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Incretin-based Therapies in Obesity Treatment: Implications for Nutritional Care and a Proposed Medical Nutrition Therapy Protocol

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ABSTRACT

Background – Obesity is a chronic, multifactorial, and highly prevalent disease whose management remains challenging due to its complex pathophysiology and high rates of weight regain. In recent decades, incretin-based therapies - such as semaglutide and tirzepatide - have emerged as effective interventions for weight reduction and cardiometabolic risk control. However, their use has raised concerns regarding the preservation of lean mass, the risk of micronutrient deficiencies, dehydration, and weight regain following treatment discontinuation.

Objective – This study aimed to evaluate the adverse effects associated with incretin-based therapies, examine their nutritional implications, and propose an evidence-based medical nutrition therapy protocol to optimize clinical outcomes and mitigate potential risks.

Methods – An integrative literature review was conducted across major databases (2019–2025), informed by PRISMA 2020 reporting recommendations.

Results – The findings demonstrate consistent reductions in body weight (up to 20.9% on average), accompanied by a substantial proportion of lean mass loss, accounting for up to 60% of total weight reduction. Additionally, inadequate protein intake and micronutrient deficiencies were reported in more than 20% of individuals across the analyzed studies. An increased risk of dehydration associated with altered fluid intake behavior was also identified, along with weight regain rates of approximately two-thirds of prior weight loss in some studies.

Conclusion – The synthesis of evidence indicates that integrating pharmacotherapy with structured nutritional intervention - implemented through medical nutrition therapy, with emphasis on adequate protein intake, hydration, and micronutrient monitoring - combined with Nutrition Education aimed at fostering critical autonomy in dietary choices, represents a key strategy for preserving lean mass, mitigating nutritional risks, and ensuring the long-term sustainability of clinical outcomes.

Keywords: Anti-Obesity Agents; Incretin-Based Therapies; Glucagon-Like Peptide 1 Receptor Agonists; Body Composition; Nutrition Therapy; Nutrition Education; Weight Loss.

Introduction

Over recent decades, obesity has come to be recognized as a chronic, complex, and multifactorial disease, resulting from the interaction of genetic, epigenetic, environmental, behavioral, and social factors, and is no longer attributed solely to individual lifestyle choices[1].

From an epidemiological perspective, obesity represents one of the most pressing global public health challenges, affecting more than 890 million adults, while approximately 2.5 billion individuals are classified as overweight. This scenario characterizes obesity as a global pandemic, with increasing clinical and economic burdens on healthcare systems[1].

In this context, prior to the introduction of Incretin-Based Therapies (IBTs), obesity management relied on behavioral interventions, pharmacotherapy, and bariatric surgery. However, anti-obesity medications have often been underutilized, lifestyle interventions do not demonstrate universal effectiveness, and bariatric surgery, although effective, remains an invasive procedure with limited accessibility and the need for long-term follow-up[2].

More recently, the introduction of IBTs, including semaglutide and tirzepatide, has transformed the pharmacological management of obesity. Clinical trials have demonstrated substantial body weight reductions, reaching approximately 20.9% in some studies, accompanied by significant improvements in metabolic parameters, including glycemic control, lipid profile, and blood pressure[3-5].

However, despite initial enthusiasm, emerging concerns and controversies have been raised. Evidence suggests that a considerable proportion of weight loss achieved with IBTs - estimated between 15% and 60% - may be attributable to reductions in lean mass, a condition that may exacerbate functional and metabolic vulnerability[6].

Concurrently, clinically relevant nutritional deficiencies have been reported, particularly involving iron, vitamin B12, and vitamin D, associated with inadequate protein intake and an overall reduction in food and fluid intake, thereby requiring careful clinical monitoring and appropriate supplementation when necessary[7-10].

Another critical issue is weight regain following treatment discontinuation, which is often rapid - occurring within months - and characterized predominantly by fat mass recovery, with no direct evidence of spontaneous restoration of lost lean mass[11,12].

This scenario highlights an important methodological gap: many clinical trials involving IBTs do not incorporate structured dietary protocols, nor do they comprehensively assess dietary quality or the long-term effects of pharmacological therapy on body composition[13,14].

From this perspective, nutritional follow-up becomes essential to optimize outcomes and mitigate risks. Strategies based on adequate protein intake, micronutrient supplementation, and resistance training contribute to the preservation of muscle mass and weight maintenance[15]. In addition, Nutrition Education and dietary behavior restructuring play a crucial role in preventing inappropriate use of pharmacotherapy and promoting sustainable behavioral changes[12,16].

Thus, the present study aims to develop a structured Medical Nutrition Therapy (MNT) protocol for patients undergoing IBTs, grounded in scientific evidence derived from an integrative literature review. This review was conducted to analyze the effects of these therapies on body composition and nutritional status, as well as to investigate the role of dietary and nutrition education interventions, implemented concomitantly with pharmacotherapy, in mitigating their adverse effects.

This study is justified by its academic and clinical relevance, as it seeks to address a gap in the integration between pharmacological and nutritional treatment, which remains insufficiently systematized in the literature, and by its potential impact on clinical practice, through the proposal of an evidence-based protocol aimed at supporting safer interventions and the sustainable management of obesity.

Materials and Methods

This study is an integrative review designed to synthesize available evidence on the effects of IBTs on body composition and nutritional health in adults with overweight or obesity, as well as to examine the implications of MNT and nutrition education in clinical management and the prevention of weight regain.

This integrative review was informed by the PRISMA 2020 reporting recommendations[17],

enhancing transparency and reproducibility. The review included studies published between 2019 and 2025, encompassing articles in Portuguese, English, and Spanish.

Eligibility criteria were defined according to the PICOS framework. The population of interest comprised adults with overweight or obesity, with or without type 2 diabetes. Interventions included therapies based on glucagon-like peptide-1 receptor agonists (GLP-1RAs) and dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1RAs, compared with placebo, usual care, or other pharmacological interventions. Studies were included if they reported outcomes related to weight loss, body composition changes, dietary intake, nutritional deficiencies, risk of dehydration, and associated nutrition therapy strategies. Eligible study designs included randomized and non-randomized clinical trials, cohort studies, observational studies, and systematic reviews with evidence synthesis.

The literature search identified 453 records across PubMed/MEDLINE, Embase, Scopus, Web of Science, Cochrane Library, SciELO, LILACS, and the CAPES Periodicals Portal. This process was complemented by manual searches and backward citation tracking. After duplicate removal and screening of titles and abstracts, studies were assessed for eligibility through full-text review. A total of 36 studies met the eligibility criteria and were included in the final synthesis.

Search strategies combined controlled vocabulary (MeSH, DeCS, and Emtree) and free-text terms related to GLP-1 receptor agonists, tirzepatide, semaglutide, obesity, body composition, nutrition therapy, protein intake, hydration, micronutrients, weight regain, weight maintenance, discontinuation of GLP-1 therapies, nutrition education, nutrition intervention, lifestyle intervention, and dietitian. Search terms were adapted according to the thematic axes of the study. The analysis of included studies prioritized methodological rigor, with emphasis on studies employing objective measures of body composition, such as dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI), as well as associated nutritional outcomes. This approach ensured greater consistency and comparability across findings.

In addition to primary evidence, the review was supported by complementary theoretical and methodological references, including international guidelines, consensus statements, narrative reviews, and official documents. This approach enabled the integration of clinical, nutritional, and behavioral aspects of IBTs in obesity management, ensuring coherence and robustness in data interpretation.

This integrative review was conducted with the aim of identifying, analyzing, and synthesizing relevant scientific evidence to support the development of a structured MNT protocol for patients undergoing IBTs. The evidence was analyzed narratively and organized into thematic domains - including body composition, nutritional challenges, and dietary and behavioral strategies - allowing for the structured integration of findings and the development of a nutrition intervention protocol oriented toward clinical practice and grounded in up-to-date evidence.

Incretin-based Therapies: Metabolic Effects and Nutritional Risks

Incretins are gut-derived hormones released in the postprandial state that enhance glucose-dependent insulin secretion, modulate glucagon release, and coordinate neurogastrointestinal responses that promote energy homeostasis[18].

In the current landscape of obesity management, IBTs have become established as effective pharmacological strategies, primarily due to their ability to reduce energy intake through appetite suppression, delayed gastric emptying, and enhanced satiety[19].

From a clinical perspective, the expected effects of IBTs include significant reductions in body weight and visceral adiposity, improvements in glycemic control, decreases in triglyceride levels and blood pressure, enhanced insulin sensitivity, and reductions in inflammatory markers. These benefits reflect the integrated effects of these agents on energy metabolism, appetite regulation, and body composition. Conversely, the most commonly reported adverse effects include nausea, early satiety, constipation or diarrhea, which are generally mild, transient, and associated with initial dose escalation[18,20].

Although clinical outcomes are substantial, the long-term use of these therapies has also revealed unintended effects that warrant careful consideration. Emerging evidence indicates that

weight loss induced by IBTs may be accompanied by reductions in lean mass and, in some cases, an increased risk of sarcopenia[6,21]. Furthermore, nutritional deficiencies have been reported, largely attributable to reduced food intake and drug-induced changes in eating behavior[8]. These findings underscore the need for an integrated, multidisciplinary approach in which MNT plays a central and indispensable role alongside pharmacological treatment, ensuring the preservation of lean mass and adequate nutritional status during and after weight loss.

Effects of Incretin-based Therapies on Body Composition: Muscle Preservation and Risk of Sarcopenia

The quality of weight loss, particularly the depletion of lean mass, is a key determinant of clinically relevant outcomes, including an increased risk of sarcopenia. According to the European consensus EWGSOP2 (European Working Group on Sarcopenia in Older People 2), sarcopenia is defined as a muscle disease characterized primarily by low muscle strength, with diagnosis confirmed by reduced appendicular lean mass. Its consequences include impaired mobility, increased risk of falls and fractures, and decline in quality of life, particularly among older adults, individuals with low baseline muscle reserves, or those with inadequate protein intake. Therefore, the effects of these therapies should be evaluated beyond total body weight changes, with the incorporation of quantitative measures such as DXA and MRI, as well as functional parameters including handgrip strength and physical performance[22]. These approaches are particularly relevant for monitoring individuals receiving IBTs during weight loss.

Evidence from phase 3 clinical trials indicates that weight loss induced by IBTs is associated with significant reductions in lean mass. In the STEP-1 trial, which evaluated semaglutide (2.4 mg/week) in adults with obesity, a DXA-based subanalysis demonstrated a mean body weight reduction of 14.9% (17.32 kg), of which 6.92 kg corresponded to lean mass, representing approximately 40% of total weight loss. This corresponds to about 13.2% of baseline lean mass, suggesting that a substantial proportion of this reduction reflects loss of muscle tissue[3].

Similarly, in the SURMOUNT-1 trial, conducted with tirzepatide (15 mg/week), body composition analyses using DXA demonstrated a predominant reduction in fat mass, accounting for approximately 75% of total weight loss, accompanied by a proportionally smaller decrease in lean mass (25%), indicating a relatively favorable distribution. Moreover, over 72 weeks, participants achieved a total weight reduction of 20.9% (23.6 kg), with an approximate 10.9% decrease in baseline lean mass[23]. In absolute terms, the magnitude of lean mass loss (approximately 5.5 kg) was comparable to that observed with semaglutide[15].

These findings are consistent with the narrative review conducted by Neeland et al.[6], which synthesized evidence from randomized clinical trials involving semaglutide and tirzepatide, estimating that between 15% and 60% of total weight loss may correspond to lean mass. However, the authors distinguish between muscle "mass" and "quality," suggesting that part of the reduction in fat-free mass measured by DXA may reflect changes in water and glycogen content rather than true loss of myofibrillar protein.

Furthermore, Neeland et al.[6] emphasized that, although such reductions are expected during rapid weight loss, they may be attenuated through supportive strategies, including adequate protein intake and regular resistance training, reinforcing the need for structured clinical management.

Another important consideration relates to the methodological quality of available studies and reviews. Although high-impact comparative reviews generally demonstrate adequate quality - characterized by systematic risk of bias assessment, comprehensive search strategies, and appropriate statistical synthesis - significant gaps persist, stemming both from limitations of primary studies and from the reviews that synthesize them[24,25].

These gaps are illustrated by heterogeneity across study populations, variability in pharmacological dosing protocols, potential bias in lean mass assessment, and direct comparisons of body composition derived from heterogeneous measurement techniques such as DXA and MRI, which assess distinct physiological dimensions[13,26].

Additionally, limited follow-up duration restricts the evaluation of the sustainability of therapeutic effects after treatment discontinuation and the full characterization of long-term sarcopenia risk, compounded by the underrepresentation of frail

older adults in clinical trials[21,26]. Furthermore, there is a lack of standardization of concomitant interventions - such as resistance training, protein intake, and nutritional follow-up - which are critical modulators of muscle preservation[6].

Consistently, recent reviews have highlighted the need to incorporate functional outcomes in the assessment of individuals receiving IBTs noting that many studies focus exclusively on lean mass without considering muscle function, namely strength and physical performance[27].

In this context, critical appraisal suggests that the substantial weight loss induced by IBTs should be interpreted in light of methodological quality and the type of outcomes reported, particularly when the focus is on body composition.

Taken together, these limitations suggest that the magnitude of lean mass loss associated with IBTs may be partially overestimated, particularly when assessed exclusively through structural measures and without adequate control of key modulating factors such as protein intake and physical activity. As such, current evidence does not allow for a robust determination of the true impact of these therapies on muscle function and long-term sarcopenia risk, but rather indicates a clinically relevant concern that warrants individualized nutritional and functional monitoring.

Nutritional Challenges and Medical Nutrition Therapy Strategies in Incretin-based Therapies: Protein Adequacy, Hydration, and Micronutrient Monitoring

During IBTs, the same mechanisms that promote weight loss may also induce changes in eating behavior, leading to reduced intake of fluids as well as macro- and micronutrients. Consequently, this may increase the risk of dehydration, muscle catabolism, and nutritional deficiencies[28-30].

Recent reviews have reinforced these findings. Christensen et al.[8] reported that patients receiving GLP-1RAs and dual incretin agonists frequently exhibit reduced dietary variety and increased food selectivity, negatively impacting overall diet quality.

Another barrier to adequate dietary adherence relates to persistent gastrointestinal adverse events - such as nausea, vomiting, early satiety, constipation, and diarrhea - commonly reported by individuals using IBTs[28,30]. However, physiological studies indicate that these adverse effects are intrinsically linked to the pharmacological mechanisms of action, including delayed gastric emptying and enhanced satiety, which further contribute to the risk of suboptimal intake[31].

From this perspective, the body of evidence indicates that, although IBTs promote substantial weight loss and significant metabolic benefits, their use is associated with a meaningful risk of nutrition-related complications. Therefore, individualized dietary recommendations, tailored to each patient's cardiovascular and metabolic risk profile, are essential - not only to prevent deficiencies but also to preserve lean mass, thereby supporting the sustainability of weight loss, optimize dietary nutrient density, mitigate gastrointestinal symptoms, and enhance treatment adherence. Moreover, such strategies contribute to improving both the efficacy and safety of therapy[9,16,19,30].

Despite these advances, it is important to acknowledge that the robustness of the available evidence remains limited by recurring methodological weaknesses, including the predominance of observational study designs, heterogeneity of study populations, and the lack of rigorous control over dietary intake and concomitant interventions. These limitations restrict causal inference and hinder the extrapolation of findings to clinical practice, particularly regarding the impact of IBTs on nutritional status. In this context, the scarcity of studies that systematically integrate dietary strategies into pharmacological protocols highlights a significant gap in the literature, reinforcing the need for more robust clinical trials.

PROTEIN ADEQUACY

Throughout treatment, prioritizing the protein density of the diet is essential to mitigate medication-related adverse effects on body composition.[30] Although the relative contribution of protein to total energy intake in individuals undergoing treatment often remains within the Acceptable Macronutrient Distribution Range (AMDR) (10–35% of total energy intake), protein intake expressed in grams per kilogram of body weight is frequently insufficient in clinical practice[10,30].

The most consistent recommendations advocate for individualized protein intake targets ranging

from 1.2 to 1.6 g/kg of adjusted body weight per day, distributed across meals (or approximately 1.5 g/kg of fat-free mass per day), with around 30 g of high-quality protein per meal. This intake provides approximately 2.8 g of leucine, a threshold considered necessary to activate the mechanistic target of rapamycin (mTOR) signaling pathway and stimulate muscle protein synthesis, particularly in older adults[15,32]. Furthermore, higher protein intake during the morning has been positively associated with increases in skeletal muscle mass and fat-free mass, likely reflecting greater muscle sensitivity to amino acids in the early hours of the day[29].

In this context, the combination of adequate protein intake and regular resistance training (2 to 3 sessions per week, with progressive overload) represents an effective strategy for preserving lean mass during weight loss by promoting a sustained anabolic stimulus[33,34]. Thus, to achieve sustainable clinical outcomes in patients receiving IBTs, the integration of pharmacotherapy with MNT constitutes a foundational approach, in which protein adequacy serves as a central pillar.

HYDRATION

Hydration management assumes particular importance, as the pharmacological effects of these agents - such as appetite suppression, delayed gastric emptying, and gastrointestinal symptoms - may compromise fluid intake and alter the regulation of fluid and electrolyte balance[35].

From a physiological perspective, the action of GLP-1RAs on the central nervous system may modulate thirst behavior through hypodipsic mechanisms, reducing neural drive for fluid intake[36]. In a randomized controlled trial conducted by Winzeler et al.[7], dulaglutide (a GLP-1 analogue) significantly reduced both fluid intake and subjective thirst perception in adults with primary polydipsia. Although the study did not include individuals with obesity, its findings provide direct evidence of GLP-1-mediated hypodipsia, reinforcing the need for preventive hydration strategies in this population.

From a hemodynamic and renal perspective, Wajdlich and Nowicki[37] reported that liraglutide (a GLP-1 analogue) induced acute modulation of natriuresis and reductions in thoracic fluid indices, suggesting transient effects on fluid and electrolyte homeostasis. These findings support the importance of periodic monitoring of renal function and fluid-electrolyte status, particularly in patients with chronic kidney disease, older adults, and individuals at increased risk of dehydration due to gastrointestinal adverse events such as vomiting and diarrhea.

In light of this body of evidence, the implementation of structured hydration plans is recommended, tailored to the patient's clinical condition and symptom profile. General targets are consistent with established clinical practice recommendations, with fractionated fluid intake throughout the day of approximately 2 to 3 liters[35].

MICRONUTRIENT MONITORING

Recent evidence indicates that individuals receiving GLP-1RAs may present mean intakes below the Dietary Reference Intakes (DRIs) for calcium, iron, magnesium, potassium, vitamins A, C, D, E, K, and choline[10,28]. Data from a cohort of 461,382 adults revealed coded diagnoses of nutritional deficiencies in 12.7% and 22.4% of users after 6 and 12 months of follow-up, respectively. Vitamin D deficiency was the most prevalent, with incidence rates of 7.5% at six months and 13.6% at twelve months. Nutritional anemia was also reported in 2.1% and 4.0% of participants over the same periods, encompassing diagnoses classified under the International Classification of Diseases, Tenth Revision (ICD-10) as anemia due to iron, vitamin B12, or folate deficiency. These findings underscore the importance of systematic clinical and laboratory monitoring throughout treatment[9].

Furthermore, Melis et al.[38] identified in a pilot study that semaglutide reduced intestinal iron absorption, thereby increasing the risk of anemia in vulnerable subgroups, including women of reproductive age, older adults, and individuals with low-iron diets or gastrointestinal disorders. In the post-bariatric setting, the initiation of semaglutide has been associated with reductions in albumin, vitamin B12, and zinc levels, warranting additional caution in this specific context[39].

In response to these findings, the position statement by Dariush Mozaffarian et al.[30] recommends baseline nutritional assessment and periodic monitoring of key micronutrients - such as iron, vitamin B12, vitamin D, calcium, and magnesium - with frequency determined according to individual risk, symptomatology, and dietary

intake. The document emphasizes that dietary correction and the use of fortified foods should precede isolated supplementation, as these approaches are associated with better tolerance and clinical adherence.

In summary, continuous monitoring of critical micronutrients enables the prevention of subclinical deficiencies, preservation of musculoskeletal function, and optimization of long-term clinical outcomes, thereby reinforcing the role of nutritional follow-up as an integral component of pharmacological obesity management[19,30].

Nutrition Education as a Strategy to Mitigate Post-treatment Weight Regain

The maintenance of weight loss achieved with IBTs depends not only on continued pharmacological treatment but also on the consolidation of behavioral patterns that promote autonomy in dietary choices and self-regulation. Evidence indicates that discontinuation of these agents leads to clinically significant weight regain, underscoring the need for educational strategies capable of sustaining more stable dietary patterns over time[12,40].

In this context, findings from the STEP-1 extension and STEP-4 trials indicate that withdrawal of semaglutide results in the regain of approximately 64% of lost weight, even when participants receive standardized guidance on diet and physical activity. This pattern suggests that, following cessation of pharmacotherapy, the biological mechanisms regulating appetite and energy balance revert toward baseline activity, thereby reducing the effectiveness of generic behavioral interventions in preventing weight regain[11,41].

Similar findings have been reported in the SURMOUNT-4 trial[42], in which discontinuation of tirzepatide led to substantial weight regain - approximately 66% - along with partial reversal of previously achieved metabolic benefits. The weight regain observed in this trial supports the concept that IBTs act not only as inducers of weight loss but also as temporary modulators of a newly established physiological set point, which tends to revert once pharmacological support is withdrawn.

Complementarily, the meta-analysis by Wu et al.[40] demonstrates that weight regain occurs in a gradual and predictable manner, beginning early after treatment discontinuation and progressing over subsequent months. Likewise, the narrative review by Quarenghi et al.[12] confirms that this phenomenon is consistent across different classes of anti-obesity medications and is proportional to the magnitude of initial weight loss.

Table 1. Weight Regain After Discontinuation of IBTs: Evidence from Clinical Trials and Reviews

Author/Year Study	Drug	Initial Weight Loss (%)	Follow-up Period After Discontinuation	Key Findings
Wilding et al., 2022 STEP-1 Extension	Semaglutide 2.4 mg	−17.3% (68 weeks)	Follow-up until week 120	After discontinuation, mean weight regain of 11.6% (≈ two-thirds of prior weight loss); faster regain observed in individuals who lost ≥20% of body weight.
Rubino et al., 2021 STEP-4	Semaglutide 2.4 mg vs placebo	−10.6% (20 weeks)	Follow-up until week 68	Participants who discontinued the drug regained 6.9% of body weight over 48 weeks.
Aronne et al., 2024 SURMOUNT-4	Tirzepatide 10–15 mg	−20.9% (36 weeks)	52 weeks after withdrawal	Discontinuation led to ~14% weight regain and partial reversal of metabolic improvements.
Wu et al., 2025 Meta-analysis	GLP-1RAs and other anti-obesity medications (AOMs)	Variable across randomized controlled trials (RCTs)	8–52 weeks post-discontinuation	Detectable weight regain occurs within 8–12 weeks and tends to stabilize between 26 and 52 weeks.
Quarenghi et al., 2025 Narrative review	Liraglutide, semaglutide, tirzepatide	14–21% (mean across RCTs)	Up to 1 year post-discontinuation	Evidence from trials indicates rapid and partial weight regain (≈ two-thirds of prior loss) following discontinuation; highlights the need for nutritional and educational strategies for weight maintenance.

References: [11,12,40-42]

Taken together, the evidence suggests that discontinuation of pharmacotherapy reactivates physiological and behavioral vulnerabilities that predispose individuals to weight regain.

In this context, the consensus proposed by Dariush Mozaffarian et al.[30] identifies Nutrition Education as a foundational component of IBTs, as it promotes autonomy in healthy dietary choices and the development of practical, patient-centered skills for managing eating behavior. Furthermore, the document highlights the importance of dynamic educational strategies - such as support groups, telemonitoring, and "Food is Medicine" programs - in which food is used as a therapeutic tool within individualized care plans. These approaches support continuity of nutritional care and enhance patients' sense of autonomy, thereby reducing the risk of relapse.

Accordingly, the role of the dietitian as an educator, through individualized care, enhances the durability of treatment outcomes by fostering understanding and informed dietary decision-making.

The studies included in this review reinforce this autonomy-centered approach grounded in critical nutrition knowledge. Despain and Hoffman[16] observed that, among dietitians managing patients receiving IBTs, the most effective practices are those that teach patients to interpret physiological cues, plan meals, and adjust portion sizes, rather than simply follow prescriptive meal plans.

A similar perspective is supported by clinical reviews. Almandoz et al.[35] recommend continuous assessment routines combined with educational feedback, with care plans adjusted based on symptoms and patient preferences. Morgan-Bathke et al.[43] and Miller[44], from a behavioral standpoint, emphasize that the educational component should be maintained even after pharmacotherapy discontinuation to consolidate new dietary patterns and reduce the likelihood of weight regain.

In this direction, the integration of Nutrition Education with Behavioral Nutrition (a field within nutrition science focused on eating behavior) may further enhance these effects. Strategies such as mindful eating, reflective food logging, and identification of emotional triggers enable patients to recognize the relationship between emotions and food intake, strengthening decision-making capacity and reducing vulnerability to obesogenic environments. This progressive learning process consolidates dietary autonomy as a therapeutic tool, enabling patients to sustain outcomes even in the absence of pharmacological support[30,45].

Although controlled clinical trials evaluating standardized Nutrition Education protocols following discontinuation of IBTs remain limited, the consistency of findings - regarding the magnitude of weight regain, the time to onset, and the underlying physiological mechanisms - supports Nutrition Education as a promising strategy for preventing weight regain[30]. However, this evidence is largely indirect for this specific context, which limits causal inference and reinforces the need for studies that systematically integrate nutritional interventions into pharmacotherapy.

Proposed Evidence-based Medical Nutrition Therapy Protocol for Patients Receiving Incretin-based Therapies

Nutritional care for patients receiving IBTs should be continuous, structured, and person-centered, beginning prior to dose titration and maintained throughout the course of treatment. Its primary objectives are to prevent nutritional deficiencies, preserve lean mass, and sustain weight loss through the integration of dietary, behavioral, and educational strategies that optimize therapeutic efficacy and ensure durable outcomes[19,30,35].

At the initial consultation, prior to the initiation of pharmacotherapy, a comprehensive nutritional assessment is recommended, including anthropometric parameters - particularly body composition analysis - as well as biochemical, clinical (past and current), dietary, and emotional factors, which together establish the baseline for subsequent follow-up[30,35].

During the dose-escalation phase, nutritional care should be intensive. According to Almandoz et al.[35], consultations should occur monthly during dose adjustment and, after stabilization, at intervals of approximately three months, depending on clinical progression and patient response. This frequency facilitates early identification of gastrointestinal symptoms and appropriate management of insufficient nutrient or fluid intake.

In parallel, international weight management guidelines[43,46] recommend that nutritional intervention be intensive during the first six months - comprising at least 14 sessions within this period - with continued regular follow-up (monthly or quarterly) for at least one year to ensure adherence and long-term weight stability. The consensus by

Dariush Mozaffarian et al.[30] reinforces this approach by emphasizing that nutritional care should continue during and after pharmacotherapy until stabilization of weight, behavioral patterns, and metabolic parameters is achieved.

Based on this body of evidence, a stepwise follow-up model is proposed, structured into five phases reflecting the clinical progression of treatment, as per table 2. The first phase corresponds to screening or the pre-initiation stage, focused on comprehensive nutritional assessment. This is followed by the initial phase, encompassing approximately the first 12 weeks of treatment, which requires intensive follow-up with weekly or biweekly consultations aimed at managing gastrointestinal symptoms, adjusting food texture and volume, and ensuring protein adequacy.

The intermediate phase, corresponding to weeks 12 to 24, is characterized by monthly consultations aimed at consolidating dietary adaptations and monitoring body composition and biochemical markers. From the sixth month onward, the stable phase begins, with bimonthly or quarterly visits focused on maintaining weight loss and strengthening dietary autonomy. In the subsequent phase, the maintenance phase aims to consolidate acquired habits and reduce the risk of weight regain following treatment discontinuation, emphasizing an autonomy-supportive approach to nutritional care until weight stabilization and sustainable dietary practices are achieved.

This progressive framework ensures continuity of care, flexibility, and individualization of interventions, allowing for adjustment of the nutritional plan according to clinical evolution and patient adherence.

Table 2. Suggested Frequency of Nutritional Follow-up During Incretin-Based Therapy

Treatment Phase	Suggested Frequency	Key Assessment Items at Each Visit
Pre-initiation Phase (Screening)	Single consultation prior to pharmaco-therapy initiation	Comprehensive nutritional assessment: past and current medical and medication history; weight history; physical activity; detailed dietary assessment (24-hour recall and food diary); emotional triggers; eating disorders; functional anthropometry (body weight, height, BMI, circumferences, handgrip strength and physical function, body composition assessed by bioelectrical impedance analysis [BIA] or DXA, when available; SARC-F screening in older adults); biochemical assessment (complete blood count, iron, ferritin, transferrin saturation, vitamin B12, vitamin D, calcium, lipid and glycemic profile, liver and renal function, albumin, and total protein). Initiate Nutrition Education and lifestyle counseling.
Initial Phase (1–3 months)	Biweekly	Review dietary recall and fluid intake; assess gastrointestinal symptoms (nausea, vomiting, early satiety, constipation, diarrhea); adjust food texture, portion size, and meal frequency; review protein adequacy and distribution; perform functional anthropometry; prescribe supplementation when indicated. Maintain Nutrition Education and lifestyle counseling.
Intermediate Phase (3–6 months)	Monthly	Repeat functional anthropometry; review food diary and protein and energy intake targets; assess dietary adherence and tolerance; evaluate persistent symptoms; adjust care plan according to clinical progression; request biochemical reassessment every 3 months. Maintain Nutrition Education and lifestyle counseling.
Stable Phase (6 months to end of pharmacological treatment)	Bimonthly or quarterly	Perform functional anthropometry and assess weight trajectory and body composition (DXA or BIA every 6–12 months); review hydration and dietary nutrient density; monitor intake and clinical symptoms; review laboratory tests. Maintain Nutrition Education and lifestyle counseling.
Maintenance Phase (post-discontinuation)	Monthly until stabilization (minimum 3 months), then quarterly for at least 1 year	Perform functional anthropometry; monitor signs of weight regain and dietary adherence; reassess satiety and energy intake; adjust dietary plan and long-term targets; reinforce protein intake and physical activity; monitor body composition and laboratory parameters semiannually until weight stabilization and development of autonomy in healthy dietary choices. Maintain Nutrition Education and lifestyle counseling.

References: [19,22,30,35,43,44,46,47]

Table 2 synthesizes the operational structure of nutritional follow-up, outlining the frequency of consultations and the main assessment parameters. It represents the macro-level framework of the protocol - that is, the organization of the care process across the different phases of treatment.

Complementarily, Tables 3 to 7 were developed to detail the specific nutritional interventions, supported by scientific evidence, for each stage of treatment. These instruments translate the scientific literature into practical actions, describing for each intervention its clinical rationale and mode of implementation. Thus, the protocol acquires an applied and reproducible character, allowing adaptation according to individual patient needs and the clinical setting.

Table 3. Interventions for the Management of Gastrointestinal Symptoms and Adaptation of Dietary Intake

INTERVENTIONS AND PRACTICAL APPLICATION
1. Assessment and Monitoring • Conduct a comprehensive assessment of gastrointestinal symptoms (nausea, vomiting, constipation, diarrhea) at every consultation. • Use standardized scales to assess symptom frequency and severity. **Clinical Rationale:** Targeted nutritional management of specific symptoms improves treatment adherence.
2. General Dietary Adaptation Strategies • Adjust meal frequency, portion size, consistency, and temperature according to individual tolerance. • During the dose-escalation phase, increase meal frequency and reduce portion size for all patients. • Avoid prolonged fasting periods. • In cases of low tolerance to solid foods, prioritize liquid or semi-solid preparations (e.g., protein shakes, soups, smoothies). • Avoid alcohol consumption. • Reduce intake of high-fat foods. • Avoid ultra-processed foods, including fast food, sugar-sweetened beverages, processed meats, concentrated sweets, and snack foods. **Clinical Rationale:** Supports adequate energy and nutrient intake, reduces the risk of energy deficit and gastrointestinal discomfort, and improves tolerance to treatment-related symptoms.
3. Symptom-Specific Adjustments • **Nausea:** Reduce meal volume and increase frequency; eat slowly; avoid high-fat, spicy foods, alcohol, and carbonated beverages. • **Vomiting:** Reduce meal volume and reinforce hydration. • **Constipation:** Increase fluid intake; introduce dietary fiber gradually; consider magnesium supplementation or osmotic laxatives (e.g., polyethylene glycol 3350) when necessary. • **Diarrhea:** Reduce intake of fat, simple sugars, caffeine, and dairy products; avoid large meals; maintain adequate hydration. **Clinical Rationale:** Gastrointestinal symptoms are common during the early phase of treatment and negatively impact intake, adherence, and overall well-being.
4. Fiber Modulation • Prioritize soluble fiber in the initial phases and introduce insoluble fiber gradually, according to gastrointestinal tolerance. • Distribute fiber intake throughout the day. • Avoid large volumes of highly fibrous foods in the first weeks (e.g., raw vegetables, whole grains) in symptomatic patients. • Encourage intake of fiber sources such as oats, chia seeds, flaxseeds, legumes, and peeled fruits. • Progress intake individually to 25–38 g/day or approximately 14 g/1000 kcal. **Clinical Rationale:** A rapid increase in insoluble fiber may exacerbate symptoms such as early satiety, nausea, and reduced appetite. In contrast, soluble fiber is better tolerated and contributes to the regulation of stool consistency.

References:[8,30,35,47]

Table 4. Interventions for Monitoring and Correction of Micronutrient Status

INTERVENTIONS AND PRACTICAL APPLICATION
1. Assessment and Monitoring • Assess critical micronutrients: iron, zinc, calcium, magnesium, potassium, and vitamins A, D, E, K, B1 (thiamine), B12, C, and choline. • Apply a checklist of clinical signs and symptoms: fatigue, hair loss, skin changes, brittle nails, muscle weakness, paresthesia, cramps, arrhythmias, delayed wound healing, and easy bruising. • Order and monitor laboratory tests according to clinical risk: complete blood count, ferritin, transferrin saturation, and micronutrient panels as indicated. **Clinical Rationale:** Hypocaloric diets and reduced food intake increase the risk of micronutrient deficiencies; timely identification and correction help prevent anemia, osteopenia, and fatigue.
2. Correction of Deficiencies and Nutritional Optimization • Prioritize dietary adjustments to increase nutrient density, tailored to individual clinical conditions and tolerance. • Use fortified foods as a first-line strategy. • Initiate individualized oral supplementation when necessary. • Guide the dietary pattern toward a Mediterranean-style diet, emphasizing fruits, vegetables, whole grains, and healthy fats, when not contraindicated. • Reassess periodically (approximately every 3 months) and adjust supplementation accordingly. **Clinical Rationale:** Ensures nutritional adequacy and safety throughout treatment.

References:[15,30,35,47]

Table 5. Interventions for Preservation of Lean Mass

INTERVENTIONS AND PRACTICAL APPLICATION
1. Body Composition Monitoring • Use methods such as dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), or functional anthropometry (body weight, BMI, circumferences, handgrip strength, and muscle function). • Apply the SARC-F questionnaire, particularly in older adults. **Clinical Rationale:** Enables assessment of the quality of weight loss and guides adjustments in protein intake and physical activity.
2. Optimization of Protein Intake • Prescribe 1.2–1.6 g/kg/day or approximately 1.5 g/kg/day of fat-free mass. • Avoid intakes <0.8 g/kg/day or ≥2.0 g/kg/day for prolonged periods. • In patients with BMI ≥30 kg/m², use adjusted body weight for protein intake calculations. **Clinical Rationale:** Preserves lean mass and bone density and reduces the risk of sarcopenia and functional decline.
3. Protein Distribution and Intake Strategy • Prioritize protein consumption at the beginning of meals. • Distribute protein intake evenly throughout the day (approximately 30 g per meal). • Adjust meal frequency according to individual tolerance. **Clinical Rationale:** Increases the likelihood of achieving daily protein targets before early satiety induced by pharmacotherapy.
4. Protein Quality and Anabolic Optimization • Prioritize high biological value proteins (meat, poultry, fish, eggs, dairy products). • Ensure an intake of approximately 2.8 g of leucine per meal. • In cases of inadequate intake, consider protein supplementation to achieve targets. **Clinical Rationale:** High biological value proteins facilitate adequate protein intake with lower food volume and improved gastrointestinal tolerance, while sufficient leucine intake supports activation of the mTOR pathway and stimulates muscle protein synthesis.
5. Integration with Physical Activity • Combine adequate protein intake with resistance exercise. • Recommend strength training 2–3 times per week, with progressive overload, supervised by a qualified professional. • Include ≥150 minutes per week of moderate-intensity aerobic activity. • For long-term weight maintenance, encourage regular physical activity of at least 60 minutes per day. **Clinical Rationale:** Preservation of lean mass depends on adequate protein intake combined with resistance exercise.

References:[8,15,30,34,35,43,46,47]

Table 6. Interventions for Maintenance of Hydration and Monitoring of Fluid and Electrolyte Balance

INTERVENTIONS AND PRACTICAL APPLICATION
1. Monitoring of Fluid Intake • Encourage regular fluid intake of approximately 2–3 L/day, individualized as needed. • Recommend the use of personal water bottles to facilitate intake tracking. • Utilize mobile applications or reminders (e.g., alarms) to support adherence to fluid intake goals. **Clinical Rationale:** Reduces the risk of dehydration associated with gastrointestinal effects and hypodipsic responses induced by IBTs.
2. Prevention and Management of Electrolyte Imbalances • Monitor clinical signs of dehydration and fluid–electrolyte disturbances. • Encourage consumption of foods rich in potassium and magnesium. • In cases of increased losses (e.g., vomiting or diarrhea), consider oral rehydration solutions. • Adjust management according to symptoms and clinical progression. **Clinical Rationale:** The high frequency of symptoms such as vomiting, diarrhea, and hypodipsia increases the risk of electrolyte imbalance.

References: [30,35,47]

Table 7. Behavioral Strategies to Enhance Treatment Adherence and Prevent Weight Regain

INTERVENTIONS AND PRACTICAL APPLICATION
1. Person-Centered Counseling (5As Model) Apply systematically at every consultation: • **Assess:** nutritional status, clinical history, motivation, and perceived barriers. • **Advise:** provide evidence-based guidance using clear, empathetic, and patient-tailored communication. • **Agree:** establish realistic, shared goals aligned with patient preferences and readiness to change. • **Assist:** offer practical strategies and ongoing support to overcome barriers. • **Arrange:** schedule regular follow-up to monitor progress, reinforce achievements, and adjust the plan as needed. **Clinical Rationale:** The 5As model supports longitudinal counseling focused on achievable goals, positive reinforcement, and shared therapeutic responsibility.
2. Ongoing Nutrition Education • Provide individual or group sessions focused on meal planning. • Encourage informed food choices and critical appraisal of the food environment. **Clinical Rationale:** Nutrition education enhances dietary autonomy, supports skill development for sustaining behavior change, reduces relapse, and improves treatment adherence.

INTERVENTIONS AND PRACTICAL APPLICATION
3. Behavioral Nutrition Strategies • Encourage mindful eating practices. • Use hunger and satiety awareness tools (e.g., Hunger–Fullness Scale, in which patients rate hunger and fullness on a 1–10 scale before and after meals). • Promote reflective dietary self-monitoring (food diaries or meal photos linking intake with emotions and physical cues). • Implement self-regulation techniques: I. Pause technique: briefly pause during meals to reassess satiety before continuing. II. Mindful bites: slow chewing with attention to texture, temperature, and flavor to enhance interoceptive awareness. • Refer for psychological support when indicated. **Clinical Rationale:** Behavioral strategies and sustained follow-up help prevent weight regain after pharmacotherapy discontinuation and facilitate recognition of food aversions, emotional eating, and the use of self-regulation and social support strategies.

References:[8,30,35,43,46,47]

The integration of planning and implementation ensures alignment between therapeutic goals and clinical practice, consistent with a person-centered approach and with the behavioral counseling principles proposed by the 5As model (Assess, Advise, Agree, Assist, Arrange), a widely used and well-established framework[30,35].

Thus, the proposed protocol operationalizes the perspective of autonomy-oriented Nutrition Education by translating scientific evidence into applicable clinical strategies, promoting the safe use of IBTs while preserving lean mass, dietary quality, and the sustainability of outcomes, and reinforcing the central role of the dietitian in the dietary management of these therapies.

Conclusion

This integrative review, conducted to support the development of a structured MNT protocol, demonstrates that IBTs represent a significant advancement in the treatment of obesity, with consistent weight reductions and improvements in cardiometabolic outcomes. However, these benefits are accompanied by important clinical challenges, including loss of lean mass, micronutrient deficiencies, dehydration, and weight regain, indicating that pharmacotherapy alone is insufficient to ensure safe and sustainable outcomes.

In this context, the proposed protocol systematically organizes evidence-based nutritional strategies - including optimization of protein intake, hydration management, micronutrient monitoring, and nutrition education and behavioral strategies - providing a clinically applicable and reproducible framework that addresses a critical gap in the integration of pharmacological and nutritional management in obesity care.

Although the available evidence is consistent, methodological limitations and gaps regarding long-term effects underscore the need for studies that structurally integrate pharmacotherapy with nutritional interventions. Accordingly, the proposed approach highlights the central role of the dietitian in delivering effective, safe, and sustainable therapeutic strategies.

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