

The challenge of weight management: Looking beyond short-term solutions

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China is currently facing a rapid increase in obesity rates. However, the greater challenge lies in the long-term maintenance of weight loss. Weight cycling, defined as the repeated pattern of intentional weight loss followed by unintentional weight regain, is highly prevalent among individuals with obesity and is independently associated with adverse cardiometabolic outcomes. Patients frequently undergo substantial initial weight reduction through

dietary interventions, pharmacotherapy, or bariatric surgery, yet many experience weight regain within a year. A systematic review of high-quality prospective studies with ≥ 3 year follow-up demonstrated that most participants who lost substantial weight through behavioural interventions regained it at approximately 0.14% body weight per month, reaching pre-intervention weight within four years. This signifies a fundamental limitation: treating

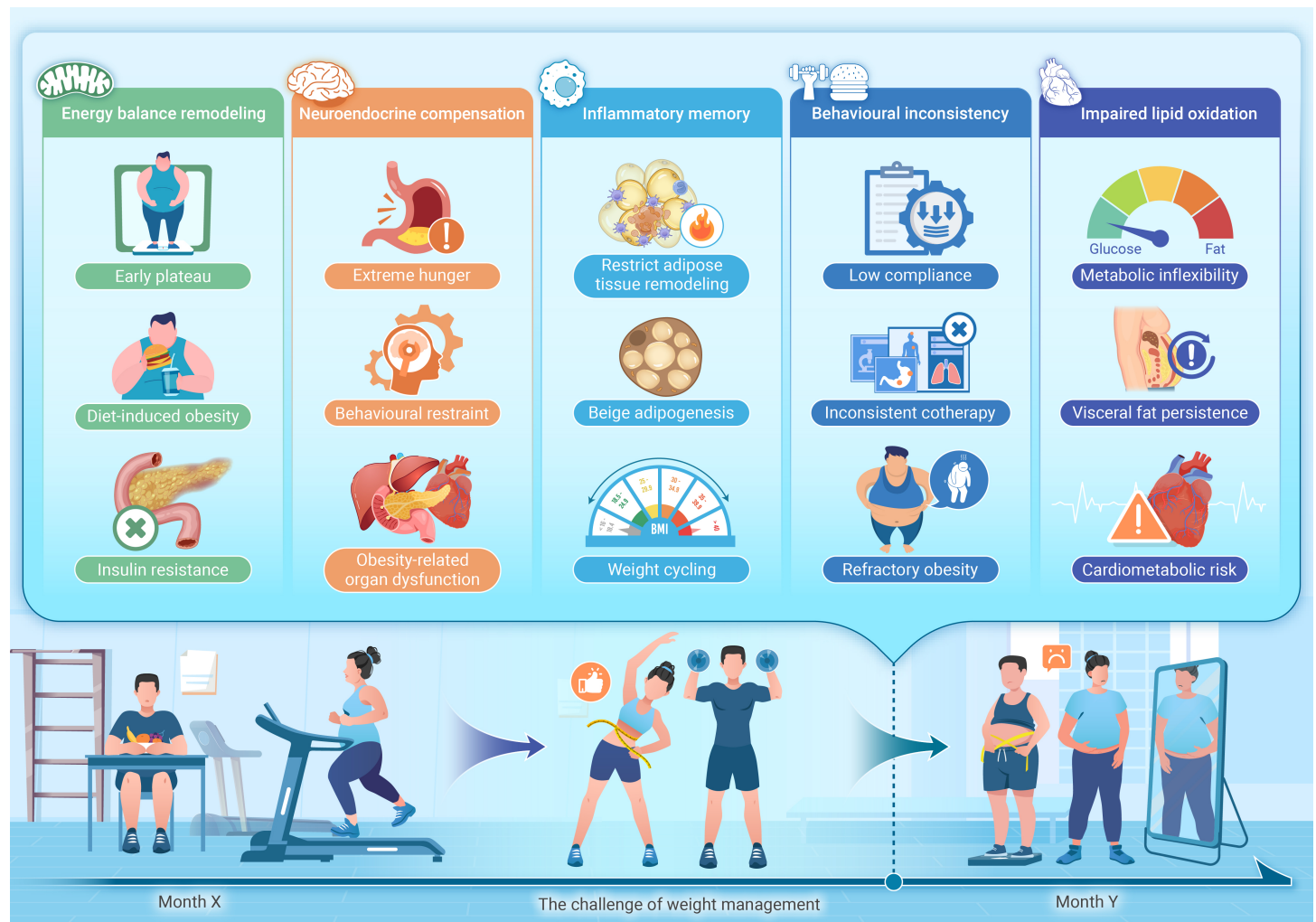


Figure 1. A mechanism-informed clinical roadmap for refractory obesity management in China. Refractory obesity arises from coordinated biological adaptations that promote weight regain after initial loss. Five mechanistic pillars are highlighted: (1) neuroendocrine compensation with reduced anorexigenic and increased orexigenic signalling; (2) adipose tissue metabolic remodeling with impaired lipid oxidation and preferential visceral fat retention; (3) adaptive energy balance remodeling via reduced sympathetic tone and impaired adipose thermogenesis; (4) adipose inflammatory memory driven by macrophage metabolic rewiring and NLRP3 inflammasome hyperactivation; and (5) behavioural–psychological loops modulating biological responses. Integrating these mechanisms with a clinical obesity framework enables stratified, function-centred intervention bundles beyond weight-centric care.

excess body weight without addressing underlying biological drivers. In China, obesity frequently manifests with early metabolic dysfunction and high visceral fat even at lower BMI levels; nationally representative data indicate that approximately 14% of Chinese adults with normal BMI (18.5–23.9 kg/m²) harbor excess visceral adiposity. Chinese guidelines define overweight as BMI ≥ 24 kg/m² and obesity as BMI ≥ 28 kg/m², with central obesity identified by waist circumference ≥ 90 cm (men) and ≥ 85 cm (women), and visceral fat

area ≥ 80 cm² as a clinically actionable threshold. Addressing this issue necessitates a long-term, mechanism-informed strategy, with nutrition at its core, to circumvent the body's tendency to regain weight.

Traditional BMI-centered definitions fail to capture obesity's heterogeneity. A recent international commission redefined clinical obesity as a chronic, systemic disease of excess adiposity impairing organ function, distinct from preclinical obesity where excess fat lacks functional damage.¹ When inte-

grated with Chinese-specific cutoffs, this framework helps identify metabolically unhealthy phenotypes—including the “thin-outside-fat-inside” presentation—disproportionately common in East Asian populations. The goal of treatment thus shifts from merely lowering weight to restoring health. This function-centric view is an essential paradigm shift for the Chinese clinical context, where conventional weight-based criteria frequently underestimate disease burden.

Neuroendocrine compensation and the role of pharmacotherapy

The durability of weight loss is challenged by a profound neuroendocrine counter-response; as adiposity declines, suppression of satiety signals and surge of orexigenic hormones induce hyperphagia and heightened food reward. In clinical practice, these imperatives partly explain why physicians and patients gravitate toward pharmacotherapy: medications directly override hunger signaling, whereas nutritional counseling demands sustained behavioural engagement and is often under-resourced in China's healthcare system. Incretin-based therapies such as GLP-1 receptor agonists have demonstrated remarkable efficacy in achieving clinically significant weight reduction. However, upon discontinuation, the underlying biology reasserts itself.² A post-treatment analysis of the S-LITE randomized controlled trial demonstrated that one year after GLP-1 receptor agonist cessation, approximately two-thirds of weight loss had been regained; post-treatment regain was 6.0 kg greater after GLP-1 RA monotherapy compared with supervised exercise alone.³ These findings confirm that neither behavioural intervention alone nor GLP-1 RA monotherapy provides durable protection against weight cycling. However, strategies including gradual dose tapering, low-dose maintenance, and sequential transition to combination therapy show promise. Notably, combined exercise plus GLP-1 RA treatment yielded a sustained weight reduction of 5.1 kg compared with GLP-1 RA alone one year post-termination, with significantly more participants maintaining $\geq 10\%$ weight loss.³ GLP-1 RAs thus retain a critical role when embedded within comprehensive nutritional, exercise-based, and behavioural frameworks. This underscores that obesity is a chronic, relapsing condition requiring indefinite, multi-modal management.

Core pathophysiological mechanisms of weight cycling

Weight regain operates through five interconnected mechanistic pillars (Figure 1). First, neuroendocrine compensation creates a hormonal milieu favoring overconsumption. Second, adipose tissue metabolic remodeling drives preferential visceral fat re-accumulation, undermining metabolic improvements even when patients remain 5–10% below baseline weight. Post-dietary adipose tissue enters a “fuel-conserving” state—particularly pronounced in populations prone to central adiposity such as Chinese adults. Third, adaptive thermogenic suppression manifests as persistent reduction in resting metabolic rate that outlasts weight loss. Disruption of peroxisome-dependent fatty acid oxidation further impairs heat production. Fourth, adipose inflammatory memory—persistent NLRP3 inflammasome activation and impaired adipose plasticity—constrains metabolic recovery.⁴ Fifth, behavioural and psychological factors—including psychological distress and disinhibited eating—amplify biological drivers of regain.⁵ Together, these mechanisms establish that effective long-term management must address each pillar through coordinated nutritional, pharmacological, exercise-based, and psychological interventions.

Nutritional co-therapy: securing the foundations of obesity management

The biological imperatives favoring weight regain necessitate that medical nutrition therapy (MNT) serves as the permanent scaffold of obesity management. Given the Chinese dietary structure—characterized by high refined carbohydrate intake—stage-specific strategies are essential. During weight-loss induction, higher protein (1.2–1.5 g/kg/day) with reduced carbohydrate is recommended; during maintenance, a localized low-glycemic-load pattern substituting whole grains, legumes, and vegetables for refined staples sustains metabolic gains. Mediterranean-Asian hybrid dietary patterns rich in unsaturated fatty acids and fiber specifically target visceral obesity.

Equally important, structured exercise—combining aerobic training to counter adaptive thermogenesis with resistance training to preserve lean mass—and psychological support addressing emotional eating and motiva-

tional barriers are indispensable.⁵ Within clinical frameworks, nutritional strategies must be elevated to “essential co-therapies”. In China's tiered healthcare system, tertiary hospitals should anchor specialized obesity clinics comprising endocrinologists, dietitians, psychologists, and exercise physiologists, while community health centers focus on long-term follow-up. Emerging evidence further suggests that digital health platforms can serve as scalable adjuncts: a multinational trial of an AI-driven lifestyle intervention demonstrated an average 14% body weight reduction, with 99% of participants losing $\geq 5\%$. By providing individualized real-time coaching and continuous behavioural support, AI-based tools hold promise for compressing weight cycling during the vulnerable maintenance phase. Integrating AI-assisted digital therapeutics with pharmacotherapy and nutritional co-therapy may represent a next-generation paradigm for sustained management. By anchoring pharmacotherapy in robust nutritional coaching, clinicians can transform fragile physiological victories into resilient cycles of metabolic health.

The fight against obesity will be won not by the initial loss of weight, but by preventing weight regain—an economic imperative as much as a medical one. Current evidence demonstrates that both behavioural interventions alone and GLP-1 RA monotherapy are insufficient for durable weight maintenance.³ Only combination strategies integrating pharmacotherapy, exercise, sustained nutrition, and AI-assisted tools can meaningfully compress the cycle of loss and regain. A sustained, nutrition-centered strategy combined with behavioural support is the linchpin for countering adaptive biological forces. Integrated nutritional co-therapy reduces long-term costs compared with pharmacotherapy alone. Aligned with the Healthy China 2030 Planning Outline, we recommend incorporating MNT into chronic disease insurance coverage, standardizing nutrition management training for primary care, and embedding obesity prevention within the national chronic disease framework. Treating nutrition as a lifelong therapy is both biologically essential and fiscally prudent. Clinicians and policymakers must prioritize integrated, durable strategies that improve not just weight metrics, but long-term health and national productivity.

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W.C. contributed to the conceptualization, resources, and funding acquisition and gave a full review and editing of the manuscript. M.W. drafted and edited the manuscript and contributed to part of the funding acquisition.

DECLARATION OF INTERESTS

Wei Chen is an Editorial Board member of The Innovation Nutrition and was blinded from reviewing or making final decisions on the manuscript. Peer review was handled independently of this member and their research group. The other authors declare no conflicts of interest.