CLOSER LOOK

MEMORANDUM

WHO issues new global guidelines on GLP-1 RA use for adults living with obesity – December 1, 2025

Recommendations highlight the need to balance long-term GLP-1 RA use and behavioral interventions with equitable access and health system readiness

The World Health Organization (WHO) published new guidelines on the use and indications of GLP-1 RAs for the treatment of obesity in adults today in *JAMA,* authored by the WHO's Dr. Francesca Celletti, Dr. Jeremy Farrar, and Dr. Luz de Regil. The WHO guidelines recognize obesity as a chronic, relapsing disease requiring lifelong care, consequently recommending long-term (defined as longer than six months) GLP-1 RA use paired with intensive behavioral therapy (IBT) for adults with obesity. Both recommendations were graded as "conditional" due to limited long-term data on GLP-1 RAs alongside targeted behavioral interventions and health system constraints globally.

These guidelines aim to support health systems and clinicians in adopting effective and equitable obesity treatment strategies.

Table of Contents

WHO issues two conditional recommendations: Long-term GLP-1 RA use and behavioral support

In today's guidelines, the WHO issued two conditional, evidence-informed recommendations:

- **Long-term GLP-1 RA therapy** may be used for adults living with obesity, based on moderate-certainty evidence demonstrating clinically meaningful weight loss and metabolic benefits across liraglutide (Novo Nordisk's Victoza), semaglutide (Novo Nordisk's Ozempic), and tirzepatide (Lilly's Mounjaro).
- **Intensive behavioral therapy (IBT)**, including structured goal setting for exercise and diet, energy intake restriction, weekly counseling sessions, and routine assessments of progress, may be combined with pharmacotherapy to reinforce weight loss, support lifestyle change, and sustain health improvements.

The guidelines explained that conditional grading reflects ongoing uncertainties around long-term safety and durability of GLP-1 RAs, their high cost, feasibility challenges across health systems around long-term adoption, and the risk of worsening access inequities.

Successful implementation will depend on three pillars, including: (i) expanding "affordable" and "fair" access to GLP-1 RAs (it was slightly challenging to interpret this across a range of geographies); (ii) preparing health systems to deliver integrated behavioral and pharmacologic care; and (iii) ensuring nondiscriminatory approaches grounded in universal access.

Current long-term evidence on GLP-1 RAs: CVOTs strengthen confidence in chronic use

The WHO also emphasized the importance of data on the extended use of GLP-1 RAs, an area where efficacy is supported by multiple large cardiovascular outcomes trials (CVOTs). Several of these trials have already demonstrated strong and prolonged safety and efficacy data for:

- **Tirzepatide (Lilly's Zepbound).** The SURMOUNT trials demonstrated substantial, durable weight loss of up to 20% with tirzepatide in people with obesity or overweight with comorbidities. Furthermore, the SURPASS-CVOT (n=13,165) trial also showed the reduction of MACE-3 risk (composite of CV death, heart attack, or stroke) by 8% compared to dulaglutide in people with T2D and CVD.
- **Semaglutide (Novo Nordisk's Wegovy).** In SELECT (n=17,604), semaglutide demonstrated a 20% reduction in major adverse cardiovascular events (MACE) in people with overweight/obesity and established CVD without diabetes. Results also showed reductions in all-cause mortality and a slowed progression to diabetes. SUSTAIN-6 (n=3,297), meanwhile, showed significant reduction of MACE in people with T2D, supporting semaglutide's cardioprotective benefits and long-term safety.
- **Liraglutide (Novo Nordisk's Saxenda).** LEADER (n=9,340) demonstrated significant reduction in primary MACE composite scores, with contributions from CV death, non-fatal MI, and non-fatal stroke in adults with T2D.

Collectively, these CVOTs offer evidence of tirzepatide, semaglutide, and liraglutide's cardiovascular and metabolic benefits, supporting their use in chronic treatment while also illustrating the need for additional evidence in conjunction with intensive behavioral therapies.

Global barriers to implementation include affordability and availability

The WHO projected that current manufacturing capacity could supply GLP-1 RAs to only ~100 million people, less than 10% of the people currently living with obesity – the WHO's own guidelines cite 890 million people are overweight, with about 10% who have obesity. The organization identified three foundational requirements for effective implementation of these guidelines:

- **Improving affordability and availability.** Strategies include voluntary licensing, tiered pricing, pooled procurement, and generic production as semaglutide patents expire in some countries (Canada) beginning in 2026. Semaglutide will be losing core patents in several additional countries next year, including a patent regarding specific formulations and delivery devices in India (March 2026) and several patents in Brazil and China.
- **Adequately preparing health systems.** Countries must strengthen primary care infrastructure, provider training, patient engagement, supply chains, and monitoring capabilities to support obesity care.
- **Ensuring person-centered universal access.** The WHO stressed that clinicians prescribing GLP-1 RAs must uphold patient autonomy and employ shared decision-making, particularly to help mitigate the discrimination patients may face in other areas of their metabolic care.

The WHO's next phase of GLP-1 RA guidelines for adult obesity care, beginning in early 2026, will focus on defining global criteria for prioritizing treatment eligibility to guide early implementation within these constraints. WHO plans to next define global prioritization criteria and examine long-term safety, cost-effectiveness, and multimodal care models.

Close Concerns' Questions

1. What further evidence does the WHO require to strengthen these guidelines beyond conditional grading?
2. What is the WHO's perspective on GLP-1 RA use in children and adolescents?

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