WeightWatchers for Business

A new frontier in weight health:

Why GLP-1 medications are game-changers for weight loss and overall health

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We've all seen the headlines, TV commercials, and social media posts. GLP-1 medications are producing exciting health results for people living with obesity, including significant weight loss, diabetes management, and reduced cardiovascular risks.

Doctors and scientists are calling glucagon-like peptide-1 (GLP-1) receptor agonists game-changers for weight health. The term is justified. In clinical trials, **patients taking GLP-1 medications achieved up to 20% weight loss**, making them nearly twice as effective as other weight-loss medications.

Not surprisingly, headline-worthy results like these spark a lot of questions.

- What's different about how GLP-1s work?
- What are the potential implications for employee health?
- What's coming next in the developing treatment of overweight and obesity?

In this report, WeightWatchers medical adviser Dr. Robert Kushner goes behind the headlines to answer these questions — and more.

Robert Kushner, M.D., has a long, distinguished career as one of the most highly respected weight health experts in the world. He is the Medical Director of the Center for Lifestyle Medicine at Northwestern University in Chicago and Professor of Medicine and Medical Education at Northwestern University's Feinberg School of Medicine.

Kushner is the past president of The Obesity Society and a founder of the American Board of Obesity Medicine, which certifies physicians in the care of patients with obesity.

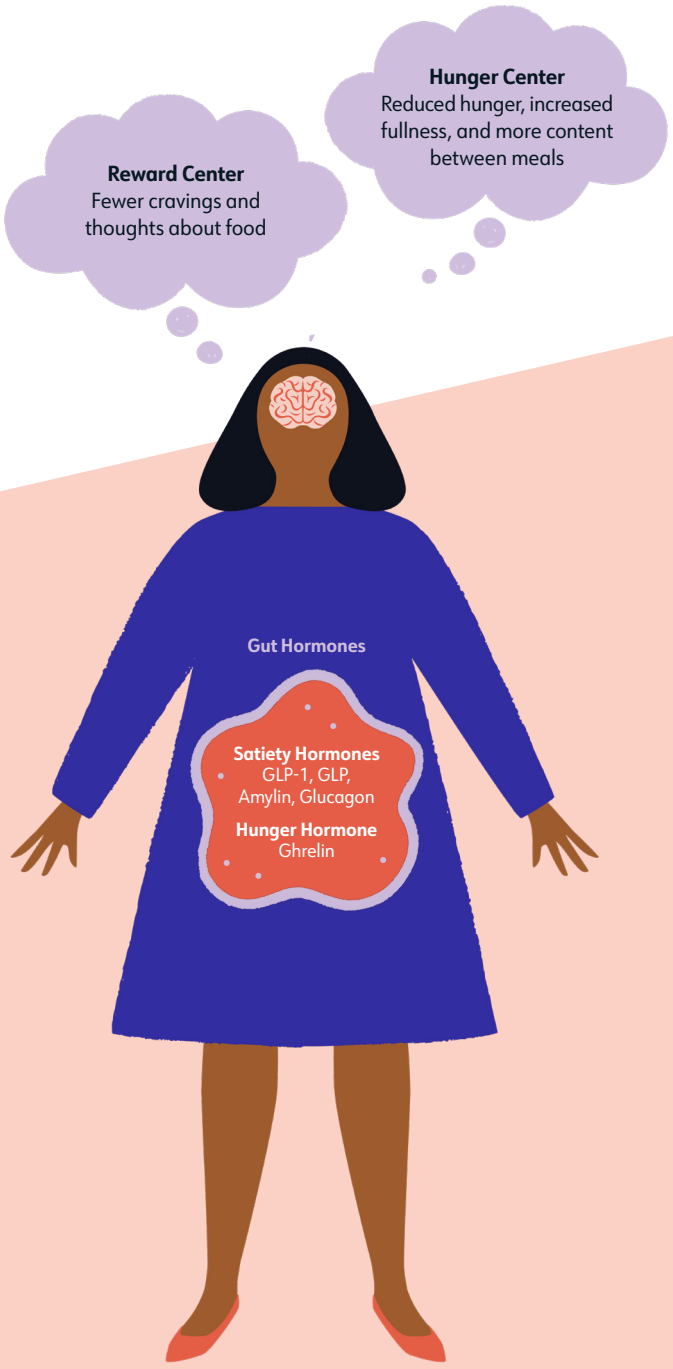
Dr. Kushner has played an integral role in the clinical research of GLP-1s, including the STEP (Semaglutide Treatment Effect in People with obesity) trial series. He has been a medical adviser for WeightWatchers since 2015.

What's different about how GLP-1s work?

For all the excitement about GLP-1 medications, they don't cause weight loss by themselves. Instead, the medications change how the brain interprets various hunger and satiety signals received, affecting a person's decisions about when and what to eat.

Here's a high-level view of how the medications work. As we ingest food, it goes through the gastrointestinal tract, ultimately releasing hormones generated from the pancreas and small intestine. These gut hormones fall into two categories:

- Hunger hormones that tell us we need to eat and
- Satiety hormones released after we eat to deliver feelings of fullness and contentment between meals.



Research has identified GLP-1 as one of the key gut hormones for weight health. To create the GLP-1 medications, the hormone is synthesized and provided to people living with obesity to address three primary purposes.

/ 01 **Impact the appetite dysregulation of the disease** (Appetite dysregulation is when a person never feels full or always feels hungry)

/ 02 **Support lifestyle interventions** by helping patients adhere to a lower-calorie diet and change their relationship with food

/ 03 **Facilitate weight loss** and improvement in health

In other words, the GLP-1 medications help quiet the mind by reducing appetite, cravings, and thoughts about food that can make it difficult for people living with obesity to make sustainable lifestyle changes that lead to weight loss. The medications work in concert with healthy eating, reduced calorie intake, and increased physical activity to address the biologic determinants of chronic obesity.

What are the potential implications for employee health?

GLP-1 medications represent a true paradigm shift in the treatment of obesity. Previously, doctors could prescribe medications that work to change the transmission of neurotransmitters within the brain, primarily targeting appetite reduction. Now, the ability to target gut hormones provides the option to treat obesity hormonally, similar to how insulin is used to treat diabetes.

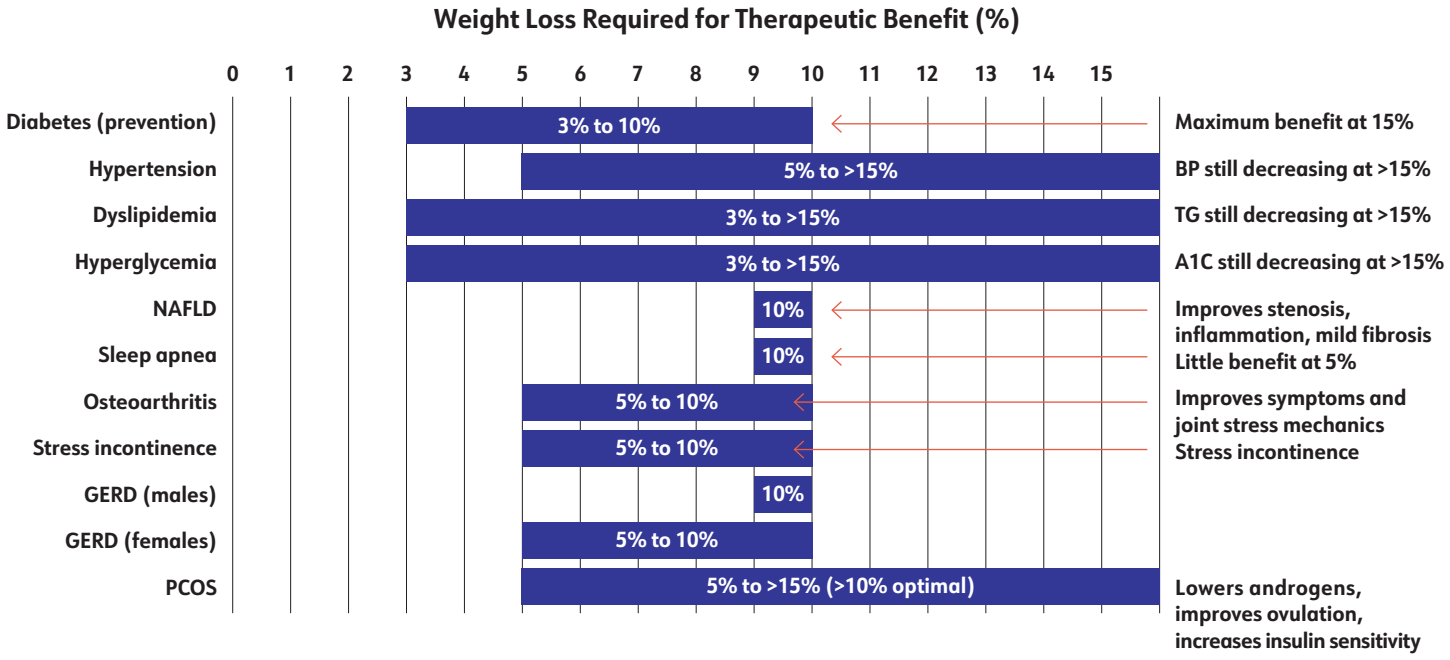
Two medications that mimic the actions of the GLP-1 gut hormone are behind the recent headlines—liraglutide (trade name Saxenda) and semaglutide (trade name Wegovy). Both drugs were originally approved in lower dosages for the treatment of diabetes, giving us greater insights into their effectiveness and proven safety.

The "first-generation" GLP-1 medication, Saxenda, produced 8% weight loss, on average. With the release of second-generation medications such as semaglutide, clinical trials produced 15% weight loss. Next up is tirzepatide (trade name Mounjaro), which is currently approved for the treatment of diabetes and has been fast-tracked for approval by the FDA for the treatment of obesity. Tirzepatide is a dual-agonist medication, meaning it brings together two gut hormones—GLP-1 and GIP. In clinical trials, tirzepatide is delivering weight-loss amounts of 21%, on average.

Losing even a small amount of weight has a positive impact on overall health and helps to reduce the medical complications that can occur for individuals living with obesity. A 3% to 5% weight loss improves high blood pressure, dyslipidemia (an imbalance of triglycerides and HDL cholesterol), hyperglycemia (elevated A1c), and osteoarthritis. When people achieve more weight loss, they can see positive impacts on other medical conditions, such as non-alcoholic fatty liver disease (NAFLD), sleep apnea, stress incontinence, gastroesophageal reflux disease (GERD), and polycystic ovary syndrome (PCOS).

> *Weight loss is beneficial for health and quality of life. From a medical point of view, individuals see significant improvements with greater weight loss.*
>
> **Dr. Robert Kushner**

As patients lose more weight, we see continued improvements across various chronic conditions. To date, a 10% weight loss has been the expectation of what a medication could help a patient living with obesity achieve. Now, GLP-1 medications are making greater percentage amounts – and greater health benefits – possible.



FDA-Approved Medication	Trade Name(s)	Mechanism of Action	Effect	Approval Date
Phentermine	Phentermine	Modified amphetamine	Appetite regulation	1959
Orlistat	Xenical, Alli	Blocks GI enzymes that absorb fat	Reduces fat absorption	1999
Phentermine/ Topiramate ER	Qsymia	Modified amphetamine	Appetite regulation	2012
Naltrexone/ Bupropion SR	Contrave	Opioid receptor blocker Increases dopamine/ noradrenaline in the brain	Appetite regulation	2014
Liraglutide	Saxenda Victoza (lower dose) approved for diabetes in 2010	Mimics action of GLP-1 gut hormone	Appetite regulation	2014
Setmelanotide	IMCIVREE	Activates specific neuro pathway (indication: obesity due to rare monogenetic forms of obesity)	Appetite regulation	2020
Semaglutide	Wegovy Ozempic (lower dose) approved for diabetes in 2017	Mimics action of GLP-1 gut hormone	Appetite regulation	2021

GLP-1s expand the toolbox for treating obesity

Understanding the impact — and potential — of GLP-1 medications

The clinical trials related to GLP-1 medications provide enhanced guidance to better understand and treat obesity as a disease. For example, wide-ranging clinical trials have been conducted to assess and understand the impact of semaglutide on weight loss and overall health. The semaglutide treatment effect in people with obesity (STEP) series of trials offers insights on average weight loss, long-term weight maintenance, the effects of lifestyle and behavioral counseling, and cardiovascular implications.

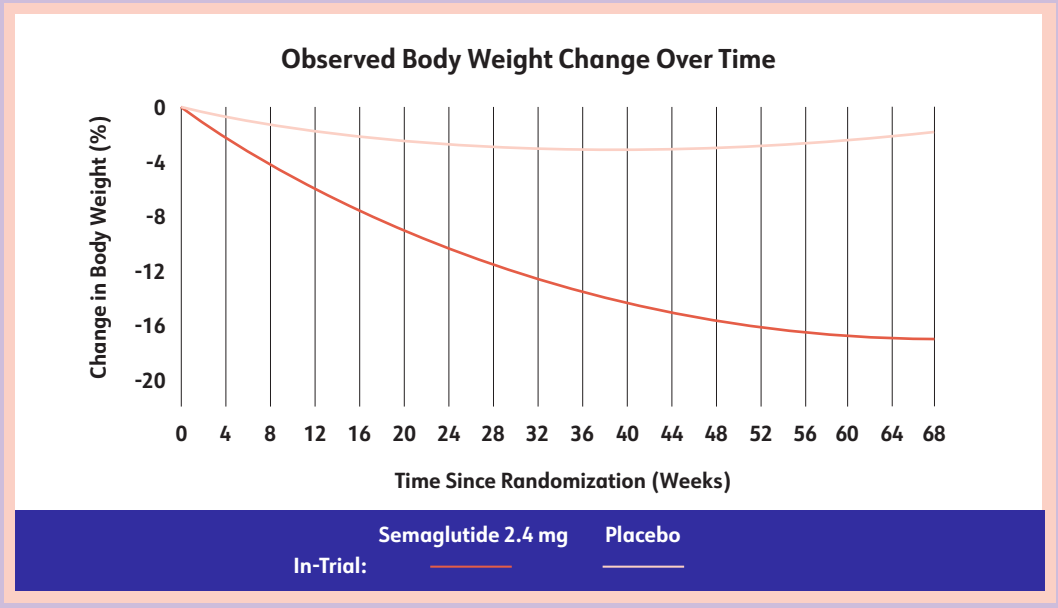
What we've learned from the clinical trials involving semaglutide

STEP Trial 1

The STEP Trial 1 examined the body weight change for people taking semaglutide.

Trial participants taking semaglutide medication lost significantly more weight over 68 weeks than patients receiving a placebo medication.

- Average weight loss: **16.9%**
- 1/3 of patients taking semaglutide saw **20%+ weight loss**
- Weight loss leveled off at around **64 weeks**



Insight:

Semaglutide produces significant weight loss for people living with obesity.

STEP Trial 5

The STEP Trial 5 tracked long-term weight management for people taking semaglutide.

Participants taking semaglutide reached their lowest weight at around 64 weeks and maintained their weight loss through 104 weeks.

Insight:

The weight loss is sustainable while continuing to take the medication.

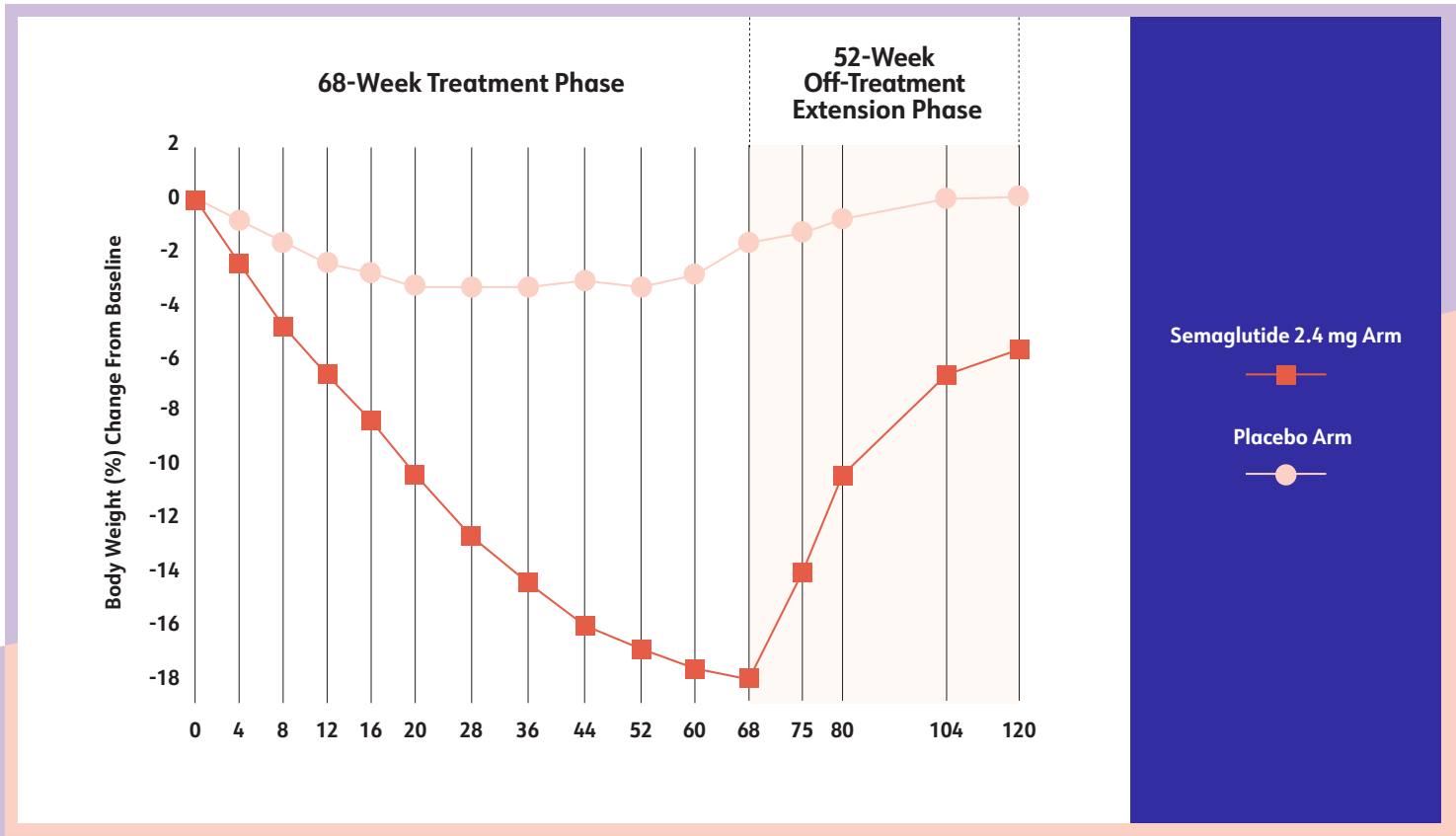
STEP Trial 1 Extension

A STEP Trial 1 Extensionl looked at what happens when patients stop taking the medication.

Patients who stopped taking semaglutide regained 2/3 of their body weight loss within a year.

Insight:

Patients regained weight when they stopped taking the medication, reinforcing that obesity is a chronic, relapsing condition.



STEP Trial 3

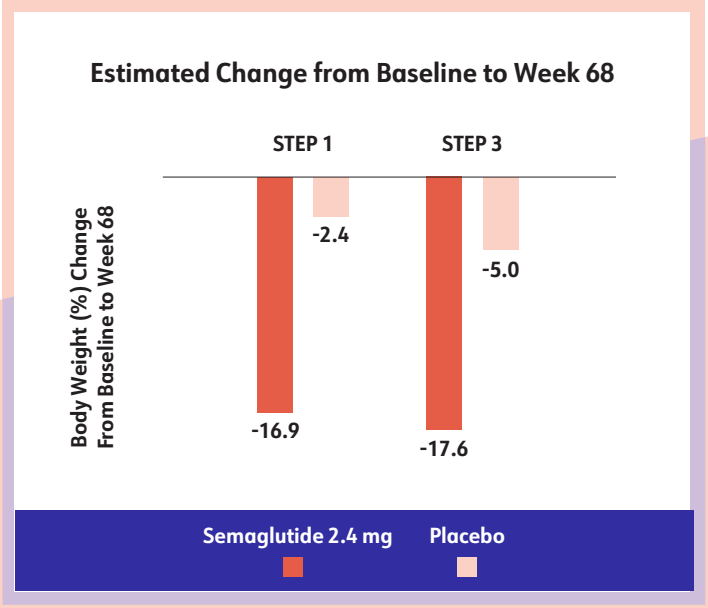
The STEP Trial 3 explored the impact of pairing the medication with intensive lifestyle counseling.

Along with receiving semaglutide or a placebo medication, participants followed a low-calorie diet, increased physical activity, and received behavioral counseling, including instruction on diet, physical activity, and behavioral strategies.

The lifestyle counseling accelerated initial weight loss for participants taking semaglutide or the placebo. At the end of the 68-week trial, overall weight loss was about 1% more for patients taking semaglutide compared to STEP Trial 1. Those taking the placebo saw a slightly greater weight loss than in STEP Trial 1.

Insight:

Lifestyle and behavioral counseling accelerate the impact of the medications.



Across the series of STEP Trials

Insight:

Semaglutide has a positive impact on overall health.

Improvement in Cardiovascular Risk Factors	Decreased Need for Medications	Improved Quality of Life
Reduced: • Blood pressure • Glucose • Triglycerides • Total cholesterol • LDL cholesterol **Increase in HDL cholesterol** **Decreased inflammatory biomarker CRP (released during tumor growth)**	**Decrease in medications:** • Anti-hypertensive • Lipid-lowering • Glucose-lowering	**Improved physical functioning** **Improved psychometric evaluation of quality of life** • Anti-hypertensive • Lipid-lowering • Glucose-lowering

SELECT Trial

The latest trial – the SELECT trial – examined semaglutide's effects on cardiovascular outcomes.

Patients living with overweight or obesity and prior cardiovascular disease were given semaglutide or a placebo over a three-year period.

Initial results show that major adverse cardiovascular events were reduced by 20% among patients taking semaglutide.

Insight:

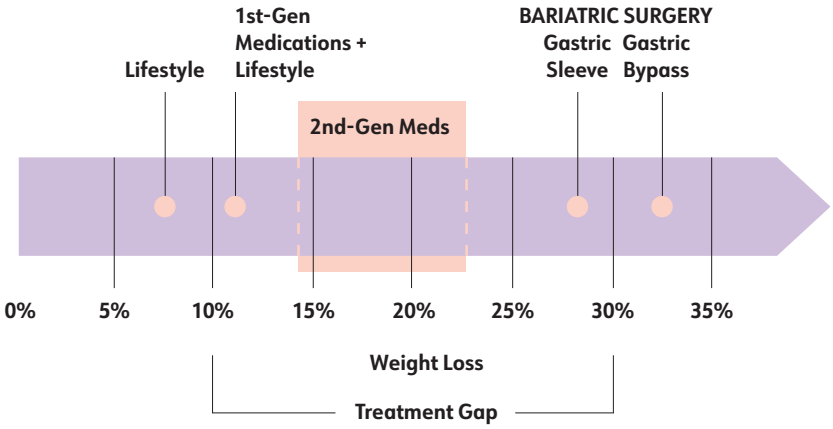
Semaglutide significantly reduces cardiovascular risk.

What's coming next in the developing treatment of overweight and obesity?

As hormone-based medications expand the toolbox for treating obesity, the research is shining a light on the biological nature of obesity as a chronic disease. It's not an overstatement to say that weight health — and our understanding of it — is at an inflection point.

The medications are continuing to advance, with exciting new options on the horizon. Semaglutide is a mono-agonist medication targeting the GLP-1 gut hormone. The medications in development are dual- and tri-agonists, targeting two and three gut hormones together for better results. At the same time, oral versions of the medications are in development, which will make them more accessible compared to the current weekly self-administered shots.

Within the spectrum of treatment options for patients with obesity, hormone-based medications are filling the gap between traditional obesity medications and surgical solutions.



While the medications are truly game-changers for weight health, they don't guarantee that people will follow a healthy diet and lifestyle. Looking ahead, it will be vital to further understand and optimize complementary behavioral and lifestyle therapies to help individuals effectively translate the biologic impact of the hormone-based medications into a healthy diet, increased activity, and sustainable weight loss.

The facts about GLP-1 medications

Hormone-based medications:

- Are approved for treating obesity, making them available for patients with a BMI of 30 or higher or a BMI of 27 or higher and at least one weight-related health condition, such as type 2 diabetes
- Must be prescribed and closely monitored by medical professionals
- Are more biologically effective in controlling appetite
- Produce greater weight loss
- Have positive impacts on overall health, including symptoms of diabetes, hypertension, and cardiovascular disease

Learn more about WeightWatchers for Business

For 60 years, WeightWatchers has been a leader in the evolving science behind weight health. Today, WeightWatchers for Business is a full-spectrum weight-health platform providing individualized pathways and experiences based on true clinical need for millions of members.

Our platform is built upon the most science-proven weight management behavioral program—and includes the following:

- Intensive, individualized behavioral programs (condition- and medication-specific)
- Virtual clinic and medication management
- Scalable coaching and communities
- Integrated personal health insights

Our goal as your organization's weight health care partner is to responsibly maximize cost control while improving the long-term health of your people.

Explore how WeightWatchers for Business can help your organization deliver personalized support and science-proven results while helping to control costs.

Learn more at ww.com/forbusiness

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