Disclosures:

Katayun Irani and all others in control of this CME activity reported no relevant financial relationships that would create a conflict of interest for CME purposes.

Katayun Irani, MD, FACS, Denver Center for weight loss, Rose Medical Center

Treating Obesity:

What we know now

Katayun Irani, MD, FACS, Denver Center for weight loss, Rose Medical Center



Katayun Irani, MD, FACS

Board Certified General and Bariatric Surgeon

Denver Center for Weight Loss and Bariatric Surgery · HCA HealthONE Rose Medical Center
Denver CO
917-499-7889 (c), 303-280-0900 (o)

Medical School

University of Texas Southwestern Medical School (2002)

Surgical Residency

NYU Grossman School of Medicine (2009)

Fellowships

Minimally Invasive & Bariatric Surgery — Good Samaritan Hospital
Tissue Engineering- Massachusetts General Hospital, Harvard Medical School

Professional societies: ASMBS, SAGES, ACS, OMA

Clinical focus: metabolic and bariatric surgery, including primary and revisional weight-loss procedures.

Discussion

01

Science & Hormones

What actually regulates body weight, and why obesity is so difficult to overcome.

02

Why Diets Fail

The physiology that turns caloric restriction into predictable weight regain.

03

Treating Obesity

Medications and Surgical Options

Obesity by the numbers

>40% Obese

of U.S. adults (20+) have obesity, BMI ≥ 30 — over 100 million people

10% Severely Obese

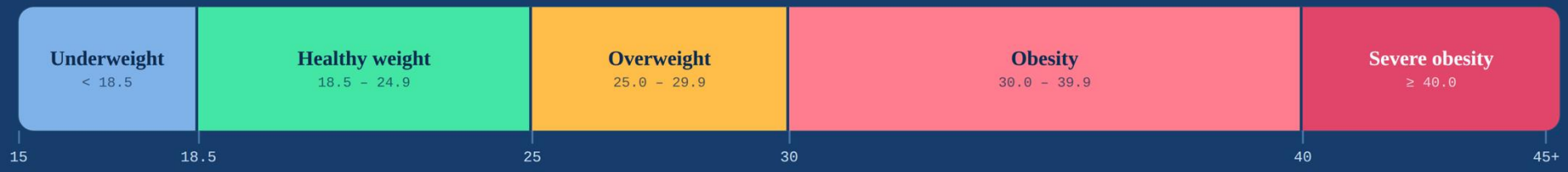
have severe obesity, BMI ≥ 40 — roughly 22 million adults

10% increase

rise in adult obesity prevalence, 1999–2000 to 2017–2020

BMI Classification

Body mass index (kg/m²) and its five clinical weight categories — **obesity begins at BMI 30**.



Class III obesity (BMI ≥ 40) is sometimes called "severe" or "morbid" obesity.

Source: CDC / WHO adult BMI classification.

BMI = weight (kg) / height (m)²

Obesity is a *disease*

energy-balance regulation — not a failure of willpower

More than a dozen hormones and neural circuits actively defend fat mass.

— **Comparative to Hypertension or diabetes**

Self-correcting physiology — not conscious choice alone.
Dysregulation leads to disease

— **Willpower works against active hormonal defense**

Behavior operates inside this biology, not independently of it.

— **Treatment intensity should match disease severity**

Lifestyle, medication, surgery: a continuum of care

The Science & Hormones Behind Obesity

The hunger-satiety circuit, the hormones that run it, and why it stops working normally in obesity.

Your *Gut* Is Running the Show

Gut hormones don't just decide when you're hungry. They quietly set your metabolic rate and your drive to move to hold your body at a particular weight.

Appetite & cravings

What and how much you eat

Metabolic rate

How many calories you burn at rest — turned up or down to defend fat mass.

Drive to move

Desire and need to exercise

Together, these signals defend a weight the body has already chosen

Six signals run this circuit — most turn against the patient

Hormone	*Source*	*Effect on the Hypothalamus*	*In obesity*
Leptin	Adipose tissue	↓ Appetite, ↑ expenditure	High, but resistant
Ghrelin	Stomach	↑ Appetite	Rises further after weight loss
GLP-1	Intestinal L-cells	↓ Appetite, ↑ insulin	Signal blunted
GIP	Intestinal K-cells	Insulin secretion, fat metabolism	Signal blunted
PYY	Intestinal L-cells	↓ Appetite	Lower post-meal rise
Insulin	Pancreatic β-cells	Central satiety + storage	Resistance common

Why Diets Don't Work

The predictable physiology that turns caloric restriction into weight regain — and why that isn't a willpower problem.

Set-Point Theory

The body defends a weight range

-The body resists deviation from a set weight/fat-mass range

-Fear of famine drove human survival — so the body resists losing weight far more than gaining it.

-A 10% weight loss can trigger a **20–25% drop in total energy expenditure**

-Hunger increases, satiety decreases, and cravings increase: Leads to *“failure”*

Results of diet and exercise programs

2% Lose 20% of body weight

1% Maintain the weight loss

-Gut hormones control the hypothalamus

-Weight decreases, triggers set point defense

-Drop in metabolism,

-Hunger and satiety hormonal rebound

-Decrease in drive to move

Success happens when we change the gut hormones

Weight-Loss Medications

What today's pharmacotherapy does well, where it ranks head-to-head, and where its ceiling sits.

Today's pharmacologic options

Drug (brand)	*Class*	*Mechanism*	*Typical weight loss*
Semaglutide (Wegovy)	GLP-1 agonist	Satiety signaling, slows gastric emptying	~15% at 2 yr
Tirzepatide (Zepbound)	GLP-1 / GIP dual agonist	Broader incretin effect	~20% at 1 1/2 years
Oral GLP-1 meds	GLP-1 agonist, daily	Same class, shorter-acting	~5–15% over 1 ½ years
Phentermine–topiramate (Qsymia)	Sympathomimetic + anticonvulsant	Appetite suppression	~8–10%
Naltrexone–bupropion (Contrave)	Opioid antagonist + antidepressant	Reward & appetite pathways	~5–6%
Orlistat (Xenical / Alli)	Lipase inhibitor	Blocks ~30% of dietary fat absorption	~3–5%

Injectable GLP-1 / GIP therapy: dosing & titration

All three are titrated upward slowly to reduce GI side effects. Higher doses than diabetes management

Medication	*Administration*	*Titration schedule*	*Maintenance dose*
Semaglutide (Wegovy)	SC, once weekly, any time of day, with or without food	0.25 mg → 0.5 mg → 1 mg → 1.7 mg • 4 weeks at each step	1.7 mg or 2.4 mg weekly
Tirzepatide (Zepbound)	SC, once weekly, any time of day	2.5 mg → 5 mg → 7.5 mg → 10 mg → 12.5 mg • 4 weeks at each step	Maintenance at 5, 10, or 15 mg
Liraglutide (Saxenda)	SC, once daily, any time of day	0.6 mg → 1.2 mg → 1.8 mg → 2.4 mg • 1 week at each step	3.0 mg daily • Reassess at 16 wk — discontinue if < 4% weight loss

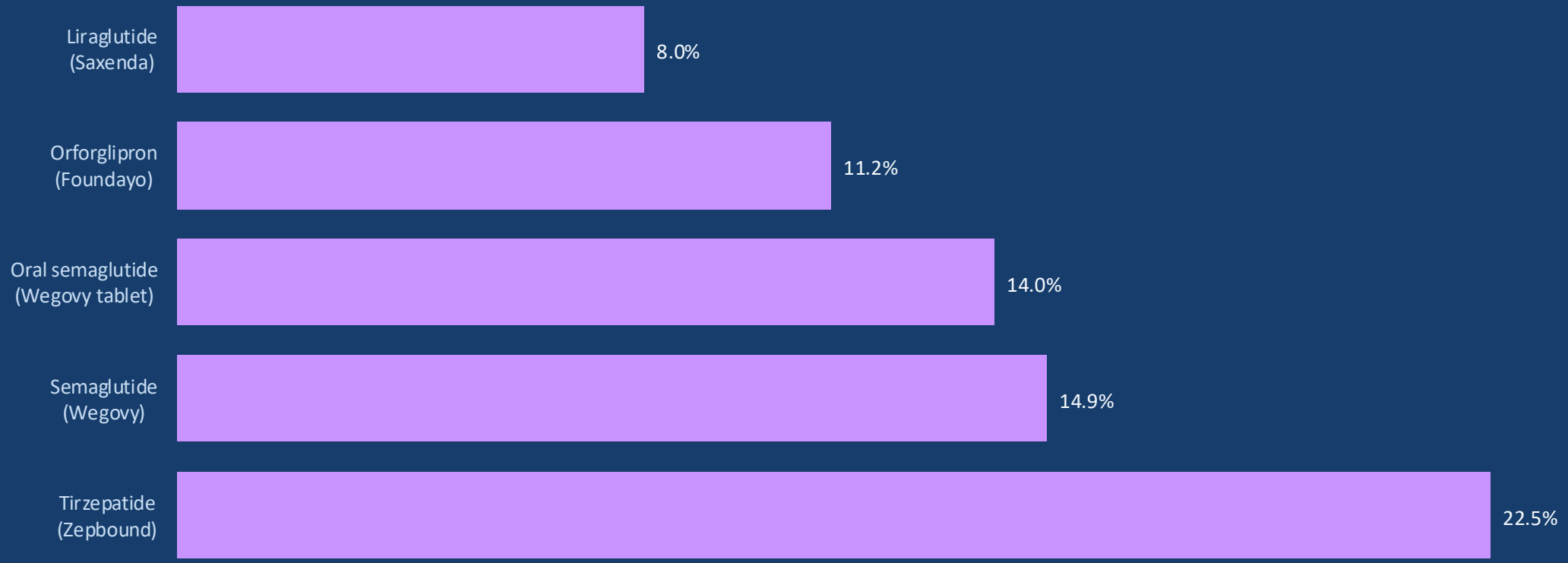
Oral GLP-1 therapy: the newest additions

Two oral options reached the market within the last year — with very different administration rules.

Medication	*Administration*	*Titration schedule*	*Maintenance dose*
Oral semaglutide 25 mg (Wegovy tablet)	Empty stomach, ≤ 4 oz water, in the morning • Wait ≥ 30 min before food, drink, or other oral meds • FDA-approved Dec 2025	1.5 mg → 4 mg → 9 mg • 30 days at each step	25 mg daily • If not tolerated: switch to Wegovy injection 1.7 mg/wk — do not just lower the tablet dose
Orforglipron (Foundayo)	Any time of day • No food or water restriction • FDA-approved April 2026	0.8 mg → 2.5 mg → 5.5 mg • ≥ 30 days at each step	9 mg → 14.5 mg →17.2 mg daily • Titrate up to weight loss goal

Total body weight loss, by medication

Mean % total body weight loss in each drug's pivotal trial — drug arm only, at its highest FDA-approved maintenance dose. Not head-to-head comparisons.



Where pharmacotherapy hits its ceiling

Side effects

Nausea, vomiting, distention, bowel obstruction, headaches
Risk of pancreatitis
Increase in resting heart rate
Thyroid C-cell tumors

Access & cost

Ongoing cost, inconsistent coverage, periodic supply constraints.
Prior authorizations—consider Lilly Direct
Compounding pharmacies (!?)

Durability

Requires indefinite adherence

Weight Regain

— Lifelong Dependence

Stop the drug and the appetite-suppressing effect
Metabolism effects of insulin resistance returns
Hunger signals in hypothalamus return
Rebound of Ghrelin, drop of leptin PPY
Food noise becomes overwhelming

— STEP 1 Trial

n = 327 (228 drug, 99 placebo)

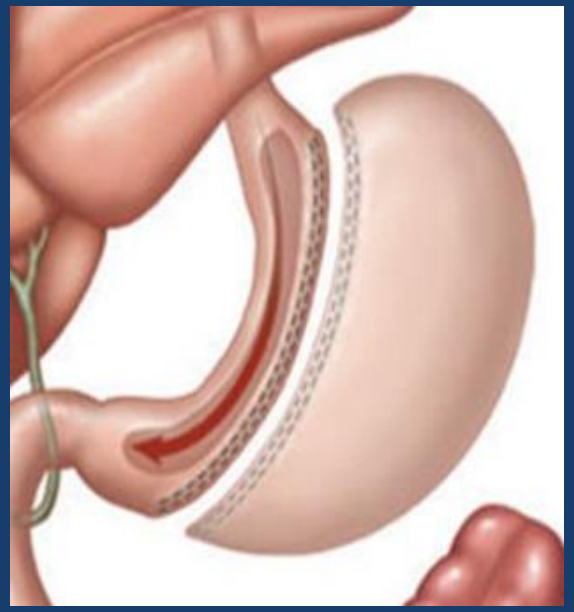
Weight regain of 11.6% TBW
Return of comorbidities

Why Surgery Is Superior

Randomized and real-world evidence on durability, remission, and cost.

What actually changes, anatomically

Sleeve Gastrectomy



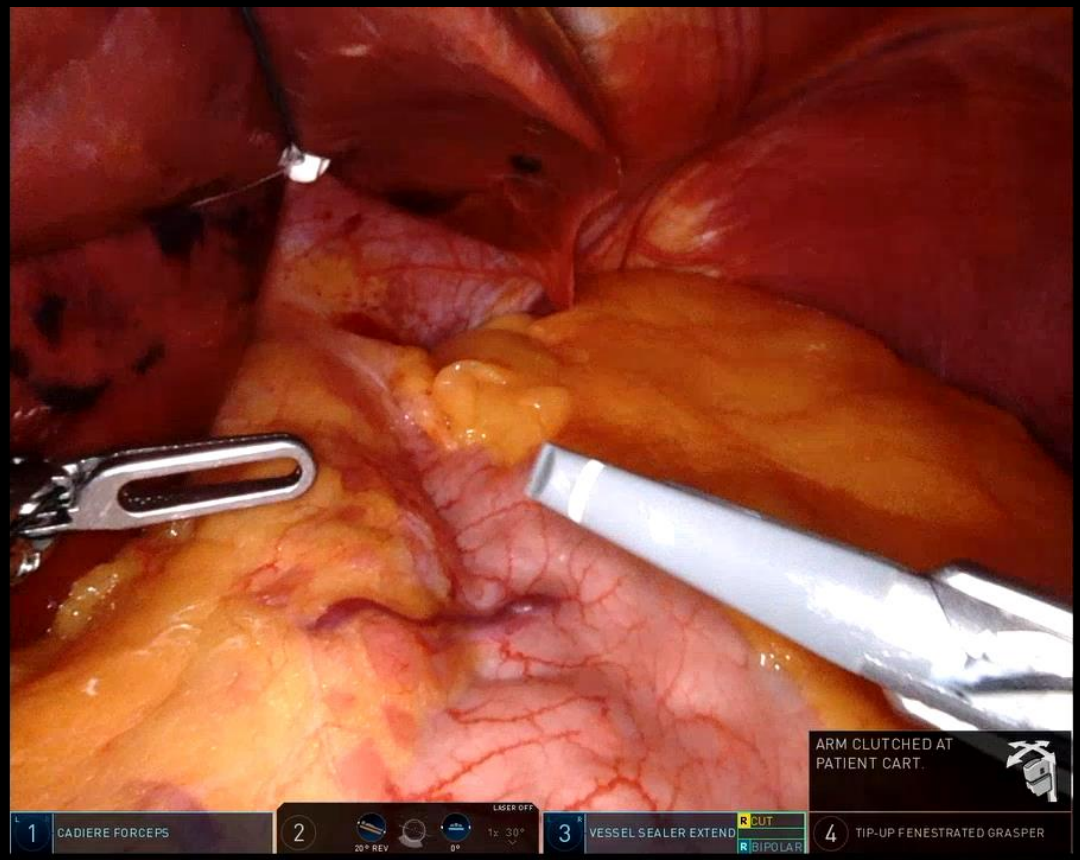
Remove 80% of the stomach
Ghrelin producing fundus is removed
Stomach resembles the sleeve of a shirt or a banana

Roux-en-Y Gastric Bypass

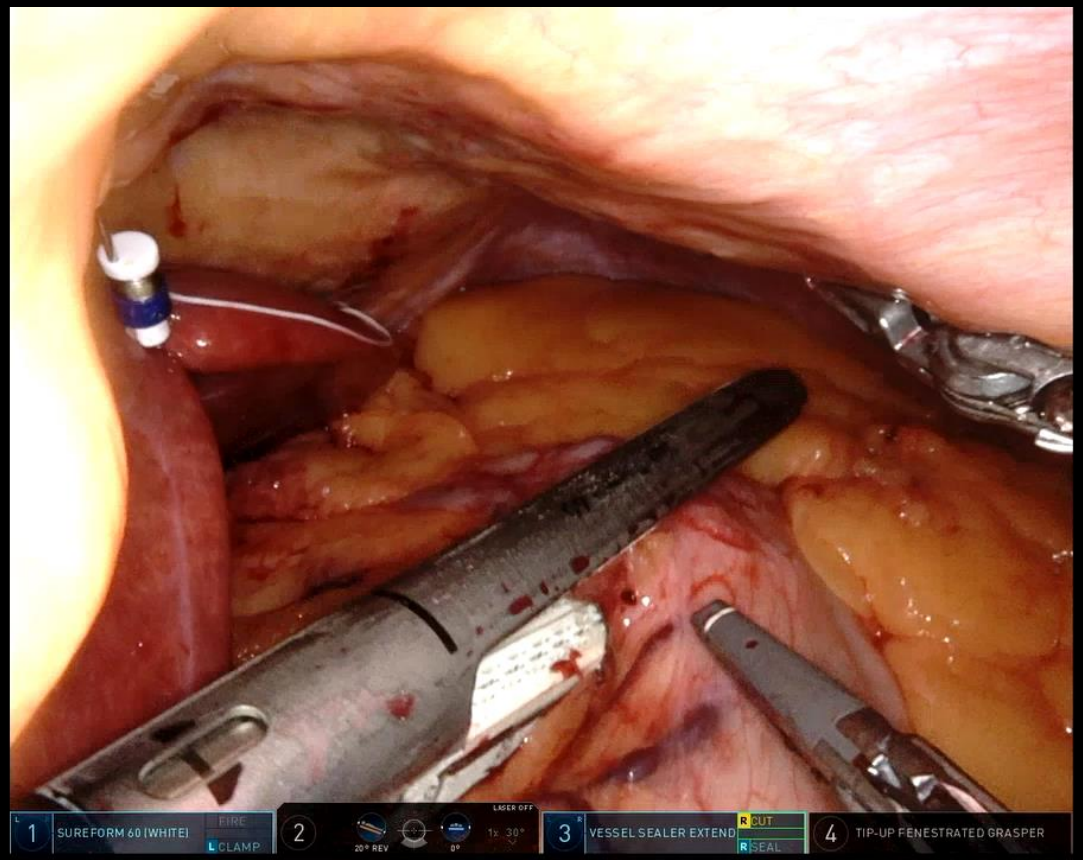


Create small pouch
Bypass portion of jejunum
Ghrelin producing fundus is excluded
Bypassed Biliopancreatic limb alters GLP-1, GIP, PYY, other hormones

Vertical Sleeve Gastrectomy



Roux en Y gastric bypass



Surgery doesn't just shrink the stomach — it rewires the hormones

Sleeve gastrectomy and Roux en Y Gastric Bypass raise post-meal GLP-1 and PYY and blunt ghrelin secretion — the same axis as medications but permanent and more dramatic

> *The difference is persistence: surgical hormonal change doesn't depend on a weekly injection or daily pill. That is the physiologic reason surgical weight loss and metabolic improvement tend to hold up as adherence-dependent therapies fade.*

What about the risks?

	Sleeve Gastrectomy	*Gastric Bypass*
30-day mortality	0.04%	0.07%
Leak rate	0.13%	0.24%
30-day morbidity	0.96%	1.25%
30-day reintervention rate	0.8%	1.9%

*Sources: ASMBS (asmbs.org), citing Stanford (mortality and 30-day morbidity rate, n≈270,000, 2007–2010) and Cleveland Clinic Florida (leak rate, n>2,400, 2005–2011) data. 30-day reoperation: Janik & Aryaie, Surg Endosc 2021, MBSAQIP 2015–2018 (n=29,165 sleeve / 11,895 bypass matched pairs). *SADI-S: Biertho et al., IFSO presentation, n=61 (not ASMBS-published); reoperation and morbidity figures not available for SADI-S in comparable form (shown as —).*

Gastric bypass: complications to recognize

Peri-operative Complications

Complication	*Watch for*
Anastomotic / staple-line leak	• Tachycardia — often the earliest sign • Fever, abdominal pain, tachypnea; typically POD 2–7
Postoperative bleeding	• Tachycardia, hypotension • Melena/hematemesis; usually within 48 hr
Gastrojejunal stricture	• Progressive dysphagia: solids → liquids • Vomiting after meals

Complication	*Watch for*
Internal hernia / SBO	• Intermittent, crampy pain ± vomiting, bloating • Subtle and easy to miss, If in doubt, call surgeon!
Marginal ulcer	• Epigastric pain, nausea, vomiting • EGD to Confirm • Carafate qid, PPI bid, Cytotec QID (refractory)
Vitamin / nutritional deficiencies	• Iron, B12, folate, calcium/vitamin D, thiamine • Fatigue, anemia, neuropathy, bone loss, dystaxia, paresthesiaa

If in doubt, call a bariatric surgeon! It could save a patient's life

— Why Surgery Is Superior · Sleeve Gastrectomy

Sleeve gastrectomy: complications to recognize

Surgical, mechanical, and nutritional complications — and the symptoms that should prompt evaluation. Gastric bypass is covered on its own slide.

Complication	*Watch for*
Staple-line leak	• Tachycardia — often the earliest sign • Fever, abdominal pain, tachypnea; typically POD 2–7
Postoperative bleeding	• Pain-Usually intra-abdominal, from the long staple line • Tachycardia, hypotension • Melena/hematemesis;
Portomesenteric vein thrombosis	• Vague abdominal pain, nausea, vomiting, diarrhea • Can progress to peritonitis/shock — easy to miss

Complication	*Watch for*
Sleeve stenosis	• Nausea, vomiting, dysphagia — worse with solids • Usually at the incisura angularis • EGD is diagnostic
New or worsening GERD	• Heartburn, regurgitation, chest pain • Refractory cases may need conversion to bypass
Vitamin / nutritional deficiencies	• Iron, B12, folate, calcium/vitamin D, thiamine • Fatigue, anemia, neuropathy, bone loss, dystaxia, paresthesiaa

— Real-World Evidence

Surgery beat GLP-1s on weight loss and cost

30,458 adults with class II/III obesity, matched by insurance claims and EMR data: 14,101 who had bariatric surgery vs 16,357 treated with a GLP-1 receptor agonist.

Total body-weight loss

- Bariatric surgery

28.3%

- GLP-1 receptor agonist

10.3%

Total cost per patient, 2 years

- Bariatric surgery

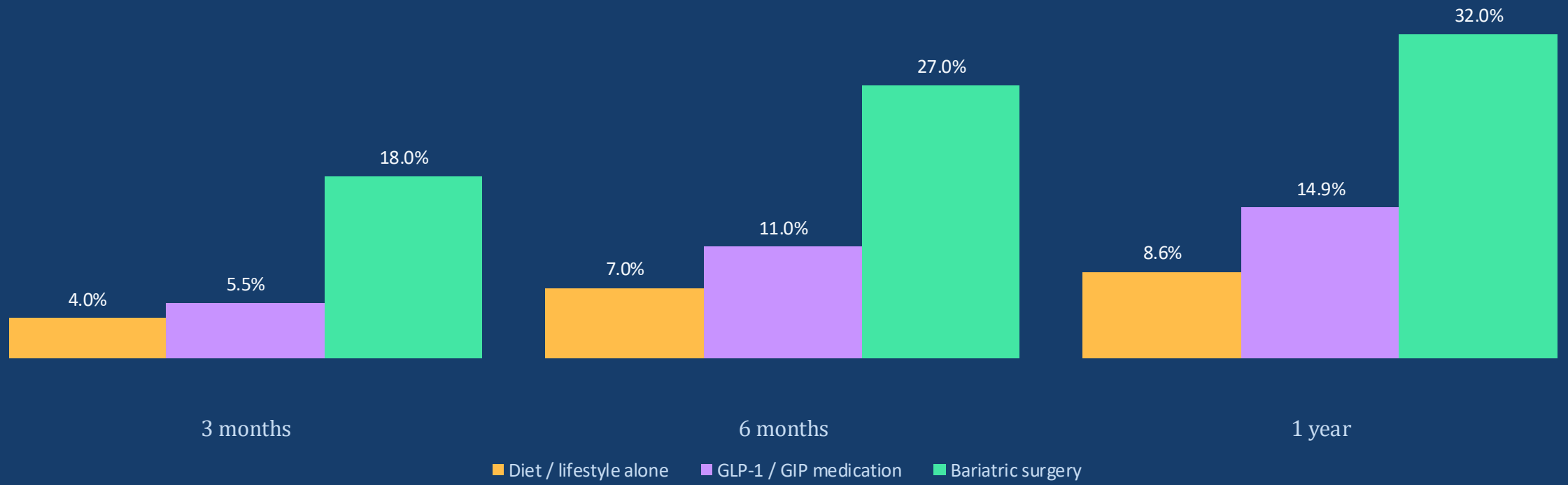
$51.8K

- GLP-1 receptor agonist

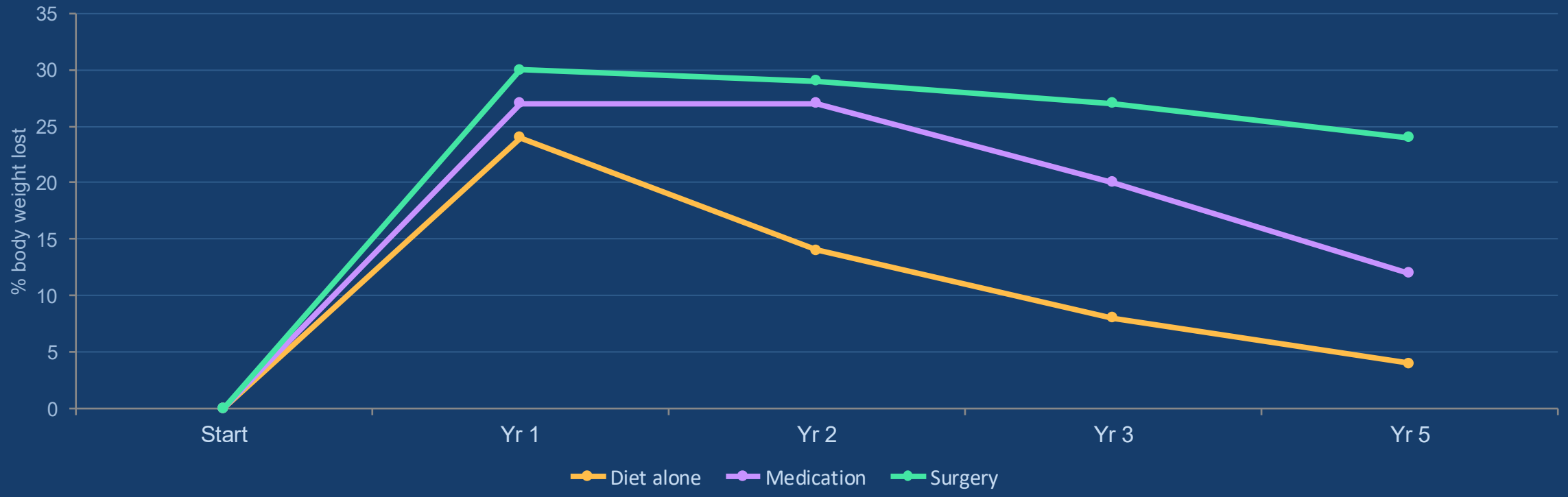
$63.5K

Source: Barrett et al., JAMA Surgery 2025 (n=30,458). GLP-1 patients carried higher sustained pharmacy costs throughout year two.

Expected weight loss: diet alone vs. GLP-1 vs. surgery



Durability favors surgery



— Real-World Evidence

Surgery cut mortality and morbidity nearly in half vs. GLP-1 therapy

3,932 adults with type 2 diabetes and obesity — 1,657 who had gastric bypass or sleeve gastrectomy vs. 2,275 treated with a GLP-1 receptor agonist

10-year cumulative all-cause mortality · 32% lower risk of death with surgery

Bariatric/metabolic surgery

9.0%

GLP-1 receptor agonist

12.4%

MACE reduction

35%

Renal Disease Reduction

47%

Diabetes Remission

24% vs 7%

TBWL

21.6 vs 6.8%

*Source: Gasoyan, Aminian, Nissen et al., "Macrovascular and microvascular outcomes of metabolic surgery versus GLP-1 receptor agonists," Nature Medicine, Oct 2025 (the "M6" study, n=3,932). Observational, doubly-robust-adjusted cohort, not a randomized trial; did not isolate the newest GLP-1 formulations. *Diabetes-remission-type outcome is from a separate cohort — Leslie et al., Lancet Diabetes & Endocrinology 2026;14:638–648 (n=45,093: 7,433 sleeve, 4,178 tirzepatide, 33,482 semaglutide) — not the M6 study above.*

Durability of Surgery

Maintenance of weight loss at 33 months. BMI >40

Bariatric surgery

96%

GLP-1 Medications

46%

3× greater weight loss with surgery
-28% vs 10% average

38%

fewer ER visits with surgery
25% fewer inpatient hospital stays

Source: Barrett et al., JAMA Surgery 2025 (n=30,458). GLP-1 patients carried higher sustained pharmacy costs throughout year two.

What about endoscopic procedures?

	Weight loss	*Complications*
Intragastric balloon	`11–15% TBWL at 12 mo`	• 0.17% severe (perforation/obstruction) • 4.4% required early removal • Temporary, removed at 6 months • Thickening of the gastric wall
Endoscopic Sleeve	`13.6% TBWL at 12 mo`	• Requires inpatient stay • 2% complication rate (abscess, bleed) • Difficult surgical revision
AspireAssist	`12.1% TBWL at 1 yr`	• 3.6% complication rate (bleeding, ulcer, dislodgement) • 30–40% peristomal irritation or infection at the site
GLP-1 / GIP therapy	`~15–22% TBWL at 12–18 mo`	• GI side effects common (nausea, GI upset) • Weight regain typical after stopping
Surgery (VSG/RYGB)	`29.5–31.9% TBWL at 1 yr, 25% TBWL at 10 years`	• Mortality 0.08–0.14% · Leak 0.3–0.4% • Morbidity 0.96–1.25% · Reoperation (30-day) 0.8–1.9%

How to lose the right weight

Prioritize Muscle to Prioritize Metabolism

Why it matters most

Skeletal muscle is the body's primary site of resting energy expenditure and insulin-mediated glucose disposal. On GLP-1 therapy specifically, DXA substudies show lean tissue makes up roughly a quarter to a third of total weight lost.

How often to recommend

2–3 nonconsecutive resistance sessions/week, 8–10 exercises covering major muscle groups, 8–12 reps/set.

It doesn't require a gym

Bodyweight movements, resistance bands, and light dumbbells are legitimate entry points. Progressive overload — not equipment — is the active ingredient; reassess and advance load as tolerance improves.

Pair it with protein

Protein distributed across the day supports the muscle-protein-synthesis response to training better than one large serving. Target ≥60 g/day, up to 1.2–1.6 g/kg/day during active weight loss.

The weight-loss journey: follow-up visits & labs

Visit	*Surgical patients*	*GLP-1 / GIP patients*
Baseline	CBC, CMP, iron studies, B12, folate, 25-OH vit D, lipids, A1c • H. pylori testing • Nutrition consult	CMP, TSH, A1c/glucose, lipids • Personal/family history of MTC or MEN2 (contraindication)
2–4 wk	Wound check; hydration & protein-intake review • Taper/d-c diabetes & BP meds as needed	Tolerability & GI side effects, Protein intake and review • confirm dose-escalation step
3 mo	CBC, iron panel, protein/albumin, vit D • Protein-intake and supplement-adherence check	Weight response check • <5% loss by now flags poor progression, consider alternative measures
6 mo	CBC+iron, B12, folate, 25-OH vit D/Ca/PTH, vit A, zinc, copper, thiamine • Reinforce vitamin/supplement regimen	CMP, A1c, lipids reassessment
12 mo & annually	CBC+iron, B12, folate, 25-OH vit D/Ca/PTH, vit A, zinc, copper, thiamine	CMP, TSH, A1c, lipids; nutritional/vitamin • Reassess goals and consider alternative measures

What this means for your next patient visit

— **Treat obesity as the chronic hormonal-regulatory disease it is**

Not a motivation problem — frame it to patients the way you'd frame hypertension or diabetes.

— **GLP-1 / GIP therapy is an effective option for a certain population of patients**

Set expectations up front: benefit is generally tied to continued use, weight loss is often not as effective as surgery.
Discuss cost, insurance coverage, and compounding pharmacy risks

— **Refer early evaluation — BMI ≥ 35, or ≥ 30 with a diabetes**

Consult is just a conversation

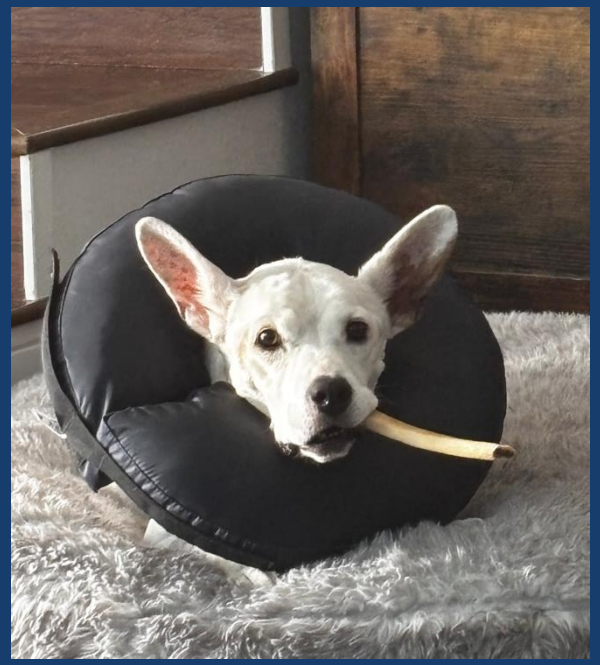
Especially with type 2 diabetes: durability and outcomes data favor earlier referral
Cure rate for diabetes with gastric bypass is 60% at 5 years for all diabetics including insulin dependency

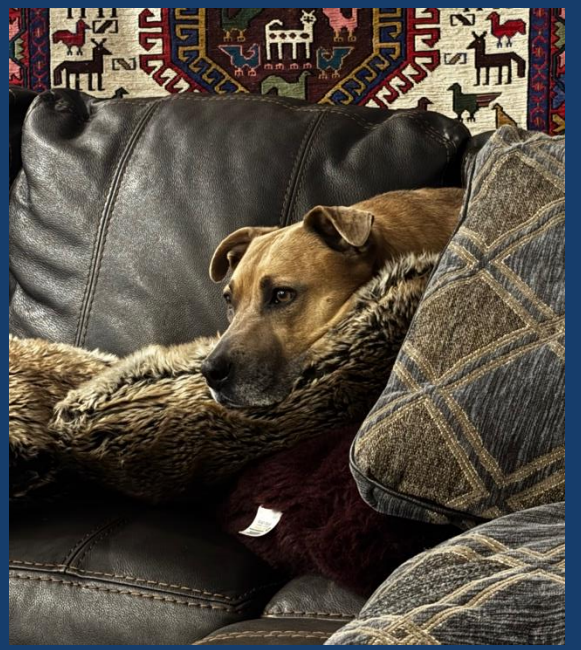
— **Medication and surgery are complementary, not competing**

Many patients benefit from GLP-1 therapy before surgery, after surgery, or both.

Questions?







Katayun (Katy) Irani, MD, FACS

Denver Center for Weight Loss and Bariatric Surgery · HCA HealthONE Rose Medical Center, Denver CO

917-499-7889 (c) 303-280-0900 (p)