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CHILDHOOD OBESITY AND GLP-1 RECEPTOR AGONISTS: CURRENT EVIDENCE, CHALLENGES AND FUTURE PERSPECTIVES – A NARRATIVE REVIEW

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ABSTRACT

Introduction: Childhood obesity has become one of the most significant global public health challenges of the twenty-first century. The prevalence of obesity among children and adolescents continues to increase worldwide, contributing to the growing burden of metabolic, cardiovascular, endocrine and psychological disorders. Traditional interventions based on lifestyle modification often demonstrate limited long-term effectiveness, highlighting the need for additional therapeutic strategies. In recent years, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have emerged as a promising pharmacological option for pediatric obesity management.

Purpose of the Study: The aim of this review is to provide a comprehensive overview of the current evidence regarding the use of GLP-1 receptor agonists in children and adolescents with obesity, with particular emphasis on their mechanisms of action, clinical efficacy, safety profile, psychological impact and future therapeutic perspectives.

Materials and Methods: The literature review was based on publications published between 2007 and 2025. PubMed, Scopus and Google Scholar databases were searched using keywords including childhood obesity, pediatric obesity, adolescent obesity, GLP-1 receptor agonists, liraglutide, semaglutide, tirzepatide, pharmacological treatment and weight management. Priority was given to randomized controlled trials, systematic reviews, meta-analyses and international clinical guidelines published in English.

Description of the State of Knowledge: Recent clinical trials have demonstrated significant efficacy of GLP-1 receptor agonists in reducing body weight and body mass index in pediatric patients with obesity. Liraglutide and semaglutide have shown clinically meaningful improvements in weight reduction, metabolic parameters and quality of life. Among currently available GLP-1 receptor agonists, semaglutide demonstrated the greatest efficacy for BMI and weight reduction in a recent network meta-analysis of pediatric obesity treatments. Although gastrointestinal adverse effects remain the most commonly reported complications, overall treatment tolerability appears favorable. Ongoing studies are evaluating long-term safety, treatment durability and the role of next-generation incretin-based therapies.

Conclusion: GLP-1 receptor agonists represent a promising advancement in the management of childhood obesity. Their ability to achieve significant weight reduction and improve obesity-related comorbidities may substantially decrease the lifetime risk of cardiovascular disease, chronic kidney disease, and premature mortality.

KEYWORDS

Childhood Obesity, Pediatric Obesity, GLP-1 Receptor Agonists, Liraglutide, Semaglutide, Adolescent Obesity, Pharmacological Treatment

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Introduction

Childhood obesity has emerged as one of the most significant public health challenges of the twenty-first century. Over the past several decades, the prevalence of overweight and obesity among children and adolescents has increased dramatically worldwide, affecting both developed and developing countries. According to the NCD Risk Factor Collaboration, the global prevalence of obesity among children and adolescents increased more than tenfold between 1975 and 2016 (NCD Risk Factor Collaboration, 2017). The growing prevalence of pediatric obesity has become a major concern for healthcare systems due to its association with numerous short- and long-term health complications.

Obesity in childhood is now recognized as a chronic, multifactorial disease resulting from complex interactions among genetic, environmental, behavioral, metabolic, and psychosocial factors (Kumar & Kelly, 2017; Hampl et al., 2023). Children with obesity are at increased risk of developing insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, metabolic dysfunction-associated steatotic liver disease (MASLD; formerly NAFLD), obstructive sleep apnea, and orthopedic complications (Kumar & Kelly, 2017).

Beyond its physical consequences, childhood obesity imposes a substantial psychological and social burden. Children and adolescents with obesity are more likely to experience depression, anxiety, low self-esteem, impaired body image, psychosocial difficulties, and reduced quality of life compared with their

healthy-weight peers (Rankin et al., 2016; Pont et al., 2017). Furthermore, weight-related stigma, teasing, and bullying are common and may contribute to social isolation, emotional distress, and adverse mental health outcomes, thereby creating additional barriers to effective obesity management (Pont et al., 2017; Rankin et al., 2016). Consequently, pediatric obesity should be regarded as a chronic medical condition requiring comprehensive and multidisciplinary care.

Current management strategies primarily focus on lifestyle interventions, including dietary modification, increased physical activity, behavioral therapy, and family-centered education. Although these approaches remain the cornerstone of treatment, their long-term effectiveness is often limited, with most interventions producing only modest reductions in BMI and body weight. Furthermore, maintaining these improvements over time remains challenging, highlighting the need for additional therapeutic options (Mead et al., 2017).

Recent advances in obesity research have led to a better understanding of the neuroendocrine mechanisms regulating appetite, satiety, energy expenditure, and body weight homeostasis. Among the most promising therapeutic developments are glucagon-like peptide-1 receptor agonists (GLP-1 RAs). GLP-1 is an incretin hormone secreted by intestinal L-cells in response to nutrient intake (Holst, 2007; Drucker, 2018). Through its effects on the central nervous system and gastrointestinal tract, GLP-1 promotes satiety, reduces appetite, delays gastric emptying, and improves glucose metabolism. Pharmacological agents targeting GLP-1 receptors have demonstrated substantial efficacy in adults with obesity and type 2 diabetes, leading to growing interest in their application within pediatric populations.

Recent evidence has shown that liraglutide and semaglutide can produce clinically meaningful reductions in BMI and body weight in adolescents with obesity, expanding the therapeutic options available for pediatric obesity management (Kelly et al., 2020; Weghuber et al., 2022). Clinical trials have demonstrated substantial reductions in body weight, BMI, and cardiometabolic risk factors with incretin-based therapies. Furthermore, emerging agents such as dual GIP/GLP-1 receptor agonists and triple GIP/GLP-1/glucagon receptor agonists have shown promising efficacy and may further expand therapeutic options for obesity management (Jastreboff et al., 2022; Jastreboff et al., 2023).

Given the rapidly expanding evidence base and increasing clinical use of GLP-1 receptor agonists, a comprehensive evaluation of their efficacy, safety, and future therapeutic potential in children and adolescents is warranted. Therefore, the aim of this narrative review is to summarize current knowledge regarding GLP-1 receptor agonists in pediatric obesity, focusing on epidemiology, pathophysiological rationale, clinical outcomes, safety considerations, and future perspectives.

Description of the Current State of Knowledge

Epidemiology of Childhood Obesity

Childhood obesity has become one of the most rapidly growing public health concerns worldwide. The prevalence of overweight and obesity among children and adolescents has increased dramatically during the past four decades across virtually all regions of the world (NCD Risk Factor Collaboration, 2017; Kerr et al., 2025). Although obesity was once considered primarily a problem of high-income countries, recent evidence demonstrates substantial increases in low- and middle-income regions, particularly in parts of Asia and Oceania (Kerr et al., 2025; World Obesity Federation, 2025).

Globally, hundreds of millions of children and adolescents are currently affected by overweight or obesity (World Obesity Federation, 2025). The prevalence varies considerably between regions, with some of the highest rates reported in North America, the Middle East, Southern Europe, and several Pacific Island nations. In many countries, obesity prevalence among adolescents has increased substantially over recent decades, highlighting the urgent need for effective prevention and treatment strategies (Kerr et al., 2025; World Obesity Federation, 2025).

In Europe, childhood obesity remains a major healthcare challenge despite increasing public health awareness (World Obesity Federation, 2025). Childhood overweight and obesity remain highly prevalent in several European countries, particularly in Southern Europe. Southern European nations, including Greece, Italy, and Spain, continue to report some of the highest prevalence rates, although increasing trends have also been observed in Central and Eastern Europe (World Obesity Federation, 2025).

The United States represents one of the most extensively studied populations regarding pediatric obesity. Data from the National Health and Nutrition Examination Survey (NHANES) have consistently demonstrated high rates of obesity among children and adolescents, with no evidence of a decline in prevalence between

1999 and 2016 (Skinner et al., 2018). Furthermore, severe obesity has become increasingly common, particularly among adolescents (Skinner et al., 2018). Disparities in obesity prevalence have been observed across racial and ethnic groups, while socioeconomic and environmental factors are also believed to contribute substantially to disease development (Sanyaolu et al., 2019).

The etiology of childhood obesity is multifactorial (Kumar & Kelly, 2017) and involves complex interactions between genetic predisposition and environmental exposures. Excessive caloric intake, increased consumption of ultra-processed foods, reduced physical activity, prolonged screen time, inadequate sleep duration, and adverse socioeconomic conditions have all been identified as important contributors (Sanyaolu et al., 2019; Kumar & Kelly, 2017). Early-life exposures, including perinatal factors, infant feeding practices, microbiota composition, and patterns of early growth, have been identified as potential contributors to childhood obesity risk (Kumar & Kelly, 2017).

The consequences of childhood obesity extend far beyond excessive body weight. Children with obesity are at significantly increased risk (Kumar & Kelly, 2017) of developing metabolic syndrome, insulin resistance, type 2 diabetes mellitus, dyslipidemia, hypertension, and metabolic dysfunction-associated steatotic liver disease (MASLD). These complications may appear during childhood and adolescence, leading to earlier onset of chronic diseases traditionally associated with adulthood.

Furthermore, longitudinal studies have demonstrated that obesity during childhood strongly predicts obesity in adulthood. Individuals affected by obesity during early life often experience persistent cardiometabolic abnormalities, increased healthcare utilization, and reduced quality of life later in life. Therefore, childhood obesity should be regarded not only as a pediatric condition but also as a major determinant of lifelong health outcomes.

The substantial global burden associated with childhood obesity has prompted growing interest in more effective therapeutic approaches. While prevention remains the cornerstone of public health strategies, the increasing prevalence of severe obesity and obesity-related comorbidities has highlighted the limitations of lifestyle interventions alone (Mead et al., 2017). Consequently, pharmacological therapies, including glucagon-like peptide-1 receptor agonists, have emerged as important components of modern obesity management, particularly among adolescents with severe disease and significant metabolic complications (Hampl et al., 2023).

Pathophysiology of Childhood Obesity

Childhood obesity is a complex, chronic, and multifactorial disease resulting from an imbalance between energy intake and energy expenditure. However, contemporary understanding of obesity extends beyond the traditional concept of excessive caloric consumption. Obesity is now recognized as a disorder involving intricate interactions among genetic, neuroendocrine, metabolic, environmental, and behavioral factors that collectively influence body weight regulation (Kumar & Kelly, 2017).

The central nervous system, particularly the hypothalamus, plays a crucial role in maintaining energy homeostasis (Kumar & Kelly, 2017; Drucker, 2018). Within the hypothalamus, the arcuate nucleus integrates peripheral hormonal and nutritional signals involved in the regulation of appetite and energy balance. Experimental studies have shown that GLP-1 receptor activation modulates hypothalamic pathways by reducing the expression of orexigenic neuropeptides such as neuropeptide Y (NPY) and agouti-related peptide (AgRP), thereby contributing to reduced food intake and weight loss (Drucker, 2018).

Several peripheral hormones influence hypothalamic appetite regulation (Kumar & Kelly, 2017). Leptin, a hormone secreted primarily by adipose tissue, signals adequate energy stores and promotes satiety. In obesity, chronically elevated leptin concentrations are associated with leptin resistance, characterized by impaired hypothalamic responsiveness to leptin signaling. Consequently, appetite suppression becomes less effective despite increased adipose tissue mass (Kumar & Kelly, 2017).

Ghrelin, often referred to as the “hunger hormone,” is produced mainly by the stomach and stimulates appetite through activation of hypothalamic NPY and AgRP neurons (Drucker, 2018). Ghrelin concentrations typically rise before meals and decrease following food intake. Alterations in ghrelin regulation may contribute to abnormal hunger signaling and excessive caloric consumption in susceptible individuals (Kumar & Kelly, 2017).

Insulin also participates in central appetite regulation in addition to its well-established metabolic functions (Drucker, 2018; Kumar & Kelly, 2017). Similar to leptin, insulin acts on hypothalamic centers to suppress food intake and regulate energy balance. The development of insulin resistance, commonly observed

in pediatric obesity, impairs these regulatory mechanisms and contributes to further weight gain and metabolic dysfunction (Kumar & Kelly, 2017).

Adipose tissue is increasingly recognized as an active endocrine organ rather than a passive energy storage site (Kumar & Kelly, 2017). Excess adiposity promotes the secretion of numerous bioactive molecules known as adipokines, including leptin, adiponectin, resistin, and inflammatory cytokines. In obesity, adipose tissue undergoes structural and functional changes characterized by macrophage infiltration and chronic low-grade inflammation. Elevated levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and other pro-inflammatory mediators contribute to systemic inflammation, insulin resistance, endothelial dysfunction, and increased cardiometabolic risk (Kumar & Kelly, 2017).

Recent research has highlighted the potential role of the gut microbiota in obesity pathogenesis (Kumar & Kelly, 2017). The intestinal microbiome influences nutrient absorption, energy harvest, immune regulation, and metabolic homeostasis. Alterations in microbial diversity and composition have been associated with increased adiposity and metabolic disturbances. Although the precise mechanisms remain incompletely understood, dysbiosis may contribute to obesity through modulation of inflammatory pathways, gut permeability, short-chain fatty acid production, and appetite-regulating hormones (Kumar & Kelly, 2017).

Genetic factors also play an important role in susceptibility to obesity (Kumar & Kelly, 2017). Genome-wide association studies have identified numerous loci associated with body weight regulation, appetite control, and energy metabolism. Nevertheless, genetic predisposition alone cannot explain the rapid increase in obesity prevalence observed during recent decades. Environmental influences, including easy access to energy-dense foods, reduced physical activity, increased screen time, inadequate sleep, and socioeconomic determinants, are believed to interact with genetic susceptibility to promote disease development (Kumar & Kelly, 2017; Sanyaolu et al., 2019).

Taken together, childhood obesity results from complex disturbances affecting multiple physiological systems involved in energy balance. Advances in understanding the complex neuroendocrine and metabolic pathways underlying obesity have facilitated the development of targeted pharmacological therapies. Among these, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have attracted considerable attention due to their ability to modulate appetite regulation, satiety signaling, glucose metabolism, and energy balance through multiple complementary mechanisms (Drucker, 2018; Müller et al., 2019).

Physiology of GLP-1 and Mechanism of Action

Glucagon-like peptide-1 (GLP-1) is an endogenous incretin hormone that plays a central role in the regulation of glucose metabolism, appetite control, and energy homeostasis. It is primarily secreted by enteroendocrine L-cells located in the distal ileum and colon in response to nutrient intake (Holst, 2007; Drucker, 2018), particularly carbohydrates and fats. Following food consumption, GLP-1 is rapidly released into the circulation, where it exerts multiple physiological effects through activation of specific GLP-1 receptors distributed throughout the pancreas, gastrointestinal tract, cardiovascular system, kidneys, and central nervous system (Holst, 2007; Drucker, 2018).

Under normal physiological conditions, GLP-1 contributes to postprandial glucose regulation through several complementary mechanisms (Holst, 2007). It stimulates glucose-dependent insulin secretion from pancreatic β -cells while simultaneously suppressing glucagon release from α -cells. As a result, hepatic glucose production decreases and postprandial glycemic control improves (Drucker, 2018). Importantly, the insulinotropic effects of GLP-1 are glucose-dependent and are therefore associated with a low risk of hypoglycemia compared with many traditional antidiabetic medications (Holst, 2007; Drucker, 2018).

Beyond its effects on glucose metabolism, GLP-1 has a profound influence on appetite regulation and body weight control (Drucker, 2018; Müller et al., 2019). One of its primary mechanisms involves signaling within the central nervous system, particularly the hypothalamus and brainstem. GLP-1 receptors are expressed in multiple regions associated with energy balance, including the arcuate nucleus, paraventricular nucleus, and nucleus tractus solitarius. Activation of these receptors enhances satiety signaling and reduces hunger perception, ultimately leading to decreased caloric intake (Müller et al., 2019).

Experimental studies have demonstrated that GLP-1 receptor activation stimulates anorexigenic pathways while suppressing orexigenic neuronal activity (Secher et al., 2014). Specifically, GLP-1 enhances the activity of proopiomelanocortin (POMC) neurons and inhibits neuropeptide Y (NPY) and agouti-related peptide (AgRP) neurons, thereby promoting satiety and reducing food-seeking behavior (Secher et al., 2014; Drucker, 2018). These neurobiological effects are considered one of the primary mechanisms responsible for the substantial weight loss observed during treatment with GLP-1 receptor agonists.

Another important mechanism involves delayed gastric emptying (van Can et al., 2014). By slowing the rate at which gastric contents enter the small intestine, GLP-1 prolongs postprandial fullness and reduces the frequency and intensity of hunger signals between meals. This effect contributes not only to appetite suppression but also to improved glycemic control by moderating postprandial glucose excursions (van Can et al., 2014).

Recent neuroimaging studies have further expanded understanding of GLP-1 activity within the central nervous system (Müller et al., 2019). Experimental and clinical studies suggest that GLP-1 receptor activation influences reward-related pathways involved in food intake and hedonic eating (Müller et al., 2019). These findings suggest that GLP-1 receptor agonists influence not only physiological hunger but also behavioral and emotional aspects of eating.

In addition to their metabolic effects, GLP-1 receptor agonists may exert beneficial actions on cardiovascular and inflammatory pathways (Drucker, 2018; Müller et al., 2019). Evidence from adult populations suggests beneficial cardiovascular and anti-inflammatory effects of GLP-1 receptor agonists beyond weight reduction and glycemic control (Drucker, 2018; Müller et al., 2019). Although data in pediatric populations remain limited, these observations suggest potential long-term benefits extending beyond weight reduction alone (Drucker, 2018).

Native GLP-1 has a very short biological half-life of approximately one to two minutes due to rapid degradation by the enzyme dipeptidyl peptidase-4 (DPP-4) (Holst, 2007). This limitation has led to the development of synthetic GLP-1 receptor agonists with prolonged duration of action. Agents such as liraglutide and semaglutide are structurally modified to resist enzymatic degradation, allowing sustained receptor activation and clinically meaningful effects on appetite regulation and body weight management (Drucker, 2018; Müller et al., 2019).

The growing understanding of GLP-1 physiology has fundamentally transformed contemporary obesity treatment. By targeting multiple pathways involved in appetite regulation, satiety signaling, gastric emptying, and glucose homeostasis, GLP-1 receptor agonists provide a biologically rational therapeutic strategy for obesity management. This paradigm shift is particularly important in pediatric populations, where neuroendocrine mechanisms often contribute to the limited effectiveness of lifestyle interventions alone. Consequently, GLP-1 receptor agonists have emerged as promising therapeutic options capable of addressing several key pathophysiological mechanisms underlying obesity development and maintenance (Drucker, 2018; Müller et al., 2019).

Liraglutide in Pediatric Obesity

Liraglutide was the first GLP-1 receptor agonist approved by the FDA and later by the EMA for chronic weight management in adolescents aged 12 years and older (Kelly et al., 2020; Agosta et al., 2024). Originally developed for the treatment of type 2 diabetes mellitus, liraglutide demonstrated substantial weight-reducing effects through appetite suppression, delayed gastric emptying, and improved regulation of energy intake. These observations prompted further investigation of its potential role in pediatric patients with obesity.

Liraglutide is a long-acting GLP-1 receptor agonist administered as a once-daily subcutaneous injection (Drucker, 2018; Agosta et al., 2024). Its molecular structure allows prolonged receptor activation compared with native GLP-1, resulting in sustained effects on satiety and caloric intake. Through activation of central nervous system pathways involved in appetite regulation, liraglutide reduces hunger perception and promotes earlier meal termination, thereby contributing to weight reduction (Pi-Sunyer et al., 2015).

The pivotal SCALE Teens trial demonstrated that liraglutide, when combined with lifestyle intervention, produced significantly greater reductions in BMI and body weight than placebo among adolescents with obesity (Kelly et al., 2020). This randomized, double-blind, placebo-controlled study evaluated adolescents aged 12 to 17 years with obesity who received liraglutide in combination with lifestyle interventions. Participants treated with liraglutide achieved significantly greater reductions in body mass index (BMI) standard deviation scores and absolute body weight compared with those receiving placebo (Kelly et al., 2020). Furthermore, a substantially higher proportion of patients in the liraglutide group achieved clinically meaningful weight-loss targets, including reductions of at least 5% and 10% of baseline body weight (Kelly et al., 2020).

Beyond weight reduction, liraglutide treatment was associated with improvements in several cardiometabolic parameters (Kelly et al., 2020). Studies have reported favorable effects on insulin sensitivity, glycemic control, and selected cardiovascular risk markers. Although long-term pediatric data remain limited,

these findings suggest that liraglutide may help reduce the risk of obesity-related complications that often emerge during adolescence and persist into adulthood (Pi-Sunyer et al., 2015).

Emerging evidence suggests potential benefits of liraglutide in children younger than 12 years; however, available data remain limited and further studies are required (Agosta et al., 2024). Preliminary evidence indicates that treatment may also be effective in children under the age of 12 years when combined with structured lifestyle interventions. These findings have expanded interest in earlier pharmacological intervention, particularly in patients with severe obesity and multiple obesity-related comorbidities.

The safety profile of liraglutide in pediatric populations appears generally consistent with observations from adult studies (Liu et al., 2024; Agosta et al., 2024). Gastrointestinal adverse events are the most frequently reported side effects and include nausea, vomiting, diarrhea, abdominal pain, and decreased appetite. These symptoms are usually mild to moderate in severity and often improve during continued treatment (Agosta et al., 2024). Gradual dose escalation is commonly employed to improve treatment tolerability (Liu et al., 2024).

Serious adverse events are relatively uncommon (Liu et al., 2024). Nevertheless, continued monitoring of long-term safety remains necessary, particularly during prolonged treatment in growing children and adolescents. Additionally, because obesity treatment may extend over prolonged periods during critical stages of growth and development, further long-term studies are required to establish the safety of chronic GLP-1 receptor agonist therapy in pediatric patients (Liu et al., 2024; Agosta et al., 2024).

Current clinical guidelines increasingly recognize liraglutide as a valuable adjunct to lifestyle modification in adolescents with obesity who fail to achieve adequate weight reduction through behavioral interventions alone (Hampl et al., 2023). Its approval has expanded available treatment options and provided clinicians with an evidence-based pharmacological strategy for managing severe pediatric obesity (Hampl et al., 2023).

Despite these promising outcomes, several challenges remain (Agosta et al., 2024; Liu et al., 2024). Treatment costs, the requirement for daily injections, variability in individual response, and uncertainty regarding long-term maintenance of weight loss continue to influence clinical decision-making. Nevertheless, liraglutide has established an important foundation for the integration of incretin-based therapies into pediatric obesity management and has paved the way for newer agents, particularly semaglutide, which has demonstrated even greater efficacy in recent clinical trials.

Semaglutide in Pediatric Obesity

Semaglutide is a second-generation glucagon-like peptide-1 receptor agonist that has attracted considerable attention due to its remarkable efficacy in obesity treatment (Weghuber et al., 2022; Wilding et al., 2021). Unlike liraglutide, which requires once-daily administration, semaglutide is administered once weekly, potentially improving treatment convenience. Through sustained GLP-1 receptor activation, semaglutide enhances satiety, reduces hunger, and decreases energy intake, resulting in substantial weight reduction (Wilding et al., 2021; Weghuber et al., 2022).

The introduction of semaglutide has significantly influenced the therapeutic landscape of obesity management (Kushner et al., 2020; Wilding et al., 2021). While lifestyle modification remains the cornerstone of treatment, the substantial weight loss observed with semaglutide has increased interest in pharmacological approaches to obesity management. Consequently, semaglutide has become one of the most extensively studied anti-obesity medications in both adult and pediatric populations.

The efficacy of semaglutide in adolescents with obesity was demonstrated in the STEP TEENS trial (Weghuber et al., 2022), a randomized, double-blind, placebo-controlled study involving adolescents aged 12 to 18 years with obesity or overweight accompanied by at least one weight-related comorbidity. Participants received once-weekly subcutaneous semaglutide at a dose of 2.4 mg in combination with lifestyle interventions, including dietary counseling and physical activity recommendations (Weghuber et al., 2022).

The STEP TEENS trial demonstrated significant efficacy in adolescent obesity treatment, with participants receiving semaglutide achieving a mean reduction in BMI of 16.1% after 68 weeks of therapy, compared with a 0.6% increase in the placebo group (Weghuber et al., 2022). In addition, significantly more participants treated with semaglutide achieved clinically meaningful weight-loss targets compared with those receiving placebo (Weghuber et al., 2022).

In addition to weight reduction, semaglutide demonstrated favorable effects on several cardiometabolic parameters (Weghuber et al., 2022). Improvements were observed in waist circumference, glycated hemoglobin levels, lipid profiles, and other cardiometabolic risk factors (Weghuber et al., 2022). These

findings are particularly important because pediatric obesity is frequently associated with metabolic abnormalities that may persist into adulthood and contribute to long-term cardiovascular risk.

The safety profile of semaglutide in adolescents appears broadly consistent with observations in adult populations (Liu et al., 2024; Weghuber et al., 2022). Gastrointestinal adverse events remain the most commonly reported complications and include nausea, vomiting, diarrhea, constipation, and abdominal discomfort. These symptoms are generally mild to moderate in severity and tend to occur during dose escalation. Most adverse events resolve spontaneously or improve with continued treatment (Weghuber et al., 2022).

Although serious adverse events are uncommon, continued monitoring of long-term safety remains necessary, particularly during prolonged treatment in growing children and adolescents (Liu et al., 2024; Weghuber et al., 2022). Long-term safety data in pediatric populations remain limited, and further studies are required to establish the safety of chronic treatment throughout critical periods of growth and development.

An additional challenge concerns weight regain following treatment discontinuation. Evidence from adult studies suggests that a substantial proportion of lost weight may be regained after cessation of pharmacological therapy (Rubino et al., 2021). Whether similar patterns occur in pediatric populations remains under investigation. These findings support the concept of obesity as a chronic, relapsing disease that may require long-term management rather than short-term intervention (Rubino et al., 2021).

Despite these limitations, semaglutide currently represents one of the most effective pharmacological options available for adolescents with obesity (Weghuber et al., 2022; Wilding et al., 2021). Its substantial impact on body weight, favorable metabolic effects, and convenient once-weekly administration have positioned it as a major advancement in pediatric obesity treatment. As additional long-term data become available, semaglutide may become an increasingly important component of comprehensive obesity management strategies and may redefine therapeutic expectations for children and adolescents affected by severe obesity (Weghuber et al., 2022).

Safety and Adverse Effects of GLP-1 Receptor Agonists

The increasing use of glucagon-like peptide-1 receptor agonists in pediatric obesity has raised important questions regarding their safety, tolerability, and long-term effects during growth and development. Although current evidence indicates that GLP-1 receptor agonists are generally well tolerated in children and adolescents, careful assessment of potential adverse effects remains essential, particularly given the chronic nature of obesity treatment (Liu et al., 2024; Kelly et al., 2020; Weghuber et al., 2022).

Gastrointestinal adverse events represent the most frequently reported side effects associated with GLP-1 receptor agonist therapy, including nausea, vomiting, diarrhea, constipation, abdominal pain, and decreased appetite (Liu et al., 2024; Kelly et al., 2020; Weghuber et al., 2022). These symptoms are most commonly observed during treatment initiation and dose escalation. They are typically mild to moderate in severity and tend to diminish over time as patients adapt to therapy; gradual dose titration is therefore recommended to improve tolerability and reduce early discontinuation (Liu et al., 2024).

Among currently available agents, semaglutide and liraglutide demonstrate broadly similar safety profiles. Clinical trials have consistently shown that gastrointestinal symptoms constitute the primary reason for treatment interruption. However, most adverse events are transient and can often be managed through dietary modifications, slower dose escalation, and supportive care measures.

Gallbladder-related complications have been reported during treatment with GLP-1 receptor agonists. Available evidence suggests that these events may be associated both with rapid weight loss and with previously observed gallbladder-related effects of GLP-1 receptor agonists. (Bergmann et al., 2023).

Although pancreatitis has been considered a potential safety concern, current evidence from semaglutide clinical trials has not demonstrated a notable increase in the incidence of acute pancreatitis (Bergmann et al., 2023). Nevertheless, patients presenting with severe abdominal pain, persistent vomiting, or elevated pancreatic enzyme levels should undergo prompt clinical evaluation.

The long-term effects of GLP-1 receptor agonists on pubertal development, bone health, and linear growth remain incompletely understood (Hampl et al., 2023; Liu et al., 2024). Current clinical trials have generally reported no significant adverse effects on growth trajectories; however, available follow-up periods remain relatively short. Additional long-term observational studies are required to determine whether chronic treatment influences endocrine development, peak bone mass acquisition, or reproductive health outcomes (Hampl et al., 2023).

Psychological safety is another important aspect of obesity management. Although weight reduction often improves self-esteem and quality of life, clinicians should remain attentive to mental health status throughout treatment. Adolescents with obesity frequently experience anxiety, depression, body image concerns, and social stigma (Hampl et al., 2023). A multidisciplinary approach involving physicians, dietitians, psychologists, and family support may help optimize both physical and psychological outcomes (Hampl et al., 2023).

An emerging challenge relates to treatment discontinuation. Evidence from adult populations indicates that cessation of GLP-1 receptor agonist therapy is often associated with partial or substantial weight regain, highlighting the chronic and relapsing nature of obesity and the potential need for long-term treatment strategies (Rubino et al., 2021). Whether similar patterns occur among pediatric patients remains an important area for future investigation.

Overall, current evidence indicates that GLP-1 receptor agonists possess a favorable benefit-risk profile in appropriately selected pediatric patients with obesity; however, continued post-marketing surveillance and long-term observational studies are necessary to further clarify safety during growth and development (Liu et al., 2024; Hampl et al., 2023).

Long-Term Safety Considerations

Long-term safety remains one of the most important unresolved issues regarding the use of GLP-1 receptor agonists in pediatric obesity (Hampl et al., 2023; Liu et al., 2024). Although short- and medium-term clinical trials have demonstrated favorable tolerability, available follow-up periods are still limited compared with the expected duration of obesity treatment. Since obesity is a chronic disease, many patients may require prolonged or repeated pharmacological therapy, potentially extending over several years.

The long-term administration of GLP-1 receptor agonists during adolescence warrants special consideration because this period is characterized by substantial physical and psychological changes. Consequently, ongoing clinical follow-up should focus not only on treatment safety and efficacy but also on broader aspects of health and development, including skeletal maturation, nutritional adequacy, and psychosocial well-being (Hampl et al., 2023; Liu et al., 2024).

Another clinically relevant issue is treatment durability. Evidence from adult populations indicates that discontinuation of GLP-1 receptor agonist therapy is frequently followed by partial weight regain, suggesting that obesity may require long-term pharmacological management in selected patients, similar to other chronic diseases (Rubino et al., 2021). However, the optimal duration of treatment in adolescents remains unknown, and further long-term studies are needed to determine the sustainability of treatment effects and the risk of weight regain after therapy discontinuation.

Psychological well-being should remain an important component of obesity management in children and adolescents (Rankin et al., 2016; Pont et al., 2017). Adolescents with obesity frequently experience reduced self-esteem, impaired quality of life, anxiety, depression, and weight-related stigma, all of which may negatively affect health outcomes and treatment adherence (Pont et al., 2017). While successful weight reduction may improve self-esteem and quality of life, ongoing assessment of psychological well-being remains important throughout treatment (Rankin et al., 2016; Pont et al., 2017). For this reason, pharmacological treatment should be integrated with psychological support, nutritional education, and family-based care (Hampl et al., 2023).

Long-term post-marketing surveillance, registry-based studies, and extended clinical trials are therefore essential. Future research should determine whether GLP-1 receptor agonists provide sustained benefits into adulthood, reduce long-term cardiometabolic risk, and maintain an acceptable safety profile during prolonged use in pediatric populations. Furthermore, the long-term consequences of treatment discontinuation and the potential need for chronic therapy remain important areas for investigation (Hampl et al., 2023; Liu et al., 2024; Rubino et al., 2021).

Psychological and Quality-of-Life Outcomes

Childhood obesity is associated not only with physical health complications but also with substantial psychological, emotional, and social consequences (Rankin et al., 2016). Increasing evidence indicates that obesity can negatively affect multiple aspects of a child's well-being, including self-esteem, body image, social relationships, emotional well-being, and overall quality of life. As a result, modern obesity management extends beyond weight reduction alone and emphasizes the importance of improving psychosocial health and long-term well-being.

Young people with obesity commonly experience stigma, teasing, and other forms of weight bias, which have been associated with adverse effects on mental health, self-esteem, and overall quality of life (Pont et al., 2017). Negative stereotypes surrounding obesity may contribute to social isolation, bullying, and reduced participation in physical or recreational activities. Such experiences can significantly impair emotional development and contribute to long-term psychological distress (Pont et al., 2017).

Numerous studies have reported increased rates of anxiety, depressive symptoms, low self-esteem, and body dissatisfaction among adolescents with obesity compared with their normal-weight peers (Rankin et al., 2016). The relationship between obesity and mental health appears to be bidirectional. Psychological distress may contribute to maladaptive eating behaviors and reduced physical activity, while obesity-related stigma and social challenges may further exacerbate emotional difficulties (Rankin et al., 2016).

Quality of life assessments consistently demonstrate lower scores among children and adolescents with obesity across physical, emotional, social, and school functioning domains (Rankin et al., 2016). Severe obesity is often associated with greater impairment, suggesting that increasing disease severity may amplify psychosocial burden. Importantly, these effects may persist into adulthood if obesity remains untreated.

Successful obesity treatment has been associated with improvements in overall health and psychosocial functioning. Weight reduction may enhance self-confidence, body image perception, social functioning, and participation in daily activities. Improvements in physical health often translate into increased engagement in sports, recreational activities, and peer interactions, further supporting psychological well-being.

Clinical trials evaluating GLP-1 receptor agonists have primarily focused on weight-related and metabolic outcomes (Kelly et al., 2020; Weghuber et al., 2022). Nevertheless, substantial weight reduction achieved with these therapies may contribute to improvements in psychosocial functioning and quality of life. While current studies indicate potential benefits of GLP-1 receptor agonist therapy on quality of life and psychosocial functioning, long-term data regarding psychological outcomes in children and adolescents remain limited and warrant further investigation.

Nevertheless, expectations surrounding treatment outcomes require careful management. Unrealistic weight-loss goals may lead to disappointment, reduced adherence, and psychological distress if anticipated results are not achieved. Healthcare professionals should therefore provide individualized counseling and emphasize sustainable health improvements rather than focusing exclusively on body weight or appearance.

The integration of psychological support into obesity management is increasingly recommended by international guidelines (Hampl et al., 2023). Multidisciplinary care involving physicians, dietitians, psychologists, and family members may enhance treatment adherence, address emotional challenges, and improve long-term outcomes. Family engagement is particularly important, as parental attitudes, lifestyle habits, and emotional support substantially influence treatment success (Hampl et al., 2023).

As the use of GLP-1 receptor agonists expands within pediatric populations, future research should investigate their long-term effects on mental health, body image, eating behaviors, and overall quality of life. Understanding these outcomes will be essential for developing comprehensive treatment strategies that address both the physical and psychosocial dimensions of childhood obesity.

Current Guidelines and Recommendations

The growing prevalence of childhood obesity and the emergence of effective pharmacological therapies have prompted major medical organizations to update their clinical recommendations regarding obesity management in pediatric populations (Hampl et al., 2023; Styne et al., 2017). Contemporary guidelines increasingly recognize obesity as a chronic disease requiring comprehensive, individualized, and multidisciplinary treatment strategies rather than solely lifestyle-based interventions (Hampl et al., 2023).

Lifestyle modification remains the foundation of pediatric obesity treatment (Styne et al., 2017; Hampl et al., 2023). International guidelines consistently recommend a combination of nutritional counseling, increased physical activity, behavioral interventions, and family-based support as first-line therapy (Styne et al., 2017). These interventions aim to establish sustainable lifestyle habits and address environmental factors contributing to excessive weight gain. However, clinical experience and research evidence suggest that lifestyle interventions alone frequently provide insufficient long-term weight reduction, particularly among adolescents with severe obesity and obesity-related comorbidities (Hampl et al., 2023).

Recent clinical guidelines from the American Academy of Pediatrics recognize pediatric obesity as a chronic disease requiring early, comprehensive, and individualized treatment. The guideline emphasizes the importance of timely intervention to prevent long-term complications and recommends that treatment should not be delayed while waiting for lifestyle interventions alone to achieve sufficient results. Furthermore,

pharmacotherapy is recommended as an adjunct to intensive health behavior and lifestyle treatment for appropriately selected adolescents with obesity (Hampl et al., 2023).

Current recommendations generally support the use of anti-obesity medications in adolescents aged 12 years and older who have obesity and have not achieved adequate weight reduction through structured lifestyle interventions alone (Hampl et al., 2023). Pharmacological treatment should always be implemented as part of a comprehensive management plan that includes nutritional, behavioral, and physical activity components (Hampl et al., 2023; Styne et al., 2017).

Liraglutide was the first GLP-1 receptor agonist approved for obesity treatment in adolescents and is currently recommended as a therapeutic option for selected patients with persistent obesity despite lifestyle modification. Clinical trial data demonstrate its ability to achieve clinically meaningful weight reduction and improve obesity-related risk factors (Kelly et al., 2020). However, treatment decisions should consider patient preferences, treatment adherence, potential adverse effects, and long-term management goals.

More recently, semaglutide has gained increasing attention following the publication of promising clinical trial results (Weghuber et al., 2022). Its once-weekly administration and superior efficacy in reducing body weight have positioned it as a potentially transformative therapy in adolescent obesity management (Weghuber et al., 2022; Wilding et al., 2021).

Although national and international recommendations continue to evolve as new evidence becomes available, semaglutide is increasingly recognized as a promising therapeutic option for adolescents with obesity following the publication of the STEP TEENS trial (Weghuber et al., 2022).

Similarly, the Endocrine Society Clinical Practice Guideline emphasizes a multidisciplinary and individualized approach to pediatric obesity treatment (Styne et al., 2017). Pharmacotherapy is generally reserved for patients with moderate-to-severe obesity, particularly when obesity-related complications such as insulin resistance, type 2 diabetes mellitus, hypertension, obstructive sleep apnea, or metabolic dysfunction-associated steatotic liver disease are present. Careful patient selection and ongoing monitoring are considered essential components of safe and effective treatment (Hampl et al., 2023).

Clinical guidelines also highlight the importance of regular follow-up during pharmacological therapy (Hampl et al., 2023). Monitoring typically includes assessment of body weight, body mass index, growth parameters, metabolic markers, treatment adherence, adverse events, and psychosocial well-being. Given the limited long-term data currently available, ongoing surveillance remains particularly important in pediatric populations (Liu et al., 2024).

Despite significant progress, several challenges remain regarding the integration of pharmacotherapy into routine clinical practice. Access to treatment, medication costs, healthcare disparities, and uncertainties regarding optimal treatment duration continue to influence implementation. Furthermore, evidence-based recommendations for long-term maintenance therapy and management following treatment discontinuation remain areas of active investigation.

Overall, contemporary clinical guidelines increasingly support the use of GLP-1 receptor agonists as part of a comprehensive and individualized obesity management strategy in carefully selected pediatric patients. As additional evidence emerges, future recommendations will further define optimal patient selection, treatment duration, monitoring strategies, and the role of next-generation incretin-based therapies in childhood obesity management (Hampl et al., 2023; Styne et al., 2017).

Comparison of GLP-1 Receptor Agonists and Bariatric Surgery in Adolescents

Bariatric surgery remains an important treatment option for selected adolescents with severe obesity. Procedures such as sleeve gastrectomy and Roux-en-Y gastric bypass have demonstrated substantial and sustained improvements in body weight, metabolic health, and obesity-related comorbidities. However, surgical treatment is invasive and requires careful patient selection, multidisciplinary assessment, and long-term follow-up (Armstrong et al., 2019).

Recent advances in pharmacological therapy have raised important questions regarding the role of GLP-1 receptor agonists as alternatives or adjuncts to bariatric surgery. The substantial weight reduction observed with semaglutide and other incretin-based therapies has narrowed the gap between medical and surgical obesity treatment, particularly in adolescents with moderate-to-severe obesity (Weghuber et al., 2022; Kelly et al., 2020).

Clinical trials have shown that semaglutide can achieve mean body weight reductions approaching 15–16% in adolescents (Weghuber et al., 2022), whereas bariatric surgery typically results in weight loss ranging from 25% to 35% depending on the procedure and duration of follow-up (Inge et al., 2016). Although surgical

intervention generally produces greater overall weight reduction, pharmacotherapy offers several advantages, including lower procedural risk, reversibility, and broader accessibility for selected patients.

In addition to weight reduction, both approaches demonstrate beneficial effects on cardiometabolic health (Inge et al., 2016; Weghuber et al., 2022). Bariatric surgery has been associated with significant improvements in type 2 diabetes mellitus, hypertension, dyslipidemia, obstructive sleep apnea, and metabolic dysfunction-associated steatotic liver disease (MASLD). Similarly, GLP-1 receptor agonists have shown favorable effects on insulin sensitivity, glycemic control, lipid metabolism, and cardiovascular risk markers. However, the magnitude and durability of these benefits remain more extensively documented for bariatric surgery due to longer follow-up data (Armstrong et al., 2019).

Safety considerations differ substantially between the two treatment modalities. Bariatric surgery carries risks related to anesthesia, postoperative complications, nutritional deficiencies, and the need for lifelong medical monitoring. In contrast, GLP-1 receptor agonists are generally associated with gastrointestinal adverse events that are usually mild to moderate in severity. Long-term safety data for GLP-1 receptor agonists in pediatric populations remain limited, especially regarding growth, pubertal development, bone health, nutritional status, and reproductive outcomes (Hampl et al., 2023; Liu et al., 2024).

Patient preferences and psychosocial factors also influence treatment selection (Armstrong et al., 2019). Some adolescents and their families may prefer a non-surgical approach due to concerns regarding operative risks or the permanent anatomical changes associated with bariatric procedures. Others may favor surgery when severe obesity significantly impairs quality of life and previous treatment attempts have failed. Shared decision-making therefore plays a central role in determining the most appropriate therapeutic strategy.

Recent advances in pharmacotherapy have significantly expanded treatment options for adolescents with obesity. Although bariatric surgery remains an important treatment option for selected patients with severe obesity, GLP-1 receptor agonists have demonstrated substantial reductions in BMI and body weight, providing an effective non-surgical alternative for many adolescents (Armstrong et al., 2019; Weghuber et al., 2022).

Future Perspectives

The therapeutic landscape of obesity management is evolving rapidly, with significant advances occurring in the field of incretin-based therapies. While liraglutide and semaglutide have already demonstrated substantial efficacy in pediatric obesity treatment, emerging pharmacological agents may further improve weight-loss outcomes and expand therapeutic possibilities for children and adolescents affected by obesity.

One of the most promising developments is tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist (Jastreboff et al., 2022). By simultaneously targeting two complementary metabolic pathways, tirzepatide has demonstrated substantial weight-loss outcomes in adult clinical trials (Jastreboff et al., 2022). In several studies, patients achieved average weight reductions exceeding those observed with currently available GLP-1 receptor agonists. Although pediatric studies remain ongoing, preliminary findings suggest that dual receptor agonists may represent the next generation of obesity pharmacotherapy.

Another highly anticipated agent is retatrutide, a novel triple agonist targeting GLP-1, GIP, and glucagon receptors (Jastreboff et al., 2023). Early phase clinical trials in adults have demonstrated substantial reductions in body weight, with some participants achieving weight loss exceeding 20% of baseline body weight (Jastreboff et al., 2023). The ability to influence multiple metabolic pathways simultaneously may offer additional benefits in appetite regulation, energy expenditure, and metabolic health. Future pediatric studies will be necessary to evaluate the safety and efficacy of these agents in younger populations.

Beyond the development of new medications, increasing attention is being directed toward personalized obesity treatment. Childhood obesity is a heterogeneous condition influenced by diverse genetic, metabolic, environmental, and behavioral factors. Consequently, treatment responses vary considerably among individuals. Advances in precision medicine may enable clinicians to identify specific patient characteristics associated with optimal responses to particular pharmacological interventions. Biomarkers, genetic profiling, and metabolic phenotyping may eventually facilitate individualized treatment selection and improve long-term outcomes (Hampl et al., 2023).

The role of pharmacotherapy may also expand to earlier stages of disease progression. Historically, anti-obesity medications have been reserved for adolescents with severe obesity and significant comorbidities. However, growing evidence suggests that earlier intervention may prevent the development of irreversible metabolic complications and improve long-term health trajectories. Future clinical trials are expected to

investigate the benefits and risks of introducing pharmacological treatment at younger ages and earlier disease stages (Hampl et al., 2023).

Nevertheless, several important challenges remain. Long-term safety data for incretin-based therapies in pediatric populations are still limited. Questions regarding treatment duration, maintenance strategies, cost-effectiveness, and management following treatment discontinuation require further investigation. In addition, healthcare systems must address issues related to medication accessibility and equitable distribution of emerging therapies.

Future research should focus not only on weight reduction but also on broader health outcomes, including cardiometabolic risk, psychological well-being, quality of life, and long-term disease prevention. Understanding how pharmacological interventions influence these outcomes throughout childhood and adulthood will be essential for optimizing treatment strategies.

Overall, the future of pediatric obesity management appears increasingly promising. Continued advances in incretin-based therapies, personalized medicine, and multidisciplinary care models may fundamentally transform the treatment of childhood obesity and significantly reduce its long-term health burden. As scientific understanding expands, the management of pediatric obesity is likely to become more effective, individualized, and comprehensive than ever before.

Limitations of Current Evidence

Despite the encouraging results reported in recent clinical trials, several important limitations remain regarding the current evidence supporting the use of GLP-1 receptor agonists in pediatric obesity. These limitations should be carefully considered when interpreting study findings and applying them in clinical practice.

First, the majority of available studies have relatively short follow-up periods. Most randomized controlled trials evaluating liraglutide and semaglutide in children and adolescents have assessed outcomes over approximately one to two years. Although these studies provide valuable information regarding short-term efficacy and safety, they do not fully address the long-term consequences of treatment extending throughout adolescence and into adulthood. As obesity is a chronic disease, longer observation periods are necessary to determine the durability of weight loss and the sustainability of metabolic improvements.

Second, data regarding the long-term safety of GLP-1 receptor agonists during critical stages of growth and development remain limited. While current evidence has not identified major safety concerns, uncertainties persist regarding potential effects on pubertal development, bone health, reproductive function, and nutritional status. Additional long-term studies are required to establish comprehensive safety profiles in pediatric populations (Liu et al., 2024; Hampl et al., 2023).

Another limitation concerns the generalizability of available trial results. Many clinical studies have been conducted in highly selected patient populations under controlled research conditions. Participants often receive intensive lifestyle counseling, frequent medical follow-up, and structured support that may not be readily available in routine clinical practice. Consequently, real-world treatment outcomes may differ from those reported in clinical trials.

Furthermore, most studies have focused primarily on changes in body weight and body mass index as primary outcome measures. Although these parameters are clinically important, obesity is a complex disease associated with numerous metabolic, cardiovascular, psychological, and social consequences. Future research should place greater emphasis on patient-centered outcomes, including quality of life, mental health, psychosocial functioning, and long-term disease prevention.

The issue of treatment discontinuation represents another significant knowledge gap. Evidence from adult populations suggests that substantial weight regain frequently occurs after cessation of GLP-1 receptor agonist therapy. However, limited data are currently available regarding long-term outcomes following treatment withdrawal in pediatric patients. Understanding whether prolonged therapy is necessary to maintain benefits remains an important clinical question.

Economic considerations also warrant attention. The high cost of GLP-1 receptor agonists may limit accessibility and contribute to healthcare disparities. Cost-effectiveness analyses in pediatric populations remain scarce, and future studies should evaluate the economic impact of widespread implementation of these therapies.

Finally, emerging agents such as tirzepatide and retatrutide show considerable promise, but evidence in children and adolescents remains extremely limited. While adult studies have demonstrated significant weight-

loss efficacy, direct extrapolation of these findings to pediatric populations should be approached with caution until dedicated pediatric trials become available.

Taken together, these limitations highlight the need for larger, longer-term, and more diverse pediatric clinical studies. Future research should focus not only on weight reduction but also on long-term safety, quality of life, treatment sustainability, and real-world effectiveness to better inform evidence-based obesity management in children and adolescents.

Practical Challenges in Pediatric GLP-1 Therapy

Despite the growing evidence supporting the efficacy of GLP-1 receptor agonists in pediatric obesity, several practical challenges continue to limit their widespread implementation in routine clinical practice. These barriers involve economic, organizational, behavioral, and healthcare-system factors that may influence treatment accessibility, adherence, and long-term effectiveness.

One of the most significant challenges is the high cost of treatment. GLP-1 receptor agonists are among the most expensive pharmacological options currently available for obesity management. In many countries, reimbursement policies remain limited or absent, requiring patients and their families to cover substantial out-of-pocket expenses. As a result, access to treatment may be restricted, particularly among socioeconomically disadvantaged populations, potentially exacerbating existing healthcare inequalities.

Another important consideration is treatment adherence. Unlike many traditional pediatric medications, GLP-1 receptor agonists are administered via subcutaneous injection. Although semaglutide offers the advantage of once-weekly administration compared with the daily dosing required for liraglutide, fear of injections may still represent a barrier for some children and adolescents. Adequate patient education, family support, and healthcare provider guidance are essential to promote acceptance and adherence.

Family involvement plays a particularly important role in pediatric obesity treatment. Parents and caregivers significantly influence dietary habits, physical activity levels, medication adherence, and healthcare utilization. Successful implementation of GLP-1 receptor agonist therapy often depends on family engagement and the ability to maintain supportive lifestyle changes alongside pharmacological treatment. Without sustained family participation, treatment benefits may be reduced.

Healthcare provider experience and training may also influence treatment outcomes. The rapid expansion of anti-obesity pharmacotherapy has created a need for increased education among pediatricians, endocrinologists, dietitians, and primary care physicians. Appropriate patient selection, dose titration, adverse event monitoring, and long-term follow-up require familiarity with these relatively new therapeutic agents.

Social perceptions of obesity treatment represent another challenge. Misconceptions that obesity is solely the result of poor lifestyle choices may contribute to reluctance regarding pharmacological intervention. Some patients, families, and healthcare professionals may view medication as unnecessary or inappropriate, despite growing recognition of obesity as a chronic biological disease. Educational efforts aimed at improving public understanding of obesity pathophysiology may facilitate broader acceptance of evidence-based treatment strategies.

Long-term treatment planning remains an area of uncertainty. Current evidence from adult populations suggests that discontinuation of GLP-1 receptor agonist therapy is frequently associated with weight regain. However, long-term pediatric data remain limited. Consequently, clinicians and families face important questions regarding treatment duration, maintenance strategies, and the balance between long-term benefits and costs. Clear evidence-based recommendations are still evolving and will likely become a major focus of future clinical research.

Finally, healthcare systems must adapt to the increasing demand for comprehensive obesity care. Effective treatment requires multidisciplinary collaboration involving physicians, dietitians, psychologists, exercise specialists, and family support services. The availability of such resources varies substantially between regions and healthcare settings, potentially affecting treatment accessibility and outcomes.

Despite these challenges, the introduction of GLP-1 receptor agonists represents a major advancement in pediatric obesity management. Addressing economic, educational, and organizational barriers will be essential to maximize the clinical benefits of these therapies and ensure equitable access for children and adolescents who may benefit from treatment.

Conclusions

Childhood obesity has become one of the most significant public health challenges worldwide, with prevalence rates continuing to rise across both developed and developing countries. The growing burden of pediatric obesity is associated with numerous metabolic, cardiovascular, endocrine, and psychological complications that may persist throughout adulthood, highlighting the urgent need for effective prevention and treatment strategies. As obesity is now recognized as a chronic, multifactorial disease, management approaches must extend beyond traditional lifestyle interventions and address the complex biological mechanisms underlying weight regulation.

Although dietary modification, physical activity, behavioral counseling, and family-based interventions remain fundamental components of treatment, their long-term effectiveness is often limited, particularly among children and adolescents with severe obesity. These limitations have stimulated the development of novel pharmacological therapies targeting appetite regulation and energy homeostasis.

Glucagon-like peptide-1 receptor agonists have emerged as one of the most important therapeutic advances in pediatric obesity management. By influencing central appetite pathways, delaying gastric emptying, and improving metabolic regulation, these agents provide a scientifically grounded approach to obesity treatment. Clinical studies have demonstrated that both liraglutide and semaglutide can achieve clinically meaningful reductions in body weight and body mass index while also improving cardiometabolic risk factors.

Among currently available GLP-1 receptor agonists, semaglutide appears to offer the greatest efficacy, producing substantial reductions in body weight and demonstrating the potential to transform treatment expectations for adolescents with obesity. In addition to weight reduction, emerging evidence suggests potential benefits for overall health, psychosocial functioning, and obesity-related comorbidities, although further research is needed to better characterize these outcomes.

Current data indicate that GLP-1 receptor agonists possess a generally favorable safety profile in pediatric populations. Gastrointestinal adverse events remain the most commonly reported complications and are usually manageable with appropriate dose escalation and clinical monitoring. Nevertheless, important questions remain regarding long-term treatment duration, maintenance of weight loss following therapy discontinuation, and the effects of prolonged treatment during critical periods of growth and development. Continued post-marketing surveillance and long-term clinical studies are therefore essential.

The future of pediatric obesity treatment appears particularly promising. Novel incretin-based therapies, including dual and triple receptor agonists such as tirzepatide and retatrutide, may further enhance therapeutic efficacy and expand available treatment options. Advances in personalized medicine and individualized treatment strategies may further improve patient selection and optimize long-term outcomes.

In conclusion, GLP-1 receptor agonists represent a major advancement in the management of childhood obesity and may significantly improve the care of children and adolescents affected by this chronic disease. While lifestyle interventions remain indispensable, pharmacological therapies are increasingly becoming an integral component of comprehensive obesity treatment. Future research should focus on long-term safety, treatment sustainability, and the development of personalized therapeutic approaches capable of reducing the lifelong burden of obesity and its associated complications.

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