

Beyond Weight Loss: The Promise and Predicament of Incretin-Based Therapies

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For decades, lifestyle modification—including dietary changes, physical activity and behavioral interventions—has remained a cornerstone of obesity management. However, growing recognition of obesity as a complex, chronic and multifactorial disease has highlighted the limitations of relying on lifestyle interventions alone for many patients (1). Metabolic and bariatric surgery has provided an effective treatment option, particularly for individuals with more severe obesity or obesity-related complications, yet it is not suitable for or acceptable to every patient (2). Consequently, effective and sustainable pharmacological therapies have become an increasingly important component of comprehensive obesity care.

The development of obesity management medications has been marked by both therapeutic advances and significant setbacks. Although several agents have offered clinically meaningful weight reduction, others have been withdrawn because of serious adverse effects, while the efficacy, tolerability or clinical applicability of available treatments has remained variable (3,4). Against this background, incretin-based therapies—particularly glucagon-like peptide-1 (GLP-1) receptor agonists and more recently, dual glucose-dependent insulinotropic polypeptide/GLP-1 receptor agonists—have substantially reshaped the pharmacological landscape of obesity treatment (5,6).

Beyond their substantial weight-loss efficacy, incretin-based therapies have demonstrated clinically meaningful benefits across several cardiometabolic and obesity-related conditions. These include improvements in glycemic control and selected lipid parameters, as well as reductions in major adverse cardiovascular events with specific agents in defined high-risk populations (5,7). Evidence has also expanded into obesity-related heart failure with preserved ejection fraction, metabolic dysfunction-associated steatohepatitis, obstructive sleep apnea and symptomatic knee osteoarthritis (8-11). Although the magnitude and certainty of benefit vary by agent, indication, and patient population, these findings highlight the potential of incretin-based therapies to address multiple complications of obesity beyond body-weight reduction.

Despite these advances, important challenges remain. Gastrointestinal adverse effects are common, and although many are manageable, the safety profiles of these agents differ across drugs and patient

populations (12). Furthermore, their expanding use raises concerns regarding long-term treatment durability, equitable access, affordability, and appropriate prescribing. The high cost of these medications and limited reimbursement in some healthcare systems may prevent eligible patients from accessing treatment, potentially widening existing health inequalities (13). At the same time, social-media promotion and the availability of non-prescription access through unregulated channels may contribute to inappropriate use and expose patients to misleading information or potentially unsafe products and may encourage demand among individuals without an established clinical indication or appropriate medical assessment (14,15). When treatment is initiated without adequate evaluation, individualized prescribing, and appropriate follow-up, opportunities to identify contraindications, to manage adverse effects, and to ensure continuity of care may be missed.

Addressing these challenges requires a coordinated approach that balances equitable access with appropriate clinical use. Incretin-based therapies should be reimbursed for eligible patients with a clear clinical indication, as part of comprehensive obesity care, to reduce financial barriers and health inequalities. Their sale without a valid prescription, including through unregulated online channels, should be prevented by effective regulatory oversight and enforcement. Public education should emphasize that incretin-based therapies are evidence-based medications to manage obesity and its complications, not cosmetic or quick-fix solutions for weight loss. Treatment should be initiated following an individualized clinical assessment by an appropriately qualified healthcare professional, with specialist input when indicated, and be supported by appropriate prescribing, monitoring, and long-term follow-up. Ultimately, the success of incretin-based therapies should be measured not only by their efficacy in reducing body weight but also by our ability to ensure their safe, appropriate and equitable long-term use in the management of obesity.

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