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GLP-1 Receptor Agonists: A New Hope in the Global Fight Against Obesity — Benefits and Health Risks

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ABSTRACT

Introduction. Global obesity has reached unprecedented levels, with approximately one billion people worldwide suffering from obesity. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have proven to be highly effective agents for weight management, resulting in significant weight loss and improvements in metabolic, cardiovascular, and renal outcomes. Nevertheless, serious concerns remain regarding long-term safety, including gallbladder disease, rare gastrointestinal complications, potential risk of pancreatitis, concerns related to perioperative aspiration, psychiatric symptoms, and significant weight regain after discontinuation of the drug.

Research objective. This review synthesizes the current evidence on the benefits and risks of GLP-1 RA use, highlighting implications for clinical practice, long-term therapy, and future research priorities.

Methodology. This review is based on a structured search of the PubMed database up to November 2025. Keywords included "GLP-1 receptor agonist," "semaglutide," "liraglutide," "tirzepatide," "obesity," "weight loss," "pancreatitis," "gallbladder," "body composition," and "safety." Priority was given to randomized controlled trials, meta-analyses, large observational studies, and WHO technical documents on the pharmacotherapy of obesity. Articles were analyzed for their relevance to efficacy, safety, or body composition outcomes.

Conclusions. GLP-1 inhibitors represent a major advance in obesity treatment, offering robust weight loss and metabolic benefits, but their use requires careful management of side effects and long-term risks. Ongoing research is needed to optimize therapy, address safety concerns, and ensure equitable access.

Keywords: GLP-1 receptor agonists, obesity, semaglutide, tirzepatide, weight loss, cardiometabolic outcomes; safety, gallbladder disease, pancreatitis, lean mass, neurocognitive benefits, thyroid cancer

1. INTRODUCTION

The problem of obesity has become one of the most important problems facing humanity [1,2]. According to the latest global analyses, in 2022 there were approximately 890 million adults worldwide who were obese (BMI ≥30), and this number is constantly growing [1,2]. Its global prevalence is rapidly increasing across all age groups and socioeconomic strata

[1,2]. This increase is observed in all regions of the world, although the highest growth rates are in Sub-Saharan Africa and Asia, where the number of overweight and obese people is expected to rise to around 3.8 billion by 2050, or more than half of the adult population [2]. Obesity is associated with many chronic diseases, including type 2 diabetes, cardiovascular disease, and cancer, placing a significant burden on healthcare systems [2,3]. Traditional treatments, such as dietary changes and physical activity, often fail to produce lasting results due to the body's biological defense mechanisms [3]. As a result, there is growing interest in drugs such as GLP-1 inhibitors, which are gaining popularity as an effective therapy to aid weight loss [1].

Glucagon-like peptide-1 (GLP-1) receptor agonists (GLP-1 RAs) are currently among the most promising drugs for the treatment of obesity [4,5]. Drugs such as liraglutide and semaglutide, originally approved for glycemic control in type 2 diabetes, have shown significant weight reduction effects in obese adults, leading to their approval at higher doses specifically for the treatment of obesity [4,5]. The mechanism of action includes appetite suppression via central nervous pathways, delayed gastric emptying, increased satiety, and improved glycemic control [6]. A new development is tirzepatide, a dual agonist of GIP and GLP-1 receptors, which is even more effective at reducing body weight than previous GLP-1 RAs, achieving up to 17.8% weight loss after 72 weeks of therapy [4,7]. The use of these drugs is growing rapidly, even among the non-diabetic population, as confirmed by data from pharmacies and surveys, and the World Health Organization is considering adding them to the list of essential medicines due to their documented benefits and the need to ensure equal access [5,8]. The most commonly reported adverse reactions are gastrointestinal symptoms such as nausea, vomiting, and diarrhea, which, however, rarely lead to discontinuation of treatment [4,8].

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are effective in reducing body weight and improving metabolic parameters, but their use is associated with certain risks and limitations. Studies indicate an increased risk of gastrointestinal side effects such as nausea, vomiting, and diarrhea, as well as an increased risk of pancreatitis, gallstones, and kidney inflammation, although serious complications are rare [9,10]. A decrease in lean body mass is also observed during weight loss, which may be significant in older people or those at risk of sarcopenia [9]. Potential risks also include questions regarding the progression of retinopathy, the risk of aspiration during the perioperative period, and psychiatric symptoms, which require further investigation [9]. However, the biggest challenge is the high rate of weight regain after discontinuing GLP-1 RAs therapy, which highlights the need for long-term monitoring and

strategies to maintain the effects [9]. Nevertheless, GLP-1 RAs have a beneficial effect on reducing the risk of cardiovascular events and strokes and improving kidney function, as confirmed by observational studies and meta-analyses [9].

2. SCALE OF USE

Over the past few years, there has been a rapid increase in the global use of GLP-1 receptor agonists (GLP-1 RAs) [11,12]. In the United States, prescriptions increased by 300% between 2020 and 2022, with 9 million prescriptions for liraglutide, semaglutide, and tirzepatide issued in the last quarter of 2022 alone [11,12]. Interestingly, nearly half of these were for adults without diabetes, reflecting the expansion of indications and off-label use for weight management [11,12]. A similar sharp increase was observed in the United Kingdom and Australia, especially after significant changes in guidelines and the approval of new drugs [13].

An estimated 750 million adults worldwide (27.6% of people aged 25–64) are eligible for GLP-1 receptor agonists based on BMI criteria and comorbidities. Eligibility is highest in high-income countries (44%) and lowest in low-income countries (11.5%), highlighting significant disparities in potential access [14]. Despite high eligibility rates, actual take-up remains significantly lower, particularly in lower-income regions and among racial/ethnic minorities [15].

3. BENEFITS OF GLP-1 RECEPTOR AGONISTS

GLP-1 receptor agonists (GLP-1 RAs), particularly semaglutide and liraglutide, have demonstrated significant and clinically relevant weight loss effects in obese adults, often surpassing older pharmacological approaches. In a randomized phase 2 study, semaglutide at doses ≥0.7 mg daily led to weight loss ranging from 8.7% to 13.8% over 52 weeks, which was significantly better than liraglutide at a dose of 3.0 mg daily, which achieved approximately 7.8% weight loss, and placebo, which achieved 2.7% [16]. In the STEP 8 study, which directly compared semaglutide 2.4 mg once weekly with liraglutide 3.0 mg once daily for 68 weeks, semaglutide resulted in a mean weight reduction of 15.8% compared to 6.4% for liraglutide, with 55.6% of participants treated with semaglutide losing ≥15% of their body weight compared to only 12% for liraglutide [17]. More than one-third of semaglutide users lost more than 20% of their body weight, highlighting its superior efficacy [17]. Tirzepatide, a dual GLP-1/GIP receptor agonist, has demonstrated even greater weight loss, with reductions exceeding 20% in some dosing regimens, and is considered highly cost-effective compared to semaglutide and liraglutide in the treatment of obesity [18]. Meta-analyses confirm that semaglutide and

liraglutide outperform older agents such as orlistat and naltrexone -bupropion, both in terms of weight and fat reduction, although potent agents such as semaglutide and tirzepatide may also reduce lean body mass by approximately 25% of total weight lost, while liraglutide tends to better preserve lean body mass [18]. GLP-1 RAs also improve cardiovascular and metabolic risk factors beyond weight loss, including glycemic control and blood pressure, contributing to their broad therapeutic benefits in the treatment of obesity [19]. Cost-effectiveness analyses indicate that semaglutide 2.4 mg is the most cost-effective pharmacotherapy for obesity in Canada and the United States, and tirzepatide also has a favorable cost-effectiveness profile [20]. Overall, semaglutide and liraglutide are highly effective, evidence-based options for significant, sustained weight loss in adults with obesity, with semaglutide offering superior efficacy and a higher percentage of patients achieving clinically meaningful weight loss thresholds [16,17,19].

GLP-1 receptor agonists provide significant metabolic benefits beyond weight reduction by affecting multiple cardiometabolic risk factors. They effectively lower HbA1c, fasting glucose, and postprandial glucose fluctuations with minimal risk of hypoglycemia thanks to a glucose-dependent insulinotropic mechanism that increases insulin secretion only when glucose levels are elevated [21]. In addition to controlling blood sugar, GLP-1 RAs lower blood pressure by approximately 4 mmHg systolic and 1.4 mmHg diastolic, improve the lipid profile by lowering triglycerides, total cholesterol, LDL cholesterol, and increasing HDL cholesterol levels, and reduce visceral obesity and markers of inflammation, contributing to overall metabolic health [22]. Studies on cardiovascular outcomes in people with type 2 diabetes consistently show that GLP-1 RAs reduce the number of serious cardiovascular events, including cardiovascular deaths , non-fatal myocardial infarctions, and strokes, highlighting their cardioprotective effects [23]. Observational studies further confirm these findings, showing a reduction in all-cause mortality and a lower incidence of a wide range of cardiovascular and metabolic conditions in real-world settings [24]. Furthermore, long-acting GLP-1 RAs appear to provide greater improvement in glycemic control and lipid parameters compared to short-acting drugs, suggesting that pharmacokinetic profiles influence the extent of metabolic benefits [25]. Overall, GLP-1 RAs provide broad cardiometabolic protection through multifaceted improvements in glycemic control, blood pressure, lipid metabolism, inflammation, and cardiovascular outcomes [23,24,25].

Recent studies indicate that GLP-1 receptor agonists may offer neurocognitive and psychiatric benefits beyond their metabolic effects [26,27]. Preclinical and clinical studies suggest that GLP-1 RAs modulate neuroinflammation, oxidative stress, and neural pathways

involved in neurodegenerative diseases such as Alzheimer's and Parkinson's disease, improving cognitive and motor function in animal models and some human studies, although clinical results remain inconclusive [26,27]. Functional neuroimaging studies show that GLP-1 and its agonists alter brain network connectivity in areas associated with cognitive function, emotion, and reward, which may underlie potential benefits in psychiatric disorders, including anhedonia and addiction [28]. Observational studies and large database studies suggest an association between GLP-1 RA use and reduced incidence of neurocognitive disorders, dementia, schizophrenia, and substance use disorders, and some evidence suggests that these effects may be partially independent of glycemic control and indirectly related to weight loss or anti-inflammatory effects [9]. However, pharmacotherapy safety data also indicate possible psychiatric adverse effects, such as depression and suicidal tendencies, particularly with semaglutide, indicating the need for careful observation in clinical practice [29]. Overall, although the neuropsychiatric benefits are promising, they need to be confirmed in well-controlled randomized trials to clarify the mechanisms, efficacy, and safety profiles in different populations [30].

Another positive aspect of using GLP-1 receptor agonists is their effect on the kidneys. Meta-analyses of randomized controlled trials (RCTs) have shown that GLP-1 receptor agonists reduce the risk of kidney disease progression in patients with type 2 diabetes by approximately 16–24%, including a reduction in composite renal endpoints such as progression of albuminuria, decline in eGFR, and need for dialysis [31,32,33]. In the FLOW study, semaglutide reduced the risk of major renal events by 24% and slowed the annual decline in eGFR in patients with chronic kidney disease and type 2 diabetes compared to placebo [31]. The renal benefits of GLP-1 RA also include improved albuminuria rates and reduced risk of major adverse kidney events (MAKE), as confirmed by meta-analyses and observational studies [32,33]. In kidney transplant patients with type 2 diabetes, the use of GLP-1 RA was associated with a slower decline in eGFR, reduced albuminuria, and lower mortality compared to patients without such treatment [34]. Protective mechanisms include natriuretic effects, reduction of hyperfiltration, modulation of the renin-angiotensin-aldosterone system (RAAS), and anti-inflammatory properties [33]. Data indicate that the renal benefits of GLP-1 RAs extend beyond glycemic effects, making them a valuable therapeutic option for the treatment of chronic kidney disease in individuals with type 2 diabetes and obesity [31,32].

Another organ where we can see positive effects is the liver. Semaglutide significantly improves the histopathological picture of metabolically associated steatohepatitis (MASH), as confirmed by the results of a large, randomized phase 3 study. Approximately 63% of patients

treated with semaglutide experienced complete resolution of hepatitis, and 37% had improvement in fibrosis without disease progression, compared to 34% and 22.5%, respectively, in the placebo group [35]. Mechanistic studies indicate that semaglutide modulates metabolic, inflammatory, and fibrotic pathways in the liver, restoring patients' proteomes to patterns observed in healthy individuals [36]. The 10–15% weight reduction achieved with semaglutide also translates into improved obstructive sleep apnea parameters, reduced joint pain, and better quality of life and physical function [35]. In animal models, semaglutide reduces steatosis, hepatocyte ballooning, and lipogenesis markers, suggesting a direct effect on the liver independent of calorie intake [37].

4. HEALTH RISKS OF GLP-1 RECEPTOR AGONISTS

The most common side effects of semaglutide affect the gastrointestinal tract and include nausea, vomiting, diarrhea, constipation, abdominal pain, and feeling full [38,39]. In STEP studies with a dose of 2.4 mg, more than 70% of patients experienced at least one gastrointestinal symptom, and in several to a dozen percent, these symptoms were so severe that they led to discontinuation of the drug [38,39]. These symptoms usually subside after a few weeks, especially with gradual dose increases, but in some patients they may prevent long-term use [40,41]. Meta-analyses confirm that semaglutide significantly increases the risk of gastrointestinal disorders compared to placebo, with nausea occurring in 2% to as many as 20% of patients, vomiting in up to 6%, and diarrhea and constipation also occurring in several percent of patients [40]. Despite these side effects, semaglutide is generally well tolerated and its clinical benefits in the treatment of diabetes and obesity outweigh the risks, provided that it is properly monitored and the dosage is adjusted [42]. In practice, it is important to educate patients about possible symptoms and to use strategies to minimize discomfort, which may improve adherence to therapy [41].

The use of GLP-1 receptor agonists is associated with a minor but statistically significant increase in the risk of acute pancreatitis (AP), especially in patients with existing risk factors such as gallstones, hypertriglyceridemia, or previous episodes of AP [9]. Randomized controlled trials (RCTs) have not shown a significant increase in the risk of AP, and some analyses even indicate no increased risk or a reduced risk in populations without comorbidities [43]. In patients with a history of severe AP, the use of GLP-1 RAs is contraindicated, and the onset of new abdominal pain requires urgent diagnosis for pancreatitis [44]. The signal is more pronounced for biliary tract diseases, where meta-analyses indicate an increased risk of gallstones and acute cholecystitis in people treated with GLP-1 RAs, which

may be due to rapid weight loss and the effect of these drugs on gallbladder motility [9]. Clinically, this means that it is necessary to monitor for symptoms of biliary colic and to consider cholecystectomy more frequently in this group of patients [45]. In summary, although the risk of AP is small and controversial, the risk of biliary complications is more well-established, requiring caution and appropriate clinical supervision during GLP-1 RA therapy [9].

Hypoglycemia is not a significant problem during monotherapy with GLP-1 receptor agonists, as their action depends on glucose levels, but the risk of hypoglycemia increases significantly when they are used together with insulin or sulfonylureas, requiring a reduction in the doses of these drugs and close monitoring of blood glucose, especially in older people and those with nephropathy [46]. GLP-1 RAs cause weight loss, of which approximately 20-40% is lean mass, including muscle, which can be problematic in older people or those with low muscle mass, increasing the risk of sarcopenia, weakness, and falls [47]. Imaging studies (DEXA, MRI) indicate that muscle mass reduction is adaptive and may be associated with improved muscle quality and insulin resistance, but older age and comorbidities increase the risk of negative effects [47]. Interventions such as increased protein intake and resistance training can effectively limit muscle mass loss during GLP-1 RA therapy, as confirmed by studies involving patients with type 2 diabetes [48]. Some studies suggest that combining GLP-1 RA with other drugs or metabolic modulators may further protect muscle mass while increasing fat loss [49]. In practice, it is recommended to monitor body composition and implement appropriate nutritional and exercise strategies to minimize the negative effects of lean mass loss during GLP-1 RA therapy [48].

The use of GLP-1 receptor agonists in humans has not shown a clear increase in the risk of medullary thyroid cancer (MTC) or pancreatic cancer in large meta-analyses of clinical trials, although the observation period is limited, and these drugs carry warnings about potential risks, especially in patients with MTC or MEN2 syndrome, based on observations of thyroid C-cell proliferation in rodents [50]. There is no evidence of a significant increase in cancer incidence, but long-term oncological safety remains under monitoring due to the lack of "proof of no risk" [50]. Regarding the risk of suicide and suicidal thoughts, meta-analyses of randomized controlled trials have not shown a statistically significant increase in the incidence of these events in patients using GLP-1 RAs compared to placebo [51]. However, due to case reports and safety signals, caution is recommended, especially in patients with depression, and mental health should be monitored during therapy [52]. Current data from observational studies and pharmacovigilance analyses suggest that rapid weight loss induced by GLP-1 RAs may affect

emotions and mental health, which requires further research and clinical vigilance [52]. In summary, there is no strong evidence of an increased risk of cancer or suicide, but due to data limitations and reports of adverse events, further monitoring of the safety of these drugs is necessary [50,51].

Delayed gastric emptying is a significant effect of GLP-1 receptor agonists, which promotes satiety but may lead to gastric retention, bloating, and even symptoms of gastroparesis in some patients [53]. In anesthesiology, delayed emptying increases the risk of residual gastric contents during procedures, which can result in aspiration despite standard fasting periods. Therefore, anesthesiology societies recommend considering discontinuing GLP-1 RA for several days to a week before major procedures, especially in patients in the dose escalation phase or with symptoms of gastroparesis [54]. Studies have shown that patients using GLP-1 RAs have a significantly higher risk of residual gastric contents during upper gastrointestinal endoscopy, which may lead to discontinuation of the procedure, although cases of aspiration are rare [55]. The effect of delayed emptying is measurable (on average about 36 minutes longer), but in most cases does not exceed standard fasting periods, although the risk is greater in people with gastric motility disorders or during the early phase of treatment [53]. Individual approaches are recommended, including prolonging the fasting period, using a liquid diet 24 hours before the procedure, and assessing the risk using gastric ultrasound on the day of the procedure, as well as cooperation between the anesthesiology, surgery, and diabetes teams [54]. In patients with advanced kidney disease, diabetic gastroparesis, or advanced age, delayed emptying can lead to more serious complications, so special caution and adjustment of therapy are required [54].

5. DISCUSSION

GLP-1 receptor agonists have rapidly changed the pharmacological treatment of obesity, narrowing the historical gap between lifestyle or older anti-obesity drugs and bariatric surgery in terms of achievable weight loss. The degree of weight reduction observed in major clinical trials of semaglutide and tirzepatide, often exceeding 15–20% of baseline body weight, clearly surpasses the results obtained with previous pharmacological therapies and lifestyle interventions alone [16–19]. These results are particularly relevant in the context of the global and ever-increasing burden of obesity, where traditional approaches often fail to achieve sustained weight loss due to homeostatic mechanisms that defend higher body weight [1–3]. The data collected in this review support the view that GLP-1 RAs should be considered the

cornerstone of modern obesity pharmacotherapy, especially in individuals with severe obesity or multiple comorbid cardiometabolic conditions [4,5,16–20].

At the same time, the evidence emphasizes that GLP-1 RAs are not a definitive cure for obesity, but rather a powerful chronic therapy whose benefits depend on long-term use. High rates of weight regain after discontinuation, documented in both randomized and observational studies, underscore the chronic, recurrent nature of obesity and challenge the concept of short-term "weight loss courses" using GLP-1 RAs [9]. These observations are consistent with data indicating biological adaptations that promote weight regain after weight loss, including changes in appetite hormones and energy expenditure [3]. From a clinical perspective, this means that decisions to initiate therapy should be made within the context of a long-term treatment plan that includes clear communication with patients about the likelihood of weight regain after discontinuation of treatment and the potential need for maintenance strategies or ongoing pharmacotherapy [3,9].

A key contribution of recent research and this review is the increasing focus on body composition rather than weight alone. The finding that approximately 20–40% of the weight lost with GLP-1 RAs can be attributed to lean body mass, including skeletal muscle, raises serious concerns, particularly in older adults and those at risk of sarcopenia [9,18,47]. Intervention studies indicating that resistance training and increased protein intake may attenuate lean body mass loss provide a practical framework for incorporating GLP-1 RAs into multimodal obesity treatment strategies [48,49]. Future studies should more systematically evaluate functional outcomes and long-term musculoskeletal health in patients treated with GLP-1 RAs, particularly in older and chronically ill populations [47–49].

The safety profile of GLP-1 RAs appears generally acceptable, but several areas warrant continued vigilance. The most common adverse events are gastrointestinal, particularly nausea, vomiting, diarrhea, and constipation, which may limit adherence or lead to discontinuation in a significant minority of patients [38–42]. Although these symptoms are often transient and can be mitigated by gradual dose escalation and patient education, they remain a clinically significant barrier to real-world use [40,41]. Signals indicating acute pancreatitis are relatively weak and inconsistent in randomized and observational trial data, but appear to be more pronounced in individuals with existing risk factors such as gallstones or hypertriglyceridemia [9,10,43,44]. In contrast, the association with gallbladder disease and acute cholecystitis is stronger and likely reflects a combination of the drug's effect on gallbladder motility and the consequences of rapid weight loss [9,45]. These findings support a risk stratification approach

that includes a thorough assessment of biliary and pancreatic disease history, monitoring of abdominal symptoms [9,43–45].

In addition to classic safety concerns, perioperative and neuropsychiatric issues are becoming increasingly important clinically. Delayed gastric emptying, a desirable mechanism for appetite regulation, may translate into increased gastric residual volume and a theoretical or observed risk of aspiration during anesthesia [53–55]. The latest recommendations for temporary discontinuation of GLP-1 RA prior to major surgery, especially in patients in the dose-escalation phase or with symptoms suggestive of gastroparesis, are therefore biologically justified and consistent with the available evidence [53,54]. Similarly, although randomized trials and meta-analyses have not shown a clear increase in the risk of medullary thyroid cancer, pancreatic cancer, or suicidal behavior, the duration of follow-up is limited, and regulatory warnings remain in place [50,51]. Case reports and signals of mood changes and suicidal tendencies, particularly with semaglutide, warrant careful psychiatric monitoring in patients susceptible to such symptoms and highlight the need for prospective clinical trials specifically designed to assess neuropsychiatric outcomes [9,29,30,52].

On the other hand, the additional metabolic benefits associated with GLP-1 RAs, particularly in the cardiovascular, renal, and hepatic systems, support their positioning not only as weight loss agents but also as systemic cardiometabolic therapies. Large studies on cardiovascular outcomes have consistently shown reductions in major cardiovascular events, all-cause mortality, and stroke in people with type 2 diabetes, and these effects appear to be only partially related to weight loss [19,21–25]. Similarly, robust evidence now indicates that GLP-1 RAs slow the progression of chronic kidney disease, reduce albuminuria, and lower the risk of major renal adverse events, including in high-risk populations such as kidney transplant recipients [31–34]. Recently described benefits in metabolic steatohepatitis, where a significant proportion of patients achieved resolution of inflammation and improvement in fibrosis, extend the potential role of GLP-1 RAs to hepatology [35–37]. Emerging data on potential neurocognitive and psychiatric benefits, including a reduction in the incidence of dementia and substance use disorders, are intriguing but remain preliminary and require careful verification in dedicated studies [9,26–30]. In summary, these findings suggest that the therapeutic value of GLP-1 RAs may extend far beyond weight reduction, positioning them as multi-organ protective agents in complex metabolic diseases.

From a population and health policy perspective, the rapid growth in global use of GLP-1 RAs raises important questions about accessibility and cost. The dramatic increase in prescriptions in high-income countries, including widespread use among non-diabetics,

contrasts sharply with limited use in low- and middle-income regions, despite significant eligibility based on BMI and comorbidities [11–15]. At the same time, the very high proportion of adults theoretically eligible for treatment (in some age groups, nearly one-third) makes universal access to treatment unrealistic in most healthcare systems [14,15]. Decision-makers will need to develop clear criteria for prioritization, for example, focusing on individuals with severe obesity, multiple comorbidities, or diagnosed cardiovascular or renal disease, while addressing inequalities related to socioeconomic status, race/ethnicity, and geographic location [11–15,20].

In light of these findings, there are several implications for clinical practice and future research. From a clinical perspective, GLP-1 RAs should be considered in patients with obesity and high cardiometabolic risk -metabolic risk, preferably as part of a comprehensive program that combines nutritional counseling, structured physical activity, and behavioral support, with a particular focus on maintaining lean body mass through resistance training and adequate protein intake [18,21,47–49]. To maximize benefits and minimize harm, a thorough baseline assessment of gallbladder disease, risk of pancreatitis, renal function, and psychiatric history is essential, as is planning for surgical procedures [9,31–33,38–45,53–55]. From a research perspective, priorities include long-term observational cohorts and clinical trials covering oncological and neuropsychiatric outcomes, studies focusing on older and frail populations, and interventions aimed at optimizing body composition and functional status during GLP-1 RA therapy [26–30,47–49,50–52]. Economic analyses across different healthcare systems, particularly in low- and middle-income countries, are also needed to ensure equitable allocation and reimbursement policies [11–15,18,20]. Overall, GLP-1 receptor agonists represent a powerful but complex tool in the fight against obesity, whose full potential and long-term safety will depend on thoughtful integration into clinical practice and health policy.

6. CONCLUSION

GLP-1 receptor agonists represent one of the most significant advances in the treatment of obesity, providing substantial and clinically relevant weight loss, improved metabolism, and beneficial effects on cardiovascular and renal outcomes, as well as on the liver and nervous system. Their safety profile is generally acceptable, although the risk of gallbladder disease, rare gastrointestinal complications, pancreatitis, and concerns about lean body mass loss require ongoing monitoring. A major limitation remains the significant weight regain after discontinuation of the drug, confirming the need for long-term treatment strategies. Future studies must clarify long-term safety, identify optimal strategies for maintaining lean body mass,

and evaluate the use of GLP-1 receptor agonists in broader populations. As their use expands, issues of cost, accessibility, and sustainability must be addressed to ensure equitable distribution of these highly effective drugs.

Disclosure

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Conflicts of Interest

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