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Weight management in China: Energy metabolism as the core principle for precision prevention and control

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China is grappling with an escalating obesity epidemic. National data show over 65% of adults would be overweight or obese by 2030, if without effective actions.[1-2] In response, China has launched a nationwide health initiative to address rising obesity prevalence, and urge comprehensive strategies to curb obesity and its metabolic consequences, as the National Health Commission declares 2025-2028 the "Weight Management Year". Various governmental agencies and medical institutions acted, including releasing guidelines on weight management and establishing weight management clinics nationwide.

This editorial reflects on key issues regarding the core scientific issues in weight management, the energy metabolic homeostasis, the long-term maintenance of weight loss and the precision management of obesity. It includes integrating insights from optimizing obesity assessment, reconsidering weight management goals, identifying new intervention targets, promoting the precision of weight management and rationally positioning of weight loss drugs (Figure 1).

TO OPTIMIZE OBESITY ASSESSMENT, FOCUSING ON THE PIVOTAL ROLE OF BODY FAT PERCENTAGE AND DISTRIBUTION

For a long time, assessment of obesity mostly refers to the international body mass index (BMI) standards, for example, the cut-off points of 25 kg/m^2 for overweight and 30 for obesity according to the WHO criteria. Because of differences in body composition and metabolic characteristics among different ethnic groups, different thresholds are introduced. In China, the threshold values of BMI for overweight are 24 kg/m^2 and 28 kg/m^2 for obesity. However, their applicability to health management remains controversial. It is imperative to establish BMI cutoffs through large, long-term cohort studies with endpoints of disease incidence and mortality. Recently, in the nationwide China Cardiometabolic Disease and Cancer Cohort (4C) study, the research team reported a BMI range of 25.0–26.0 kg/m^2 as the inflection point for mortality in general population,[3] evoking further discussion about the optimal standards of overweight or obesity in Chinese and other ethnic populations.

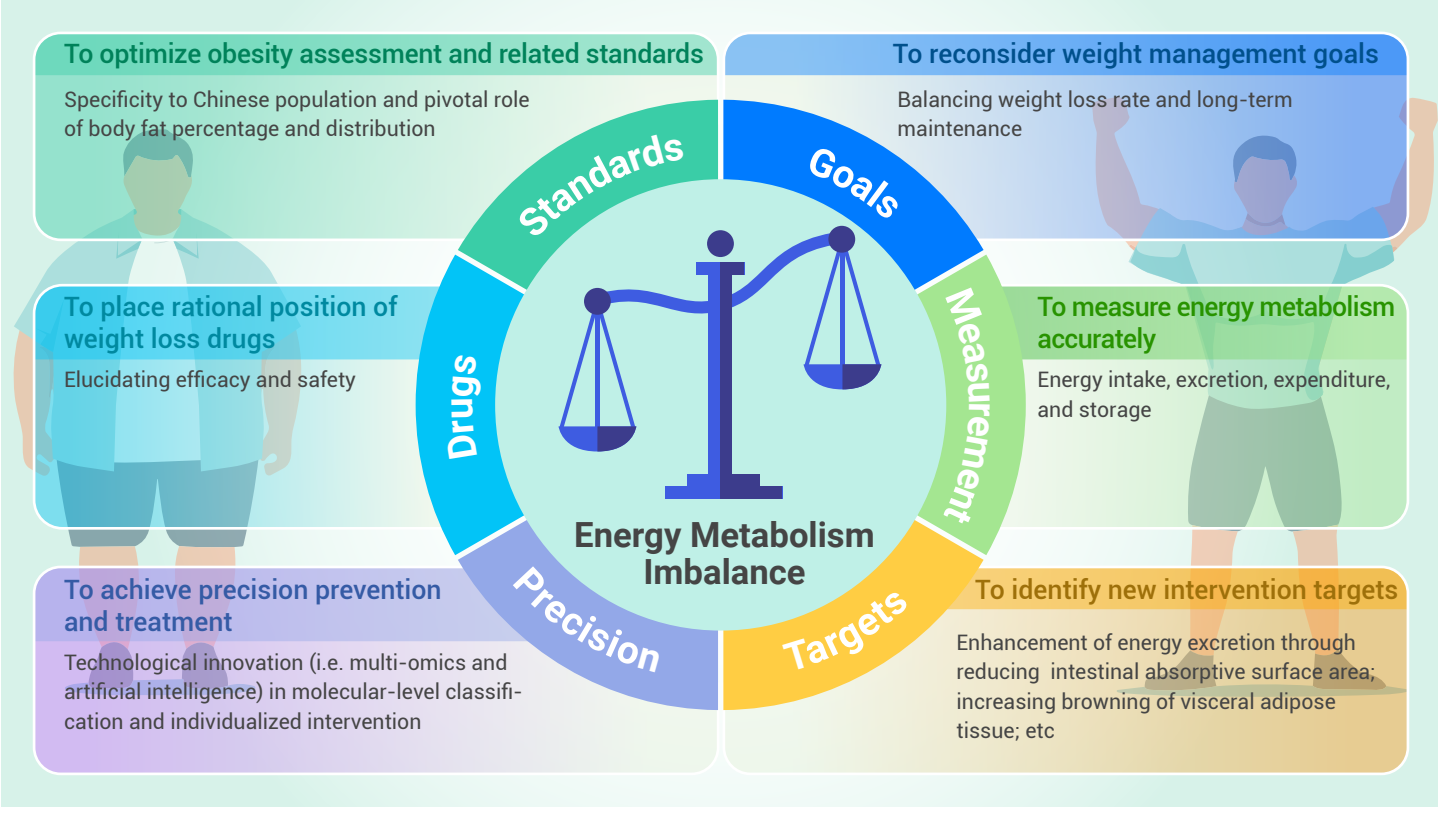

Figure 1. Several key issues for life-course weight management.

However, BMI itself cannot tell the whole story. Excessively high visceral fat, the fat in or surrounding the abdominal organs, such as the liver, pancreas, kidneys, and intestines, has been recognized as a risk factor for diabetes, hypertension, cardiovascular diseases and certain kinds of cancers. Shifting the assessment focus from superficial body weight to deep-seated body composition and distribution will receive more attention in weight management. These can be measured by waist circumference, waist-to-hip ratio, waist-to-height ratio, CT/MRI or bioelectrical impedance analysis. A precise and health-oriented weight loss should focus on decreasing inappropriately accumulated adipose tissue, while preserving the mass of bone, muscle, and visceral organs.

TO MEASURE ENERGY METABOLISM ACCURATELY, AND TARGET IMPROVING ENERGY EXCRETION

The fundamental scientific question of sustaining energy metabolism

homeostasis entails accurate quantification of the balance among the four dimensions: energy intake, excretion, expenditure, and storage. Even if individuals have the same weight and age, significant differences exist in their basal metabolic rate, active metabolic rate (energy consumption from exercise) and thermic effect of food (energy consumption from digestion and absorption). Through accurate measurements, such as human room calorimetry system or indirect calorimetry or metabolomics analysis, the primary cause of "energy surplus/deficit" will be identified (e.g., whether energy accumulation is caused by low metabolism or excessive dietary intake). Further proactively modifying one or more of the four dimensions to maintain energy metabolism homeostasis is the primary strategy for weight loss.

For enhancement of energy excretion, the underexplored yet valuable strategy involves gastrointestinal and renal pathways. Certain antidiabetic agents increase glucose excretion to augment energy loss. For example, SGLT2 inhibitors achieve this through urinary glucose excretion; orlistat inhibits intestinal fat absorption, while acarbose reduces carbohydrate absorption, both enhancing energy excretion. Exploring targeted modulation of excretory pathways to reduce energy absorption represents a promising choice for weight management. Recently, it was first demonstrated that inactivation of a subpopulation of the dorsal motor nucleus of vagus (DMV) neurons that project to the jejunum shortens the length of gut microvilli, thereby reducing fat absorption and consequently causing weight loss.[4] Interestingly, puerarin can induce intestinal fat loss depending on the inhibition of DMV neurons and the subsequent shortening of length of microvilli.[4] This work demonstrates the regulability of intestinal microvilli and intestinal absorptive surface area, presenting a completely novel perspective for weight loss.

TO RECONSIDER WEIGHT MANAGEMENT GOALS, ACHIEVING LONG-TERM MAINTENANCE

Most current weight intervention programs focus on the weight loss phase, but neglect maintenance strategies after weight loss. Preventing weight regain remains a scientific gap in our current understanding. Several issues underlie this challenge. Methods used to control weight gain may not be adequate to reduce the risk of weight regain, because the mechanisms causing weight regain seem to differ from those of developing the initial weight gain. The pro-inflammatory imprint formed by macrophages during the period of obesity may be one of the key reasons for the deterioration of metabolic status following weight regain. These "experienced" immune cells render adipose tissue abnormally vulnerable when confronted with new energy challenges. Another proposed mechanism is loss of lean body mass, which results in reduced energy expenditure and increased energy intake. Obesity-induced or weight loss-induced changes in the gut environment may be causally associated with weight regain, for these factors may affect the direct energy intake and expenditure.

In addition to disentangling the mechanisms in weight regain, the practical strategies for weight management at present are highly recommended including solidifying healthy dietary behaviors, developing exercise habits, and providing psychological support. Based on reduced total energy intake, strategies include restricting consumption of high-calorie, high-lipid, high-sugar, refined carbohydrate, and ultra-processed foods, and prioritizing those rich in dietary fiber, high-quality protein, and unsaturated fats, with an increased proportion of vegetables, fruits, and whole grains (e.g., the Jiangnan Diet, a Chinese alternative to the Mediterranean Diet). Individualized measures should be improved by incorporating additional environmental and biological evaluation (e.g., social determinants of health, microbiome, sex, age, medical and weight history, BMI category) that may influence long- term success. Using technology to facilitate adherence can support weight loss and maintenance. For instance, sensor-based devices, such as smartwatches, can objectively detect behavioral patterns (e.g., eating, exercise and sleep). Smartphones and smart home devices (e.g., connected refrigerators, scales, voice assistants and health monitoring devices) can further promote self- monitoring through real- time, objective feedback.

TO DEVELOP PRECISION METHODS FOR WEIGHT LOSS, THROUGH SCIENCE BREAKTHROUGHS AND TECHNOLOGICAL INNOVATION

Precision management for obesity lies in two aspects, one is prevention and the other is treatment. Development of technologies such as genomics (identifying obesity genetic loci), proteomics (analyzing the functions of metabolism-related proteins), and artificial intelligence (predicting trend of weight change and optimizing intervention plans) facilitates characterizing an individual's profile that reflects specific responses to different dietary and exercise interventions, identifying biomarkers that have the potential to predict intervention efficacy, classifying individuals according to intervention outcomes, and developing personalized intervention measures based on metabolic comorbidity subtypes. An example is the A. muciniphila (AKK), which is a promising target of gut microbiota modulation for managing obesity and type 2 diabetes. Supplementation with AKK resulted in significant reductions in body weight, fat mass, and glucose levels among patients with type 2 diabetes who had low baseline AKK levels, whereas it showed poor colonization and no significant clinical improvements in those with high baseline AKK levels.[5]

Besides, the genetic-based (e.g. the poly genetic score, the key genetic variant in candidate genes of high susceptibility or specific response to treatments), brain and central nerve system-based (the appetite, eating behavior, etc.) precision have been investigated and proposed. Treatment-based multitrait phenotypes, such as multi-omics data, can improve weight loss outcomes. However, because the phenotyping methods are burdensome and costly, further exploration of their applicability is needed.

TO PLACE RATIONAL POSITION OF WEIGHT LOSS DRUGS AND BALANCE EFFICACY AND SAFETY

Some weight loss drugs require combination with diet and exercise to take effect, and the boundary of their "purely pharmacological effects" needs to be clarified (e.g., whether they work only by suppressing appetite and promoting metabolism, or rely on the synergistic effect of lifestyle interventions). This avoids overestimating the efficacy of drugs. Weight loss drugs may be associated with side effects such as gastrointestinal reactions (e.g., nausea, diarrhea), cardiovascular risks (e.g., blood pressure fluctuations), and neuroendocrine impacts (e.g., mood changes). It is important to emphasize individualized risk assessment—the benefits and potential risks of drugs must be weighed based on the patient's age, underlying diseases, metabolic status, etc., to avoid "one-size-fits-all" medication.

In total, weight management could be a systematic strategy. In the short term, medications or bariatric surgery can be used to achieve goals as soon as possible. In the medium term, with the support of digital instruments like energy metabolism rings and monitoring watches, individuals can engage in active personal lifestyle management to prevent weight regain. In the long-term, establish standardized metabolic management centers in medical institutions to provide accurate assessment and diagnosis of obesity and related diseases, achieving a steady healthy lifestyle and personalized weight management. China's "Weight Management Year" presents a pivotal opportunity to integrate cutting-edge science with policy action. Success will require collaboration between clinicians, researchers, policymakers, and communities to transform evidence into impact, ultimately curbing the obesity epidemic and improving metabolic health for generations to come.

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DECLARATION OF INTERESTS

The authors declare no competing interests.