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Comparative Effectiveness of Contemporary Weight-Loss Injections and Established Bariatric Procedures.

Abstract

Obesity management has shifted from a traditional 'lifestyle-versus-surgery' framework to a broader continuum that now includes highly effective injectable anti-obesity medications. This review compares the principal injectable therapies currently used in routine obesity care—liraglutide 3.0 mg, semaglutide 2.4 mg, and tirzepatide 5–15 mg—with major bariatric operations, especially sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), and selected duodenal switch (DS) procedures. The central outcome of interest is reduction in total body weight, complemented by durability, cardiometabolic benefit, treatment burden, safety, and practical clinical positioning. Across pivotal trials, mean weight reduction was approximately 7.4% for liraglutide at 56 weeks, 14.9% for semaglutide at 68 weeks, and 20.9% for tirzepatide 15 mg at 72 weeks. In randomized or comparative bariatric literature, 5-year total weight loss was about 22.5% after SG and 26.0% after RYGB, while DS can exceed this in selected high-BMI populations. The strongest overall conclusion is that metabolic/bariatric surgery remains the most durable treatment for severe obesity, but modern injections have narrowed the efficacy gap substantially and broadened individualized treatment options. For many patients, the optimal strategy is not an either/or choice but a staged or combined pathway.

Key takeaways

 Among currently marketed broad-indication injectable anti-obesity medicines, tirzepatide produces the largest mean weight loss in pivotal trials, followed by semaglutide and liraglutide.

 Among bariatric operations, Roux-en-Y gastric bypass generally yields greater long-term weight loss than sleeve gastrectomy, while duodenal switch can be even more potent but

is usually reserved for selected patients because nutritional risk is higher.

 Surgery remains the most durable intervention overall, but injections offer a non-surgical, reversible, and increasingly evidence-based option, especially for patients who prefer medical treatment, are not surgical candidates, or need bridge therapy before surgery.

Cross-trial comparisons must be interpreted cautiously because populations, follow-up horizons, adherence, and outcome definitions differ.

Scope and method

This article is a structured narrative review based on pivotal clinical trials, recent long-term follow-up studies, FDA prescribing information, bariatric guideline literature, and selected contemporary systematic reviews. To maximize academic rigor, the evidence hierarchy prioritized randomized controlled trials, long-term extensions, guideline statements, official prescribing information, and meta-analyses over narrative commentary or promotional material. The quantitative comparisons are intentionally restricted to interventions with established clinical uptake and reasonably robust published data. The review emphasizes adults with obesity or overweight plus obesity-related complications. Rare-disease therapies such as setmelanotide were not included in the main comparative tables because their indication is fundamentally different from common obesity management. Likewise, newly marketed semaglutide formats approved in 2026 are noted but not used as the core comparator set because the best long-term comparative literature still centers on liraglutide, semaglutide 2.4 mg, and tirzepatide.

An important limitation is that the medication–surgery comparison is largely indirect. Drug trials and surgical cohorts differ in entry criteria, baseline body mass index, co-morbidity load, behavioral support, follow-up completeness, and the definition of weight-loss endpoints. Therefore, the figures below should be interpreted as clinically informative benchmarks rather than exact head-to-head treatment effects.

Current injectable anti-obesity therapies

The current broad-market injectable therapies with major obesity indications are liraglutide 3.0 mg (daily GLP-1 receptor agonist), semaglutide 2.4 mg (weekly GLP-1 receptor

agonist), and tirzepatide 5–15 mg (weekly dual GIP/GLP-1 agonist). In March 2026, the FDA also aligned labeling around newer Wegovy formats, including oral tablets and a higher-dose injection pathway, illustrating how rapidly the pharmacotherapy landscape is evolving. In practice, however, the three agents above remain the most established anchors for comparing efficacy and real-world treatment strategy.

Table 1. Main currently marketed injectable obesity therapies

Drug

Dosing

Mechanism

Pivotal efficacy endpoint

Mean weight change

Notes

Liraglutide 3.0 mg (Saxenda)

Daily SC injection

GLP-1 receptor agonist

56 weeks

−7.4%

Earliest widely used obesity GLP-1; daily dosing is less convenient and average weight loss is smaller than with newer agents.

Semaglutide 2.4 mg (Wegovy)

Weekly SC injection

GLP-1 receptor agonist

68 weeks

−14.9%

Strong weight-loss efficacy; also has high-quality cardiovascular outcome evidence in obesity without diabetes.

Tirzepatide 5–15 mg (Zepbound)

Weekly SC injection

Dual GIP/GLP-1 agonist

72 weeks

−15.0% to −20.9%

Highest average weight loss among established injectables in pivotal trials; long-term data now extend to 176 weeks.

Established bariatric procedures

The dominant surgical comparators are sleeve gastrectomy and Roux-en-Y gastric bypass. Sleeve gastrectomy removes roughly 80% of the stomach, reduces gastric volume, and influences gut hormones, while preserving intestinal continuity. Roux-en-Y gastric bypass creates a small gastric pouch and bypasses part of the proximal small bowel, combining restriction, hormonal change, and modest malabsorption. Duodenal switch and related operations generally achieve the greatest weight loss but require particularly careful nutritional surveillance. Adjustable gastric banding, although historically important, has a much smaller role today because long-term weight loss and reoperation profiles are less favorable.

According to the 2022 ASMBS/IFSO guidance, metabolic/bariatric surgery is recommended for BMI ≥35 kg/m² regardless of the presence, absence, or severity of obesity-related conditions, and should be considered in patients with BMI 30–34.9 kg/m² when metabolic disease is present or when durable weight loss is not achieved with nonsurgical therapy. These guidelines reflect the maturation of surgery from a last-resort intervention to a standard evidence-based option in selected patients.

Table 2. Major bariatric operations used in comparative practice

Procedure

Core mechanism

Typical comparative efficacy

Durability

Main strengths

Main limitations

Sleeve gastrectomy (SG)

Restrictive + hormonal

~22.5% total weight loss at 5 years

Good

Technically simpler than bypass; strong efficacy; no intestinal bypass

Reflux may worsen; some weight regain over time; less potent than RYGB

Roux-en-Y gastric bypass (RYGB)

Restrictive + hormonal + mild malabsorption

~26.0% total weight loss at 5 years

Very good

Greater average weight loss; strong diabetes and GERD benefits

More complex operation; micronutrient deficiencies and dumping syndrome require long-term follow-up

Duodenal switch (DS/BPD-DS)

Restrictive + stronger malabsorption

Can exceed 30% total weight loss in selected high-BMI cohorts

Excellent in selected patients

Most powerful weight-loss procedure for severe obesity

Highest nutritional burden; not first-line for most patients

Adjustable gastric banding (historical comparator)

Restrictive

Inferior long-term performance

Variable

Reversible and less anatomically disruptive

High revision/removal rates; now much less favored

Comparative efficacy: what the numbers show

The central pattern is straightforward: each generation of injectable therapy has improved upon the previous one, but surgery still produces the largest and most durable mean

weight reduction overall. In the adult obesity population without diabetes, liraglutide 3.0 mg produced a mean weight change of about −7.4% at 56 weeks. Semaglutide 2.4 mg nearly doubled that benchmark to −14.9% at 68 weeks. Tirzepatide extended the pharmacologic ceiling further, reaching −20.9% at 72 weeks with the 15 mg dose. By contrast, 5-year randomized comparative data show approximately 22.5% total weight loss after sleeve gastrectomy and 26.0% after Roux-en-Y gastric bypass.

Figure 1. Selected weight-loss outcomes. Values are drawn from pivotal medication trials and major surgical comparative studies. The duodenal switch value reflects a selected super-obesity cohort and should not be generalized to all obesity populations.

Two clinical inferences follow. First, tirzepatide is now close enough to sleeve gastrectomy that treatment choice can reasonably pivot on patient preference, risk tolerance, access, and the need for durability rather than on the assumption that all medication is 'mild.' Second, the difference between semaglutide and tirzepatide is large enough to be clinically meaningful, especially when the treatment goal is a ≥15% or ≥20% body-weight reduction.

Milestone responders and clinical meaning

Average weight loss is useful but incomplete. Clinicians also care about the proportion of patients who cross major clinical thresholds because many metabolic improvements begin around 5% weight loss, while fatty liver disease, obstructive sleep apnea, insulin resistance, and orthopedic symptoms often improve more substantially as patients approach the 10–20% range. In the pivotal liraglutide trials, 33.9% of participants achieved at least 10% weight loss. With semaglutide 2.4 mg, 47.9% achieved at least 15% weight loss. With tirzepatide 15 mg, 70.6% achieved at least 15% weight loss, and 56.7% achieved at least 20% weight loss.

Figure 2. Milestone responders in pivotal drug trials. Because liraglutide labels prominently report ≥10% response whereas semaglutide and tirzepatide are frequently discussed at ≥15%, this figure compares the most clinically cited milestone from each source and

should not be interpreted as a strict like-for-like endpoint.

Durability, maintenance, and relapse

Durability is where surgery still holds the clearest overall advantage. Pharmacotherapy works while it is continued; surgery often continues to work after the perioperative period because it permanently alters anatomy, appetite regulation, eating tolerance, and in some procedures nutrient handling. In the STEP 4 semaglutide withdrawal trial, patients who continued semaglutide after a run-in period lost an additional 7.9% from week 20 to week 68, whereas those switched to placebo regained 6.9%. A later extension analysis found that much of the lost weight returned after medication withdrawal. By contrast, semaglutide maintained clinically meaningful weight reduction to 208 weeks in the SELECT program when treatment was continued, and tirzepatide maintained approximately −18.7% to −19.7% weight change at 176 weeks in SURMOUNT-1.

Surgical durability is also not absolute; weight regain can occur after every bariatric procedure, especially after the first two to three years. Nonetheless, long-term randomized and meta-analytic data consistently show durable superiority of RYGB over SG and, in carefully selected very-high-BMI groups, even greater durability with duodenal switch.

Figure 3. Selected durability outcomes. Negative values indicate weight reduction; positive values indicate regain. Horizons differ across studies, so the graph is best read as a durability overview rather than a direct efficacy ranking.

Cardiometabolic outcomes beyond body weight

Weight reduction is not the only outcome that matters. Semaglutide 2.4 mg has the strongest direct cardiovascular outcomes evidence among current obesity injections: in SELECT, semaglutide reduced major adverse cardiovascular events by 20% (hazard ratio 0.80) in adults with overweight/obesity and established cardiovascular disease, but without diabetes. Tirzepatide has shown highly favorable glycemic and diabetes-prevention signals, including long-term reduction in progression from prediabetes in the SURMOUNT-1 program, although direct cardiovascular outcome evidence in obesity

remains less mature than semaglutide's.

Bariatric surgery also provides major cardiometabolic benefits, especially for type 2 diabetes remission, obstructive sleep apnea, blood pressure improvement, and dyslipidemia. RYGB often has an advantage over SG for diabetes remission and reflux control, whereas SG may be preferred in patients who prioritize technical simplicity or wish to avoid intestinal bypass. In this sense, 'effectiveness' depends on the target outcome: semaglutide currently leads the medication class for hard cardiovascular-outcomes evidence, tirzepatide leads for mean trial-based weight loss, and surgery leads for durability plus broad metabolic impact.

Safety, burden, and trade-offs

The safety discussion must distinguish acute procedural risk from chronic treatment burden. Modern bariatric surgery has become much safer than older perceptions suggest: contemporary laparoscopic series report 30-day mortality typically below 0.2%. However, surgery still carries operative risks such as leak, bleeding, venous thromboembolism, bowel obstruction, strictures, and long-term micronutrient deficiencies, especially after bypass-type procedures. These risks are front-loaded but potentially serious.

Injectable therapy avoids anesthesia and operative recovery, but side effects are often chronic and adherence-dependent. Across FDA labels, gastrointestinal adverse events—especially nausea, vomiting, diarrhea, constipation, and abdominal discomfort—are the dominant class effects for liraglutide, semaglutide, and tirzepatide. Class warnings also include gallbladder disease, pancreatitis concerns, and contraindication in patients with personal or family history of medullary thyroid carcinoma or MEN2. Treatment discontinuation because of adverse effects is common enough to matter in routine practice, and real-world effectiveness often underperforms trial efficacy because patients stop treatment, cannot access sustained coverage, or fail to escalate to full dose.

This table summarizes the adverse-effect patterns most relevant to patient counseling. Frequency varies across studies and labels, and surgical risk also depends on center

volume, patient frailty, and procedure-specific expertise.

Figure 4. Selected common adverse-effect frequencies in adult obesity trials for liraglutide, semaglutide, and tirzepatide. Percentages are drawn from adult FDA label tables and are not perfectly head-to-head because study populations, follow-up duration, and dose-escalation protocols differ.

Intervention

Common side effects

Important/serious risks

Clinical notes

Liraglutide 3.0 mg

Nausea, vomiting, diarrhea, constipation, abdominal discomfort, decreased appetite

Gallbladder disease, pancreatitis warning, dehydration or renal injury, boxed thyroid C-cell warning

Daily injections may worsen treatment fatigue; slower titration can improve tolerance.

Semaglutide 2.4 mg

Nausea, vomiting, diarrhea, constipation, abdominal pain, headache, fatigue

Gallbladder disease, pancreatitis warning, dehydration or renal injury, boxed thyroid C-cell warning

Weekly dosing is convenient, but long-term adherence still determines real-world effectiveness.

Tirzepatide 15 mg

Nausea, diarrhea, vomiting, constipation, abdominal pain, dyspepsia

Gallbladder disease, pancreatitis warning, dehydration or renal injury, boxed thyroid C-cell warning

Highest drug efficacy, but GI tolerability may limit escalation in some patients.

Sleeve gastrectomy

Postoperative pain, nausea, vomiting, reduced intake, reflux symptoms

Staple-line leak, bleeding, VTE, dehydration, micronutrient deficiencies, worsening GERD

Requires lifelong follow-up; reflux risk is a major differentiator.

Roux-en-Y gastric bypass

Postoperative pain, nausea, dumping symptoms, altered food tolerance

Leak, bleeding, internal hernia, bowel obstruction, VTE, micronutrient deficiencies, hypoglycemia

Often stronger metabolic effect than sleeve, but nutritional surveillance is more demanding.

Duodenal switch

Frequent stools or steatorrhea, altered tolerance, postoperative GI symptoms

Highest nutritional deficiency burden, protein malnutrition, fat-soluble vitamin deficiency, surgical complications

Reserved for selected patients and centers experienced in intensive follow-up.

Table 4. Side-effect profile by intervention

For bariatric surgery, side effects are best separated into early postoperative complications and long-term sequelae. Early complications include bleeding, leak, infection, venous thromboembolism, nausea or vomiting, dehydration, and—depending on the procedure—bowel obstruction or internal hernia. Longer-term issues include iron, vitamin B12, folate, calcium, vitamin D and fat-soluble vitamin deficiencies; dumping syndrome after bypass; GERD after sleeve gastrectomy; hypoglycemia in selected post-bypass patients; gallstones during rapid weight loss; and the possibility of weight regain or need for revisional surgery.

However, the side-effect profile is not limited to nausea. FDA labeling also highlights clinically important risks such as gallbladder events, pancreatitis warnings or precautions, acute kidney injury in the setting of dehydration, increased heart rate, and the class boxed warning related to medullary thyroid carcinoma and MEN2. In routine care, tirzepatide may offer greater potency at the cost of more challenging gastrointestinal tolerability in some patients, whereas liraglutide's daily injection schedule adds adherence burden.

Semaglutide often occupies the middle ground: stronger weight loss than liraglutide, more

mature cardiovascular-outcomes evidence than tirzepatide, and a familiar weekly format.

For injectable therapy, the most common adverse effects are gastrointestinal and dose-related. Liraglutide, semaglutide, and tirzepatide all commonly cause nausea, vomiting, diarrhea, constipation, abdominal pain, and reduced appetite, especially during dose escalation. These symptoms are usually most intense early in treatment and often improve with slower titration, smaller meals, reduced dietary fat, better hydration, and temporary dose de-escalation when clinically appropriate.

Drug-specific adverse effects: practical summary

Table 3. Practical comparison for clinical decision-making

Dimension

Liraglutide / Semaglutide / Tirzepatide

Sleeve gastrectomy

Roux-en-Y gastric bypass

Comment

Reversibility

High (treatment can be stopped)

Low

Low

Drugs are reversible; surgery is generally permanent.

Durability without ongoing therapy

Limited

Moderate-to-good

Good-to-very-good

A major differentiator favoring surgery.

Early treatment burden

Dose escalation, GI symptoms, insurance/access

Operation + recovery

Operation + recovery

The burdens differ rather than one being universally easier.

Nutritional monitoring

Usually modest

Required

Required and more intensive

Bypass/DS demand the most structured supplementation.

Best-fit patient profile

Prefers medical therapy, lower surgical readiness, bridge therapy, recurrence after surgery

Needs strong efficacy with simpler anatomy

Needs maximal durability, diabetes/GERD benefit

Shared decision-making remains essential.

Which option is 'more effective'?

The answer depends on the endpoint and the time horizon. If the question is immediate, non-surgical efficacy with a reversible treatment, tirzepatide currently offers the highest average weight loss among established injections. If the question is durable long-term body-weight reduction, surgery remains more effective overall, with RYGB generally outperforming SG and DS exceeding both in selected patients at the cost of greater nutritional complexity. If the question is cardiovascular outcomes evidence in obesity without diabetes, semaglutide currently has the most direct randomized evidence. If the question is broad clinical practicality, the best treatment is the one a patient can safely start, tolerate, continue, and integrate into long-term follow-up.

Therefore, the modern clinical framework is increasingly sequential and personalized. Some patients should begin with medication, some should go directly to surgery, and some benefit most from combination care—such as preoperative pharmacologic weight reduction, postoperative treatment of regain, or medication use when surgery is contraindicated or declined. The historical tendency to contrast injections and surgery as competitors is giving way to a chronic-care model in which both belong to the same therapeutic continuum.

Conclusion

Modern weight-loss injections have transformed obesity care and significantly narrowed the gap between nonsurgical and surgical treatment. Tirzepatide has raised the pharmacologic efficacy ceiling to a level that approaches sleeve gastrectomy in some comparative frames, while semaglutide has added robust cardiovascular-outcomes evidence that strengthens the medical case for treating obesity as a disease rather than as a lifestyle failure. Even so, bariatric surgery—particularly Roux-en-Y gastric bypass and, in selected cases, duodenal switch—still provides the greatest long-term and most durable weight loss. The most defensible conclusion is not that one modality has universally replaced the other, but that clinicians now have multiple high-efficacy options and should match them to patient goals, risk profile, co-morbidities, and readiness for lifelong follow-up.

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