



International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	INCRETIN-BASED THERAPIES FOR OBESITY MANAGEMENT: THE IMPACT OF PATIENT EDUCATION AND LIFESTYLE MODIFICATION ON LONG-TERM TREATMENT OUTCOMES
----------------------	---------------------------------------------------------------------------------------------------------------------------------------------

DOI	https://doi.org/10.31435/ijitss.4(48).2025.4225
------------	---------------------------------------------------------------------------------------------------------------

RECEIVED	29 September 2025
-----------------	-------------------

ACCEPTED	15 December 2025
-----------------	------------------

PUBLISHED	23 December 2025
------------------	------------------

LICENSE



The article is licensed under a **Creative Commons Attribution 4.0 International License**.

© The author(s) 2025.

This article is published as open access under the Creative Commons Attribution 4.0 International License (CC BY 4.0), allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

INCRETIN-BASED THERAPIES FOR OBESITY MANAGEMENT: THE IMPACT OF PATIENT EDUCATION AND LIFESTYLE MODIFICATION ON LONG-TERM TREATMENT OUTCOMES

Natalia Senatorska (Corresponding Author, Email: senatorska.natalia@gmail.com)

Medical University of Lodz, Łódź, Poland

ORCID ID: 0009-0009-8167-9839

Katarzyna Kleszczewska

Independent Public Health Care Complex in Myszków, Myszków, Poland

ORCID ID: 0009-0009-4177-089X

Agnieszka Pruska

University Clinical Center in Gdansk, Gdańsk, Poland

ORCID ID: 0000-0002-4439-5126

Julia Rarok

Faculty of Medicine, University of Opole, Opole, Poland

ORCID ID: 0009-0009-7433-2175

Daria Godlewska

Medical University of Warsaw, Warsaw, Poland

ORCID ID: 0009-0001-3640-3552

Hanna Pietruszewska

Medical University of Lodz, Łódź, Poland

ORCID ID: 0009-0000-7626-2996

Monika Banaszek

Independent Public Healthcare Center in Puławy, Puławy, Poland

ORCID ID: 0009-0006-4696-8756

Agata Panfil

Prof. K. Gibiński University Clinical Centre of the Medical University of Silesia in Katowice, Katowice, Poland

ORCID ID: 0009-0008-9589-4305

Julia Błocka

4th Military Clinical Hospital, Wrocław, Poland

ORCID ID: 0009-0000-1698-4591

Agata Lurka

Provincial Hospital in Poznan, Poznań, Poland

ORCID ID: 0009-0005-6851-3763

ABSTRACT

Obesity represents one of the most pressing global health challenges, driven by complex biological, behavioral, and environmental factors. Incretin-based pharmacotherapies, such as GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists, have redefined the clinical approach to obesity management by enabling substantial and sustained weight reduction. However, long-term treatment success extends beyond pharmacological efficacy alone. This review examines the role of patient education and lifestyle modification as critical determinants of adherence, behavioral change, and sustainability of weight loss during incretin therapy. Integrating pharmacotherapy with structured education, digital coaching, and telehealth-based interventions enhances motivation, reduces treatment fatigue, and promotes lasting metabolic improvement. The interdisciplinary model proposed in this study positions patient empowerment and health literacy as key drivers of therapeutic success. By combining medical innovation with behavioral and social approaches, incretin therapy can evolve into a cornerstone of holistic, technology-supported chronic obesity management.

KEYWORDS

Incretin Therapy, GLP-1 Receptor Agonists, Tirzepatide, Obesity Management, Patient Education, Behavioral Therapy, Lifestyle Modification, Adherence, Chronic Disease Model, Telehealth

CITATION

Natalia Senatorska, Katarzyna Kleszczewska, Agnieszka Pruska, Julia Rarok, Daria Godlewska, Hanna Pietruszewska, Monika Banaszek, Agata Panfil, Julia Błocka, Agata Lurka. (2025). Incretin-Based Therapies for Obesity Management: The Impact of Patient Education and Lifestyle Modification on Long-Term Treatment Outcomes. *International Journal of Innovative Technologies in Social Science*. 4(48). doi: 10.31435/ijitss.4(48).2025.4225

COPYRIGHT

© The author(s) 2025. This article is published as open access under the **Creative Commons Attribution 4.0 International License (CC BY 4.0)**, allowing the author to retain copyright. The CC BY 4.0 License permits the content to be copied, adapted, displayed, distributed, republished, or reused for any purpose, including adaptation and commercial use, as long as proper attribution is provided.

1. Introduction

Obesity is a chronic, multifactorial, and relapsing metabolic disorder that has reached epidemic proportions worldwide. According to the World Health Organization (WHO), more than 650 million adults were classified as obese in 2016, and this number is projected to exceed 1.2 billion by 2030 (Emmerich et al., 2024). Recent global analyses published in *The Lancet* indicate that the prevalence of obesity continues to rise across all income levels, with particularly rapid increases observed in younger adults and low- to middle-income countries (Ng et al., 2025). The condition represents one of the most significant public health challenges of the 21st century due to its strong association with cardiometabolic comorbidities, including type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, and several cancers, all of which contribute to reduced life expectancy and quality of life (Wilding et al., 2022).

Conventional management strategies for obesity—primarily lifestyle interventions involving caloric restriction and physical activity, as well as bariatric surgery—often result in limited long-term efficacy. High relapse rates and the challenge of maintaining weight loss highlight the chronic and relapsing nature of the disease (Berg et al., 2025). These limitations have prompted the development of pharmacological agents that target hormonal and neural pathways regulating appetite and energy balance.

Incretin-based pharmacotherapies have emerged as a major advance in obesity treatment. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) mimic endogenous gut hormones that regulate appetite, satiety, and glucose metabolism. Agents such as semaglutide have demonstrated substantial efficacy in clinical trials, producing mean body weight reductions of approximately 15% compared with placebo (Qin et al., 2024).

More recently, dual agonists targeting both GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors have set new benchmarks in obesity pharmacotherapy. Tirzepatide, the first approved dual GLP-1/GIP agonist, has shown mean weight reductions exceeding 20% in the SURMOUNT-1 and SURMOUNT-4 clinical programs, significantly outperforming semaglutide and earlier incretin analogues (Jastreboff et al., 2022). Head-to-head studies published in *The New England Journal of Medicine* in 2025 further confirmed superior efficacy of tirzepatide compared with semaglutide for weight loss and metabolic improvement (Aronne et al., 2025).

Despite these unprecedented results, sustaining weight loss after discontinuation remains a clinical challenge. Evidence shows that cessation of GLP-1 receptor agonist therapy leads to partial or complete weight regain, underscoring the need for continued treatment and comprehensive management (Berg et al., 2025). Therefore, pharmacotherapy should be considered one element within a holistic, patient-centered framework that also incorporates lifestyle modification and behavioral support.

Patient education represents a cornerstone of such an integrated approach. A deeper understanding of the mechanisms of action, expected benefits, and potential side effects of incretin-based medications enhances adherence, motivation, and self-efficacy among patients. Furthermore, combining pharmacotherapy with structured behavioral and educational interventions has been shown to improve long-term outcomes and treatment sustainability (Wang et al., 2024).

The objective of this review is to provide an up-to-date overview of incretin-based therapies for obesity management, emphasizing the synergistic role of patient education and lifestyle modification in maintaining therapeutic efficacy. By integrating pharmacological advances with behavioral science, this paper highlights the importance of an interdisciplinary and patient-centered model for the long-term management of obesity.

2. Incretin therapies – mechanisms and general characteristics

2.1. The role of incretins in metabolism regulation

Incretins are gastrointestinal hormones that play a fundamental role in postprandial glucose regulation and appetite control. The two primary incretins—glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP)—are secreted by enteroendocrine L and K cells, respectively, in response to nutrient ingestion (Campbell et al., 2023). GLP-1 enhances glucose-dependent insulin secretion, inhibits glucagon release, slows gastric emptying, and promotes satiety, collectively contributing to reduced caloric intake and improved glycemic control. GIP also stimulates insulin secretion but exhibits a more complex role in lipid metabolism and adipose tissue regulation, with ongoing research exploring its differential impact on energy balance (Boer et al., 2023; Müller et al., 2019).

2.2. Classic incretin therapies

The first generation of incretin-based drugs comprised GLP-1 receptor agonists (GLP-1 RAs), such as liraglutide, exenatide, and semaglutide. These agents mimic endogenous GLP-1, producing clinically significant weight loss and improved metabolic control in patients with obesity and type 2 diabetes. Semaglutide, in particular, has demonstrated mean weight reductions of approximately 15% compared to placebo in large-scale trials (STEP program) and has become the reference agent for next-generation incretin therapies (Rodriguez et al., 2024; Wilding et al., 2021).

GLP-1 RAs act through both central and peripheral pathways—reducing appetite via hypothalamic signaling and enhancing insulin sensitivity in peripheral tissues (Rodriguez et al., 2024).

2.3. Modern incretin therapies

Modern incretin therapies extend beyond monoreceptor agonism to target multiple metabolic pathways simultaneously. The most notable example is tirzepatide, a dual GLP-1/GIP receptor agonist that produces synergistic effects on insulin secretion, glucagon suppression, and appetite regulation (Cai et al., 2024; Rodriguez et al., 2024).

Clinical trials from the SURMOUNT program have shown that tirzepatide achieves mean weight losses of 20–25%, surpassing the efficacy of semaglutide (Aronne et al., 2024; Cai et al., 2024).

Newer dual and triple incretin agonists—such as retatrutide (GLP-1/GIP/glucagon agonist)—are currently under investigation and show promising results, with mean weight reductions of up to 24% in phase 2 studies (Jastreboff et al., 2023). Such multimodal agents represent the next frontier in metabolic pharmacotherapy.

2.4. Mechanisms of action of incretin therapies

The clinical efficacy of incretin-based drugs is mediated through a combination of central (hypothalamic) and peripheral mechanisms. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual agonists enhance glucose-dependent insulin secretion, thereby reducing postprandial glucose excursions. At the same time, they suppress glucagon secretion, which leads to a decrease in hepatic glucose production. By delaying gastric emptying, these agents increase satiety and prolong the sensation of postprandial fullness. Furthermore, they exert central effects by acting on hypothalamic centers such as the arcuate nucleus, where they modulate

appetite through neuronal populations expressing pro-opiomelanocortin (POMC) and neuropeptide Y (NPY) (Boer et al., 2023; Campbell et al., 2023).

Dual and triple agonists may further improve adipose tissue metabolism and energy expenditure through mild glucagon receptor activation, promoting lipolysis and thermogenesis (Brandt et al., 2018).

2.5. Efficacy and safety of incretin therapies

Clinical evidence consistently demonstrates that incretin-based therapies are both effective and safe in the management of obesity. Tirzepatide achieved average body weight reductions of 21–25% in pivotal phase 3 trials, with significant improvements in glycemic control, lipid profiles, and markers of insulin resistance (Cai et al., 2024; Jastreboff et al., 2023).

Common adverse effects include transient gastrointestinal symptoms—nausea, vomiting, diarrhea, and constipation—typically resolving after a few weeks of therapy (Chetty et al., 2024). Rare events such as gallstones or pancreatitis may occur, often associated with rapid weight loss rather than direct drug toxicity (Cai et al., 2024). Importantly, long-term surveillance has not confirmed any increased risk of medullary thyroid carcinoma or other major safety concerns in humans (Chetty et al., 2024).

Overall, incretin-based pharmacotherapy represents a paradigm shift in obesity management, combining metabolic efficacy with an acceptable safety profile.

3. The effectiveness of incretin therapies in the treatment of obesity – data from clinical trials

3.1. Introduction

Over the past five years, incretin-based pharmacotherapies have revolutionized obesity management. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) and dual GLP-1/GIP receptor agonists have shown clinically meaningful and sustained weight reduction, accompanied by improvement in glycemic control, lipid profile, and blood pressure (Kosiborod et al., 2023; Wadden et al., 2021; Wilding et al., 2021).

These effects extend beyond energy balance regulation—recent analyses demonstrate significant improvements in cardiometabolic outcomes, liver steatosis, and inflammatory biomarkers, positioning incretin agonists as metabolic disease-modifying agents rather than solely appetite suppressants (Caruso et al., 2024; Giordano et al., 2023).

The pivotal clinical trial programs—STEP for semaglutide and SURMOUNT for tirzepatide—have set a new benchmark in the evidence-based pharmacotherapy of obesity. Their robust design, long duration, and inclusion of diverse populations provide a high level of clinical certainty regarding both efficacy and safety (Aronne et al., 2024; Kosiborod et al., 2023; Wilding et al., 2021).

Importantly, the integration of pharmacotherapy with behavioral interventions, as seen in the STEP-3 study, underscores the potential of a multidimensional treatment model for chronic weight management (Wadden et al., 2021).

3.2. Efficacy of semaglutide in the treatment of obesity

Semaglutide, a long-acting GLP-1 receptor agonist administered once weekly, remains the most thoroughly studied incretin-based drug for obesity treatment.

The STEP 1 randomized controlled trial demonstrated a mean weight reduction of 14.9% at 68 weeks with semaglutide 2.4 mg compared to 2.4% in the placebo group among adults with obesity but without diabetes (Wilding et al., 2021). In STEP 3, which combined semaglutide with intensive behavioral therapy, the mean weight loss reached 16.0% vs. 5.7% with placebo, confirming a synergistic effect between pharmacological and behavioral strategies (Wadden et al., 2021).

Subsequent meta-analyses and real-world studies have confirmed the reproducibility of these outcomes, showing sustained weight reductions of 10–15% and marked improvements in glycemic control, triglycerides, and systolic blood pressure (Ghusn et al., 2022; Giordano et al., 2023). In a 2-year follow-up (STEP 5), semaglutide maintained weight loss and improved cardiometabolic parameters without new safety concerns (Kosiborod et al., 2023).

Collectively, semaglutide represents a breakthrough in obesity pharmacotherapy—an agent that combines potent efficacy, cardiometabolic benefits, and a safety profile consistent with long-term use. It also established the clinical foundation for next-generation incretin-based agents such as tirzepatide and retatrutide.

3.3. Dual GLP-1/GIP agonists – a new direction in obesity treatment

Dual incretin receptor agonists represent the next major advancement in obesity pharmacotherapy. Tirzepatide, the first dual GLP-1/GIP agonist approved for clinical use, has demonstrated superior efficacy compared with GLP-1 monotherapy. In the SURMOUNT-1 trial, adults with obesity but without diabetes achieved an average weight loss of 20.9% with tirzepatide 15 mg weekly versus 3.1% in the placebo group after 72 weeks (Jastreboff et al., 2022). Body composition analyses confirmed that approximately 33.9% of the reduction corresponded to adipose tissue mass, while 10.9% involved lean tissue, indicating preferential fat loss (Look et al., 2025).

A head-to-head trial comparing tirzepatide and semaglutide showed even greater weight reduction with tirzepatide (−20.2% vs −13.8%) and superior improvements in glycemic parameters and lipid metabolism (Rodriguez et al., 2024). Furthermore, tirzepatide has been associated with favorable cardiovascular and hepatic outcomes, including reductions in liver fat and inflammatory markers (Kosiborod et al., 2023).

The next generation of incretin-based drugs—such as retatrutide, a triple GLP-1/GIP/glucagon receptor agonist—shows promise in early trials, achieving weight loss exceeding 24% in 48 weeks and further enhancing metabolic flexibility (Jastreboff et al., 2023).

3.4. Sustainability of effects and the problem of weight regain

Despite impressive short-term efficacy, maintaining weight loss after discontinuation of incretin therapy remains a major clinical challenge. In the STEP 4 trial, patients who continued semaglutide treatment maintained or enhanced their weight loss (−7.9%), while those switched to placebo regained 6.9% of body weight within 48 weeks (D. Rubino et al., 2021). Similarly, the SURMOUNT-4 study found that continued tirzepatide therapy was necessary to prevent substantial weight regain, confirming the chronic nature of obesity and the need for ongoing treatment (Aronne et al., 2024).

Mechanistically, discontinuation leads to reactivation of homeostatic neurohormonal systems that favor weight regain—such as increased ghrelin and decreased leptin and peptide YY levels—highlighting the physiological drive to restore energy balance (Van Baak & Mariman, 2025). These findings underscore the need for a chronic-disease management model combining pharmacotherapy, lifestyle intervention, and ongoing patient education to ensure durable outcomes.

3.5. Safety profile of incretin therapies

Incretin-based therapies exhibit a favorable safety and tolerability profile across multiple clinical trials and real-world studies. The most common adverse events are mild to moderate gastrointestinal symptoms—nausea, vomiting, diarrhea, and constipation—which typically occur during the dose-escalation phase and resolve within several weeks (Chetty et al., 2024).

Serious adverse events are rare. The initially hypothesized risk of medullary thyroid carcinoma observed in rodent studies has not been confirmed in human trials or post-marketing surveillance (Chetty et al., 2024). Isolated cases of pancreatitis and gallbladder disease have been reported, particularly during rapid weight loss, but causality remains uncertain (Cai et al., 2024; Iorga et al., 2020).

Overall, the long-term safety profile of GLP-1 and dual GLP-1/GIP agonists is favorable, supporting their use as first-line pharmacologic options for chronic obesity management. Ongoing cardiovascular-outcome and renal-outcome trials will further clarify their systemic benefits and long-term risk–benefit balance (Iorga et al., 2020; Rodriguez et al., 2024).

4. The importance of patient education and lifestyle modification in the long-term treatment of obesity using incretin therapies

4.1 Introduction

Obesity is a chronic, multifactorial condition in which biological, behavioral, and environmental factors interact to disrupt energy homeostasis. While incretin pharmacotherapy (GLP-1 receptor agonists and dual GLP-1/GIP agonists) has enabled unprecedented weight reduction, maintaining this effect requires sustained behavioral and educational support. Integrated care models combining pharmacotherapy with structured lifestyle interventions have consistently shown superior long-term outcomes compared with pharmacotherapy alone (D. Rubino et al., 2021; Tronieri et al., 2020; Wadden et al., 2021).

4.2 Patient education — definition, goals, and mechanisms of influence

Patient education encompasses systematic, evidence-based interventions aimed at improving health literacy, self-management, and adherence to therapeutic recommendations. Its primary objectives are to enhance patients' understanding of obesity pathophysiology and drug mechanisms, develop self-monitoring skills (e.g., dietary tracking, physical activity logging), strengthen motivation and self-efficacy and prevent relapse by promoting behavioral resilience (Tronieri et al., 2020).

Education improves clinical outcomes through several mechanisms: improved adherence, early identification of barriers, and increased engagement in treatment (Tronieri et al., 2020; Wang et al., 2024). When integrated into multidisciplinary care, it transforms patients from passive recipients into active participants in long-term therapy (American Diabetes Association Professional Practice Committee et al., 2024; Garvey et al., 2016; Kraschnewski et al., 2023).

4.3 Education and adherence in clinical trials with incretins

Evidence from the STEP and SURMOUNT programs demonstrates that the intensity of behavioral support directly correlates with weight outcomes. In STEP 3, semaglutide combined with intensive behavioral therapy produced a threefold greater weight loss than behavioral intervention alone (Wadden et al., 2021). Adherence metrics—such as session attendance, dietary self-monitoring, and physical activity tracking—have been shown to predict both early and long-term weight outcomes (Tronieri et al., 2020).

A recent review emphasized the phenomenon of treatment fatigue—a gradual decline in motivation and adherence after 6–12 months of pharmacotherapy—which can significantly reduce long-term treatment effectiveness (Berg et al., 2025; Van Baak & Mariman, 2025; Wilding et al., 2022). Structured education and coaching interventions mitigate this problem by sustaining motivation and fostering adaptive coping strategies (Irvin et al., 2023; Unick et al., 2024; Wang et al., 2024).

4.4 Education models and formats: individual, group, remote (telehealth), and hybrid

Different educational models have been examined for their effectiveness and potential for broad implementation. Individual counseling provides personalized feedback and psychological support but requires considerable time and professional resources. Group-based programs improve motivation through social interaction and are generally more cost-effective. Remote approaches, such as telehealth and eHealth, have shown similar effectiveness to in-person sessions and proved especially useful for maintaining participation during the COVID-19 pandemic (Kraschnewski et al., 2023; Kupila et al., 2023; Ross et al., 2022; Unick et al., 2024).

Hybrid and adaptive formats that combine periodic face-to-face meetings with remote coaching appear to offer the best balance between outcomes and cost (Kupila et al., 2023; Tronieri et al., 2020). In addition, digital health coaching platforms supported by artificial intelligence and behavioral analytics are emerging as effective tools for improving adherence and promoting long-term lifestyle change (Irvin et al., 2023; Tronieri et al., 2020).

4.5 Integrating education with incretin pharmacotherapy — evidence and practical implications

Clinical data indicate clear synergy between pharmacotherapy and behavioral therapy. Combining GLP-1 receptor agonists with intensive behavioral interventions leads to greater and more durable weight loss than either treatment alone (American Diabetes Association Professional Practice Committee et al., 2024; Wadden et al., 2021). Continuous monitoring of adherence and engagement enables early intervention in non-responders and reduces dropout rates (Tronieri et al., 2020).

Telehealth delivery expands access to educational programs, allowing scalable support in resource-limited settings (D. Rubino et al., 2021; Tronieri et al., 2020). This justifies a model of long-term or conditional continuation of pharmacotherapy in parallel with an educational program. Long-term or conditional continuation of incretin therapy, combined with ongoing education, is now recommended as a model of chronic obesity management (Kraschnewski et al., 2023; Kupila et al., 2023; Ross et al., 2022; Unick et al., 2024).

4.6 Implementation barriers and proposed solutions

Common barriers in clinical practice include lack of reimbursement for educational services, limited clinician time, and insufficient staff training. Potential solutions involve hybrid program development, integration of mobile technologies for automated monitoring, and short motivational-interview training for healthcare providers. Structured referral pathways to multidisciplinary teams (physicians, dietitians, psychologists, and nurses) can further improve coordination and sustainability (Kupila et al., 2023; Ross et al., 2022).

Patient education and sustained lifestyle modification are indispensable components of successful obesity treatment with incretin therapies. Optimal long-term outcomes are achieved when pharmacotherapy is embedded in an interdisciplinary framework that includes behavioral training, monitoring, and ongoing support. In the era of digital health, combining GLP-1–based pharmacotherapy with adaptive, technology-enhanced education models may define the future standard of care for obesity management (Irvin et al., 2023).

5 Discussion

Incretin-based therapies have redefined the pharmacologic management of obesity, offering an efficacy profile that rivals metabolic surgery for selected patients. The data from pivotal clinical trials—STEP, SURMOUNT, and early retatrutide studies—confirm that GLP-1 and dual GLP-1/GIP receptor agonists produce sustained and clinically meaningful weight reduction with favorable cardiometabolic benefits (Iorga et al., 2020; Jastreboff et al., 2022; Montan et al., 2019; Wadden et al., 2021).

However, the translation of these outcomes into long-term clinical practice requires an understanding of obesity as a chronic, relapsing disease rather than a condition with a definitive cure. Treatment discontinuation almost invariably leads to partial or complete weight regain, as demonstrated in STEP 4 and SURMOUNT 4 (Aronne et al., 2024; Iorga et al., 2020; D. Rubino et al., 2021). Therefore, a long-term, patient-centered management approach—combining pharmacotherapy, education, and lifestyle intervention—should be considered the standard of care.

5.1. Integration of pharmacotherapy and behavioral strategies

Incretin therapies produce the greatest benefits when combined with structured behavioral support (Caruso et al., 2024). The synergy between GLP-1 receptor agonists and behavioral therapy, as observed in the STEP 3 trial, underscores the critical role of education and sustained self-regulation (Tronieri et al., 2020; Wadden et al., 2021; Wang et al., 2024). Behavioral adherence determines long-term success, with poor adherence linked to attenuated weight loss and early discontinuation (Berg et al., 2025; Tronieri et al., 2020; Wang et al., 2024).

Emerging data also highlight *treatment fatigue*, a gradual decline in motivation and adherence after several months of pharmacotherapy. To counteract this, periodic counseling, digital monitoring, and adaptive education models are recommended to sustain engagement and enhance long-term outcomes (Irvin et al., 2023).

5.2. The evolving concept of precision obesity medicine

Recent research has shifted the paradigm toward precision obesity medicine, which aims to individualize pharmacologic treatment according to metabolic phenotype, behavioral profile, and genetic background (Espinosa et al., 2025). For instance, baseline insulin resistance, appetite phenotype, and early weight response may predict the efficacy of GLP-1 versus dual GLP-1/GIP agonists (Kyriakidou et al., 2022). Future clinical algorithms may incorporate molecular and behavioral markers to optimize therapy selection and duration, maximizing benefit while minimizing treatment burden.

5.3. Long-term implications and public health perspective

The expanding use of incretin-based therapies also carries implications for healthcare systems. While cost remains a limiting factor, economic modeling suggests that long-term use may be cost-effective due to reductions in diabetes incidence, cardiovascular events, and liver disease progression (Iorga et al., 2020). Nevertheless, equitable access, patient education, and post-treatment follow-up remain critical to ensuring sustainable benefits at a population level.

6 Conclusions

Incretin-based pharmacotherapy has transformed the modern approach to obesity management, offering unprecedented efficacy in weight reduction and metabolic improvement. Nevertheless, the available clinical and real-world evidence clearly demonstrates that pharmacological intervention alone is insufficient to achieve durable outcomes in a chronic, relapsing disease such as obesity. The long-term success of therapy depends on the integration of medication with structured patient education, behavioral modification, and sustained lifestyle support (D. Rubino et al., 2021; Tronieri et al., 2020; Wadden et al., 2021).

The use of GLP-1 receptor agonists and dual GLP-1/GIP agonists, such as semaglutide and tirzepatide, represents a milestone in metabolic medicine. These drugs not only facilitate substantial weight loss—averaging 15–25% in major clinical trials—but also improve glycemic control, lipid profile, and cardiovascular

risk markers (Aronne et al., 2024; Jastreboff et al., 2022; Wilding et al., 2021). However, evidence from the STEP and SURMOUNT trials consistently indicates that discontinuation of treatment leads to significant weight regain, underlining that obesity should be managed as a chronic condition requiring long-term therapy and ongoing behavioral support (Aronne et al., 2024; D. Rubino et al., 2021; Wilding et al., 2022).

Patient education plays a pivotal role in maintaining the effects of pharmacotherapy. By increasing patients' understanding of disease mechanisms and the rationale for incretin-based treatment, educational interventions enhance adherence, empower self-management, and reduce the likelihood of treatment discontinuation (Tronieri et al., 2020). Integrating behavioral therapy with incretin pharmacotherapy—especially in hybrid or telehealth formats—provides a scalable, cost-effective model that can be successfully implemented in diverse healthcare settings (Kraschnewski et al., 2023; Kupila et al., 2023; Ross et al., 2022; Unick et al., 2024).

Clinically, these findings advocate for a paradigm shift from short-term, weight-centered interventions toward a comprehensive chronic care model for obesity. This model should combine pharmacological, behavioral, psychological, and educational strategies delivered by interdisciplinary teams. Regular follow-up, adherence monitoring, and adaptive treatment adjustments are essential to prevent relapse and sustain long-term benefits (American Diabetes Association Professional Practice Committee et al., 2024; Garvey et al., 2016).

From a healthcare systems perspective, implementing structured education and behavioral support alongside pharmacotherapy can improve quality of life and reduce long-term healthcare costs associated with obesity-related comorbidities (Lee et al., 2020; F. Rubino et al., 2020). The development of digital tools and AI-supported coaching systems may further enhance patient engagement and facilitate personalized treatment pathways in the future.

In summary, incretin-based therapies have revolutionized obesity treatment by offering safe and effective pharmacological tools. However, enduring success relies on empowered patients, continuous education, and an integrated, multidisciplinary approach. The future of obesity care will depend not only on drug innovation but also on the capacity of healthcare systems to combine pharmacotherapy with sustainable behavioral and educational support—transforming short-term success into lifelong metabolic health.

Conflicts of Interest: All authors have read and approved the manuscript. The authors declare no conflict of interest.

REFERENCES

1. American Diabetes Association Professional Practice Committee, ElSayed, N. A., Aleppo, G., Bannuru, R. R., Bruemmer, D., Collins, B. S., Ekhlaspour, L., Hilliard, M. E., Johnson, E. L., Khunti, K., Kushner, R. F., Lingvay, I., Matfin, G., McCoy, R. G., Perry, M. L., Pilla, S. J., Polsky, S., Prahalad, P., Pratley, R. E., ... Gabbay, R. A. (2024). 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Care in Diabetes—2024*. *Diabetes Care*, 47(Supplement_1), S145–S157. <https://doi.org/10.2337/dc24-S008>
2. Aronne, L. J., Horn, D. B., Le Roux, C. W., Ho, W., Falcon, B. L., Gomez Valderas, E., Das, S., Lee, C. J., Glass, L. C., Senyucel, C., & Dunn, J. P. (2025). Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. *New England Journal of Medicine*, 393(1), 26–36. <https://doi.org/10.1056/NEJMoa2416394>
3. Aronne, L. J., Sattar, N., Horn, D. B., Bays, H. E., Wharton, S., Lin, W.-Y., Ahmad, N. N., Zhang, S., Liao, R., Bunck, M. C., Jouravskaya, I., Murphy, M. A., SURMOUNT-4 Investigators, Fretes, J. O., Coronel, M. J., Gutnisky, L. L., Frechtel, G. D., Gellersztejn, E., Aizenberg, D., ... Nardandrea, J. P. (2024). Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity: The SURMOUNT-4 Randomized Clinical Trial. *JAMA*, 331(1), 38. <https://doi.org/10.1001/jama.2023.24945>
4. Berg, S., Stickle, H., Rose, S. J., & Nemec, E. C. (2025). Discontinuing glucagon-like peptide-1 receptor agonists and body habitus: A systematic review and meta-analysis. *Obesity Reviews*, 26(8), e13929. <https://doi.org/10.1111/obr.13929>
5. Boer, G. A., Hay, D. L., & Tups, A. (2023). Obesity pharmacotherapy: Incretin action in the central nervous system. *Trends in Pharmacological Sciences*, 44(1), 50–63. <https://doi.org/10.1016/j.tips.2022.11.001>
6. Brandt, S. J., Müller, T. D., DiMarchi, R. D., Tschöp, M. H., & Stemmer, K. (2018). Peptide-based multi-agonists: A new paradigm in metabolic pharmacology. *Journal of Internal Medicine*, 284(6), 581–602. <https://doi.org/10.1111/joim.12837>
7. Cai, W., Zhang, R., Yao, Y., Wu, Q., & Zhang, J. (2024). Tirzepatide as a novel effective and safe strategy for treating obesity: A systematic review and meta-analysis of randomized controlled trials. *Frontiers in Public Health*, 12, 1277113. <https://doi.org/10.3389/fpubh.2024.1277113>

8. Campbell, J. E., Müller, T. D., Finan, B., DiMarchi, R. D., Tschöp, M. H., & D'Alessio, D. A. (2023). GIPR/GLP-1R dual agonist therapies for diabetes and weight loss—Chemistry, physiology, and clinical applications. *Cell Metabolism*, 35(9), 1519–1529. <https://doi.org/10.1016/j.cmet.2023.07.010>
9. Caruso, I., Cignarelli, A., Sorice, G. P., Perrini, S., & Giorgino, F. (2024). Incretin-based therapies for the treatment of obesity-related diseases. *Npj Metabolic Health and Disease*, 2(1), 31. <https://doi.org/10.1038/s44324-024-00030-5>
10. Chetty, A. K., Rafi, E., Bellini, N. J., Buchholz, N., & Isaacs, D. (2024). A Review of Incretin Therapies Approved and in Late-Stage Development for Overweight and Obesity Management. *Endocrine Practice*, 30(3), 292–303. <https://doi.org/10.1016/j.eprac.2023.12.010>
11. Emmerich, S., Fryar, C., Stierman, B., & Ogden, C. (2024). *Obesity and Severe Obesity Prevalence in Adults: United States, August 2021–August 2023*. National Center for Health Statistics (U.S.). <https://doi.org/10.15620/cdc/159281>
12. Espinosa, M. A., Rivera Gutierrez, R. D. J., Villamarin, J., & Acosta, A. (2025). Precision Medicine for Obesity Treatment. *Journal of the Endocrine Society*, 9(9), bvaf102. <https://doi.org/10.1210/jendso/bvaf102>
13. Garvey, W. T., Mechanick, J. I., Brett, E. M., Garber, A. J., Hurlley, D. L., Jastreboff, A. M., Nadolsky, K., Pessah-Pollack, R., & Plodkowski, R. (2016). American Association of Clinical Endocrinologists and American College of Endocrinology Comprehensive Clinical Practice Guidelines For Medical Care of Patients with Obesity. *Endocrine Practice*, 22, 1–203. <https://doi.org/10.4158/EP161365.GL>
14. Ghush, W., De La Rosa, A., Sacoto, D., Cifuentes, L., Campos, A., Feris, F., Hurtado, M. D., & Acosta, A. (2022). Weight Loss Outcomes Associated With Semaglutide Treatment for Patients With Overweight or Obesity. *JAMA Network Open*, 5(9), e2231982. <https://doi.org/10.1001/jamanetworkopen.2022.31982>
15. Giordano, U., Kobińska, J., & Pilch, J. (2023). Semaglutide as a chance for obesity treatment. *Medical Research Journal*, 8(3), 262–264. <https://doi.org/10.5603/MRJ.a2023.0034>
16. Iorga, R., Bacalbasa, N., Carsote, M., Bratu, O., Stanescu, A. M., Bungau, S., Pantis, C., & Diaconu, C. (2020). Metabolic and cardiovascular benefits of GLP-1 agonists, besides the hypoglycemic effect (Review). *Experimental and Therapeutic Medicine*. <https://doi.org/10.3892/etm.2020.8714>
17. Irvin, L., Madden, L. A., Marshall, P., & Vince, R. V. (2023). Digital Health Solutions for Weight Loss and Obesity: A Narrative Review. *Nutrients*, 15(8), 1858. <https://doi.org/10.3390/nu15081858>
18. Jastreboff, A. M., Aronne, L. J., Ahmad, N. N., Wharton, S., Connery, L., Alves, B., Kiyosue, A., Zhang, S., Liu, B., Bunck, M. C., & Stefanski, A. (2022). Tirzepatide Once Weekly for the Treatment of Obesity. *New England Journal of Medicine*, 387(3), 205–216. <https://doi.org/10.1056/NEJMoa2206038>
19. Jastreboff, A. M., Kaplan, L. M., Frias, J. P., Wu, Q., Du, Y., Gurbuz, S., Coskun, T., Haupt, A., Milicevic, Z., & Hartman, M. L. (2023). Triple-Hormone-Receptor Agonist Retatrutide for Obesity—A Phase 2 Trial. *New England Journal of Medicine*, 389(6), 514–526. <https://doi.org/10.1056/NEJMoa2301972>
20. Kosiborod, M. N., Bhatta, M., Davies, M., Deanfield, J. E., Garvey, W. T., Khalid, U., Kushner, R., Rubino, D. M., Zeuthen, N., & Verma, S. (2023). Semaglutide improves cardiometabolic risk factors in adults with overweight or obesity: STEP 1 and 4 exploratory analyses. *Diabetes, Obesity and Metabolism*, 25(2), 468–478. <https://doi.org/10.1111/dom.14890>
21. Kraschnewski, J. L., Kong, L., Bryce, C. L., Francis, E. B., Poger, J. M., Lehman, E. B., Helbling, S., Soleymani, T., Mancoll, R. E., Villalobos, V., & Yeh, H.-C. (2023). Intensive behavioral Therapy for weight loss in patients with, or At-Risk of, type 2 Diabetes: Results from the PaTH to health diabetes study. *Preventive Medicine Reports*, 31, 102099. <https://doi.org/10.1016/j.pmedr.2022.102099>
22. Kupila, S. K. E., Joki, A., Suojanen, L.-U., & Pietiläinen, K. H. (2023). Correction: The Effectiveness of eHealth Interventions for Weight Loss and Weight Loss Maintenance in Adults with Overweight or Obesity: A Systematic Review of Systematic Reviews. *Current Obesity Reports*, 12(4), 544–545. <https://doi.org/10.1007/s13679-023-00530-3>
23. Kyriakidou, A., Kyriazou, A. V., Koufakis, T., Vasilopoulos, Y., Grammatiki, M., Tsekmekidou, X., Avramidis, I., Baltagiannis, S., Goulis, D. G., Zebekakis, P., & Kotsa, K. (2022). Clinical and Genetic Predictors of Glycemic Control and Weight Loss Response to Liraglutide in Patients with Type 2 Diabetes. *Journal of Personalized Medicine*, 12(3), 424. <https://doi.org/10.3390/jpm12030424>
24. Lee, M., Lauren, B. N., Zhan, T., Choi, J., Klebanoff, M., Abu Dayyeh, B., Taveras, E. M., Corey, K., Kaplan, L., & Hur, C. (2020). The cost-effectiveness of pharmacotherapy and lifestyle intervention in the treatment of obesity. *Obesity Science & Practice*, 6(2), 162–170. <https://doi.org/10.1002/osp4.390>
25. Look, M., Dunn, J. P., Kushner, R. F., Cao, D., Harris, C., Gibble, T. H., Stefanski, A., & Griffin, R. (2025). Body composition changes during weight reduction with tirzepatide in the SURMOUNT -1 study of adults with obesity or overweight. *Diabetes, Obesity and Metabolism*, 27(5), 2720–2729. <https://doi.org/10.1111/dom.16275>
26. Montan, P. D., Sourlas, A., Olivero, J., Silverio, D., Guzman, E., & Kosmas, C. E. (2019). Pharmacologic therapy of obesity: Mechanisms of action and cardiometabolic effects. *Annals of Translational Medicine*, 7(16), 393–393. <https://doi.org/10.21037/atm.2019.07.27>
27. Müller, T. D., Finan, B., Bloom, S. R., D'Alessio, D., Drucker, D. J., Flatt, P. R., Fritsche, A., Gribble, F., Grill, H. J., Habener, J. F., Holst, J. J., Langhans, W., Meier, J. J., Nauck, M. A., Perez-Tilve, D., Pocai, A., Reimann, F., Sandoval, D. A., Schwartz, T. W., ... Tschöp, M. H. (2019). Glucagon-like peptide 1 (GLP-1). *Molecular Metabolism*, 30, 72–130. <https://doi.org/10.1016/j.molmet.2019.09.010>

28. Ng, M., Gakidou, E., Lo, J., Abate, Y. H., Abbafati, C., Abbas, N., Abbasian, M., Abd ElHafeez, S., Abdel-Rahman, W. M., Abd-El salam, S., Abdollahi, A., Abdoun, M., Abdulah, D. M., Abdulkader, R. S., Abdullahi, A., Abedi, A., Abeywickrama, H. M., Abie, A., Aboagye, R. G., ... Vollset, S. E. (2025). Global, regional, and national prevalence of adult overweight and obesity, 1990–2021, with forecasts to 2050: A forecasting study for the Global Burden of Disease Study 2021. *The Lancet*, 405(10481), 813–838. [https://doi.org/10.1016/S0140-6736\(25\)00355-1](https://doi.org/10.1016/S0140-6736(25)00355-1)
29. Qin, W., Yang, J., Deng, C., Ruan, Q., & Duan, K. (2024). Efficacy and safety of semaglutide 2.4 mg for weight loss in overweight or obese adults without diabetes: An updated systematic review and meta-analysis including the 2-year STEP 5 trial. *Diabetes, Obesity and Metabolism*, 26(3), 911–923. <https://doi.org/10.1111/dom.15386>
30. Rodriguez, P. J., Goodwin Cartwright, B. M., Gratzl, S., Brar, R., Baker, C., Gluckman, T. J., & Stucky, N. L. (2024). Semaglutide vs Tirzepatide for Weight Loss in Adults With Overweight or Obesity. *JAMA Internal Medicine*, 184(9), 1056. <https://doi.org/10.1001/jamainternmed.2024.2525>
31. Ross, K. M., Carpenter, C. A., Arroyo, K. M., Shankar, M. N., Yi, F., Qiu, P., Anthony, L., Ruiz, J., & Perri, M. G. (2022). Impact of transition from face-to-face to telehealth on behavioral obesity treatment during the COVID-19 pandemic. *Obesity*, 30(4), 858–863. <https://doi.org/10.1002/oby.23383>
32. Rubino, D., Abrahamsson, N., Davies, M., Hesse, D., Greenway, F. L., Jensen, C., Lingvay, I., Mosenzon, O., Rosenstock, J., Rubio, M. A., Rudofsky, G., Tadayon, S., Wadden, T. A., Dicker, D., STEP 4 Investigators, Friberg, M., Sjödin, A., Dicker, D., Segal, G., ... Warren, M. L. (2021). Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity: The STEP 4 Randomized Clinical Trial. *JAMA*, 325(14), 1414. <https://doi.org/10.1001/jama.2021.3224>
33. Rubino, F., Puhl, R. M., Cummings, D. E., Eckel, R. H., Ryan, D. H., Mechanick, J. I., Nadglowski, J., Ramos Salas, X., Schauer, P. R., Twenefour, D., Apovian, C. M., Aronne, L. J., Batterham, R. L., Berthoud, H.-R., Boza, C., Busetto, L., Dicker, D., De Groot, M., Eisenberg, D., ... Dixon, J. B. (2020). Joint international consensus statement for ending stigma of obesity. *Nature Medicine*, 26(4), 485–497. <https://doi.org/10.1038/s41591-020-0803-x>
34. Tronieri, J. S., Wadden, T. A., Walsh, O., Berkowitz, R. I., Alamuddin, N., & Chao, A. M. (2020). Measures of adherence as predictors of early and total weight loss with intensive behavioral therapy for obesity combined with liraglutide 3.0 mg. *Behaviour Research and Therapy*, 131, 103639. <https://doi.org/10.1016/j.brat.2020.103639>
35. Unick, J. L., Pellegrini, C. A., Dunsiger, S. I., Demos, K. E., Thomas, J. G., Bond, D. S., Lee, R. H., Webster, J., & Wing, R. R. (2024). An Adaptive Telephone Coaching Intervention for Patients in an Online Weight Loss Program: A Randomized Clinical Trial. *JAMA Network Open*, 7(6), e2414587. <https://doi.org/10.1001/jamanetworkopen.2024.14587>
36. Van Baak, M. A., & Mariman, E. C. M. (2025). Physiology of Weight Regain after Weight Loss: Latest Insights. *Current Obesity Reports*, 14(1), 28. <https://doi.org/10.1007/s13679-025-00619-x>
37. Wadden, T. A., Bailey, T. S., Billings, L. K., Davies, M., Frias, J. P., Koroleva, A., Lingvay, I., O'Neil, P. M., Rubino, D. M., Skovgaard, D., Wallenstein, S. O. R., Garvey, W. T., & STEP 3 Investigators. (2021). Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. *JAMA*, 325(14), 1403. <https://doi.org/10.1001/jama.2021.1831>
38. Wang, D., Benito, P. J., Rubio-Arias, J. Á., Ramos-Campo, D. J., & Rojo-Tirado, M. A. (2024). Exploring factors of adherence to weight loss interventions in population with overweight/obesity: An umbrella review. *Obesity Reviews*, 25(9), e13783. <https://doi.org/10.1111/obr.13783>
39. Wilding, J. P. H., Batterham, R. L., Calanna, S., Davies, M., Van Gaal, L. F., Lingvay, I., McGowan, B. M., Rosenstock, J., Tran, M. T. D., Wadden, T. A., Wharton, S., Yokote, K., Zeuthen, N., & Kushner, R. F. (2021). Once-Weekly Semaglutide in Adults with Overweight or Obesity. *New England Journal of Medicine*, 384(11), 989–1002. <https://doi.org/10.1056/NEJMoa2032183>
40. Wilding, J. P. H., Batterham, R. L., Davies, M., Van Gaal, L. F., Kandler, K., Konakli, K., Lingvay, I., McGowan, B. M., Oral, T. K., Rosenstock, J., Wadden, T. A., Wharton, S., Yokote, K., Kushner, R. F., & STEP 1 Study Group. (2022). Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. *Diabetes, Obesity and Metabolism*, 24(8), 1553–1564. <https://doi.org/10.1111/dom.14725>