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What to Know About the WHO's New GLP-1 Drug Guideline

Kate Schweitzer

For more than 30 years, global obesity rates have gone in one discouraging direction. Between 1990 and 2022, the worldwide prevalence of obesity more than doubled. But, in the US, after peaking at a record high of nearly 40% 3 years ago, the obesity rate among adults has changed course. The rate declined to 37%—representing an estimated 7.6 million fewer obese adults—in 2025. The timing of this shift coincides with a notable uptick in the use of glucagon-like peptide-1 (GLP-1) receptor agonists, a class of drugs including semaglutide (Wegovy) and tirzepatide (Zepbound) that were approved for the treatment of obesity in the US market this decade.

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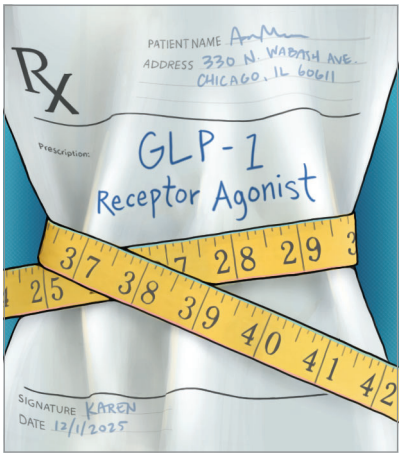
"Obesity is an epidemic that year on year, no country has reversed," said Jennifer Manne-Goehler, MD, ScD, assistant professor of medicine at Brigham and Women's Hospital at Harvard Medical School. "Nobody has managed to reverse it—not by eating less and moving more, not by sugary beverages taxes….But now there's this transformative tool that has the potential to mute that endless rise, and we now have to learn how to use it to bend that curve."

To harness that potential, the World Health Organization (WHO) has issued its first guideline on the use of GLP-1 drugs and glucose-dependent insulinotropic polypeptides (GIP)/GLP-1 dual agonists to treat obesity.

According to Francesca Celletti, MD, PhD, senior advisor of obesity within the WHO's department of nutrition and food safety, this marks a "groundbreaking" shift in the way the agency has historically framed obesity treatment. Previously citing lifestyle changes—namely diet and exercise—as the hallmark recourse for an illness that affects more than 1 billion people globally, the WHO now endorses, conditionally, the use of GLP-1 drugs.

"GLP-1s are the first efficacious [medication] for obesity and for a population that has been neglected by society and by the health system," said Celletti, who led the development of the guidance, which took 15 months to complete and covered issues of implementation, feasibility, and scale. "The fact that we have new science to address the neglected needs and to reboot the system is an amazing opportunity for the world that we shouldn't miss."



Here are some of the key learnings from the new WHO guideline:

Obesity Is Framed as a Chronic, Relapsing Disease

The guidance recognizes obesity as a "complex, relapsing, chronic disease" that requires ongoing, lifelong care.

It officially puts obesity in the same category as conditions such as hypertension and diabetes that relapse with medication discontinuation, explained Louis J. Aronne, MD, an obesity medicine specialist and professor of metabolic research at Weill Cornell Medical College, who was not involved with the new publication.

"For us, it's a quite consolidated notion, but still many countries in the world do not recognize obesity as a disease, never mind a complex one," Celletti said. "It's driven by such diverse root causes that encompass genetics, behavioral, biological, metabolic, the social environment, you name it."

The hope in articulating this within the guidance is that it may continue to temper the stigma surrounding obesity and its care within the health system.

"Somehow it's OK for someone to be told their blood pressure is 5 points too high but for whatever reason, if you're 10 lbs [4.5 kg] overweight, it's seen as your fault," Manne-Goehler, who served as a content expert advisor for the WHO guidance, said. "I actually credit GLP-1s with helping flip the script," she added.

The WHO's designation, Celletti said, stands to increase engagement among both patients and clinicians. "This includes more early diagnosis, assessment of comorbidities, and implementation of a set of interventions that include behavioral changes, pharmacotherapy, or surgery," she noted.

The Recommendations Are Conditional

The new guidance contains 2 key conditional recommendations: GLP-1 therapies may be used by adults, excluding pregnant women, for long-term obesity treatment and "intensive behavioral interventions" may be offered to those prescribed GLP-1 medications.

The guidance states that the efficacy of GLP-1 drugs is evident not only in treating obesity but in improving metabolic health outcomes. Still, long-term data are limited and some instances of low-certainty evidence exist.

"There is an evidence gap," said Celletti, who coauthored a Special Communication in *JAMA* about the guidance. "First of all, we don't know if this is a lifelong therapy. The long-term use and safety of the medicine are not actually known."

She referenced rare adverse events, such as gastrointestinal issues—nausea, vomiting, and diarrhea—and potential risks of acute pancreatitis or nonarteritic anterior ischemic optic neuropathy.

"If hundreds of millions of people are receiving this medicine in the next 10 years, even the most rare of adverse effects can become a considerable absolute number," she said. "The current safety data is very inconclusive. We need many more studies."

The conditional recommendation was also put in place to account for health systems that may not be ready to implement necessary changes just yet. Time is needed to adapt for chronic, integrated care, Celletti added.

Additionally, the guideline is considered "living," in that it will be continuously updated and expanded following the emergence of new real-world data or discoveries. Such updates could include the safety, feasibility, and effectiveness of oral GLP-1 drugs, such as the newly approved once-daily Wegovy pill.

GLP-1 Medications Aren't a "Magic Bullet"

The guidance positions the drugs not as a standalone fix but as part of a comprehensive treatment strategy that combines pharmacology, behavioral support focused on a healthy diet and physical activity, and long-term follow-up.

In other words, GLP-1 drugs "aren't a magic bullet," Manne-Goehler said.

Aronne echoed this: "While these therapies represent a breakthrough in obesity treatment, medicine alone will not solve the problem."

The guidance suggests a "multimodal clinical algorithm" involving GLP-1 drugs and intensive behavioral therapy, which entails goal-setting on physical activity and diet, restriction of energy intake, and counseling sessions. Research has indicated that GLP-1 drugs may be more effective when combined with select lifestyle modifications. However, the WHO did not recommend some cointerventions that have been found to have little to no effect, including meal replacement and lead-in phases with lifestyle changes.

"Structured intervention and continuous monitoring are useful in addressing obesity, but they also amplify the effectiveness of the medicine, which should not be used in isolation," Celletti said. "They must be used in association with the therapy that aims to change unhealthy behavior."

Still, Aronne, who directs the Comprehensive Weight Control Center at Weill Cornell, said such a strategy is "very difficult" to implement considering "we lack systems to easily address behavior and lifestyle in primary care." His obesity treatment center, which he calls an outlier, dedicates registered dietitians and pharmacy liaisons to support patients, all in addition to medical staff.

Equitable Access Is Critical to Curb Obesity Worldwide

The need for global guidance on GLP-1 drugs may seem incongruous with their limited global uptake so far.

"Their use is really limited to just a few countries, including the US," Manne-Goehler said, and even then, less than 5% of those individuals in the US with an obesity diagnosis used a GLP-1 drug in 2024, according to one source.

"Ensuring equitable access and strengthening health systems will be essential to prevent widening health disparities," Aronne said.

The guidance discussed the importance of affordability through both policy levers and market forces. In November, Novo Nordisk, which manufactures GLP-1 drugs Wegovy and Ozempic, cut self-pay prices from $499 to $349 per month.

It's not just price that creates a barrier to equitable access. Supply shortages have hindered GLP-1 use in the past, and "production capacity is still very limited," Celletti said. "Even in the highest projected scenario with our current capacity, we will only be able to cover less than 10% of the people that currently meet the need." The guidance cites pooled procurement, local production, and compulsory licensing as strategies to boost the supply of GLP-1 drugs.

Distribution concerns, particularly in regions where cold chain or injection delivery pose challenges, may soon be solved with the production of more oral formulations, Aronne said.

But ensuring the drugs are affordable and available aren't enough if health systems don't offer them.

"The whole health system has to be strengthened to be able to offer sustainable, quality care and universal access to that care, which comes to the medicine being free at the point of delivery," Celletti said. This, Manne-Goehler said, will require a public health transformation considering "most doctors have approached obesity as 'it's hopeless, good luck.'" For his part, Aronne believes that the WHO guidance will encourage both insurers and employers to "cover both the medications and the behavioral support."

The WHO emphasized that without deliberate policies, GLP-1 drug access may remain limited—projected to reach less than 10% of eligible people by 2030—and could exacerbate health inequities.

Long-Term Sustainability Must Be Considered

A critical area of consideration within the guidance surrounds the long-term, or possibly lifetime, sustainability of GLP-1 drugs. Although more than half of individuals who initiate the medication may discontinue it within a year, the WHO notes that terminating treatment often leads to weight regain.

The extent to which individuals stop taking GLP-1 drugs may align with access issues such as price toxicity, Manne-Goehler said, but other questions about sustained use remain.

"It's not clear that the medications will work for everyone forever, so how do we mitigate any negative health impacts of starting and stopping?" said Manne-Goehler, who coauthored a Viewpoint about the pathways to sustainable obesity care.

She noted that some individuals may be amenable to maintenance dosing—prescribing lower or less frequent doses of a GLP-1 drug until achieving a regimen that allows for weight maintenance—and that some studies show that exercise in tandem with GLP-1 drug use leads to more sustained weight loss after stopping medication.

"Obesity is a lifelong condition that needs lifelong care, but it's not clear to me that every person with every form of obesity needs lifelong GLP-1 therapy," she said.

The Drugs' Potential Is Still Untapped

The WHO guidance is a first step, Manne-Goehler said. "There's still a ton to be learned about the impact of the medicines on a number of potential obesity-related complications that are relevant, and they're not even addressed in the guidance because they are still emerging," she added, citing the promise GLP-1 drugs offer in treating metabolic dysfunction–associated steatotic liver disease, for example.

Aronne also predicted that it "will become clearer" in the coming years that treating obesity "can treat the majority of metabolic disease and then some." One trial, for example, found that treatment with a GLP-1 drug over nearly 4 years reduced progression from prediabetes to diabetes by 94%. "Think about what that means: fewer heart attacks, strokes, kidney failure, dialysis, amputations." He added that "it also reduces sleep apnea, osteoarthritis pain, and immobility. Why would a public health department not prevent diabetes if they can?"

The WHO guidance seeks to reorient current approaches toward a 3-pronged practice: creating healthier environments that prevent obesity, protecting individuals at high risk of developing obesity, and ensuring access to lifelong care for those with obesity.

"This isn't an individual problem to solve but a societal one," Celletti said, adding that the next 5 years will be "our window of opportunity to do something tangible to bend the curve down."

Manne-Goehler envisions a very different GLP-1 drug landscape by 2030: "If we can get it to who needs it the most for a price that is getable with a system around it that's sensical and rational, it will be so transformative for so many of the highest-burden, highest-cost health issues that we face as a human population." ■

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Conflict of Interest Disclosures: Dr Manne-Goehler reported serving as a consultant to the WHO Department of Nutrition and Food Safety and the WHO Department of Non-Communicable Diseases, receiving a K23 Career Development Award from the National Institutes of Health and National Institute of Diabetes and Digestive and Kidney Diseases, and serving as a lecturer for Academic Medical Education/Virology Education. Dr Aronne reported receiving consulting fees from and serving on advisory boards for Altimmune, Amgen, Atria, Boehringer Ingelheim, Carmot Therapeutics/Roche, CinFina Pharma, Corteria, Currax Pharma, Eli Lilly, Enterin, Helicore Biopharma, Jamieson Wellness, Juvena Therapeutics, Kallyope, MBX Bioscience, Morphic Medic/GI Dynamics, Novartis, Novo Nordisk, Pfizer, Prosciento, Senda Biosciences, Skye Bio/Cbeyond, Summit Clinical, Syntis Bio, Verdiva, Veru Pharmaceuticals, and Zealand Pharmaceuticals; receiving research funding from Eli Lilly, Novo Nordisk, Skye Bioscience, and Viking Therapeutics; having equity interests in ClicBio, ERX Pharmaceuticals, Flyte Health, Jamieson Wellness, Juvena Therapeutics, Kallyope, MBX Bioscience, Mediflix, Skye Bio/Cbeyond, Syntis Bio, Verdiva, and Veru Pharmaceuticals; and serving on the board of directors for ERX Pharmaceuticals, Flyte Health, and Jamieson Wellness. No other disclosures were reported.

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