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Beyond the Treatment Peak: Why We Need Pharmacotherapeutic Follow-Up Protocols for the Withdrawal of Metabolic Weight-Loss Therapies

João Pedro FD*

Clinical Pharmacist, UnyLeya College, Brazil

***Corresponding author:** João Pedro FD, Clinical Pharmacist, UnyLeya College, Santa Casa de Belo Horizonte, Belo Horizonte, Minas Gerais, Brazil

Opinion

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Abstract

The advent of next-generation incretin therapies has revolutionized the management of obesity and cardiometabolic diseases, achieving significant and historically unprecedented weight reductions in pharmacotherapy. However, the commercial appeal and aesthetic pressure from social media have transformed these medications into short-term body remodeling tools, creating a false perception of a "definitive solution" and diverting attention from the need for long-term management. This opinion article examines the global impact of these therapies and critiques the lack of clinical guidelines addressing the post-achievement phase of therapeutic goals. Abrupt discontinuation or loss of follow-up triggers compensatory neuroendocrine adaptations, resulting in weight cycling and the development of sarcopenic obesity due to disproportionate regain of visceral fat. It is concluded that obesity management should not stop at the peak phase of treatment. The implementation of structured deprescribing protocols (gradual tapering) co-managed by the endocrinologist and the clinical pharmacist, integrated into the interdisciplinary team, is advocated, transforming discontinuation into an active and safe step for the continuous maintenance of cardiometabolic health.

Keywords: GLP-1 Receptor Agonists; Obesity; Deprescribing; Pharmacotherapeutic Monitoring; Weight Regain; Interdisciplinary Team

Introduction

Globally, the debate is intensifying regarding advances in the management of obesity, cardiovascular risk, and renal protection resulting from the use of SGLT-1/SGLT-2 inhibitors, as well as GLP-1 receptor agonists (glucagon-like peptide 1) and dual GIP/GLP-1 agonists (glucose-dependent insulinotropic polypeptide) in their injectable or oral pharmaceutical forms.

However, both in lay discourse and in scientific forums on weight management, there is an uncritical overvaluation of the performance of these molecules, often portrayed in an almost mythical sphere, with effects considered 'miraculous.' This reductionist approach restricts the focus to immediate weight loss outcomes and diverts attention from the imperative need for longitudinal planning, beyond the active period of drug use.

The efficacy of these molecules in the management of obesity and its associated comorbidities is undeniable and extensively supported by large clinical trials, which are essential for regulatory approval and commercialization. Studies on GLP-1 receptor agonists, such as semaglutide,

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demonstrate average weight reductions of approximately 15% of total body weight [1], whereas dual GIP/GLP-1 agonists, such as tirzepatide, achieve substantial losses exceeding 20% [2], levels historically attainable only through bariatric surgery. Additionally, this metabolic response is accompanied by significant improvements in glycemic parameters and cardiovascular risk markers [3,4].

From a critical perspective, however, the very nature of these pre-commercialization clinical trials imposes significant methodological limitations, being confined to follow-up periods that rarely exceed five years of efficacy and safety assessment. Given the recent introduction of these molecules to the market, there is a pronounced scarcity of observational and real-world evidence studies focusing on the long-term follow-up of individuals.

A profound lack of bibliographic evidence becomes evident in the proposal of clear clinical and pharmacotherapeutic approaches for the phase following the achievement of therapeutic goals, representing an obvious scientific gap regarding the management of result maintenance, discontinuation, and the risk of weight regain.

In this context, a central question arises for interdisciplinary clinical practice: How can care be safely transitioned after achieving weight-related goals, by structuring a guided discontinuation plan that prevents metabolic regain and ensures the long-term maintenance of outcomes?

The Appeal to Thin Aesthetics and the Role of Social Media

In parallel with the clinical expansion of these drugs, there is a massive appropriation of the topic by digital influencers and social media ecosystems, driving trending topics that reshape public perception of pharmacotherapy [5]. This unrestrained adherence is fueled by the historical centrality of the ideal of thinness, in which conformity to visual standards is frequently prioritized over actual cardiometabolic health needs [6].

When subjected to body image pressures, metabolic therapy loses its role as continuous care for obesity, a chronic and multifactorial disease, and becomes instrumentalized as an aesthetic shortcut. This idealization of rapid weight loss transforms the use of GLP-1 and GIP receptor agonists from a long-term management tool into a mere instrument of temporary body reshaping, promoting a functionalist and disposable approach to treatment [7].

This reductionist dynamic not only distorts clinical rationality but also encourages short-sighted behaviors that critically overlook post-treatment phase planning. The danger of metabolic rebound and disproportionate weight regains lies precisely at the intersection of aesthetic pressure and the inevitable cessation of these therapies, requiring endocrinologists, clinical pharmacists, and other members of the interdisciplinary team to adopt a firm stance to refocus the intervention from superficial appearance to the genuine sustainability of health.

Global Market Opening and Exploration of Commercial Niches

In the aftermath of the Covid-19 pandemic, the world was undergoing economic restructuring with a significant emphasis on prioritizing individual health; in this context, the launch of cutting-edge therapies sparked an unprecedented expansion in the pharmaceutical retail sector.

The commercial appeal has turned incretins into global revenue phenomena, generating tens of billions of dollars annually and causing atypical demand spikes that overload the formal supply chain [8]. Nevertheless, this mass consumption, often facilitated without proper continuous pharmacotherapeutic monitoring or driven by off-label prescriptions and the informal market, reflects a short-term pursuit of weight outcomes, ignoring the health risks of premature discontinuation and the total absence of structured tapering protocols.

This pursuit of rapid results is directly connected to the rise of the wellness industry, whose global market was valued at USD 5.6 trillion and is projected to surpass USD 7.3 trillion by 2028 [9]. It is important to emphasize that this scenario reveals a fundamental paradox: although the sectors of gyms, physical exercise, and lifestyle products are posting record revenues, global obesity rates continue to advance at an alarming pace [10].

It is precisely in the gap between the demands of the fitness standard and the physiological complexity of maintaining exhaustive routines that injectable therapies emerge as a 'biological shortcut.' The promise of a lean body unattached to sustained effort becomes the main catalyst for this rampant consumption, concealing the imperative need for pharmaceutical monitoring protocols during the post-goal phase.

The Pathophysiology of Weight Cycling and the "Yo-Yo Effect"

The abrupt and unplanned discontinuation of these therapies triggers a complex metabolic phenomenon known in the literature as weight cycling, commonly referred to as the "yo-yo effect." This process is not merely the regain of lost

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weight but entails a compensatory physiological adaptation to the energy deficit, characterized by reactive hyperphagia, decreased resting energy expenditure, and profound changes in the satiety hormonal profile, such as sustained suppression of leptin and hypersecretion of ghrelin [11,12].

From the standpoint of body composition, rapid weight loss induced by GLP-1 receptor agonists and dual agonists involves a significant portion of skeletal lean mass; however, during post-discontinuation weight regain, recovery occurs predominantly as visceral adipose tissue [13]. This imbalance in tissue reconstruction culminates in the worsening of visceral adiposity and the development of discontinuation-induced sarcopenic obesity, amplifying insulin resistance, low-grade inflammation, and cardiovascular risk above the pre-treatment metabolic state [14].

Deprescribing/Gradual Tapering and the Importance of Clinical Intervention

In light of this neuroendocrine vulnerability, deprescribing or gradual tapering (step-down/deprescribing) is established as a planned, individualized, and indispensable clinical intervention [15]. Abrupt discontinuation exposes the patient to rapid weight regain, metabolic imbalance, and psychological distress arising from the sense of therapeutic failure, thereby perpetuating the cycle of dependence or abandonment [7,16-21].

To mitigate these risks, management should be co-directed in an integrated manner. The endocrinologist is responsible for agreeing on the gradual tapering of doses based on clinical and metabolic stability, whereas the clinical pharmacist is responsible for structuring continuous pharmacotherapeutic follow-up, monitoring early markers of relapse, advising the patient on dose tapering, and ensuring adherence to lifestyle modifications.

Deprescription ceases to be merely the termination of an intervention and becomes an active, necessary, and strategic phase of the care plan, focusing on monitoring body composition and the gradual management of energetic and endogenous homeostasis mechanisms [22-26].

Conclusion

The advancement of incretin-based metabolic therapies marks a milestone in modern endocrinology, yet their clinical benefits risk being undermined by the logic of instant gratification and the lack of planning for the conclusion of the therapeutic cycle. Treating obesity, a chronic, complex, and recurrent condition, requires acknowledging that achieving the target weight does not signify the end of the intervention, but rather the beginning of one of the most critical phases of care: the consolidation of outcomes.

The erroneous assumption that these molecules serve as definitive solutions must be countered with a rigorous and ethical clinical approach. Abrupt discontinuation of treatment without adequate support exposes the patient to weight cycling and aggravated metabolic risk, perpetuating a frustrating cycle of pharmacological dependence and weight regain.

It thus becomes imperative that the scientific community and international guidelines incorporate formal protocols for deprescribing and gradual tapering. This transition should be synergistically led by the endocrinologist and the clinical pharmacist, supported by the interdisciplinary team. Only through continuous pharmacotherapeutic follow-up, focused on monitoring body composition, health education, and lifestyle restructuring, will it be possible to disconnect treatment success from indefinite drug use and ensure the sustainability of long-term metabolic health.

Conflicts of Interest

The author declares no conflicts of interest, financial, commercial, or personal, that could have influenced the preparation or content of this opinion article.

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