

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

43 approved in 2026 are noted but not used as the core comparator set because the best long-term
 44 comparative literature still centers on liraglutide, semaglutide 2.4 mg, and tirzepatide.

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

49 **Current injectable anti-obesity therapies**

50 The current broad-market injectable therapies with major obesity indications are liraglutide 3.0 mg (daily
 51 GLP-1 receptor agonist), semaglutide 2.4 mg (weekly GLP-1 receptor agonist), and tirzepatide 5–15 mg
 52 (weekly dual GIP/GLP-1 agonist). In March 2026, the FDA also aligned labeling around newer Wegovy
 53 formats, including oral tablets and a higher-dose injection pathway, illustrating how rapidly the
 54 pharmacotherapy landscape is evolving. In practice, however, the three agents above remain the most
 55 established anchors for comparing efficacy and real-world treatment strategy.

56 **Table 1. Main currently marketed injectable obesity therapies**

Drug	Dosing	Mechanism	Pivotal efficacy endpoint	Mean weight change	Notes
Liraglutide 3.0 mg (Saxenda)	Daily injection SC	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 injection SC	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 injection SC	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.

57 **Established bariatric procedures**

58 The dominant surgical comparators are sleeve gastrectomy and Roux-en-Y gastric bypass. Sleeve
 59 gastrectomy removes roughly 80% of the stomach, reduces gastric volume, and influences gut hormones,
 60 while preserving intestinal continuity. Roux-en-Y gastric bypass creates a small gastric pouch and
 61 bypasses part of the proximal small bowel, combining restriction, hormonal change, and modest
 62 malabsorption. Duodenal switch and related operations generally achieve the greatest weight loss but
 63 require particularly careful nutritional surveillance. Adjustable gastric banding, although historically

64 important, has a much smaller role today because long-term weight loss and reoperation profiles are less
 65 favorable.

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

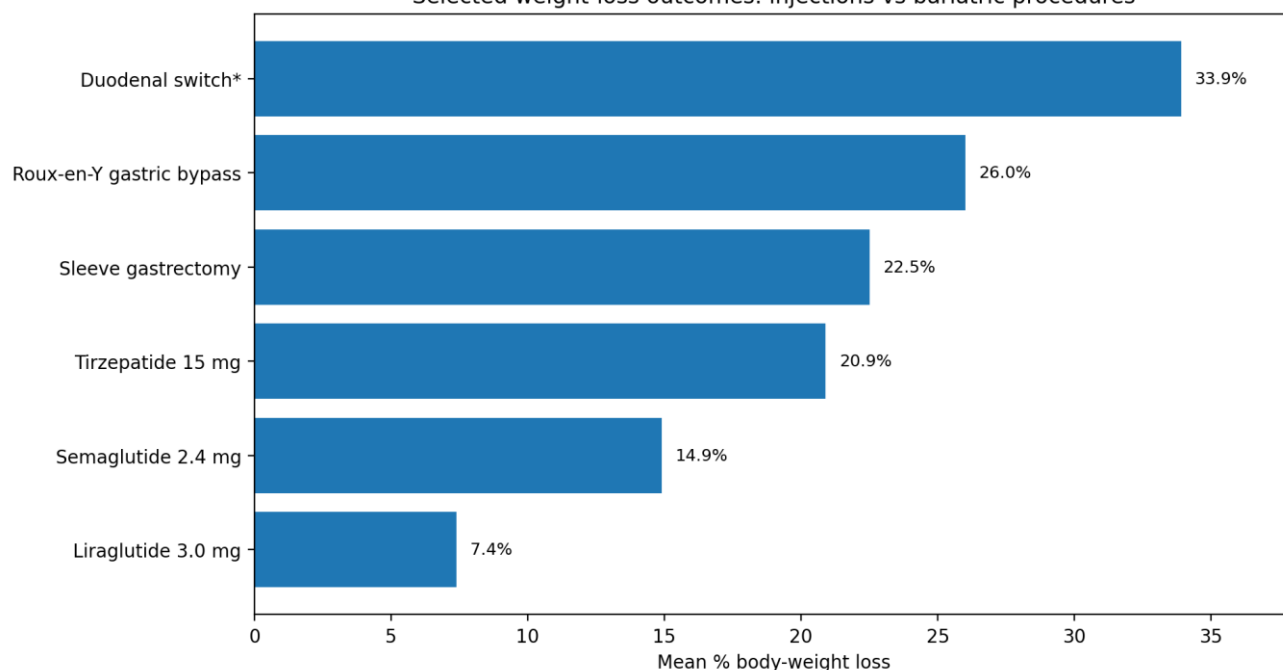
71 **Table 2. Major bariatric operations used in comparative practice**

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

72 Comparative efficacy: what the numbers show

73 The central pattern is straightforward: each generation of injectable therapy has improved upon the
 74 previous one, but surgery still produces the largest and most durable mean weight reduction overall. In the
 75 adult obesity population without diabetes, liraglutide 3.0 mg produced a mean weight change of about
 76 -7.4% at 56 weeks. Semaglutide 2.4 mg nearly doubled that benchmark to -14.9% at 68 weeks.
 77 Tirzepatide extended the pharmacologic ceiling further, reaching -20.9% at 72 weeks with the 15 mg dose.
 78 By contrast, 5-year randomized comparative data show approximately 22.5% total weight loss after sleeve
 79 gastrectomy and 26.0% after Roux-en-Y gastric bypass.

Selected weight-loss outcomes: injections vs bariatric procedures



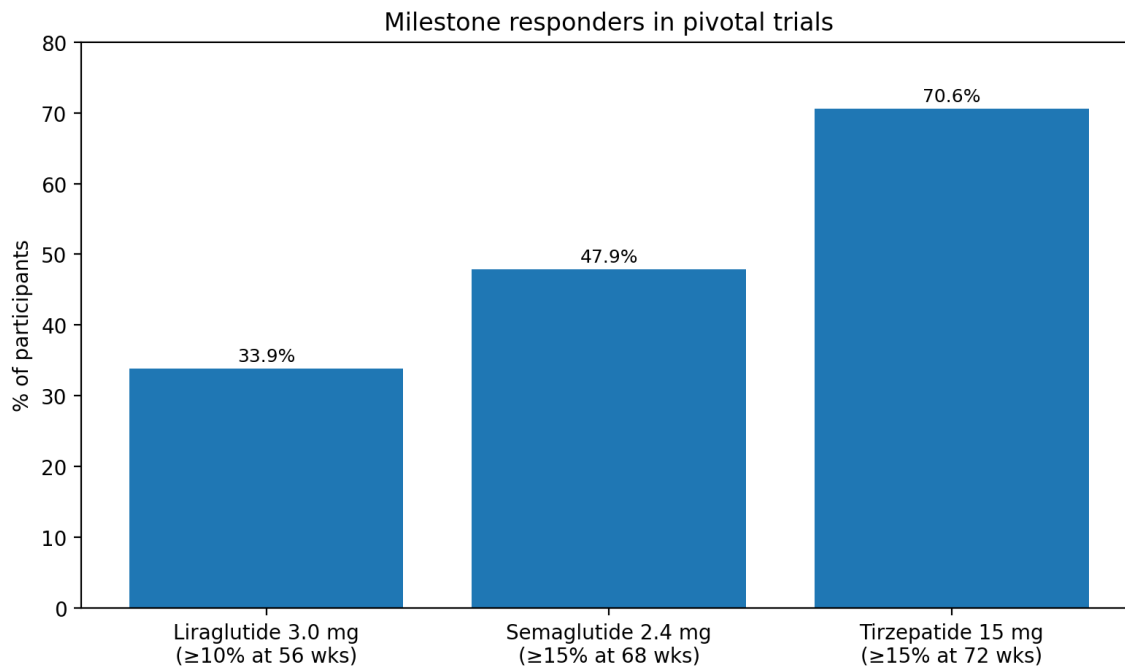
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81 *Figure 1. Selected weight-loss outcomes. Values are drawn from pivotal medication trials and major surgical comparative*
82 *studies. The duodenal switch value reflects a selected super-obesity cohort and should not be generalized to all obesity*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

84 Two clinical inferences follow. First, tirzepatide is now close enough to sleeve gastrectomy that treatment
85 choice can reasonably pivot on patient preference, risk tolerance, access, and the need for durability rather
86 than on the assumption that all medication is 'mild.' Second, the difference between semaglutide and
87 tirzepatide is large enough to be clinically meaningful, especially when the treatment goal is a $\geq 15\%$ or
88 $\geq 20\%$ body-weight reduction.

89 Milestone responders and clinical meaning

90 Average weight loss is useful but incomplete. Clinicians also care about the proportion of patients who
91 cross major clinical thresholds because many metabolic improvements begin around 5% weight loss, while
92 fatty liver disease, obstructive sleep apnea, insulin resistance, and orthopedic symptoms often improve
93 more substantially as patients approach the 10–20% range. In the pivotal liraglutide trials, 33.9% of
94 participants achieved at least 10% weight loss. With semaglutide 2.4 mg, 47.9% achieved at least 15%
95 weight loss. With tirzepatide 15 mg, 70.6% achieved at least 15% weight loss, and 56.7% achieved at least
96 20% weight loss.



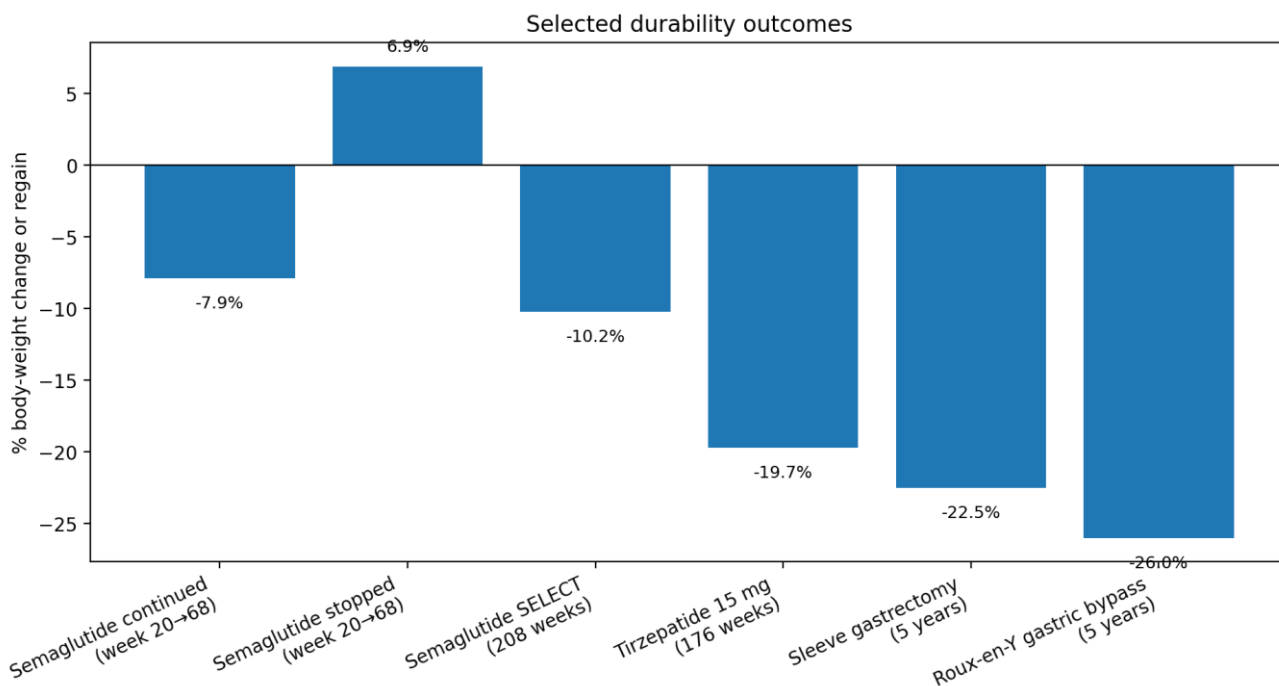
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98 *Figure 2. Milestone responders in pivotal drug trials. Because liraglutide labels prominently report ≥10% response whereas*
 99 *semaglutide and tirzepatide are frequently discussed at ≥15%, this figure compares the most clinically cited milestone from*
 100 *each source and should not be interpreted as a strict like-for-like endpoint.*

101 Durability, maintenance, and relapse

102 Durability is where surgery still holds the clearest overall advantage. Pharmacotherapy works while it is
 103 continued; surgery often continues to work after the perioperative period because it permanently alters
 104 anatomy, appetite regulation, eating tolerance, and in some procedures nutrient handling. In the STEP 4
 105 semaglutide withdrawal trial, patients who continued semaglutide after a run-in period lost an additional
 106 7.9% from week 20 to week 68, whereas those switched to placebo regained 6.9%. A later extension
 107 analysis found that much of the lost weight returned after medication withdrawal. By contrast, semaglutide
 108 maintained clinically meaningful weight reduction to 208 weeks in the SELECT program when treatment
 109 was continued, and tirzepatide maintained approximately -18.7% to -19.7% weight change at 176 weeks
 110 in SURMOUNT-1.

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



115

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

118 **Cardiometabolic outcomes beyond body weight**

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

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

133 **Safety, burden, and trade-offs**

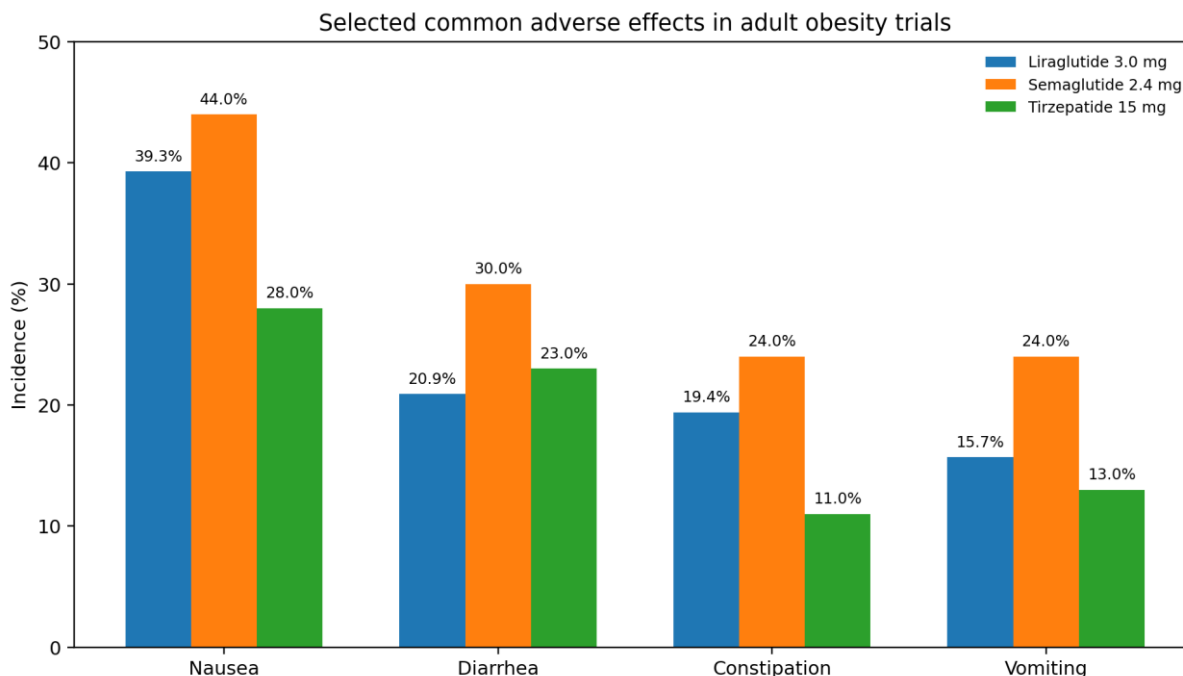
134 The safety discussion must distinguish acute procedural risk from chronic treatment burden. Modern
 135 bariatric surgery has become much safer than older perceptions suggest: contemporary laparoscopic
 136 series report 30-day mortality typically below 0.2%. However, surgery still carries operative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

139 Injectable therapy avoids anesthesia and operative recovery, but side effects are often chronic and
 140 adherence-dependent. Across FDA labels, gastrointestinal adverse events—especially nausea, vomiting,
 141 diarrhea, constipation, and abdominal discomfort—are the dominant class effects for liraglutide,

142 semaglutide, and tirzepatide. Class warnings also include gallbladder disease, pancreatitis concerns, and
 143 contraindication in patients with personal or family history of medullary thyroid carcinoma or MEN2.
 144 Treatment discontinuation because of adverse effects is common enough to matter in routine practice, and
 145 real-world effectiveness often underperforms trial efficacy because patients stop treatment, cannot access
 146 sustained coverage, or fail to escalate to full dose.

147 *This table summarizes the adverse-effect patterns most relevant to patient counseling. Frequency varies across studies and*
 148 *labels, and surgical risk also depends on center volume, patient frailty, and procedure-specific expertise.*

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



152

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.

Intervention	Common side effects	Important/serious risks	Clinical notes
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.

153 **Table 4. Side-effect profile by intervention**

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

161 However, the side-effect profile is not limited to nausea. FDA labeling also highlights clinically important
 162 risks such as gallbladder events, pancreatitis warnings or precautions, acute kidney injury in the setting of
 163 dehydration, increased heart rate, and the class boxed warning related to medullary thyroid carcinoma and
 164 MEN2. In routine care, tirzepatide may offer greater potency at the cost of more challenging
 165 gastrointestinal tolerability in some patients, whereas liraglutide's daily injection schedule adds adherence
 166 burden. Semaglutide often occupies the middle ground: stronger weight loss than liraglutide, more mature
 167 cardiovascular-outcomes evidence than tirzepatide, and a familiar weekly format.

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

173 **Drug-specific adverse effects: practical summary**

174 **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.

175 Which option is 'more effective'?

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

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

190 Conclusion

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

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