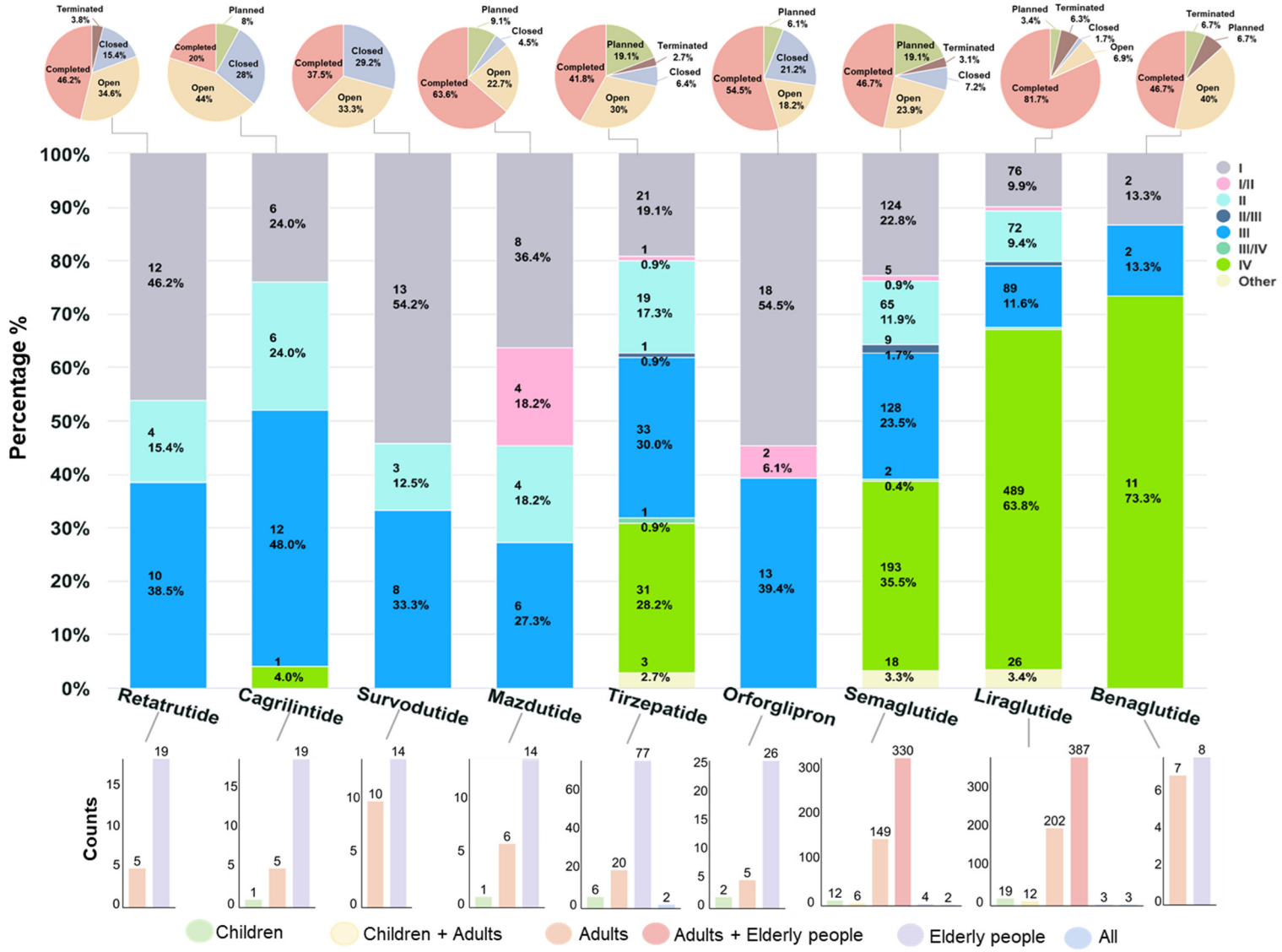

Figure 2. Profile of clinical trials for nutrient-stimulated hormone-based medications, detailing their distribution by phase (I–IV), current status (e.g., recruiting, completed), and enrolled patient age groups. Pie charts illustrate the status of clinical trials for each drug, showing the proportion of registered trials in the databases that are open (ongoing), planned, completed, terminated, or closed. The bar charts show the number of trials conducted for different population groups, including children, adults, elderly individuals, or their combinations.

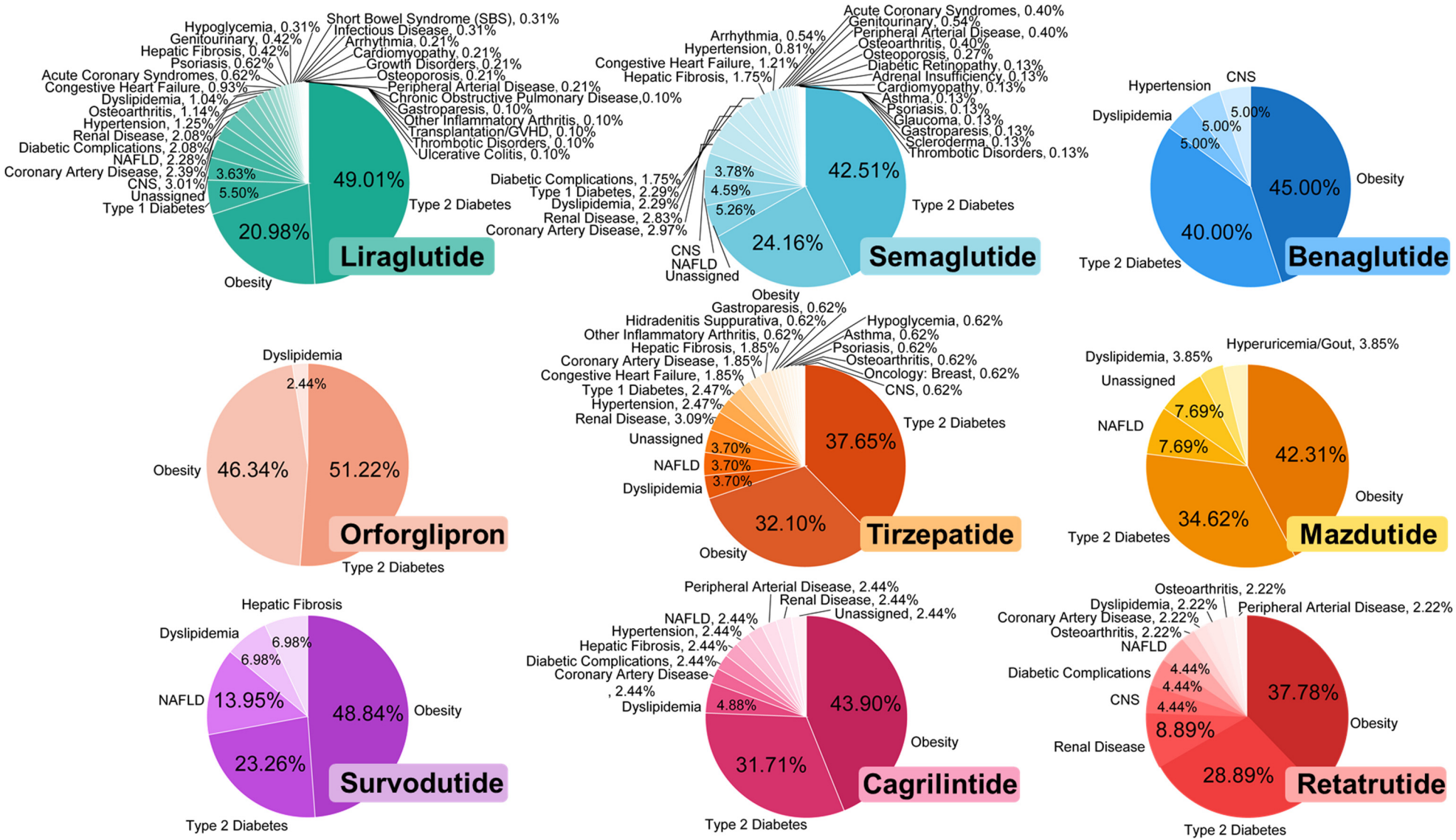

Figure 3. Therapeutic scope of nutrient-stimulated hormone-based medications, presenting the range of diseases targeted by each drug in clinical development.

4. GLP-1 Mono RAs on Weight Loss and Weight Loss Maintenance

4.1. Liraglutide

Liraglutide is a GLP-1RA with 97% homology to human GLP-1 with the half-life to 11 to 15 h. It was initially approved for the treatment of T2D in the United States in 2010 at doses up to 1.8 mg once daily subcutaneous administration. It was subsequently approved for obesity treatment at doses up to 3.0 mg once daily in 2014 for adults (Table 1), and in 2020 for adolescents aged ≥12 years.

A meta-analysis included 18 randomized controlled trials (RCTs) of weight-lowering drugs in 6321 participants from inception to 23 March 2021, reported that, compared with placebo, liraglutide was associated with a 4.7% weight reduction (95%CI, 4.1–5.3%) among adults with obesity [10]. A randomized, open-label, 68-week, phase IIIb trial conducted at 19 US sites in adults with BMI of 30 or greater or 27 or greater with 1 or more weight-related comorbidities, without diabetes, once-daily subcutaneous liraglutide, 3.0 mg reduced the body weight by average 6.4% [11], establishing its efficacy in general obesity management. Notably, the BARI-OPTIMISE assessed the efficacy and safety of liraglutide (3.0 mg) on weight reduction in patients with poor weight loss and suboptimal GLP-1 response at least 1 year after metabolic surgery [12]. Estimated change in percentage body weight from baseline to week 24 was average −8.82 with liraglutide vs. −0.54 with placebo. This 40% efficacy difference between general obesity and post-surgical populations implies potential mechanistic differences in drug response related to the altered gut hormone signaling after bariatric procedures.

Beyond weight reduction in adults, Mashayekhi et al. reported improvements in insulin sensitivity and glycemic control in prediabetic individuals, effects not replicated through diet-induced weight loss alone [13]. Foghsgaard et al., reported that once daily subcutaneous liraglutide 1.8 mg for 52 weeks reduced bodyweight [−3.9 (−6.2 to −1.6) kg], fasting plasma glucose [−0.2 (−0.4 to −0.1) mmol/L] and HbA1c [−2.2 (−3.5 to −0.8) mmol/mol] in women with overweight/obesity and previous gestational diabetes mellitus [14].

In 2020, the SCALE TEENS trial, was conducted among 251 obese adolescents (average age: 14.6 years) to evaluate the effectiveness of 3.0 mg of liraglutide administered daily compared to placebo over a 56-week period. Liraglutide demonstrated a placebo-subtracted weight reduction of 5% [15]. However, there are currently no approved medications for treating non-monogenic, non-syndromic obesity in children aged under 12 years.

Most recently, researchers from the SCALE Kids Trial Group conducted a phase III trial, with a 56-week treatment period and a 26-week follow-up, to evaluate the efficacy and safety of daily subcutaneous liraglutide (3.0 mg or maximum tolerated dose) in children aged 6 to <12 years with obesity (n = 56) compared to placebo (n = 26), in combination with lifestyle interventions [16]. Liraglutide resulted in a 5.8% reduction in BMI, with an estimated difference of 7.4% (95% CI: −11.6 to −3.2) compared to placebo. Besides, a long-term, open-label extension study lasting up to 2 years in patients with T2D found liraglutide to be well-tolerated, and had a lower risk of hypoglycemia compared to glimepiride [17]. However, studies assessing the long-term safety of liraglutide are limited (Table S2). These population-specific responses underscore the importance of tailored treatment approaches when prescribing liraglutide.

4.2. Semaglutide

Semaglutide represents the next-generation of chemically modified GLP-1RAs, which was designed for once-weekly subcutaneous administration with a prolonged half-life of 183 h. Semaglutide was initially approved for the treatment of T2D in the United States at doses up to 1.0 mg once weekly in 2017 and at 2.0 mg once weekly in 2022. It was subsequently approved at doses up to 2.4 mg once weekly for chronic weight management in the setting of obesity for adults in 2021 and in 2022 for adolescents (Table 1). Overall, semaglutide achieves greater than 10% weight reduction in diverse populations. It has shown to reduce energy intake, increase satiety and satiation, and improve glycemic control. Semaglutide was also approved to reduce the risk of major adverse cardiovascular events in adults with established cardiovascular disease and either obesity or overweight in 2024 [18].

The semaglutide Treatment Effect in People with Obesity Program (STEP) constitutes the largest phase 3 double-blinded, randomized, multicenter, and multinational trials evaluating the efficacy, safety, and tolerability of semaglutide 2.4 mg, administered subcutaneously once weekly in adults with obesity or overweight (Table S3). Specifically, STEP 1 (NCT03548935; n = 1961) demonstrated a 14.8% weight reduction in people with obesity or overweight after 68 weeks of semaglutide treatment alongside lifestyle intervention (i.e., 500-kcal per day deficit relative to the estimated total energy expenditure calculated at randomization together with a recommended 150 min per week of physical activity). STEP 2 (NCT03552757; n = 807) used a similar design but enrolled participants with T2D, resulting in a 9.6% weight reduction. STEP 3 incorporated intensive behavioral therapy, including a hypocaloric diet, physical activity, and behavioral counseling, which led to a 16.6% weight loss in people with obesity or overweight. STEP 4 (NCT03548987; n = 902) followed the STEP 1 protocol but included a 20-week run-in period with dose escalation and 4 weeks at the target dose, underscoring sustained efficacy during maintenance. STEP 5 confirmed durable weight loss, with a 12.6% reduction maintained over two years, highlighting its potential for long-term weight management.

Table 1. Summary on the weight loss efficacy, dosages and adverse events of 9 drugs.

Drugs	Targets	Weight Loss Efficacy	Dosage	Duration	GI Adverse Events	Other Adverse Events
Liraglutide	GLP-1	✓ Adults: 4.7–6.4% reduction ✓ Adolescents: ~5% reduction (56 weeks)	3.0 mg S.C. once daily	56–68 weeks	Nausea, vomiting, diarrhea	Pancreatitis (rare), increased risk in rodents
Semaglutide	GLP-1	✓ Adults (Global): 10–15.8% reduction ✓ Adults (East Asian): −14.3% reduction ✓ Adolescents: ~16.1% reduction (68 weeks)	2.4 mg S.C. once weekly or 50 mg P.O. once-daily	68–208 weeks	Nausea, vomiting, diarrhea	Pancreatitis, fat-free mass loss (25–40% of total weight loss), dysesthesia (abnormal skin sensation)
Beinaglutide	GLP-1	✓ Adults: ~6% reduction (16 weeks)	0.1 mg S.C. three times daily	12–16 weeks	Nausea, diarrhea	/
Orforglipron	GLP-1	✓ Adults: 8.6–12.6% reduction (36 weeks)	12–45 mg P.O. once daily	36–72 weeks	Nausea, diarrhea, constipation, vomiting	/
Tirzepatide	GLP-1 and GIP	✓ Adults without T2D: 15–20% reduction (72 weeks) ✓ Adults with T2D: 12.8–14.7% reduction	5–15 mg S.C. once weekly	72–96 weeks	Nausea, vomiting, diarrhea (dose-dependent)	/
Mazdutide	GLP-1 and glucagon	✓ Adults: ~6.22% reduction	2–9 mg S.C. once weekly	24–48 weeks	Nausea, diarrhea, vomiting	/
Survodutide	GLP-1 and glucagon	✓ Adults without diabetes: 6.2–14.9% reduction (46 weeks)	0.6–6.0 mg S.C. once weekly	46–48 weeks	Nausea, diarrhea, vomiting	
Cagrilintide	Amylin and calcitonin	✓ Adults with obesity: 10-17% reduction (with semaglutide)	0.16–4.5 mg S.C. once weekly (alone or with semaglutide)	20–32 weeks	Lower vomiting incidence compared to semaglutide/liraglutide	/
Retatrutide	GLP-1, GIP and glucagon	✓ Adults: 17.5% (24 weeks), 24.4% (48 weeks) reduction	2–12 mg S.C. weekly	24–89 weeks	Nausea, vomiting, diarrhea	/

S.C.: subcutaneous, P.O.: per Os.

The racial composition of STEP 1–5 is primarily white, whereas STEP 6 demonstrated semaglutide's efficacy in East Asian adults, showing superior bodyweight reduction (−8.7% vs. −1.2% with placebo) and visceral fat loss (−40.3 cm^2 vs. −6.4 cm^2) at 68 weeks [19]. STEP TEENS reported significant BMI reduction in adolescents (−16.1% vs. +0.6% with placebo) [20], while STEP 8 established semaglutide's superiority over liraglutide (−15.8% vs. −6.4% weight loss) and higher treatment persistence [11].

In 2024, the SELECT trial, a longest clinical trial comparing the effects of semaglutide versus placebo on weight, demonstrated the safety and durability of semaglutide for weight loss and maintenance in a geographically and racially diverse population of adults in obesity without diabetes [17]. Patients treated with semaglutide across all sexes, races, body sizes, and geographic regions achieved clinically significant weight loss that persisted for 65 weeks and was maintained for up to 4 years. At 208 weeks, semaglutide resulted in mean reductions in weight (−10.2%), waist circumference (−7.7 cm), and waist-to-height ratio (−6.9%) compared to placebo (−1.5%, −1.3 cm, and −1.0%, respectively).

Besides, a randomized, double-blind, placebo-controlled, phase 3 OASIS 1 trial (Oral semaglutide 50 mg taken once per day in adults with overweight or obesity) conducted in nine countries in Asia, Europe, and North America (n = 334), demonstrated a mean weight reduction of 12.7% from baseline over 68 weeks [21]. This efficacy is comparable to that of once-weekly subcutaneous semaglutide (2.4 mg) [22]. Semaglutide holds great promise to be the only GLP-1RA available in both an injectable and an oral formulation for the management of obesity, with similar efficacy and safety profiles affording patients more choices.

4.3. Beinaglutide

Beinaglutide, is a novel recombinant human GLP-1RA with a 100% human protein sequence (7-36 GLP-1), which was approved for the treatment of Chinese patients with T2D in 2016 [23]. The recommended dosage of beinaglutide is 0.1 mg (Table 1), administered three times daily via subcutaneous injection in the upper arm, thigh, or abdomen. The dosage may be increased to 0.2 mg three times daily if the glycemic control is inadequate.

Trials of beinaglutide with published results are limited (Table S4). A 12-week beinaglutide resulted in a 5–10% reduction in body weight among patients with overweight or obesity, with or without T2D [24,25]. The weight regain rate 12 weeks after beinaglutide was only 0.78%. In a phase III trial, a 16-week subcutaneous beinaglutide reduced body weight by average 6% and caused significant greater waist circumference reduction than the placebo in non-diabetic Chinese adults with a BMI of 24–27.9 kg/m^2 and of 28 kg/m^2 or higher [24].

4.4. Orforglipron

Orforglipron (LY3502970), a potent a once-daily oral agent, has a mean half-life ranges from 28.7 to 49.3 h [26], which demonstrates unique advantages including extended half-life, food/water-unrestricted oral administration, and a greater effect on cyclic AMP signaling than on β-arrestin recruitment, compared to other GLP-1RAs.

Efficacy and safety of orforglipron have been reported in Phase I and 2 trials (Table S5): Pratt et al., conducted a double-blind, placebo-controlled Phase I trial involving healthy adults, with BMI ranging from 20 to 40 kg/m^2 and an HbA1c of 47.5 mmol/mol (<6.5%) [26]. The 4-week administration led to a significant weight loss, reaching up to 5.4 kg, whereas the placebo group caused 2.4 kg weight loss. Another Phase I trial evaluated different dosing regimens of orforglipron in people with T2D [26]. Orforglipron led to a mean HbA1c reduction ranging from −1.5% to −1.8% across all doses, compared to a −0.4% reduction with placebo. Additionally, body weight changes ranged from −0.24 kg to −5.8 kg across doses, versus a 0.5 kg increase with placebo.

A phase II multicenter RCT (n = 272, average age, 54.2 years; average BMI, 37.9 kg/m^2) evaluated the weight loss efficacy of orforglipron administration at different doses (12, 24, 36, or 45 mg) versus a placebo for a duration of 36 weeks [27]. Orforglipron led to the mean reduction in weight ranged from −8.6 (95% CI, −10.2 to −6.9) to −12.6 (95% CI, −14.1 to −11.1) at different doses, compared to −2.0 (95% CI, −3.6 to −0.4) for those on a placebo. Moreover, a recent phase 2 trial revealed that orforglipron at doses of 12 mg or greater significantly reduced HbA1c and bodyweight compared with placebo or dulaglutide in adults with T2D treated with diet and exercise [28]. Although mild to moderate gastrointestinal side-effects, such as nausea, diarrhea, constipation and vomiting, were noted, the discontinuation rate due to adverse events ranged from 10% to 17% among participants, which was lower than that observed with liraglutide, thereby supporting the continued clinical development of orforglipron [27].

Systematic validation of orforglipron's therapeutic profile across diverse populations, benchmarked against established therapies, is crucial. According to the Trialtrove database (Table S5), 13 Phase III trials of orforglipron have been conducted. Among these, 11 trials involved adults, while 2 focused on adolescents and children under 17 years old, notably the ADVANCE (NCT06672549) and ADVANCE-ATTAIN-ADOLESCENTS

(NCT06672939) trials. The ATTAIN trials evaluate the weight management potential of once-daily oral orforglipron, with ATTAIN-1 designed to enroll 3,000 participants with obesity or overweight from the US, Europe, and Asia who will receive orforglipron or placebo for 72 weeks, expected to conclude in September 2027 (NCT05869903). ATTAIN-2 will evaluate efficacy and safety versus placebo in adults with obesity or overweight and T2D (NCT05872620), while ATTAIN-J (NCT05869903) focuses on Japanese adults with obesity, including 236 participants with BMI 27–35 kg/m^2 and at least two comorbidities or BMI ≥ 35 kg/m^2 with at least one comorbidity. ATTAIN-MAINTAIN (NCT06584916) will assess weight loss maintenance in 300 participants with obesity or overweight. Additionally, the ACHIEVE trials (1–5; NCT05971940, NCT06192108, NCT06045221, NCT05803421, NCT06109311) focus on T2D patients, evaluating orforglipron versus insulin glargine, semaglutide, or dapagliflozin in adults with T2D and obesity or overweight, while ACHIEVE-J (NCT06010004) assesses long-term safety in Japanese adults with T2D and inadequate glycemic control.

5. Dual RAs on Weight Loss and Weight Loss Maintenance

5.1. Tirzepatide

Tirzepatide is a long-acting, single-molecule GIP/GLP-1RAs with a 117 h half-life with weekly subcutaneous administration. Tirzepatide was approved for the indication of T2D by the FDA and by the European Medicines Agency in 2022 based on data from the SURPASS Diabetes trials [29–31]. It was subsequently approved for obesity treatment in adults in 2023 [8]. The efficacy and safety of tirzepatide for weight reduction in individuals were tested in the global phase III SURMOUNT program (i.e., SURMOUNT 1–5), including a series of double-blind, randomized, controlled trials. Results are recently published.

The SURMOUNT-1 investigated the effect of tirzepatide for weight reduction in 2,539 individuals with obesity without T2D, who were randomized to receive tirzepatide 5 mg, 10 mg, or 15 mg, or placebo for 72 weeks [32]. Over 50% participants underwent tirzepatide 10 mg or 15 mg lost ≥ 20% body weight versus 3.1% achieving this target in the placebo group. The SURMOUNT-2 trial evaluated the impact of tirzepatide on weight management in 938 individuals with obesity and T2D [33]. The mean body weight reduction with tirzepatide 10 mg and 15 mg was −12.8% and −14.7%, respectively, significantly greater than the −3.2% reduction observed with placebo. More than 70% of participants treated with tirzepatide achieved a bodyweight reduction of 5% or more, compared to those receiving placebo.

The SURMOUNT-3 demonstrated a significant additional reduction in body weight with tirzepatide at 10 or 15 mg following intensive lifestyle interventions in 806 adults with overweight or obesity [34]. Tirzepatide reduced 18.4% body weight compared to a 2.5% reduction in the placebo group. Among participants receiving tirzepatide, 87.5% achieved an additional weight reduction of ≥5%, whereas only 16.5% of those in the placebo group met this criterion.

In 2023, the SURMOUNT-4 trial reported, for the first time, the long-term benefits of tirzepatide in maintaining weight reduction among 670 participants with obesity or overweight [35]. These participants completed 36 weeks of tirzepatide treatment and achieved a significant weight loss of approximately 20.9%. During the 52-week follow-up period, those who discontinued tirzepatide experienced substantial weight regain. In contrast, participants who continued treatment maintained their initial weight reduction and further reduced their weight by an average of 4.5%.

Most recently, the SURMOUNT-J [36] and SURMOUNT-CN [37] trials, demonstrated the efficacy and safety profiles of tirzepatide in Japanese adults with obesity (BMI ≥ 25 kg/m^2 and excessive fat accumulation) and in Chinese adults with BMI ≥ 28 or BMI ≥ 24 accompanied by at least one weight-related comorbidity, excluding diabetes. Results consistently indicate that once-weekly administration of 10 mg or 15 mg of tirzepatide led to statistically significant and clinically relevant weight loss, accompanied by an acceptable safety profile, in East Asian populations.

Ongoing clinical programs are currently evaluating the effectiveness of tirzepatide for combating obesity in various populations, while also making comparisons with other available pharmacotherapies (Table S6). The SURMOUNT-5 (NCT05822830) aims to compare the efficacy of tirzepatide and semaglutide, specifically targeting individuals with obesity. Another noteworthy trial, the SURMOUNT-MAINTAIN study (NCT06047548), aims to explore the potential for long-term weight maintenance following an initial weight loss phase achieved over a 60-week open-label period using tirzepatide. SURMOUNT-Adolescents (NCT06075667) and SURMOUNT-Adolescents-2 (NCT06439277) studies are phase III trials that will investigate the safety and efficacy of tirzepatide specifically in adolescents aged 12 to 17 years who are affected by obesity, expanding the understanding of how this treatment can be beneficial for younger populations. The outcomes of these studies are anticipated to contribute significantly to the ongoing discourse on effective weight management interventions.

5.2. Mazdutide

Mazdutide (IBI362 or LY3305677), a dual agonist targeting both GLP-1R and glucagon, exhibits an extended half-life of 150.9 to 403.5 h. It is recommended for subcutaneous administration once weekly (Table 1). A meta-analysis of five phase I and two phase II RCTs, involving 680 participants, demonstrated that mazdutide was more effective in reducing body weight (mean difference = −6.22%, 95% CI: −8.02% to −4.41%) than placebo [38]. Additionally, mazdutide improved obesity-related indicators, including blood pressure (SBP: −7.57 mmHg; DBP: −2.98 mmHg), total cholesterol, triglycerides (TC: −16.82%; TG: −43.29%), and both low- and high-density lipoproteins. Notably, subgroup analyses revealed greater weight loss in non-diabetics and with longer treatment duration (24 weeks), though gastrointestinal AEs were more frequent with mazdutide.

A total of 22 registration records for RCTs using mazdutide were identified in the Trialtrove database, including only 6 phase III trials (Table S7). The ongoing phase III GLORY program explores its anti-obesity efficacy through distinct dosing strategies: the GLORY-1 (NCT05607680) enrolled 600 participants with BMI ≥ 28 kg/m^2, or ≥24 kg/m^2 and at least 1 concomitant cardiometabolic comorbidity. Participants will receive a weekly subcutaneous dose of 2 mg mazdutide for 4 weeks and thereafter 4 mg for 44 weeks or 2 mg for 4 weeks, followed by 4 mg for 4 weeks, followed by 6 mg for 40 weeks. The GLORY-2 (NCT06164873) extends this evaluation to a 9 mg dose in 450 participants (BMI ≥ 30 kg/m^2) with a BMI ≥ 30 kg/m^2 and with at least 1 unsuccessful dietary effort to lose weight. The DREAMS phase III programs (DREAMS 1-2; NCT05628311 and NCT05606913), represent multicenter, randomized, double-blind, placebo-controlled studies targeting on T2D patients. The DREAMS 1 will evaluate the efficacy and safety of mazdutide in Chinese people with T2D or with poor glycemia control only through diet and exercise. The DREAMS 2 will compare mazdutide vs. Dulaglutide as add-on to Metformin and/or sodium-glucose cotransporter 2 (SGLT2) inhibitor or TZD in subjects with T2D. Potential results from those trials could position mazdutide as a versatile therapeutic agent across the diverse metabolic diseases.

5.3. Survodutide

Survodutide (BI 456906), is a glucagon/GLP-1 dual RA with a half-life of 100 h in humans. Two randomized, double-blind, placebo-controlled, dose-finding phase II trials assessed efficacy and safety profiles of survodutide for weight control. The first trial was conducted across 43 centers in 12 countries [39]. Participants (aged 18–75 years, BMI ≥ 27 kg/m^2, without T2D) were randomized to receive once-weekly subcutaneous survodutide (0.6, 2.4, 3.6, or 4.8 mg) or placebo for 46 weeks, which included a 20-week dose-escalation phase and a 26-week maintenance period. The treatment resulted in dose-dependent weight loss, ranging from 6.2% to 14.9%, compared with 2.8% in the placebo group. However, gastrointestinal adverse events were more frequent with survodutide (75% vs. 42% with placebo). Another study assessed a 16-week treatment of survodutide (up to 0.3, 0.9, 1.8 or 2.7 mg once weekly or 1.2 or 1.8 mg twice weekly) in participants aged 18–75 years with T2D, an HbA1c level of 53–86 mmol/mol (7.0–10.0%) and a BMI of 25–50 kg/m^2 alongside with a standardized metformin therapy [40]. Both studies revealed dose-dependent anti-obesity effects of survodutide, while accompanying with gastrointestinal adverse events.

There are 3 phase III RCTs recently launched to investigate the long-term effects of survodutide administered subcutaneously (76-week) compared with placebo in patients with obesity disease in people with overweight or obesity and T2D (NCT06176365, NCT06066528 and NCT06066515, Table S8). A phase III trials aiming to enroll 300 Chinese with a BMI ≥ 28 kg/m^2 or BMI ≥ 24 kg/m^2 with at least one weight- related complication is expected to complete in July 2025 (NCT06214741). Besides, 2 phase III RCTs will focus on participants with compensated non-alcoholic steatohepatitis/metabolic dysfunction are expected to complete in 2029 (NCT06632457) and 2031 (NCT06632444).

The SYNCHRONIZE-CVOT trial (NCT06077864) is currently enrolling participants with overweight or obesity with established cardiovascular disease or chronic kidney disease, and/or at least two weight-related complications or risk factors cardiovascular disease. This RCT is expected to be completed in 2026 to determine its cardiovascular safety and efficacy in participants. Given the high prevalence of cardiovascular complications in obese patients, if survodutide shows positive results, it could be a significant addition to the treatment options.

5.4. Cagrilintide

Cagrilintide, a novel long-acting dual amylin and calcitonin receptor agonist with a half-life of 168–192 h, is primarily being developed for synergistic action with the semaglutide. This investigational combination therapy aims to leverage complementary mechanisms for enhanced weight loss.

A Phase Ib trial investigating doses of cagrilintide up to 4.5 mg co-administered with semaglutide 2.4 mg in participants with overweight or obesity reported a mean bodyweight reduction of 17% with cagrilintide 2·4 mg

and semaglutide 2.4 mg versus 10% with co-administered semaglutide 2.4 mg and placebo after 20 weeks [41]. In a Phase II dose-response study of individuals with overweight or obesity, hypertension, or dyslipidemia, and without T2D, 2.4 mg of cagrilintide combined with diet and exercise, led to a 10% reduction in body weight compared to a 3% reduction with placebo after 26 weeks [42]. A recent 32-week, multicenter, double-blind, phase II trial in the USA evaluated adults with T2D and a BMI ≥ 27 kg/m^2 [43]. Participants received once-weekly subcutaneous cagrilintide (0.16–4.5 mg) or placebo, co-administrated with semaglutide (2.4 mg) resulted in significantly greater weight loss of 15.6% compared to 8.1% with cagrilintide alone and 5.1% with semaglutide alone. A meta-analysis of 3 RCTs involving 430 individuals revealed that patients receiving Cagrisema (semaglutide with cagrilintide, both at 2.4 mg) weekly had significantly stronger effects compared to semaglutide, leading to a greater weight-loss [mean difference −9.11 kg (95%CI: −12.84, −5.39)] [44]. These results underscore the superior efficacy of this combination therapy. Cagrilintide monotherapy demonstrated comparable efficacy to semaglutide/liraglutide while exhibiting substantially lower vomiting incidence (9% vs. 22–25%) [44].

There are 11 phase III trials on CagriSema that focus on people with diverse health conditions (Table S9), including adults with overweight or obesity with (NCT05394519, NCT06221969, NCT06065540, NCT06323174, NCT06323161 and NCT06534411) or without T2D (NCT05567796, NCT06131437, NCT06388187), with established cardiovascular disease (NCT05669755), with east Asian participants with overweight or obesity (NCT05813925), with particular Chinese participants (NCT05996848). Targeting populations disproportionately affected by obesity-related comorbidities (e.g., T2D, cardiovascular risks), the outcomes could mitigate lifelong disease burdens and reduce socioeconomic disparities in healthcare access.

Intriguingly, a pioneering 68-week Phase IV trial (TrialTroveID-480883), set to conclude in 2030, is the first to specifically investigate the cagrilintide/semaglutide combination in children and adolescents with obesity. It aims to evaluate the therapy's pharmacokinetics, efficacy, and safety as an adjunct to lifestyle intervention, thereby filling a major gap in pediatric evidence for hormone-based anti-obesity therapies.

6. The Triple RA on Weight Loss and Weight Loss Maintenance

Currently in development, multi-receptor agonist drugs present a promising avenue to address unmet medical needs. Retatrutide, a single peptide composed of 39 amino acids, is engineered from a GIP peptide backbone to activate GLP-1, GIP, and glucagon receptors, providing enhanced glycemic control and greater weight loss compared to single or dual Ras [45,46]. Retatrutide possesses a prolonged half-life of approximately 6 days, allowing for its administration as a once-weekly subcutaneous injection [47]. This extended half-life is advantageous for maintaining consistent plasma drug levels, thereby contributing to its sustained efficacy in reducing body weight and improving glucose regulation [48]. Retatrutide is metabolized primarily in the liver, with excretion pathways yet to be fully elucidated. Its mechanism of action involves a synergistic interaction among these receptors, resulting in increased insulin secretion, improved glucose homeostasis, and refined appetite modulation [45,46].

Coskun et al. (2022) conducted a first-in-human, single ascending dose [49], Phase I study in Singapore with 47 healthy participants to assess the safety and pharmacokinetics of retatrutide. Of these, 45 received at least one dose of the drug or a placebo. The study found dose-related increases in fasting insulin and C-peptide, and a decrease in fasting glucagon at higher doses (4.5 and 6.0 mg). In a phase I trial with T2D patients, retatrutide was deemed relatively safe, with pharmacokinetics suitable for once-weekly dosing.

It is worth noting that retatrutide shows promise for sustained weight loss, with a multicenter, double-blind, placebo-controlled phase II trial indicating effective results and a relatively good safety profile [50]. Retatrutide led to an average weight losses of 17.5% at 24 weeks and 24.4% at 48 weeks among overweight and obese adults. Long-term studies are needed to fully assess its benefits and risks. Adverse events led to discontinuation in 6% to 16% of retatrutide users (4 mg), compared to none in the placebo group, with gastrointestinal issues being the most common. These were mostly mild to moderate and could be reduced with a lower starting dose (2 mg).

In addition, 10 phase III trial are recently registered for retatrutide (Table S10). TRIUMPH-1 aims to include 2100 participants with obesity or overweight (plus at least 1 weight-related comorbidity) who will receive undisclosed doses of retatrutide or placebo subcutaneously once weekly for approximately 89 weeks (NCT05929066). The trial is expected to be completed in May 2026. TRANSCEND-T2D-1 aims to investigate the efficacy and safety of retatrutide in adults with T2D and inadequate glycemic control with diet and exercise alone, while TRANSCEND-T2D-2 comparing retatrutide with semaglutide in adults with T2D and inadequate glycemic control with metformin with or without SGLT2 inhibitor. An ongoing trial is designed to compare the efficacy and safety of retatrutide with tirzepatide in 800 adults who have obesity (NCT06662383). Other trials target on participants who have obesity or overweight and osteoarthritis of the knee (NCT05931367), chronic

kidney disease (NCT05936151, TrialTroveID-493355), established cardiovascular disease (NCT05882045), renal impairment (NCT06297603, NCT06383390), which will be completed in 2026 or 2029.

7. Comparative Studies on Efficacy and Adherence of GLP-1RAs

Comparative studies on GLP-1RAs regarding weight loss have provided significant insights into their effectiveness and challenges in real-world settings. Dual agonists targeting GLP-1R and GIPR, such as tirzepatide, have shown more pronounced efficacy than single GLP-1RAs, like semaglutide in clinical trials. The magnitude of weight loss achieved with retatrutide (up to 24%) is notably impressive than that reported for GLP-1R agonists alone [50]. This suggests that the addition of glucagon receptor (GCGR) and/or GIPR agonism to GLP-1R agonism may provide additive benefits for weight loss.

Specifically, tirzepatide demonstrated dose-dependent reductions in weight loss (−0.9 kg to −11.3 kg). A recent network meta-analysis evaluated the efficacy and safety of tirzepatide compared to semaglutide and orlistat in the treatment of overweight and obesity [51]. Tirzepatide (15 mg) ranked in the top three across weight-related parameters, glycated hemoglobin, lipid parameters (total cholesterol, HDL-C, LDL-C and triglycerides), and blood pressure. For achieving ≥15% weight loss, tirzepatide had the highest efficacy compared with placebo (risk ratio 10.24, 95% CI: 6.42–16.34). Consistently, using SURMOUNT-1 and STEP 1 data, le Roux CW et al. (2023) reported a greater reductions in percentage change in body weight were observed with tirzepatide [52]. More participants achieved 5% or greater weight loss with tirzepatide 10 mg and 15 mg compared with semaglutide 2.4 mg.

8. Concerns on GLP-1RAs Associated Adverse Events

Apart from the promising potentials, the widespread application of GLP-1RAs is hindered by challenges including high costs, technical complexities, and importantly, adverse effects. A real-world study based on the US FDA Adverse Event Reporting System database found significant disproportionality in adverse events, particularly gastrointestinal disorders, metabolism and nutrition disorders, drug-induced pancreatitis and the loss of lean mass, as well ashepatobiliary disorders [53].

Mechanistically, GLP-1RAs slow down stomach emptying, the motility of the small bowel and colon, which may lead to symptoms such as nausea, vomiting, and constipation [54]. It may modulate enteric immune responses through the intestinal intra-epithelial lymphocyte GLP-1 receptors [55]. Disruptions in this signaling network could potentially contribute to gastrointestinal adverse events[55]. While these medications can lead to substantial weight loss, high discontinuation rates, ranging from 20% to 50% within the first year, possibly due to the high prevalence of gastrointestinal adverse events, negatively impact the effectiveness of GLP-1RAs in real-world settings [56].

A network meta-analysis consisting of 31 RCTs involving more than 35,000 patients revealed that both semaglutide and tirzepatide and GLP-1RA across all doses had significant increases in gastrointestinal adverse effects compared to placebo [51]. More recently, a meta-analysis of 10 studies encompassing 960 participants with metabolic dysfunction-associated steatotic liver disease revealed a significantly higher overall incidence of adverse events, notably gastrointestinal adverse events in the GLP-1RAs group compared to the control group [55]. Adverse events, has been shown to occur in 89% of participants with liraglutide. Gastrointestinal adverse events and vomiting were significantly higher with Cagrisema compared to semaglutide. In a retrospective analysis of patient-level data, within each treatment group of different GLP-1RAs, a higher percentage of women reported gastrointestinal adverse events [57].

Gastrointestinal adverse effects are common early after initiation, affecting 20% to 44% of users, these typically subside within the first few months of therapy [8]. Do et al. (2024) reported the overall prevalence of GLP-1RAs discontinuation was 26.2%, 30.8%, and 36.5% at 3, 6, and 12 months among 195,915 new adult users with T2D or obesity respectively [58]. Nearly 30% of individuals discontinued semaglutide in the SELECT trial, with real-world estimates for GLP-1RA discontinuation in the range of 50% to 75% at 12 months [58].

Nausea (transient and mild-to-moderate) was the most common adverse event in the beinaglutide group (49.3% vs. 7.1% [placebo]), resulting to a higher percentage of patients in the beinaglutide group (5.9%) discontinued treatment than in the placebo group (0.7%) [59]. The risk of nausea was dose-dependent for long-acting GLP-1RAs and across all GLP-1RA, and a similar trend was observed for vomiting and diarrhea [59]. Prince et al. (2025) conducted a real-world adverse events analysis of GLP-1RAs in the US using data retrieved from the FAERS Database [60]. Results show that semaglutide was linked to higher prevalence of nausea, vomiting, and delayed gastric emptying. Although specific data on the relationship between age and GLP-1RAs related adverse events is limited, in general, elderly patients may be more vulnerable to adverse events due to aging related physiological changes.

Moreover, GLP-1RAs may induce clinically significant lean mass loss, despite inconsistent reporting. The proportion of lean mass lost can be substantial: semaglutide has been linked to a loss constituting up to 40% of total weight loss, and liraglutide up to 60%. In the SURMOUNT-1 trial, tirzepatide reduced lean mass by 25.7% of the total weight lost. Conversely, a study comparing semaglutide 1 mg and tirzepatide with placebo in patients with T2D showed lean mass reductions of approximately 15% or less of total weight loss across all groups. Such heterogeneity may be attributed to differences in drug molecules, dosing regimens, study duration, assessment methods, patient populations, and concomitant lifestyle interventions designed for the trials.

Apart from the gastrointestinal adverse effects , a recent study systematically evaluated risks of incident GLP-1RA use (n = 215,970) compared to subjects without additional new therapy (n = 1,203,097) [61]. GLP-1RA use was associated with an increased risk of abdominal pain (OR =1.12 (1.10–1.13)), hypotension (OR = 1.06 (1.04–1.09)), syncope (OR = 1.06 (1.03–1.1)), sleep disturbances (OR = 1.12 (1.10–1.14)), headaches (OR = 1.10 (1.08–1.13)), arthritis (OR = 1.11 (1.09–1.13)), arthralgia (OR = 1.11 (1.09–1.13)), tendinitis and synovitis (OR = 1.10 (1.07–1.12)), interstitial nephritis (OR = 1.06 (1.03–1.09)) and nephrolithiasis (OR = 1.15 (1.12–1.19)), and drug-induced acute pancreatitis (OR = 2.46 (2.05–2.96)). Rodent studies indicate dose-dependent thyroid C-cell hyperplasia, prompting recommendations for calcitonin monitoring in high-risk patients[62]. The high discontinuation rates of GLP-1RAs are likely driven by adverse events that compromise patient satisfaction, highlighting the need for comprehensive risk-benefit assessments when prescribing these therapies.

9. Future Perspectives

9.1. Research Priorities on Comparative Effectiveness and Their Efficacy in Special Populations

Comparative effectiveness studies are needed to evaluate GLP-1RAs against other anti-obesity therapies, clarifying their relative efficacy, safety, and optimal positioning in treatment algorithms. Further investigation into potential synergies with lifestyle interventions or bariatric therapies is also warranted to enhance therapeutic outcomes. Moreover, critical research gaps persist regarding GLP-1RA use in pediatric populations and special clinical contexts, such as pregnancy and perioperative care. Addressing these areas represents both an urgent public health need and a significant therapeutic opportunity, especially amid the rising pediatric obesity epidemic.

9.2. Research Priorities on Long-Term Safety and Post-Treatment Management

Optimized management strategies, including gradual dose escalation and patient education, are essential for GLP-1RAs treatments adherence [63]. Although cardiovascular safety has been established over medium-term follow-up (e.g., SELECT trial), real-world evidence on extended use (>5 years) and rare adverse events (e.g., gastroparesis) requires further characterization. Additionally, emphasis is placed on the necessity for further research to elucidate the underlying causes of adverse events, which could facilitate the development of more tailored preventive and treatment strategies, ultimately improving the safety and effectiveness of GLP-1RA-based therapy.

Equally important is the management of post-discontinuation weight trajectories, given that therapy cessation frequently triggers rapid weight regain, while continued treatment maintains efficacy. Indeed, the STEP 1 trial extension showed that participants regained two-thirds of their lost weight one year after stopping semaglutide (2.4 mg) and lifestyle intervention [64]. The development of structured post-therapy protocols, including ongoing lifestyle support, is needed to mitigate such rebound effects.

9.3. Research Priorities on Personalized Treatment Strategies

Multi-omics approaches (genomics, microbiomics, metabolomics) show promise in predicting treatment response and adverse events, enabling more personalized GLP-1RA therapy. Recent studies reveal considerable inter-individual variation in semaglutide response, with a subset of patients failing to achieve clinically meaningful weight loss(i.e., non-responders defined as at least a 5% reduction in weight) [8]. Lundgren et al. demonstrated that combining liraglutide with individualized lifestyle interventions significantly improves weight maintenance compared to monotherapy [65], reinforcing the value of patient-tailored strategies, further highlighting the need for tailored treatment strategies. Prediction models incorporating clinical variables (e.g., age, gender, gastrointestinal history) and omics signatures could help identify high-risk patients and non-responders, facilitating personalized treatment selection through tools such as nomograms.

10. Limitations

While extensive efforts were made to ensure a thorough search of the literature, including comprehensive database searches and manual screening of reference, there is still a possibility of missing relevant studies.

Additionally, restricting the inclusion criteria to articles published in English may introduce language bias and overlook pertinent research published in other languages.

11. Conclusions

The rising prevalence of obesity poses a significant global health challenge. GLP-1RAs demonstrate remarkable efficacy in weight loss, glycemic control, and potential cardiovascular benefits in preclinical and clinical studies, suggesting their potential to become a cornerstone in the treatment of obesity and related metabolic disorders. This has implications for reducing the global burden of these conditions on both individuals and healthcare systems. Future research must address critical gaps in our understanding of GLP-1RAs, including their long-term effects in underrepresented populations, the determinants of inter-individual variation in treatment response and body composition, and the characterization of non-gastrointestinal adverse outcomes.

Supplementary Materials: The following supporting information can be downloaded at: https://media.sciltp.com/articles/others/2601151741020785/HM-2508000237-SM.zip, Figure S1: The annual number of clinical trials focusing on NuSH-based medications across the world; Figure S2: The number of clinical trials conducted in different countries; Figure S3: Data on clinical trials for the application status of each drug: as a single use or in combination with other medications; Table S1: Numbers of clinical trials conducted across 71 countries; Table S2: Detailed information of liraglutide retrieved from databases; Table S3: Detailed information of semaglutide retrieved from databases; Table S4: Detailed information of benaglutide retrieved from databases; Table S5: Detailed information of orforglipron retrieved from databases; Table S6: Detailed information of tirzepatide retrieved from databases; Table S7: Detailed information of mazdutide retrieved from databases; Table S8: Detailed information of survodutide retrieved from databases; Table S9: Detailed information of cagrilintide retrieved from databases; Table S10: Detailed information of retatrutide retrieved from databases.

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List of Abbreviations

Abbreviations	Definitions
GLP-1RAs	Glucagon-like peptide-1 receptor agonists
FDA	Food and Drug Administration
T2D	Type 2 diabetes
MASH	Metabolic dysfunction-associated steatohepatitis
GIP	Glucose-dependent insulinotropic polypeptide
GIPR	Glucose-dependent insulinotropic polypeptide receptor
RCTs	Randomized controlled trials
BMI	Body mass index
STEP	Semaglutide Treatment Effect in People with Obesity Program
SGLT2	Sodium-glucose cotransporter 2
GCGR	Glucagon receptor

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