



# The Muscle Problem Nobody Talks About

And Five Evidence-Based Ways to Solve It

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Evidence-based | Provider-reviewed | No BS

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# The Number That Started the Panic

You have probably seen the headlines. "GLP-1 drugs are eating your muscle." "Ozempic face is destroying your body." "The hidden danger of weight loss drugs."

Some of that is real. Most of it is missing context. Here is what the science actually says — and what you can do about it right now, whether you are on semaglutide, tirzepatide, or considering treatment.

**25–40%**

of total weight lost may be lean mass

*STEP 1 and SURMOUNT-1 clinical trial data*

When you lose weight — through **any** method — you lose a combination of fat and lean mass. Lean mass includes muscle, but also organs, bone, fluids, and water stored in fat tissue. This is not unique to GLP-1 medications. It happens with dieting. It happens after bariatric surgery. It happens any time your body is in a sustained caloric deficit.

A UC Davis research team found that much of the reported 40% lean mass loss with GLP-1 use comes from the liver — not from skeletal muscle. When your liver shrinks because it is no longer storing excess fat, that registers as lean mass loss on a DEXA scan. Your biceps did not disappear. Your liver got healthier.

A 2024 network meta-analysis across 22 randomized controlled trials confirmed that GLP-1 medications reduced lean mass by approximately 25% of total weight lost — but critically, the **percentage of lean mass relative to total body weight remained unchanged**. In plain English: your body composition ratio stays similar or improves because you are losing proportionally more fat.

# Why This Matters More Than Headlines Suggest

The real concern is not lean mass loss in general. It is **skeletal muscle loss specifically** — the muscle that moves your body, supports your joints, maintains your metabolic rate, and protects you as you age. Here, the picture is more nuanced than the panic suggests.

## Adaptive Response

A 2025 Circulation review found muscle changes during GLP-1 treatment are likely adaptive — a normal physiological response to carrying less weight. When you lose 50-70 lbs, your body naturally recalibrates.

## Insulin Sensitivity Improves

GLP-1 medications improve insulin sensitivity, and insulin plays a key role in muscle protein synthesis. Treatment may improve the quality of muscle you retain, even if total volume decreases slightly.

*The question is not whether to worry about muscle loss — it is what to do about it. Muscle matters enormously for long-term health, metabolic rate, mobility, and aging. The five strategies in this guide are your evidence-based action plan.*

# The Glucagon Advantage: Why Retatrutide May Change This

Current GLP-1 medications work primarily by reducing appetite. You eat less, your body enters a caloric deficit, and you lose weight. The caloric deficit is what drives muscle loss — not the drugs themselves.

Retatrutide introduces a third mechanism that current medications lack: **glucagon receptor activation**. This promotes preferential fat burning over lean mass loss and increases energy expenditure — meaning your body burns more calories at rest.

## Fat Mobilization

Glucagon mobilizes fat stores for fuel rather than breaking down muscle

## Preferential Fat Burning

Weight loss shifts toward fat mass with less impact on lean mass

## Increased Metabolic Rate

Energy expenditure increases — you burn more calories at rest

## Muscle Preservation

Phase 2 data: 24.2% weight loss primarily from fat mass reduction

# Five Strategies You Can Start Today

Whether you are on semaglutide, tirzepatide, or any weight loss program, these five strategies are supported by current evidence and recommended by the medical community. They are listed in order of impact.

1

## Prioritize Protein — and Hit Your Number

This is the single most important thing you can do to preserve muscle during weight loss. Current evidence supports 1.2 to 2.0 grams of protein per kilogram of body weight per day. For a 200-pound person, that translates to roughly 110 to 180 grams of protein daily. Aim for 30 to 40 grams at each meal. Prioritize complete protein sources — eggs, poultry, fish, dairy, legumes. A Mass General Brigham review found that combining a high-protein diet with consistent exercise had the greatest benefit in preserving bone and muscle mass.

**110–180g**

daily protein target for a 200 lb person

1.2–2.0 g/kg body weight during active weight loss

2

## Resistance Train 2 to 4 Times Per Week

This is non-negotiable. Resistance training is the most powerful signal you can send your body to preserve muscle during weight loss. It tells your muscles: you are still needed. Focus on compound movements — squats, deadlifts, rows, presses, lunges — that recruit the most muscle fiber. Two to four sessions of 30 to 45 minutes is sufficient. The key is consistency over intensity. Progressive overload keeps the preservation signal strong.

# Five Strategies (continued)

**3**

## Do Not Undereat

This seems counterintuitive during weight loss, but it is critically important. GLP-1 medications can suppress appetite so effectively that some patients eat dangerously little — sometimes under 800 calories per day. At that level of restriction, your body will break down muscle for energy regardless of protein intake or training. Work with your provider to ensure your caloric intake stays in a moderate deficit range. Extreme restriction does not accelerate results — it accelerates muscle loss.

**4**

## Monitor Body Composition, Not Just Weight

The scale tells you one number. It cannot tell you whether you lost five pounds of fat or five pounds of muscle. Options range from simple to clinical: waist-to-hip ratio measurements at home, bioelectrical impedance scales (available for under \$50), and DEXA scans for the most accurate picture. The goal is not a specific weight — the goal is losing fat while retaining muscle. Those are different objectives requiring different measurements.

**5**

## Consider Creatine

Creatine monohydrate is one of the most studied supplements in sports science, with decades of safety data. It supports muscle energy production, may improve strength output during resistance training, and has emerging evidence for cognitive benefits. For patients on GLP-1 medications who are actively resistance training, creatine supplementation (3 to 5 grams daily) may provide additional muscle preservation support. It is inexpensive, widely available, and has no known interactions with GLP-1 medications.

*Creatine is not a magic bullet. It is a small edge that compounds over time — and it only works if you are already doing the first four strategies.*

# The Bigger Picture: Muscle Is Your Metabolic Engine

Here is why all of this matters beyond aesthetics.

**“Preserving muscle during weight loss is not about looking a certain way. It is about ensuring that the weight you lose stays lost.”**

Muscle is the largest glucose-disposal organ in your body. It is responsible for a significant portion of your resting metabolic rate. It protects your joints, supports your spine, and is the single strongest predictor of physical independence as you age.

## Metabolic Rate

Patients who lose significant muscle have lower metabolic rates afterward, making weight regain more likely

## Long-Term Outcomes

Patients who preserve muscle maintain higher metabolic rates and have better long-term weight maintenance outcomes

This is where the combination of medical treatment and lifestyle intervention produces results that neither can achieve alone. The medication handles appetite and metabolic signaling. You handle the resistance training and protein. Your provider handles the monitoring and dose optimization.

The weight loss medication landscape is evolving fast. Today's medications work. Tomorrow's — like retatrutide — may work even better at preserving the muscle that matters most. But regardless of which medication you use, the five strategies in this guide are your foundation.

# Sources & References

This guide draws on peer-reviewed research, clinical trial data, and expert consensus. Below are the primary sources cited throughout.

## STEP 1 Trial

Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. New England Journal of Medicine. 2021;384(11):989-1002.

## SURMOUNT-1 Trial

Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. New England Journal of Medicine. 2022;387(3):205-216.

## Network Meta-Analysis

Karakasis P, et al. Lean mass changes across 22 randomized controlled trials of GLP-1 receptor agonists. Metabolism. 2025.

## UC Davis Research

UC Davis Health GLP-1 Symposium. Lean mass composition findings: hepatic vs. skeletal muscle contributions to DEXA measurements. 2025.

## Circulation Review

GLP-1 receptor agonists and skeletal muscle: adaptive vs. maladaptive changes during pharmacological weight loss. Circulation. 2024.

## Mass General Brigham

Grand Rounds presentation: Protein intake and exercise interventions for bone and muscle preservation during GLP-1 treatment. 2025.

## Creatine + GLP-1

Tinsley GM, et al. Case series: Creatine monohydrate supplementation combined with resistance training in GLP-1 RA-treated patients. 2025.

## Retatrutide Phase 2

Jastreboff AM, Kaplan LM, Frias JP, et al. Triple-hormone-receptor agonist retatrutide for obesity. New England Journal of Medicine. 2023;389(6):514-526.

*All clinical data referenced in this guide was current as of February 2026. Retatrutide is an investigational medication not yet approved by the FDA. Clinical trial results represent averages; individual outcomes may vary.*



## Ready to Build Your Plan?

Talk to a licensed provider about which weight loss treatment is right for you — and how to protect your muscle mass while you lose fat.

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