CLOSER LOOK

MEMORANDUM

Endocrine Society calls for obesity treatment goals to move beyond percent weight loss – September 9, 2026

The GLP-1 RA era shifting obesity care toward individualized health outcomes, raising questions about long-term treatment, precision prescribing, safety, and maintenance

The Endocrine Society released a momentous statement today, "Obesity science, research gaps, and opportunities in the new era of obesity medicines," reviewing major research gaps created by the rapid evolution of obesity pharmacotherapy. The authors, including Dr. Daniel Drucker (University of Toronto), Dr. Ania Jastreboff (Yale University), and Dr. Donna Ryan (Pennington Biomedical Research Center) et al., emphasize that GLP-1 RAs have enabled unprecedented weight reduction and have expanded the field's focus from achieving weight loss toward optimizing broader health outcomes. Key priorities include (i) understanding obesity biology; (ii) explaining heterogeneity in treatment response; (iii) redefining treatment targets; (iv) determining optimal long-term treatment strategies; and (v) strengthening evidence around safety and real-world use.

The statement is not intended as treatment guidance. Instead, it lays out a research "roadmap" for how the field should evolve as highly effective obesity medicines become increasingly available and as therapies expand beyond semaglutide and tirzepatide to oral agents, multi-agonists, and longer-acting approaches.

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Moving beyond percent weight loss: Redefining success in obesity treatment

Percent change in body weight remains the predominant, primary efficacy endpoint used in obesity drug development. Yet, authors assert that it overlooks major variation in treatment response, fat distribution, and body composition.

The statement therefore calls for more meaningful treatment targets that incorporate measures such as visceral and ectopic adiposity, organ function, cardiometabolic health, physical function, and patient-reported outcomes. Accordingly, authors highlighted the STEP-3 trial, where semaglutide combined with intensive lifestyle intervention produced weight loss within ~1% of the STEP-1 trial, which used standard lifestyle intervention. These data underscore lifestyle support as adding relatively little additional weight loss, but having the potential to deliver broader health benefits such as improved nutrition quality, physical activity, sleep, and stress management. As obesity medicines become more powerful, the question is shifting from "how much weight did a patient lose?" to "how much treatment is needed to meaningfully improve this patient's health?"

Precision obesity therapy remains on the horizon despite substantial variation in treatment response

The statement repeatedly emphasized heterogeneity in obesity and treatment response. Individuals taking GLP-1 RAs may achieve considerably different results weight loss magnitude, side effects, and weight regain after discontinuation. Existing genetic approaches have not yet been able to reliably predict clinically meaningful differences in response to GLP-1 RAs.

The authors therefore call for better clinical, genetic, and behavioral biomarkers that could help identify the optimal medication and dose for an individual patient. This may become especially important as obesity treatment options expand, requiring clinicians to make increasingly complex and individualized decisions about therapy.

Long-term maintenance strategies are a major clinical question

Phase 3 withdrawal studies demonstrate that discontinuing GLP-1 RAs and GIP/GLP-1 RA leads to substantial weight regain and metabolic relapse, reinforcing the view of obesity as a chronic disease that often requires long-term treatment. However, the optimal maintenance strategy remains uncertain. The statement highlights the significance of trials aimed at comparing continued full-dose treatment with lower doses, intermittent dosing, or lifestyle-supported maintenance.

Long-term safety evidence will need to keep pace as obesity medicines are used by millions of people for multiple years

Although GLP-1 RAs and GIP/GLP-1 RAs have been evaluated in tens of thousands of participants, trials are generally too short and too small to reliably identify rare adverse events or establish long-term safety across diverse populations. Many patient populations, including those with T1D, pregnancy, certain renal or psychiatric conditions, and histories of cancer, have also been excluded from pivotal trials, leaving critical evidence gaps as real-world use expands. The authors also raised concerns about the consequences of rapid, substantial weight loss, including loss of lean mass and bone in susceptible individuals. The statement highlighted the need for research on resistance exercise, adequate protein intake, slower weight-loss strategies, and emerging muscle-preserving therapies to support safe long-term treatment with GLP-1 RAs.

Close Concerns' Questions

1. How should payers weigh the upfront cost of obesity treatment against longer-term reductions in obesity-related complications and healthcare utilization?
2. How much weight regain occurs with different maintenance approaches, and at what point does weight regain begin to erode the health benefits achieved during treatment?
3. Which clinical features or biomarkers might eventually help determine whether an individual is more likely to respond better to mono-agonist, dual-agonist, or emerging triple-agonist obesity therapy?
4. How will coverage and reimbursement models evolve to ensure equitable access as obesity medicines scale to chronic, long-term use?
5. As powerful therapies reshape obesity care, how do we ensure prevention efforts remain a central priority?

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