Diabetes, Metabolic Syndrome and Obesity

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EDITORIAL

The Future of Obesity Management: Bridging Pharmacologic Innovation and Public Health

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Global Obesity Trends

Obesity remains one of the most pressing global health challenges, with its prevalence continuing to rise across socioeconomic and geographic boundaries. While historically, it predominantly impacted high-income countries, obesity now disproportionately affects low- and middle-income countries (LMICs), where rapid urbanization and economic development have led to dramatic lifestyle and behavioral changes. This "nutrition transition" has redefined population health, fueling increases in type 2 diabetes, cardiovascular disease, and metabolic dysfunction-associated steatotic liver disease.[1,2]

The determinants of obesity are multifactorial, encompassing economic growth, sedentary behavior, and increased consumption of energy-dense, ultra-processed foods.[3] Many LMICs, particularly in Asia, Latin America, the Middle East, and parts of Sub-Saharan Africa, have witnessed rapid increases in overweight and obesity. China exemplifies this trend: traditional plant-based diets have been supplanted by high-calorie, animal-based and processed foods, while both occupational and leisure-time physical activity have declined sharply.[4] Consequently, China now hosts the world's second-largest population of adults living with obesity. Asian populations are especially susceptible to visceral adiposity and related metabolic complications at a lower body mass index (BMI) compared with individuals of European ancestry.[5] These distinctions highlight the necessity for region-specific diagnostic criteria and treatment paradigms.

Incretin-Based Therapies: A Turning Point

Recent pharmacologic advances have redefined therapeutic possibilities for obesity. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, exemplifies this innovation. By simultaneously activating GIP and GLP-1 pathways, tirzepatide enhances insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety, producing more pronounced weight reduction and glycemic control than GLP-1 receptor agonists alone.[6] Emerging triple agonists, such as retatrutide, demonstrate even greater efficacy by targeting GLP-1, GIP, and glucagon receptors.

The SURMOUNT-CN trial evaluated tirzepatide in Chinese adults with overweight or obesity, using Asian-specific BMI thresholds (≥23 kg/m^2 for overweight, ≥28 kg/m^2 for obesity).[7] Participants achieved mean weight reductions of 13.6–17.5% at 52 weeks, comparable to the global SURMOUNT-1 trial.[8] Tirzepatide also preferentially reduced visceral and abdominal fat, offering potential cardiometabolic benefits for populations prone to central obesity. These findings are particularly salient for Asian populations, who develop metabolic complications at lower BMIs. Tirzepatide's targeted effect on abdominal adiposity may help mitigate cardiometabolic risk even in individuals with relatively modest BMI elevations. Nonetheless, additional research is needed to assess long-term impacts on clinically meaningful cardiometabolic outcomes in this population.

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Balancing Promise and Practicality

Despite its efficacy, the widespread adoption of tirzepatide faces significant barriers. High costs and limited availability pose particular challenges in LMICs, where obesity prevalence is rising most rapidly. Equitable access will require coordinated efforts among governments, healthcare systems, and pharmaceutical companies to negotiate pricing, expand insurance coverage, and facilitate generic production post-patent expiration.[9]

Evidence from SURMOUNT-CN suggests that tirzepatide, in combination with lifestyle interventions, can produce substantial weight loss, even among individuals at the lower end of the overweight or obesity spectrum. However, discontinuation often leads to rapid weight regain, indicating the need for sustained, potentially lifelong therapy.[10] Additionally, lean mass loss, a concern with incretin-based therapies, raises important considerations for aging populations and long-term health management.

This reality raises concerns about adherence, affordability, and long-term safety, particularly among younger patients or those without severe obesity-related comorbidities. Ethical frameworks and clinical guidelines must therefore balance therapeutic benefit against potential risks and financial burden.

Integrating Pharmacotherapy with Lifestyle and Behavioral Approaches

Although pharmacologic therapy represents a breakthrough, lifestyle modification remains central to obesity management. Dietary counseling, physical activity, and behavioral support are essential for achieving and sustaining weight loss. Combining medication with lifestyle therapy can enhance both efficacy and sustainability, aligning with a chronic-disease management model rather than an episodic treatment paradigm.[11] A notable concern with incretin analogues such as tirzepatide is the loss of lean body mass, particularly skeletal muscle. This effect is especially relevant for older adults and individuals with sarcopenia, as appetite suppression can reduce overall calorie and protein intake, with some trials reporting muscle loss of 10% or more.[12,13] Although lean mass reduction is common in weight loss interventions, it poses particular risks for frail or elderly patients. Mitigation strategies include consuming adequate high-quality protein and engaging in both aerobic and resistance exercises. Emerging approaches, such as co-administration of myostatin inhibitors with incretin analogues, aim to selectively preserve lean mass while promoting fat loss, though their effectiveness remains under investigation.[14]

Further research is needed to fully understand the impact of tirzepatide and other incretin analogues on body composition. Ongoing studies using dual-energy X-ray absorptiometry (DEXA) are assessing both lean mass and bone mineral density, providing critical insights to optimize interventions for preserving lean mass during treatment. Current evidence suggests that combining nutritional strategies with structured exercise remains essential for maintaining lean mass and metabolic health during therapy.

Implications for Clinical Practice, Pubic Health, and Policy

Findings from SURMOUNT-CN and related trials highlight the importance of contextualizing obesity treatment within population-specific frameworks. In Asia, where BMI thresholds for metabolic risk are lower, these results could guide updates to clinical guidelines, incorporating tirzepatide and other incretin-based agents as adjuncts to lifestyle interventions.[7,8] Beyond individual treatment, policy initiatives should address the upstream determinants of obesity by improving access to healthy foods, regulating marketing of energy-dense products, and promoting active built environments.[15]

Currently, tirzepatide and similar therapies remain largely inaccessible to most patients in LMICs due to high costs and limited availability. As additional agents enter the market and competition increases, prices may decrease, and the eventual introduction of generics could further improve access. In the meantime, obesity management in LMICs will continue to rely primarily on prevention and traditional strategies, including dietary modification and increased physical activity. Given constraints in healthcare infrastructure and medication access, prevention remains the most cost-effective and equitable approach. Public-private partnerships, community education, and fiscal policies targeting the built environments can complement pharmacologic advances, supporting sustainable and population-wide obesity control.

Equitable access to incretin mimetics such as tirzepatide remains a major challenge in low-resource settings. Limited supply, high demand driven by their weight-loss effects, and prohibitive costs restrict availability for many populations. Policy interventions could include stricter regulation of prescriptions and sales, prioritizing treatment for individuals with weight-related comorbidities. Governments should also negotiate lower prices, expand insurance coverage, and support the production of generics as patents expire, all of which could enhance affordability and accessibility in resource-limited contexts.

Finally, the increasing use of compounded GLP-1 receptor agonists, such as tirzepatide, for weight management raises important safety concerns. According to the US Food and Drug Administration (FDA), these compounded formulations are not reviewed for safety, efficacy, or quality, and there have been reports of dosing errors, contamination, and mislabeling. Their clinical effectiveness and long-term safety have not been clearly demonstrated, emphasizing the need for caution and regulatory oversight.[16]

Future Directions and Long-Term Obesity Management

Long-term data on tirzepatide's safety, durability of weight loss, and impact on cardiometabolic outcomes are still emerging. Research must include diverse populations, particularly from Asia, Africa, and Latin America, to ensure generalizability of efficacy and safety. For example, SURMOUNT-CN and prior meta-analyses of tirzepatide for the treatment of diabetes both demonstrated higher incidence of gastrointestinal adverse events for Asian populations compared to individuals of other geographic origins. Further studies are also needed to assess effects on cardiometabolic diseases, metabolic dysfunction-associated fatty liver disease, chronic kidney disease, and body composition, particularly with respect to lean mass preservation.

Findings from the SURMOUNT-CN study can shape future clinical guidelines for obesity treatment in China and across other Asian countries, and lessons can be drawn for global obesity management. The results from SURMOUNT-CN indeed set a positive precedent for expanding the use of tirzepatide in clinical practice across Asian countries, as an adjunct to lifestyle interventions. These agents may also reduce the need for bariatric surgery, especially considering the lower BMI thresholds for surgery in China. As more data becomes available, particularly from ongoing trials in Japan and other Asian countries, it will be crucial to integrate these medications into clinical guidelines in a way that maximizes both efficacy and accessibility.

Long-term success requires not only access to pharmacologic therapies but also structural changes that enable healthier lifestyles across populations. Relying solely on pharmacologic agents poses significant sustainability challenges for healthcare systems. A practical and durable approach may involve using incretin analogues to induce weight loss, followed by maintenance through lifestyle modification. Alternatively, treatment could begin with dual or triple incretin agonists to achieve weight reduction, then transition to a single GLP-1 receptor agonist for long-term weight maintenance, bridging cutting-edge pharmacology with public health and prevention efforts.

From a systems perspective, the success of incretin-based therapies will depend on integration with preventive health policies. Pharmacologic advances offer an unprecedented opportunity to reduce obesity-related morbidity, but they must be deployed within a broader framework of health equity, affordability, and population-level prevention.

Conclusion

Incretin receptor agonists such as tirzepatide represent a transformative advance in obesity and cardiometabolic disease management. However, pharmacologic innovation alone cannot reverse the global obesity epidemic. The most durable progress will result from combining these agents with lifestyle modification, policy reform, and structural changes that enable healthy living. Bridging clinical innovation with public health action offers a path toward sustainable, equitable solutions for obesity and its consequences.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analyzed in this study.

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FQ and LW was responsible for Conceptualization, Formal Analysis, Writing – original draft and Writing – review and editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been. submitted; and agree to be accountable for all aspects of the work

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