M5.1 — Final Narration Script for Clinical Review

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Audience: Dr. Jeffrey Gross MD **Purpose:** Read-through of the exact narration in the v10 audio (33:30, M5.1-FINAL.mp4) **Source:** `Internal/Module-5-Video-Pipeline/M5.1/M5.1-narration.txt` (with phonetic spellings reversed to canonical drug names for clinical readability) **Generated:** 2026-05-26

What this document is

This is the exact word-for-word script spoken in the M5.1 video lesson v10. The narration text fed to ElevenLabs contained phonetic respellings like “sem-uh-GLOO-tide” so the voice model pronounced drug names correctly. Those phonetic spellings have been reversed here back to canonical forms (semaglutide, tirzepatide, etc.) for your reading.

The script reflects ALL clinical edits from your earlier review (PMID-traced ying/yang glucagon paragraph, MASH expansion, anti-aging framing, etc.) PLUS the new B2 hormone-framing update from Daria’s recent direction (peptide therapy can run alongside hormone optimization; specific baseline lab categories).

Reading time: ~25 minutes at clinical-review pace. **Audio playback time:** 33:30.

The script

Welcome to Module 5.1 — Pharmacology of Weight-Loss Peptides.

Here’s what this lesson covers.

The biology that defends weight — five hormone axes, the hypothalamic set point, and the data on why diets fail over years.

The nine compounds that have reshaped this field in the last five years — including the first small-molecule GLP-1.

The safety profile across five fronts — cancer, pancreatitis, NAION, suicidality, pregnancy.

The four conversations that come up repeatedly when any of these medications is being considered.

And the adjunctive layer — what gets added to the GLP-1 backbone for lean-mass preservation, visceral-fat targeting, and skin laxity.

The frame is biology, not blame. Without blaming anyone for the last fifteen years, and without overpromising the next fifteen.

Now — the story that makes all of this matter.

Fifteen years of diets. Atkins. Weight Watchers. Whole30. Keto. Intermittent fasting.

Every one of them worked — for a while. Twenty pounds lost, then twenty-plus back. Each time, she blamed herself. Eat less, move more, try harder.

Her sister is on semaglutide. Lost forty pounds. Says the food noise is gone.

The questions she's bringing are real. Will it work for me. Is it cheating. Will I gain it all back the moment I stop.

That's the conversation we're here to have.

How that conversation goes depends on whether obesity is understood as a willpower problem or as a chronic neuroendocrine disease — with a defended set point and decades of hormonal and metabolic adaptation working against the person trying to lose weight.

The next eighteen months are bringing new compounds into the field that most people have not heard of yet. The pipeline is not slowing.

And the people who can adapt as the evidence evolves are the ones who understand the underlying biology. The neuroendocrine signaling. The set-point defense. The receptor pharmacology. Not just the current dosing chart.

One note before we go further. These peptides work best on a known terrain.

Get a baseline. Thyroid. Sex hormones. Metabolic markers. Inflammation. Plus the lifestyle pillars — sleep, stress, nutrition, training.

Peptide therapy can run alongside hormone optimization. sermorelin, CJC-1295 with ipamorelin, kisspeptin, gonadorelin, BPC-157, and thymosin alpha-one cover that work — those live in other modules of this course.

For decades, mainstream medicine told people with obesity their problem was behavioral. Eat less. Move more. If it didn't work, you weren't trying hard enough.

That advice has failed two generations. And the data showing why has been sitting in the literature the whole time.

Here's the central idea.

The body has a thermostat for weight. Not one you set — one that's already set, somewhere in the hypothalamus, calibrated to a target.

When weight rises above that target, the brain ratchets the target up. When weight drops below it, the brain defends. And it defends hard.

That target is the set point.

We have data going back to the early nineties showing what happens when people lose weight through caloric restriction alone.

The body doesn't just stop losing — it actively pushes back.

Resting metabolic rate drops. Hunger hormones rise. Satiety hormones fall. Thyroid signaling shifts. The brain treats the weight loss as a problem to solve.

And it stays in problem-solving mode. Not for weeks. Not for months. For years.

The classic metabolic-chamber work showed that after about a ten percent body-weight loss, total energy expenditure drops on the order of three to four hundred kilocalories per day for a typical adult.

That headwind persists.

The Biggest Loser cohort — contestants from the TV show — were followed for six years after the competition. At year six, the metabolic adaptation was still there. Roughly five hundred kilocalories per day below baseline.

So when someone who lost forty pounds finds the weight coming back even though their behavior hasn't changed, the question isn't what did they do wrong.

The question is: how is the biology defending the lower weight they fought to achieve?

This is the frame shift.

Obesity is not a failure of discipline. It's a chronic, biologically defended state. The brain perceives the higher weight as correct, and it spends years trying to get back there.

By the way, this is how we treat chronic disease in every other system. We don't tell hypertensive patients to relax more. We treat the biology at the cellular level.

And in the last five years, for the first time, we have a portfolio of medications that genuinely intervene in the biology of weight regulation. That portfolio is widening.

When years of shame from failed diets shape someone's story of themselves, the pharmacology isn't just delivering a treatment. It's rewriting that story.

The new story is true: the body has been defending a higher set point with measurable changes no one could have overridden through willpower. The medications we'll talk about reduce the size of that defense. They don't replace the work. They make the work biologically achievable.

That reframe is not preamble to obesity care.

It is obesity care.

So if obesity is hormonally defended — what hormones are we talking about?

There are four to know well, and now in 2026, a fifth axis that the new generation of peptide medications has brought into clinical relevance.

Fat tissue is not inert. It's an endocrine organ.

Adipocytes — fat cells — release a hormone that travels to the brain and tells it the fuel tanks are full. That hormone is leptin.

Healthy lean physiology works like this: you eat, you store, leptin rises, the brain hears the signal, appetite drops. The thermostat works.

In established obesity, circulating leptin is high — sometimes very high — but the hypothalamus stops responding to it. The signal is screaming, and the receiver has gone deaf.

That's leptin resistance. It's analogous to insulin resistance. Plenty of hormone in the bloodstream, but no functional response at the target tissue.

People with obesity are not failing to feel full because they're greedy. They're failing to feel full because the satiety signal isn't being received. The brain perceives a state of fuel deficit even when fat stores are excessive.

From the inside, it feels like hunger. And it is hunger — real hunger, mediated by the same circuits that tell a starving person to eat.

Now the opposite signal. Ghrelin. The hunger hormone.

Released from the stomach when it empties. Rises before meals. Falls after eating.

In established obesity, ghrelin patterns are dysregulated, and during caloric restriction, ghrelin climbs higher and stays elevated for years.

That's part of why diets fail in year three when they worked in month three. This is the main reason behind yo-yo dieting.

Third, insulin.

In the context of weight, insulin is anabolic: it pushes glucose into cells, suppresses lipolysis, and promotes fat storage. Too much fat storage equals obesity.

Insulin resistance, common in obesity, means more circulating insulin is required to do the same metabolic work. More insulin means more storage signal, and the system spirals. Carbohydrates, particularly simple sugars, trigger insulin release — and over time, act as pro-inflammatory drivers.

Fourth, the incretins. GLP-1 and GIP.

But first, you need to know about glucagon. Like most body chemistry, there is a ying and yang. A response, and an anti-response to dampen and control these pathways, unless they get over-run. Glucagon, a hormone in the secretin family, is released when blood sugar drops. Where insulin is the anabolic driver (growth), glucagon is the catabolic driver (burning mode).

GLP-1 is glucagon-like peptide one, released from the L-cells of the distal small intestine after meals. It does three things that matter for weight. It slows gastric emptying, which keeps you feeling full since your stomach maintains food in it longer. It enhances glucose-dependent insulin secretion. And critically, it acts on hypothalamic and brainstem circuits, at the reward center, to reduce appetite and food intake.

GIP, glucose-dependent insulinotropic polypeptide, is a parallel incretin from the K-cells of the proximal small intestine. Overlapping and distinct biology from GLP-1.

We are constantly learning more about GIP's role in adipose tissue, and the GIP biology is part of why the dual coagonists like tirzepatide, retatrutide, and others, have the impact that they do.

And now the fifth axis, amylin.

Amylin is co-secreted with insulin by the pancreatic beta-cell. It has two roles that matter for weight. It slows gastric emptying, mechanism-overlapping with GLP-1. And it acts on the area postrema and nucleus tractus solitarius in the brainstem to drive satiety, also at reward centers.

Think of amylin's receptor as a locked door in the brainstem.

Native amylin signals through the calcitonin receptor, but only when that receptor is complexed with a receptor-activity-modifying protein — RAMP one, RAMP two, or RAMP three.

The RAMP proteins are like keys that change the shape of the lock. Without a RAMP attached, amylin doesn't fit. With a RAMP attached, amylin binds perfectly and delivers the stop-eating message.

That's the receptor architecture. Three RAMP variants create three receptor subtypes, AMY one, AMY two, AMY three, and that's where compounds like cagrilintide engage.

Why does all this matter now?

Because cagrilintide, a long-acting synthetic amylin analog, entered clinical relevance in this past year as studies show fat loss benefits, and it is the amylin half of cagrisema.

We have, for the first time in obesity pharmacology, a deliberate dual-axis intervention: GLP-1 plus amylin. The two pathways converge on satiety but engage different receptor families, different brain circuits, and different post-meal time windows.

You can also tie the parasympathetic vagal afferents into this. Gastric stretch, nutrient sensing in the duodenum, vagal signaling to the hindbrain — those circuits are how the gut tells the brain it's been fed.

Many of the new compounds modulate that pathway directly or indirectly.

So that's the cast.

Leptin. Ghrelin. Insulin. The incretins — GLP-1 and GIP. And amylin. Five axes.

The medications we'll discuss intervene at one, two, three, or all of these. That's not metaphor — that's the actual receptor pharmacology.

And anyone with established obesity has every one of these axes working against them.

Look AHEAD is one of the most important diabetes-obesity trials ever conducted.

Five thousand patients with type 2 diabetes. Randomized to intensive lifestyle intervention or standard care. Eight years of follow-up.

At year one, the intervention group had lost about eight and a half percent of body weight. Real success.

At year nine — median follow-up — they were at about six percent below baseline. Still better than control, but the trajectory was clear: the body had been steadily clawing back what they fought to lose.

The Diabetes Prevention Program — three thousand patients at high diabetes risk, randomized to lifestyle, metformin, or placebo. The lifestyle arm did reduce diabetes incidence by 58 percent. But the average weight loss at follow-up was about five and a half kilograms.

Meaningful for diabetes prevention. Modest for obesity care.

These were the gold-standard, intensively-resourced lifestyle interventions in modern medicine. And the answer was: lifestyle works partially, modestly, and the biology fights back continuously.

What was missing from the equation was a way to reduce the defense itself. To turn down the gain on the hunger signal. To lower the set point.

That's what changed in the last decade or so.

So here's where the field actually is right now, in 2026.

For the first time, there is a portfolio of agents that intervene directly in the neuroendocrine biology of weight regulation. The classes are worth knowing because all of them are being asked about.

semaglutide, an incretin mimetic, as a glucagon-like peptide one agonist, is the anchor peptide. Weekly subcutaneous injection.

The two anchor studies.

STEP-1 study in 2021 showed about fifteen percent body weight loss at 68 weeks.

SELECT study in 2023 showed a twenty percent reduction in major adverse cardiovascular events, in patients with obesity and established cardiovascular disease. A hard cardiovascular outcome — not just weight.

So semaglutide is not “a weight-loss drug.” It’s an intervention with cardiovascular, kidney, and hepatic benefit, and weight reduction is one of several outcomes. And by weight loss, we are really talking mostly, but not only, adipose tissue.

liraglutide is the daily-injection predecessor. It is also a glucagon-like peptide one agonist.

Approved for type 2 diabetes in 2010, for weight management in 2014, and uniquely, for adolescents with obesity.

liraglutide remains relevant, particularly for pre-conception use given its short two-day washout versus semaglutide’s roughly thirty-five days, and for pediatric obesity where it has the longest clinical track record. Clearly though, it is less convenient than semaglutide.

Then there’s Rybelsus, oral semaglutide. Same molecule as the injectable.

Oral peptide absorption is normally negligible, so the formulation uses a permeation enhancer called SNAC, sodium N-eight, two-hydroxybenzoyl amino caprylate, to get clinically meaningful absorption.

It has to be taken on an empty stomach with thirty minutes of water-only waiting.

That formulation context matters.

tirzepatide. One molecule, dual receptor activity at both GLP-1 and GIP.

The two anchor studies: SURMOUNT-1 study in 2022 showed 20.9% body weight loss at 15 mg at 72 weeks. SURMOUNT-5 study in 2025 was the direct head-to-head between those two peptides, tirzepatide at 20.2% versus semaglutide at 13.7% at week 72.

That is the only head-to-head we have.

tirzepatide is approved for marketing claims across three indications: type 2 diabetes, chronic weight management, and moderate-to-severe obstructive sleep apnea with obesity.

retatrutide. One molecule, three receptors: GLP-1, GIP, and glucagon.

The glucagon component adds a thermogenic, catabolic, dimension that the dual coagonists don’t have.

The TRIUMPH-4 study reported 28.7% body weight loss at the 12 mg dose.

survodutide is in late-stage development, with Breakthrough Therapy designation in MASH, previously called non-alcoholic fatty liver accumulation. Topline obesity readout was about 16.6% body weight loss.

cagrilintide as a standalone study demonstrated about 11.8% body weight loss at 68 weeks. Single-mechanism, different from anything else in the field discussed so far.

cagrisema combines cagrilintide and semaglutide. The combo arm reported about 22.7% body weight loss in obesity without diabetes.

And note the structural distinction. cagrisema is two separate molecules co-administered in one injection, not a single-molecule multi-agonist like tirzepatide. Different strategy for similar pharmacological footprint.

Then icosema, insulin icodec plus semaglutide, is a Type 2 diabetes-focused combination.

orforglipron. We discuss it here since it fits in the topic discussion nicely.

This is not a peptide. It’s a spiropiperidine small molecule.

Think of a peptide like semaglutide as a long, delicate string of pearls. Stomach acid snips it apart easily. A spiropiperidine is more like a tightly interlocked 3D cage made of carbon and nitrogen rings. Stomach acid can’t break those bonds.

That’s why orforglipron needs no permeation enhancer, no empty-stomach timing window, full oral bioavailability.

The Phase 3 study readouts in 2025 showed about 11.2% body weight loss in obesity. Smaller magnitude than the high-dose injectables, but the oral platform opens access in ways injection-only therapeutics cannot.

Among practitioners working at the frontier, retatrutide is increasingly the agent being reached for first when it becomes accessible.

The triagonist mechanism — the glucagon component on top of the GLP-1 and GIP coagonism — has translated, in real-world use, to additional benefits, fewer side effects in people who didn’t tolerate prior compounds, and more effective weight-loss magnitude.

Practice population and individual judgment will calibrate this for any specific case.

The lesson here is that the field is moving toward triagonist therapy fast enough that thinking should be in that direction now, even before formal approval changes the access landscape.

Seven mechanism distinctions.

The question “which peptide” is no longer a one-on-one choice. It’s a phenotype-guided selection problem across seven mechanism distinctions. Access is also a factor.

We’ll dig into each compound in the lessons that follow. The roadmap is on screen now. Each compound gets its own deep-dive lesson, followed by the adjunct lessons on visceral fat, lean-mass preservation, skin laxity, titration, labs, and case construction.

For now, the pearl is this. The question is no longer whether pharmacology can move obesity. It does.

The question is how to match the right peptide to the right phenotype, monitor the right things, and walk through what is and isn’t known. Patient preparation, education, and informed consent are always paramount.

Safety questions come up. Five fronts are worth knowing.

A moderate-certainty 2026 systematic review pooled forty-eight randomized trials with nearly 95,000 patients across eleven cancer types plus multiple myeloma and meningioma.

Bottom line: GLP-1 receptor agonists show little or no effect on the risk of obesity-related cancers in the populations studied, at the durations studied.

There are individual database signals that pull against this — a French national database in 2023 found a positive thyroid cancer signal that has not been consistently reproduced.

So we know one positive signal in one large dataset, alongside a moderate-certainty meta-analysis showing little or no effect at the class level. That’s the honest picture.

The thyroid C-cell concern in particular goes back to rodent studies showing C-cell proliferation on chronic GLP-1 receptor agonist exposure.

That finding led to the medullary thyroid carcinoma label in the United States.

It’s important to know that rodents have much higher C-cell density and much higher GLP-1 receptor density on those cells than humans, and the prospective human signal has not converged.

Personal or family history of medullary thyroid cancer remains a label-level contraindication, and it should be acted on. But for the broader population, the meta-analysis is what the evidence shows.

For pancreatitis, a 2025 systematic review pooling sixty-two trials and sixty-six thousand patients found a pooled relative risk of acute pancreatitis of about 1.44 — statistically significant, modest in absolute terms.

Pancreatic cancer separately was at a relative risk of 1.30, with confidence interval crossing one — not statistically significant.

Personal history of pancreatitis pushes the risk-benefit assessment toward a different agent class.

Non-arteritic anterior ischemic optic neuropathy — NAION.

Multiple analyses across 2024 and 2025 — including a Danish nationwide cohort of over 400,000 — confirmed a signal with semaglutide.

The tirzepatide signal is absent at the same statistical threshold — but that needs to be interpreted carefully, because tirzepatide has been on the market for a much shorter time.

The European Medicines Agency has labeled the semaglutide signal explicitly. NAION risk is low in absolute terms — but the eye-symptom-monitoring conversation matters, particularly for people who already have predisposing factors.

For suicidality, the major 2024 case-time-control analysis reported an odds ratio of about 0.62 — protective, not harmful — in GLP-1-exposed people versus comparators.

This is reassuring in the short-term psychiatric safety domain, and worth knowing given the social-media coverage that has been less reassuring.

For pregnancy, pooled regulatory-submitted exposure data across semaglutide, liraglutide, dulaglutide, and class-related compounds showed congenital abnormality incidence appearing relatively low. Sample size is limited; exposures were unplanned-pregnancy contexts.

Standard practice when pregnancy occurs or is planned: discontinue. For planned pregnancy on semaglutide, that's a roughly two-month washout because of the elimination half-life. On liraglutide it's roughly two days.

That difference is part of how to select between the two if the person is in reproductive years and pregnancy is on the horizon.

The class is well-characterized at this point.

The risks are quantified, the contraindications are clear, and the absolute event rates for the rare signals — NAION, pancreatitis — are low.

This isn't a black-box class. It's a well-characterized one — known signals, known contraindications, known monitoring approach.

Compounded semaglutide and tirzepatide are real-world clinical options used by a substantial patient population.

They emerged during the 2022 to 2024 shortage periods and continue through 503A state-licensed pharmacies and 503B FDA-registered outsourcing facilities for specific use cases.

The 503A and 503B regulatory enforcement landscape has evolved through 2025. Check the current state at the time of each prescription.

Here's what you tell patients who ask.

Compounded GLP-1 is a real option used by many patients. The operational differences from Wegovy or Ozempic or Mounjaro are real.

Lyophilized vial requiring reconstitution rather than pre-filled pen.

Different oversight pathway.

Different storage profile.

Costs are typically lower. The patient self-administers using technique similar to insulin self-injection.

You do not lead with “it’s not Wegovy” or “it’s not approved.” The molecule, semaglutide, tirzepatide, is approved for marketing claims for its on-label indications. What differs in the compounded preparation is the supply pathway, not the molecule’s approval status.

You will find patients seeking these peptides, and they will likely benefit from them even if their regular doctor, or worse, their insurance, would not prescribe or cover the cost.

You lead with what it is. A real clinical option with operational characteristics you and the patient evaluate together. The decision is theirs to make with full information.

If your patient is considering compounded, review the specific compounding pharmacy’s quality practices.

Sterility testing per USP 797 and 800.

Per-batch certificate of analysis showing peptide content, purity, residual solvents, and endotoxin.

Cold-chain shipping documentation.

State-licensure verification or FDA registration verification.

Walk through reconstitution training with the patient. Be specific. Bacteriostatic water volume. Drawing technique with a thirty-gauge insulin syringe. Storage at 2 to 8 degrees Celsius for the reconstituted vial across the dosing window.

That training is part of how the decision gets made well.

Three patient conversations come up repeatedly.

The first is the comparison between peptides.

Both semaglutide and tirzepatide are evidence-based weight-management options.

The direct head-to-head, SURMOUNT-5 study in 2025, showed tirzepatide produced about 6.5% more weight loss than semaglutide at the doses each had achieved by week 72. So tirzepatide does produce more weight reduction in average terms.

Beyond that, the peptides differ on cardiovascular outcomes evidence, on MASH approval status, on kidney outcomes evidence, on ophthalmologic-signal differentiation, on side-effect profiles, on cost, and on access.

Those are the dimensions to discuss based on individual situation.

The second is the question about microdosing or use in lean bodies for general longevity.

The cardiovascular benefit of semaglutide was demonstrated in adults with body mass index of 27 or higher who already had established cardiovascular disease. The weight-management benefit was demonstrated in adults with obesity or with overweight and a weight-related comorbidity. The kidney benefit was demonstrated in type 2 diabetes with chronic kidney disease.

So when the question is microdosing for general longevity or metabolic optimization in a lean person without those diagnoses, we're extrapolating beyond the trial populations to a question the trials weren't designed to answer.

And just so we are on the same page, microdosing could be simply a lower weekly dose, or even lower twice-weekly doses, that are below the weight-loss effect, but enough to continue to enhance the insulin glucagon and other hormonal axes for long-term benefits.

The known side effect profile, gastrointestinal effects, gallbladder events, the pancreatitis signal, the NAION signal, applies whether the use case is in the studied population or not. Whether the cardiovascular and metabolic benefit extrapolates is research-state-incomplete.

The conversation is honest. Here's what's known, here's what's an open question, and here's what monitoring would matter if the decision is to proceed.

The third is what happens when the medication stops.

Body weight is a chronically defended physiologic variable. When the medication stops, the biology that was being modulated returns.

The STEP-1 study extension data and the SURMOUNT-4 study withdrawal arm both showed that on average, people regain a substantial fraction of the weight lost after stopping. Some keep more of the loss than others.

That doesn't mean the treatment failed. It means weight management is a chronic-disease management problem, similar to how hypertension and dyslipidemia work.

Long-term planning is the same conversation as antihypertensive therapy. Stopping is an option. Tapering is an option. Lower-dose maintenance is an option some people use. The plan can adjust as it goes.

A word about the injection itself, because patients sometimes ask.

Self-injection is a routine clinical skill. We teach it every day for insulin, for fertility hormones, for biologics, for the weekly GLP-1 therapeutics.

The needle is fine, twenty-nine to thirty-two gauge. The depth is subcutaneous, not muscle, skin-deep. We demonstrate the technique in one office visit, and patients refine it over the first two or three self-administrations.

The pre-filled auto-injector pens, Wegovy, Ozempic, Zepbound, Saxenda, make it even simpler. You click a button. The dose is pre-measured. The needle retracts.

For compounded preparations, add reconstitution and drawing with an insulin syringe, also a learned skill.

The thing the patient is going to ask you about three weeks in is not the injection. It is dose-titration tolerance, the gastrointestinal effects, the escalation cadence, the side-effect management.

That is the substantive question. The injection itself is a routine clinical skill, not a barrier to treatment.

The thread connecting all three conversations is the same.

Present facts. Don’t steer toward an answer. Invite shared decision-making.

One more concept before we close, because Module 5 has lessons on it.

GLP-1 class compounds produce weight loss that is, on average, about 25 to 40 percent lean mass loss alongside fat-mass loss.

That’s not a defect — it’s how the body unloads tissue when fuel intake drops. But it has clinical consequences: Reduced lean mass means reduced resting metabolic rate. Reduced physical function. And it’s a contributor to weight regain when the medication stops.

The adjunctive layer in Module 5 — lessons five through seven — addresses this: tesamorelin and AOD-9604 for visceral and adipose-fat targeting. CJC-1295 with ipamorelin and MOTS-c for lean-mass preservation through pulsatile growth hormone signaling. GHK-Cu for post-weight-loss skin laxity through collagen and elastin synthesis stimulation.

The evidence base for the adjunctive layer is thinner than for the GLP-1 backbone.

We’ll be specific about what’s mechanism-strong but trial-state-incomplete.

The framing for those lessons is honest: the choice to add an adjunctive intervention is based on mechanism rationale plus practitioner experience plus a willingness to monitor in the absence of definitive Phase 3 evidence for that specific use case.

That’s a legitimate clinical decision space. It’s how peptide therapy practice works, and it’s how it should be discussed.

So — back to the person with fifteen years of failed diets and a sister on semaglutide.

The conversation:

This is biology, not blame.

There’s a class of medications that genuinely intervene in the biology of weight regulation, and a portfolio of compounds within that class to choose from.

Walk through the choices, in plain language. Let the dimensions that matter for the individual life pick themselves — magnitude, cardiovascular history, kidney status, oral versus injection, cost, access, the long-term planning question.

State what's known about safety, and what's still being characterized.

This is chronic-disease management — like blood pressure — and the plan adjusts as it goes.

What walks out with a prescription is two things. A treatment. And a story about a body that's truer than the one walked in with.

That's obesity care in 2026. It is body composition management. It is visceral fat loss. It is healthy metabolic adjustment, and much more.

Next lesson — M5.2 — we go deep on semaglutide itself.

The trial portfolio. The dosing escalation. The titration. The clinical decisions specific to that compound. And the conversations your patients will bring you about it.

See you there.

End of script. See accompanying M5.1-DR-GROSS-REVIEW-PACKET.md for the document-by-document review brief covering the 12 supporting docs that ship with this lesson.