https://doi.org/10.1038/s41591-026-04210-2

Unintended risks of sarcopenic obesity during weight-loss interventions in older people

Older adults over 65 years of age with obesity are physically not all the same, exhibiting distinct trajectories and responses to weight-loss interventions. Incretin mimetic drugs (IMDs) such as semaglutide and tirzepatide are increasingly prescribed and can induce substantial weight loss[1], often accompanied by reductions in fat and muscle. Given the central role of muscle in strength, mobility and independence, its preservation has clinical relevance in older adults. These shifts in body composition have renewed interest in muscle—fat dynamics, particularly sarcopenic obesity, defined by increased fat mass and reduced muscle health[2]. Regardless of its definition, sarcopenic obesity is consistently associated with worse physical function, lower quality of life and higher mortality than either sarcopenia or obesity alone[3].

Data have shown that lifestyle-based, structured diet and exercise programs supported by behavioral counseling reduce obesity-related complications but may cause unintended losses in lean mass, which includes muscle mass, connective tissue, viscera, and bone density and content; this necessitates a careful balance of benefits and harms[4]. In older adults, these losses are clinically meaningful, translating to declines in strength, balance and resilience. Most trials report body composition changes over 6–12 months, with limited long-term data.

With more-intensive weight loss interventions, including surgery and pharmacotherapy, muscle and bone losses occur early and may persist[5]. IMDs also produce this loss. In the STEP-1 and SURMOUNT trials[6,7], approximately 24–40% of weight loss was attributed to lean mass loss, with absolute losses of about 6 kg, a magnitude comparable to a decade or more of age-related muscle decline[1]. However, older adults were under-represented in these trials, and outcomes were not stratified by age or sex. Thus, clinicians must extrapolate safety and efficacy data to older populations without adequate evidence on the outcomes that matter most to patients. In addition, bone health is frequently overlooked in obesity management, as weight loss with IMD therapies may accelerate bone loss unless mitigated by exercise. For older adults already at risk for osteoporosis, this raises concerns about fracture risk during and after weight loss.

Loss of lean mass does not inevitably result in functional decline, especially when weight loss is paired with targeted exercise-based strategies. Caloric restriction combined with aerobic and resistance exercise improves physical performance more than either intervention alone, despite modest losses in lean mass[4]. Resistance exercise seems to be essential for preserving strength, even when some lean mass is lost. Adequate protein intake (about 1.2–1.5 g per kilogram body weight per day) may further mitigate muscle loss.

When liraglutide is combined with resistance exercise, lean mass is preserved and cardiorespiratory fitness improves despite greater weight loss, which illustrates that how weight is lost matters as much as how much weight is lost. Importantly, no randomized trials have evaluated newer IMDs specifically in older adults with established or incipient sarcopenic obesity. In pooled analyses of semaglutide trials in adults with heart failure[8], modest improvements in 6-minute walking distance were observed but did not reach clinically important thresholds. This measure also lacks specificity for sarcopenia-related functional decline[9], which underscores the need for targeted performance assessments.

Discontinuation of IMDs is also increasingly common in older adults, often due to dose-dependent gastrointestinal side effects. Weight cycling is therefore a realistic concern. When weight is regained, fat mass is preferentially gained over lean mass. In a study of post-menopausal women, substantially less lean mass was regained per kilogram of fat gained than was lost during weight loss[10]. Clinically, this suggests that repeated cycles of weight loss and regain may progressively erode muscle reserves, increasing vulnerability to falls, frailty and fractures. Therefore, identifying a patient's position along the sarcopenia trajectory may guide safe and effective initiation or intensification of treatment.

These observations have clear implications. Screening and diagnosis should extend beyond body mass index alone. Older adults considered for pharmacological weight-loss therapy should be routinely evaluated for muscle strength, physical performance and bone health, particularly when weight-loss targets exceed 10–15% of initial body weight. Although assessments during clinical encounters remain operationally challenging, they are essential for tailoring intervention intensity. These include simple measures of visceral adiposity, objective physical function and body composition, where available. Existing electronic health record data from routine computed tomography or magnetic resonance imaging could be harnessed to enhance reporting. Emerging digital health-based technologies may offer cost-effective solutions once they are validated to identify patients at heightened risk.

Harmonization efforts such as the Global Leadership Initiative on Sarcopenia[9] and the Sarcopenic Obesity Global Leadership Initiative[2] continue to propose a conceptual framework that integrates muscle mass, strength and muscle-specific strength. They also provide clinicians with a pragmatic algorithm for screening, diagnosing and staging sarcopenic obesity, designed for primary care, using cost-effective and accessible tools. Identifying patients using these criteria may be more actionable than precise phenotyping. Functional decline should be treated as a critical outcome of obesity therapy in older adults, not a secondary consideration.

The availability of highly effective IMDs calls for a cautious, individualized approach aligned with the geriatric principles of 'starting low and going slow' when titrating doses, with enhanced monitoring for adverse effects and prioritization of functional preservation. Importantly, safe thresholds for weight loss in older adults remain poorly defined — in particular, how much muscle can be lost without compromising strength, independence or long-term health[3]. Until such thresholds are established, prioritizing functional preservation over maximal weight reduction should remain central to clinical decision-making.

A multidisciplinary care team consisting of providers, dietitians, exercise professionals

and care managers is essential for guiding treatment decisions, supporting individualized nutrition and exercise strategies, and promoting long-term adherence. Financial burden and social support are often overlooked, particularly in aging populations. Health systems and payers must also address barriers to nutrition and exercise access, particularly in this population. Patients should be informed about weight regain and uncertain long-term effects on sarcopenia.

Further research is needed to determine whether people with sarcopenic obesity derive benefits from IMDs comparable to those observed for lifestyle-based weight-loss interventions. Broader use of IMDs underscores the need to move beyond body mass index alone and to integrate body-composition assessments into routine clinical practice. Whether patients with diabetes who are treated with IMDs and remain overweight are at increased risk of sarcopenia remains unknown.

Emerging artificial intelligence-driven tools may help to synthesize biomarkers by applying a precision medicine framework to match the right intervention to the right patient[3]. As IMDs become more widely adopted, integrating assessments of muscle mass, lean mass and bone into routine obesity care and evaluating the impact of weight-loss trajectories on body composition and physical function will be critical. IMDs should be tools that help align treatment goals with healthy aging, not just with weight loss.

John A. Batsis[1,2] ✉, **Lorenzo M. Donini**[3] **& Carla M. Prado**[4]

[1]Division of Geriatric Medicine, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, USA. [2]Department of Nutrition, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. [3]Department of Experimental Medicine, Sapienza University, Rome, Italy. [4]Department of Agricultural, Food, and Nutritional Sciences, University of Alberta, Edmonton, Alberta, Canada.
✉e-mail: john.batsis@unc.edu

Published online: 05 February 2026

References

1. Locatelli, J. C. et al. *Diabetes Care* **47**, 1718–1730 (2024).
2. Gortan Cappellari, G., Zanetti, M., Donini, L. M. & Barazzoni, R. *Curr. Opin. Clin. Nutr. Metab. Care* **27**, 402–409 (2024).
3. Prado, C. M., Batsis, J. A., Donini, L. M., Gonzalez, M. C. & Siervo, M. *Nat. Rev. Endocrinol.* **20**, 261–277 (2024).
4. Villareal, D. T. et al. *N. Engl. J. Med.* **376**, 1943–1955 (2017).
5. Nuijten, M. A. H. et al. *Obes. Rev.* **23**, e13370 (2022).
6. Wilding, J. P. H. et al. *N. Engl. J. Med.* **384**, 989–1002 (2021).
7. Jastreboff, A. M. et al. *N. Engl. J. Med.* **387**, 205–216 (2022).
8. Butler, J. et al. *Lancet* **403**, 1635–1648 (2024).
9. Beaudart, C. et al. *Aging Clin. Exp. Res.* **37**, 100 (2025).
10. Beavers, K. M. et al. *Am. J. Clin. Nutr.* **94**, 767–774 (2011).

Competing interests

J.A.B. has consulted for Regeneron, Abbott Nutrition and MedaCorp. C.M.P. has previously received honoraria and/or paid consultancy from Abbott Nutrition, Nutricia, Nestlé Health Science and Novo Nordisk.