

KEYNOTE · SLEEP & METABOLIC MEDICINE

Obesity, Obstructive Sleep Apnea & the New Treatment Landscape

From airway management to metabolic disease modification

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BEFORE



140 LBS OF SUGAR



140 LBS OF POTATOES

ROBERT'S STORY

14

ten-pound bags

140 lbs

lost

“Doc, that’s how much weight I was carrying on me.”

No medications.
Nutrition and behavior change
alone.

THE QUESTION

Are we treating OSA... or just managing symptoms?

For decades, our standard of care has been mechanical airway support — powerful, but it leaves the underlying disease untouched. With obesity rising and PAP adherence stubbornly low, is that enough?

The Patient in Your Sleep Clinic Today

BMI

41 kg/m²

AHI

52 /hr

BLOOD PRESSURE

Hypertensive

GLYCEMIA

Prediabetes

LIVER

MASLD

TESTOSTERONE

Low

THE CLINICAL QUESTION

Is this purely obstructive sleep apnea — or an integrated metabolic phenotype that needs disease-modifying therapy?

We'll return to this patient at the end.

Learning Objectives



Pathophysiology & CPAP

- How adiposity collapses the airway
- What CPAP treats — and misses
- How weight change moves AHI



Clinical Trial Evidence

- SURMOUNT-OSA: AHI & hypoxic burden
- SURMOUNT-1 & -3: lifestyle + medication
- SURMOUNT-4: what sustains results



Reassessment & Endocrine

- When to re-evaluate PAP
- Getting patients Inspire-ready
- Hormones & MHT in men and women



The Need for Integrated Care

- Medication + nutrition + behavior change
- Dosing, plateaus & side effects
- Continuity when coverage changes

PART 1

The Problem

Why an open airway isn't the same as a treated disease

Why Excess Adiposity Collapses the Airway



Upper-airway fat

Parapharyngeal and tongue fat directly narrow the lumen and raise collapsibility.



Reduced lung volume

Lower functional residual capacity weakens caudal tracheal traction on the pharynx.



Abdominal load

Visceral fat restricts the diaphragm, especially during supine sleep.



Inflammatory signaling

Adipokine and cytokine imbalance blunts upper-airway dilator muscle responsiveness.

Obesity is the leading modifiable cause of upper-airway collapse.

OSA Triggers a Downstream Cascade



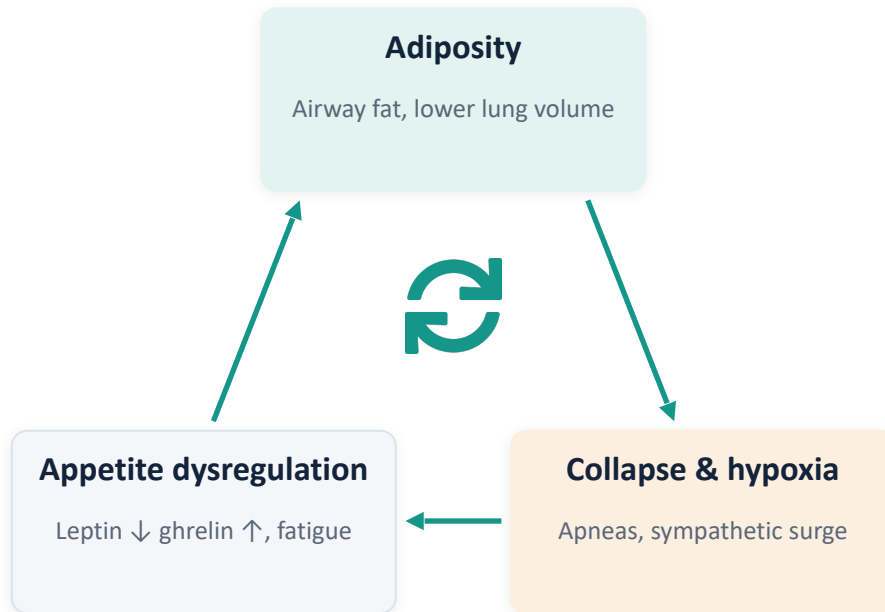
Leading to coexisting cardiometabolic disease



Obesity and OSA Feed Each Other

Weight gain increases airway collapse. Nocturnal hypoxemia and fragmented sleep then disrupt leptin and ghrelin signaling — driving daytime fatigue, hyperphagia and further weight gain.

Treating the airway alone leaves the underlying metabolic driver active.



What CPAP Does Very Well — and What It Doesn't



CPAP does very well

- Acts as a pneumatic splint against upper-airway collapse
- Eliminates apneas and hypopneas when used
- Improves daytime sleepiness and quality of life
- Modestly lowers blood pressure in adherent patients



CPAP does not

- Reduce adipose tissue or visceral fat
- Correct insulin resistance, MASLD or dyslipidemia
- Alter appetite or energy dysregulation
- Work on the nights it isn't worn — adherence is the limit

CPAP treats the airway. It does not treat the disease driving the airway.

Small Changes in Weight Move AHI Substantially

+32%

AHI with a 10% weight gain

-26%

AHI with a 10% weight loss

-57%

Mean AHI with ~20% BMI
loss

The response is non-linear: meaningful OSA improvement comes well before a normal BMI.

Peppard PE et al. JAMA 2000 (10% change data); meta-analytic data (~20% BMI loss).

PART 2

The Evidence

A medication that treats OSA at its source

Obesity Is a Chronic, Biologically Defended Disease



Genetics

Polygenic risk



Neuroendocrine

Hypothalamic appetite resistance



Insulin resistance

Altered nutrient partitioning



Sleep disruption

Higher nocturnal cortisol



Adaptation

Lower resting energy expenditure



Hormonal drivers

Hypogonadism, thyroid shifts

The body defends its set point

- Ghrelin rises (more hunger)
- GLP-1 and PYY fall (less satiety)
- Adaptive thermogenesis lowers energy expenditure

Anti-obesity medications act on these central pathways to make weight loss durable.



PATIENT SPOTLIGHT · NEW VIVA MD

100 lbs lost

Biology pushes back — but it can be overcome.

Medication quiets the drive to regain. Nutrition and behavior change turn that window into lasting habits.

40–50% of body weight
lost

5+ yrs maintained, since
2019

Shown with patient permission. Individual results vary.

Weight Management Is Part of OSA Treatment

American Thoracic Society (2018): all adults with OSA who are overweight or obese should receive comprehensive weight-loss intervention.



Reduced-calorie diet



Physical activity



Behavioral counseling

ADJUNCTS TO CONSIDER

- Anti-obesity medication
- Medical weight loss program
- Tirzepatide now FDA-approved for OSA (2024)

Hudgel DW et al. Am J Respir Crit Care Med 2018.

The Anti-Obesity Medication Landscape



GLP-1 receptor agonists

Liraglutide · Semaglutide

Glucose-dependent insulin secretion, satiety and slowed gastric emptying.



Dual GIP / GLP-1 agonist

Tirzepatide

Complementary GIP + GLP-1 activation; largest mean weight loss; FDA-approved for OSA.



Oral, centrally acting

**Phentermine/topiramate ·
Naltrexone/bupropion**

Appetite suppression via central catecholamine and reward pathways.

Only tirzepatide carries a specific indication for obstructive sleep apnea.

Tirzepatide: Dual Agonism, Dose-Dependent Loss

GIP receptor agonism

Nutrient sensing & lipid metabolism

+

GLP-1 receptor agonism

Satiety & delayed gastric emptying

**≈21% mean weight loss at 72 weeks
(15 mg)**

SURMOUNT-1: Adding Tirzepatide to Lifestyle

THE STUDY

NEJM 2022 · n=2,539 · 72 weeks

- Obesity, or overweight + complication; no diabetes
- Tirzepatide 5, 10 or 15 mg vs placebo
- Everyone received lifestyle counseling

57% vs 3%

reached $\geq 20\%$ weight loss,
tirzepatide vs placebo

95% vs 62%

prediabetes reverted to
normal glucose

CONCLUSION Not medication vs lifestyle — lifestyle plus medication vs lifestyle alone.

AHI Fell by Roughly Half — With or Without PAP

TRIAL 1 • DIFFERENCE VS PLACEBO

−20.0 /hr

−50.7% vs −3.0% AHI change · P<0.001

TRIAL 2 • DIFFERENCE VS PLACEBO

−23.8 /hr

−58.7% vs −2.5% AHI change · P<0.001

Response Rates and Weight Loss at Week 52

	Trial 1 · Tirzepatide	Trial 1 · Placebo	Trial 2 · Tirzepatide	Trial 2 · Placebo
Mean % change in AHI	−50.7%	−3.0%	−58.7%	−2.5%
≥50% AHI reduction	61.2%	19.0%	72.4%	23.3%
Mean body-weight change	−17.7%	−1.6%	−19.6%	−2.3%

Magnitude of weight loss tracked closely with the magnitude of AHI improvement.

Benefits Extend Past the Event Count



Hypoxic burden

Significant reduction in depth, duration and frequency of desaturation.



Systolic blood pressure

Statistically significant reductions vs placebo.



hsCRP

Marked decrease in systemic inflammation.



Patient-reported outcomes

Less sleep-related impairment and sleep disturbance (PROMIS).

Why it matters: hypoxic burden predicts cardiovascular mortality more strongly than AHI alone.

What We Can Confidently Conclude



Tirzepatide substantially reduces OSA severity in adults with obesity

AHI fell ~51–59% over 52 weeks in moderate-to-severe OSA, with or without PAP.



Benefits extend beyond the event count

Hypoxic burden, systolic BP, hsCRP and patient-reported sleep outcomes all improved.



Metabolic therapy and PAP are complementary

Adding tirzepatide to ongoing PAP produced further improvement — the therapies work on different targets.

What the Data Does NOT Establish



That tirzepatide replaces PAP

Many patients retained clinically significant OSA; PAP remains indicated until objective retesting says otherwise.



Long-term hard outcomes

No data yet on cardiovascular events or mortality in OSA; the trials ran 52 weeks.



Durability after stopping — or use outside the trial population

Weight regain after discontinuation is expected; mild OSA and OSA without obesity were not studied.

December 20, 2024

FDA approves Zepbound® (tirzepatide) for moderate-to-severe obstructive sleep apnea in adults with obesity



First medication approved to treat OSA itself — not just daytime sleepiness



Used together with a reduced-calorie diet and increased physical activity

PART 3

Beyond the Prescription

What turns a trial average into a lasting result

Obesity Isn't Treated Like Hypertension

Condition	Treatment model	Medication alone enough?	Role of lifestyle	Disease mechanism
Hypertension	Antihypertensives	Yes — usually reaches target	Supportive	Single pathway: vascular tone / volume
Hyperlipidemia	Statins ± combination	Yes — routinely normalizes LDL	Supportive	Single pathway: hepatic synthesis
COPD	Inhaled therapies	Yes — primary driver of control	Smoking cessation matters	Single organ: airway inflammation
Obesity	Medication + nutrition + exercise + behavior + hormones	No — incomplete, often unsustained	Required, not optional	Multifactorial: genetic, hormonal, neuroendocrine, behavioral

Obesity is a chronic, multisystem disease. It needs a multisystem treatment plan.

In Obesity, a Higher Dose Isn't Always More Weight Loss

Hypertension · Lipids

- Higher dose → more BP / LDL lowering
- Titrate to a numeric target
- Predictable dose–response

Obesity

- Higher dose ≠ more weight loss for every patient
- Response is individual; may peak at a lower dose
- Side effects increase with dose

SURMOUNT-1: THE CURVE FLATTENS

+4.5 pts 5 → 10 mg

+1.4 pts 10 → 15 mg

Escalate



Weight loss has stalled and the current dose is well tolerated

Hold



Steady weight loss, or mild side effects still settling

De-escalate



Side effects limit protein, fluids or daily life — or entering maintenance

Titration monitoring is the most crucial step. The goal is the lowest effective dose, not the maximum dose.

Do Patients “Adapt” to GLP-1 Medications?

Sometimes — but it’s not simply “GLP-1 resistance.”



Weight loss slows

The body adapts as weight falls; a plateau is common



Appetite effects persist

Hunger stays lower and satiety higher, even after loss slows



Gastric emptying adapts

The stomach-slowing effect fades with continued treatment



The body fights back

Lower weight means lower energy needs and stronger regain signals

A PLATEAU ≠ MEDICATION FAILURE

Before changing therapy, check:

- Dose and adherence
- Nutrition and activity
- Sleep (including untreated OSA)
- Weight-promoting medications
- Underlying metabolic and hormonal factors

Key takeaway: a plateau often reflects normal biological adaptation to weight loss — not resistance to GLP-1 therapy.

Nutrition & Behavior Are Part of the Treatment

THE STUDY

Joint advisory: ACLM · ASN · OMA · The Obesity Society (2025) + scoping review of 129 GLP-1 trials

- Nutrition priorities for GLP-1 therapy
- Pivotal trials all paired drug with lifestyle counseling
- How often trials actually tracked diet

15–21%

Weight loss in STEP 1,
STEP 3 and
SURMOUNT-1 — drug
plus lifestyle
counseling

28%

of 129 GLP-1 trials
assessed dietary intake

8%

actually reported it

CONCLUSION Trial results assume nutrition support. Build it in — don't leave it to the patient.

SURMOUNT-3: What If They've Already Tried Hard?

THE STUDY

Nature Medicine 2023 • n=579 • 12 + 72 weeks

- 12-week intensive lifestyle program first
- Then tirzepatide (10 or 15 mg) vs placebo
- Patients had already lost weight before any drug

12 wks

of intensive lifestyle therapy before
randomization

~24.5%

mean total weight loss from original
baseline with tirzepatide

CONCLUSION Medication doesn't replace effort — it builds on it.

Beyond the Trial Average: What a Program Adds

THE EVIDENCE

~21%

SURMOUNT-1: mean loss, medication + standard counseling

~25%

SURMOUNT-3: total loss when intensive lifestyle therapy came first



Structured nutrition

Protein-forward plans that protect lean mass



Behavior change

Coaching on habits, hunger cues and emotional eating



Accountability

Frequent in-clinic weigh-ins and dose adjustment



Movement

Resistance training to preserve muscle

Medication treats the biology. Nutrition and behavior change are what let patients go further.



PATIENT SPOTLIGHT · NEW VIVA MD

151 lbs lost

Trials report the average. Our patients can go further.

SURMOUNT-OSA averaged 18–20% weight loss. With structured nutrition, coaching and close follow-up, some of our patients go much further — and stay there.

40–50% of body weight
lost

5+ yrs maintained, since
2019

Shown with patient permission. Individual results vary.

Preserving Lean Mass During GLP-1/GIP Therapy

THE STUDY

Recent GLP-1/GIP trials + 2025 cohort (n=200) +
2025 multi-society advisory

- Strength training ≥3×/week
- ≥150 min/week aerobic activity
- Protein 1.2–2.0 g/kg/day
- Consider creatine 3–5 g/day

26–40%

of weight lost is lean tissue without
targeted support

13% → 3%

Weight lost vs muscle lost with
strength training + protein (6 months)

CONCLUSION Muscle loss is modifiable. Prescribe protein and strength training with every GLP-1.

Tirzepatide Safety & Tolerability



Common GI effects

- Nausea, diarrhea, constipation
- Vomiting, dyspepsia / GERD
- Mostly mild–moderate, during escalation



Contraindications

- Personal or family history of medullary thyroid carcinoma
- MEN 2 syndrome (boxed warning)
- Prior serious hypersensitivity



Monitor & counsel

- Pancreatitis, gallbladder disease
- Hypoglycemia with insulin / sulfonylurea
- Oral contraceptives; peri-anesthesia aspiration risk

Preserve lean mass during weight loss: adequate protein and resistance training.

Manage Side Effects Early to Keep Patients on Therapy

WHY IT MATTERS

~1 in 3

patients still on a GLP-1 for weight loss at 1 year (real-world claims data)

GI side effects are a leading reason patients stop. Every avoided dropout protects the weight loss — and the OSA benefit.



Nausea & vomiting

Small meals, stop at fullness, avoid greasy food; slow titration



Constipation

Fluids, fiber, activity; bowel regimen early



Reflux & diarrhea

Avoid late and high-fat meals; hydration



Fatigue & dehydration

Protein and fluid targets; check intake



Hair shedding & muscle loss

Adequate protein, resistance training



Red flags

Severe abdominal pain, persistent vomiting — evaluate promptly

Check in after every dose increase · slow or hold titration instead of stopping · counsel before the first dose

Sustaining Weight Loss: What the Evidence Shows

SURMOUNT-4 · JAMA 2024

Stop the drug, lose the result

- 36 weeks of tirzepatide, then randomized
- Continue tirzepatide vs switch to placebo
- Both groups received diet & exercise counseling

−5.5% kept losing +14% regained on placebo

eCLINICALMEDICINE REVIEW · 2026

Regain is biology, not willpower

- Driven by metabolic adaptation, hunger, behavior
- Lifestyle alone has limited effect
- Exercise + liraglutide: ~5 kg less regain at 1 yr
- Gradual tapering beats abrupt stopping

CONCLUSION A hybrid model: continued or tapered medication plus ongoing nutrition and behavior support.

Real Patients: 1,089 Pounds Lost Among Ten



40–50% of body weight lost · maintained for 5+ years, since our clinic opened in 2019

Selected patients shown with permission. Individual results vary.

Zepbound Is Not the Only Path

Anti-obesity medications



Tirzepatide

Zepbound · OSA indication



Semaglutide

Wegovy · injection or oral



Liraglutide

Saxenda · daily injection



Phentermine/topiramate

Qsymia · oral



Naltrexone/bupropion

Contrave · oral



Phentermine & others

Lower-cost oral options

NO MEDICATION? STILL POSSIBLE

Some patients succeed with an integrative approach alone

- Structured nutrition
- Behavior change coaching
- Physical activity & strength
- Sleep & stress management
- Frequent follow-up

Match the tool to the patient.

Only tirzepatide is FDA-approved specifically for OSA.

Losing Coverage Doesn't Mean Stopping Obesity Care



Appeal & re-authorize

Document OSA and comorbidities; the OSA indication can open coverage, including Medicare Part D



Self-pay programs

Manufacturer direct-pay options at lower cash prices



Switch medication

A covered alternative or lower-cost oral option



Intensify the program

More nutrition and behavior support to protect results



Keep close follow-up

Catch early regain and adjust the plan quickly



Protect the airway

Recheck OSA symptoms and PAP needs if weight rises

Stopping abruptly leads to regain (SURMOUNT-4). Plan the transition — never just stop care.

PART 4

The Whole Patient

Airway, Inspire and hormones

Synergy, Not Competition: An Integrated Workflow



CPAP

Targets upper-airway collapse · works from night one



Tirzepatide

Targets the metabolic phenotype · works over months

1

Phenotype

BMI, AHI, BP, glycemia, liver, hormones



2

Airway care

Initiate PAP or oral appliance



3

Metabolic care

Add anti-obesity pharmacotherapy



4

Monitor

Weight, symptoms, PAP data, labs

When to Re-evaluate PAP — and How



Sustained weight loss

15–20% loss maintained



Pressure intolerance

Complaints that pressure feels too high



Symptom resolution

No residual daytime sleepiness



Medical weight loss

Reaching maintenance in a structured program



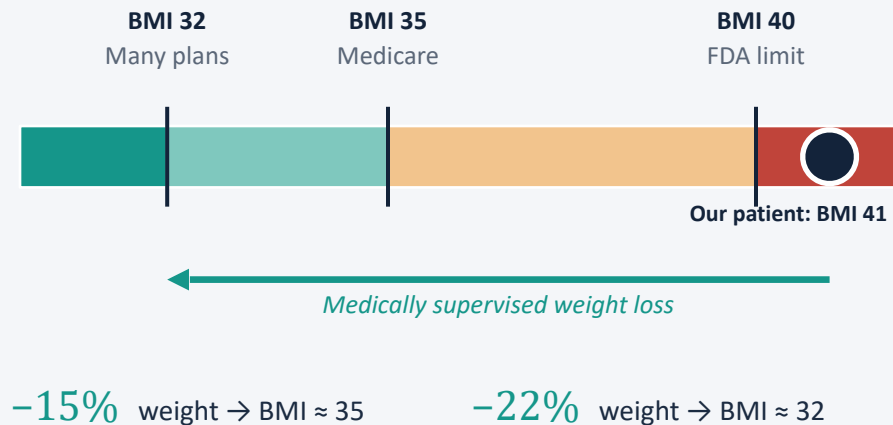
Never assume remission

Retrognathia, positional apnea and residual soft-tissue collapse can sustain OSA despite major weight loss.

Objective testing (HSAT or PSG) before discontinuing PAP.

Weight Loss Opens the Door to Inspire

BMI thresholds for Inspire



Eligibility

Lower BMI meets payer cutoffs (≤ 35 Medicare; $\leq 32-35$ many plans)



Better outcomes

Odds of success drop ~17% per BMI point above 32



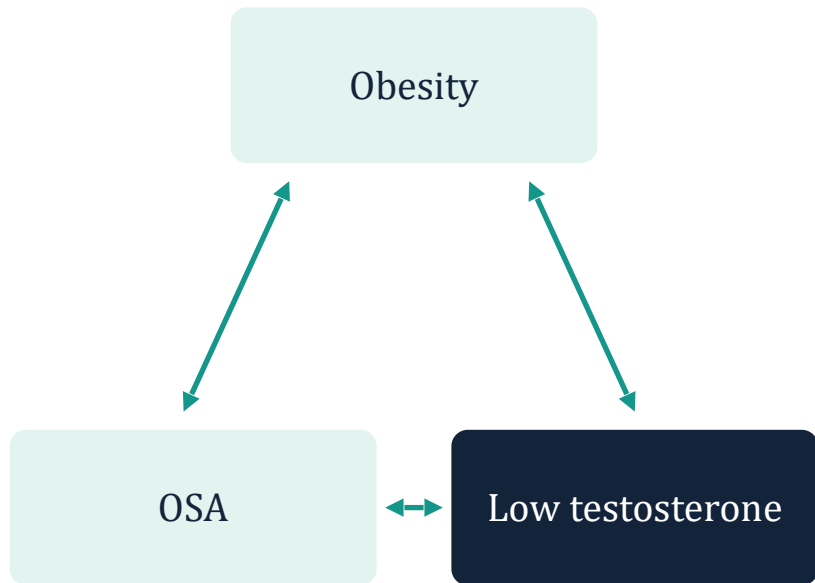
Favorable anatomy

Less airway fat; may bring very high AHI into the 15–100 range



Refer patients above the BMI cutoff. We lower BMI, coordinate retesting, and return them Inspire-ready.

The Hypogonadal–Metabolic Triad in Men



Functional hypogonadism

Visceral fat raises aromatase activity and lowers SHBG.

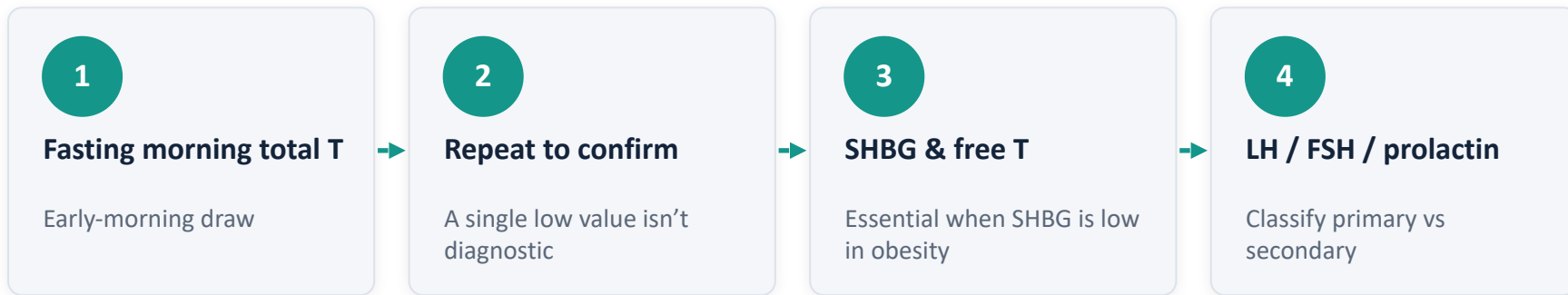
Sleep-axis disruption

Recurrent apneas and fragmentation blunt nocturnal LH pulsatility.



Testosterone therapy can worsen OSA.
Screen for and treat OSA before starting TRT.

Evaluating Testosterone in Men with OSA and Obesity



EMERGING DATA · 2025 PILOT

83

men with obesity & low T

After 2 months of tirzepatide: fat mass fell, while SHBG, total and free testosterone, LH/FSH and erectile function scores rose. Uncontrolled pilot — hypothesis-generating.

Women: Hormones, Weight and Sleep

How hormones and weight interact



Menopause transition

Estrogen loss → visceral fat, lean-mass loss, insulin resistance; OSA risk rises as progesterone's respiratory drive falls



PCOS

Insulin resistance and androgen excess; 5–10% weight loss can restore ovulation



As weight falls

Fertility may return — counsel on contraception, especially with tirzepatide

WHY HRT BELONGS IN WEIGHT CARE

- Treats hot flashes and night waking that disrupt sleep and adherence
- May limit central fat gain and improve insulin sensitivity
- Supports lean mass and bone, with resistance training

16% vs 12%

weight loss on semaglutide at 1 year, with vs without HT
(Mayo Clinic retrospective)

For symptomatic peri- and postmenopausal women, HRT is a key partner in weight loss and maintenance · [individualize](#)

Tirzepatide + Hormone Therapy After Menopause

THE STUDY

Mayo Clinic · ENDO 2025 / J Endocr Soc; full cohort in Lancet Obstet Gynaecol Women's Health

- Retrospective matched cohort, n=120
- 40 tirzepatide + MHT vs 80 tirzepatide alone
- MHT: estrogen ± progesterone; ~18 months
- Observational — association, not causation

17% vs 14%

Median weight loss,
with vs without MHT
(p=0.01)

45% vs 18%

Reached ≥20% weight
loss (p=0.001)

19% vs 14%

Mean loss at last
follow-up (full Lancet
cohort)

CONCLUSION MHT was associated with greater tirzepatide weight loss — randomized trials still needed.

Don't Just Treat the Weight. Treat the Biology.

SURMOUNT-1, -3, -4 post hoc (2025): tirzepatide worked in pre-, peri- and postmenopausal women.



Metabolic biology

Insulin resistance, appetite signaling



GLP-1 / GIP therapy



Menopausal hormonal biology

Estrogen loss, vasomotor symptoms, poor sleep



MHT when clinically indicated



Body composition

Lean-mass and bone loss risk



Nutrition + resistance training

Together: one long-term weight-management strategy, with close follow-up.

Applying the Integrated Model

OUR PATIENT

BMI 41 kg/m²

AHI 52 /hr

Hypertension

Prediabetes

MASLD

Low testosterone



Airway

Start PAP now; retest objectively after sustained loss



Weight

Tirzepatide + nutrition and resistance training



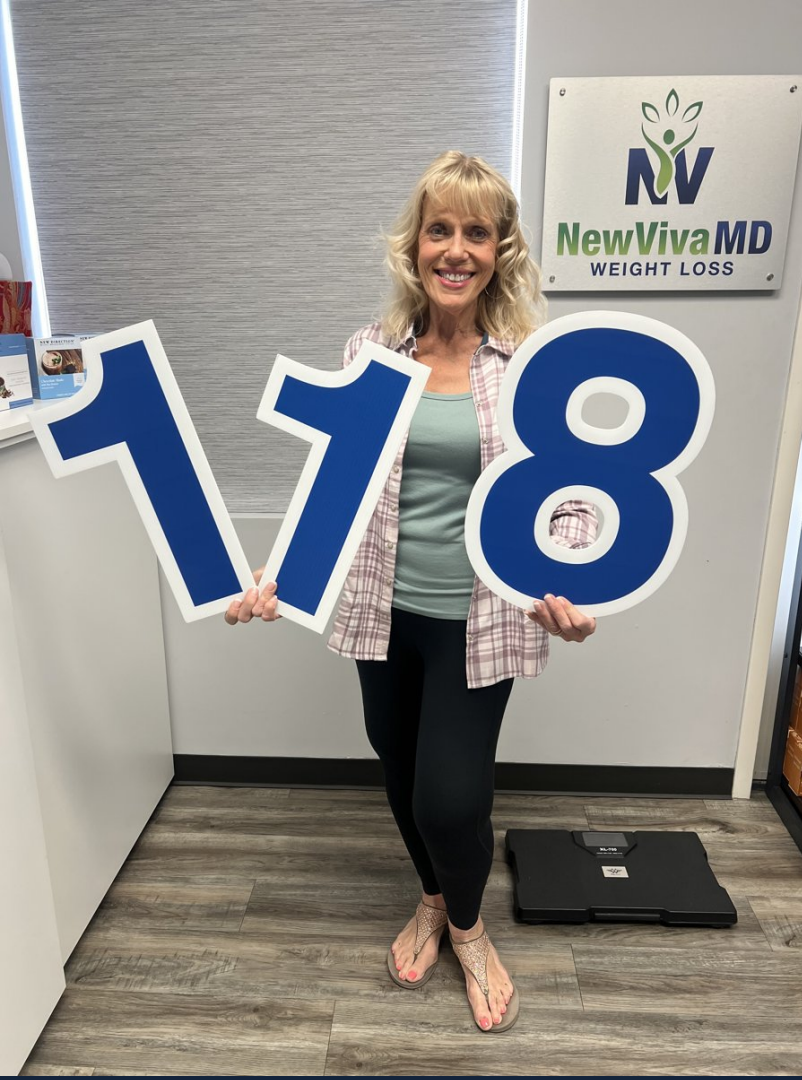
Metabolic

Treat and track BP, glycemia, liver fat



Hormones

Confirm low T; recheck once OSA and weight improve



PATIENT SPOTLIGHT · NEW VIVA MD

118 lbs lost

This is what treating the whole patient looks like.

Medication, nutrition, behavior change and follow-up — working together, not one number at a time.

40-50% of body weight
lost

5+ yrs maintained, since
2019

Shown with patient permission. Individual results vary.

TAKE-HOME

“We don’t have to choose between treating the airway and treating the patient.”

So — are we treating OSA, or managing symptoms? Now we can truly treat it.



Airway

PAP / oral appliance



Weight

Anti-obesity Rx



Metabolic

Glucose · BP · lipids



Hormones

Endocrine evaluation

New Viva MD: Your Weight-Management Partner

NEW VIVA MD

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"One Doctor, One Team, One Plan, One Place"

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We accept insurance

Weight loss and hormone programs



Telemedicine

Virtual visits across Arizona



Easy referrals

Fax (480) 571-3613 · or via EMR



Since 2019

Patients maintaining results for 5+ years

Refer: OSA with obesity · CPAP-intolerant patients · patients above Inspire BMI cutoffs

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