FREE GUIDE · PEPSRX

The Tirzepatide Guide

What the big trials actually found, in plain English.



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Tirzepatide in 60 seconds

Six numbers from the biggest trials. **Each one gets its own page.**

~20% P.05

Body weight lost, head to head with semaglutide's ~14%

3/4 P.06

Of every pound lost **was fat**, on body scans

90%+ P.07

Lower risk of **type 2 diabetes** over three years

38% P.08

Fewer **heart failure events** or heart deaths

62% P.09

Saw **liver inflammation resolve** on the top dose

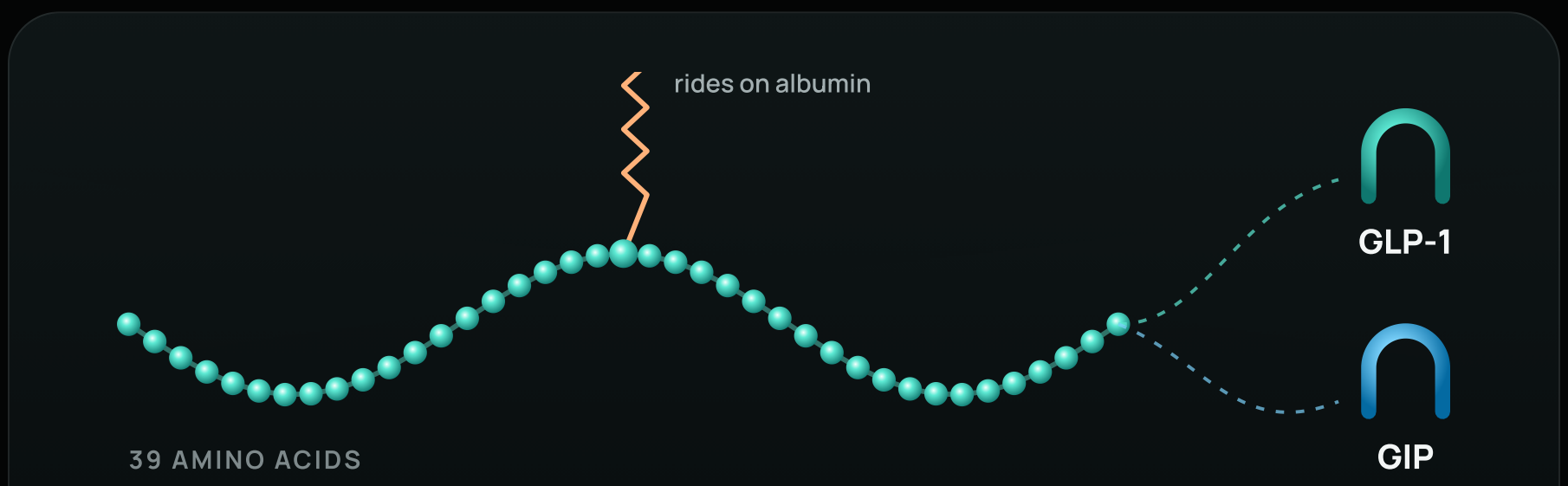
~1/2 P.10

Fewer **breathing stops** in sleep apnea

HOW IT WORKS

One molecule, two switches

Tirzepatide is one peptide chain, **39 amino acids long**, built to switch on two of your gut-hormone receptors at once. Semaglutide only switches on one.



• GLP-1

The familiar one. **Appetite quiets**, the stomach empties slower, and insulin rises when blood sugar is high.

• GIP

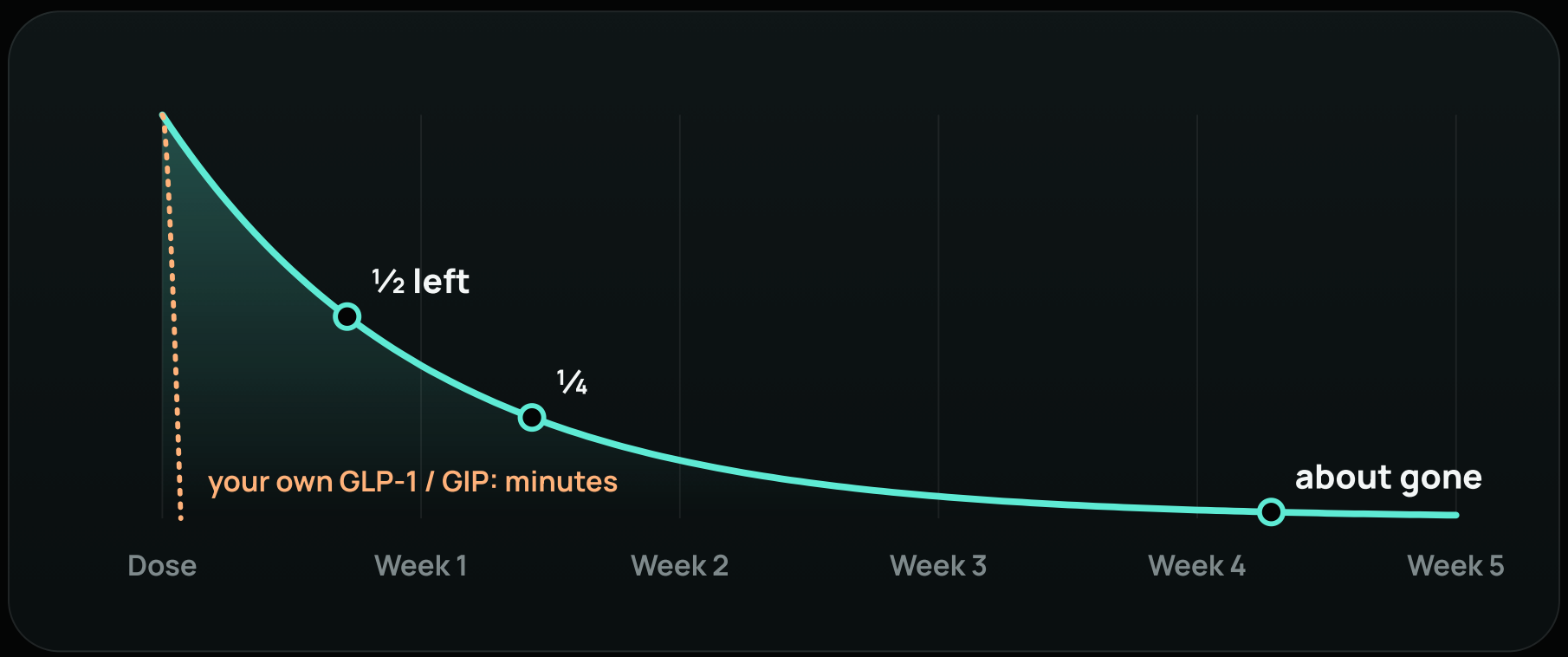
The extra piece. It works on **insulin release and on fat tissue**. This is what semaglutide doesn't touch.

Sources: Mounjaro / Zepbound and Wegovy prescribing information.

WHY IT'S WEEKLY

One shot, a whole week

Your own GLP-1 and GIP are cut apart **within minutes**. Tirzepatide carries a small fatty tail that grabs onto **albumin**, the most common protein in your blood, which is too big for your kidneys to filter out. So it rides along, protected, for days.



~5 days
Half-life, so it's taken once a week

~99%
Of the drug rides on albumin

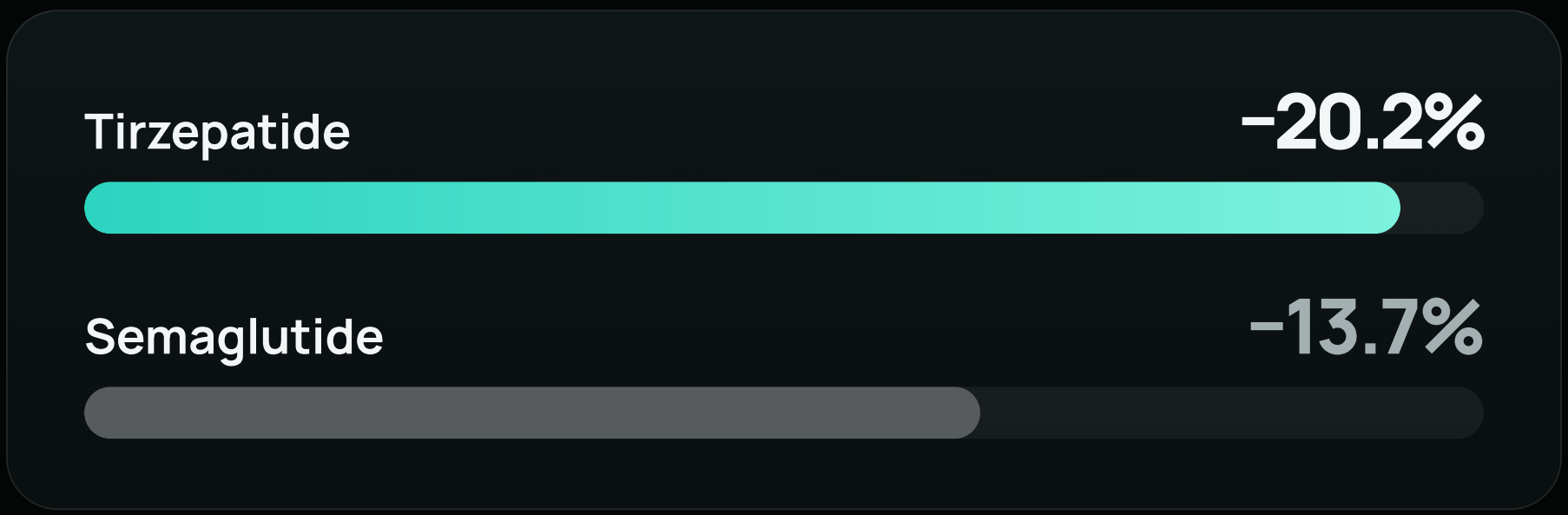
~1 month
To fully clear after the last dose

Sources: Lilly medical information (Mounjaro/Zepbound half-life and clearance); NCBI StatPearls, Tirzepatide; Drucker DJ, incretin physiology review.

WEIGHT

Same race, clear winner

Most comparisons stack two separate trials. This one put both drugs in the **same race**: 751 adults with obesity, same rules, 72 weeks.



WAISTLINE

−18.4 cm vs −13.0

About 7 inches versus 5

QUIT OVER STOMACH EFFECTS

2.7% vs 5.6%

Fewer people stopped tirzepatide

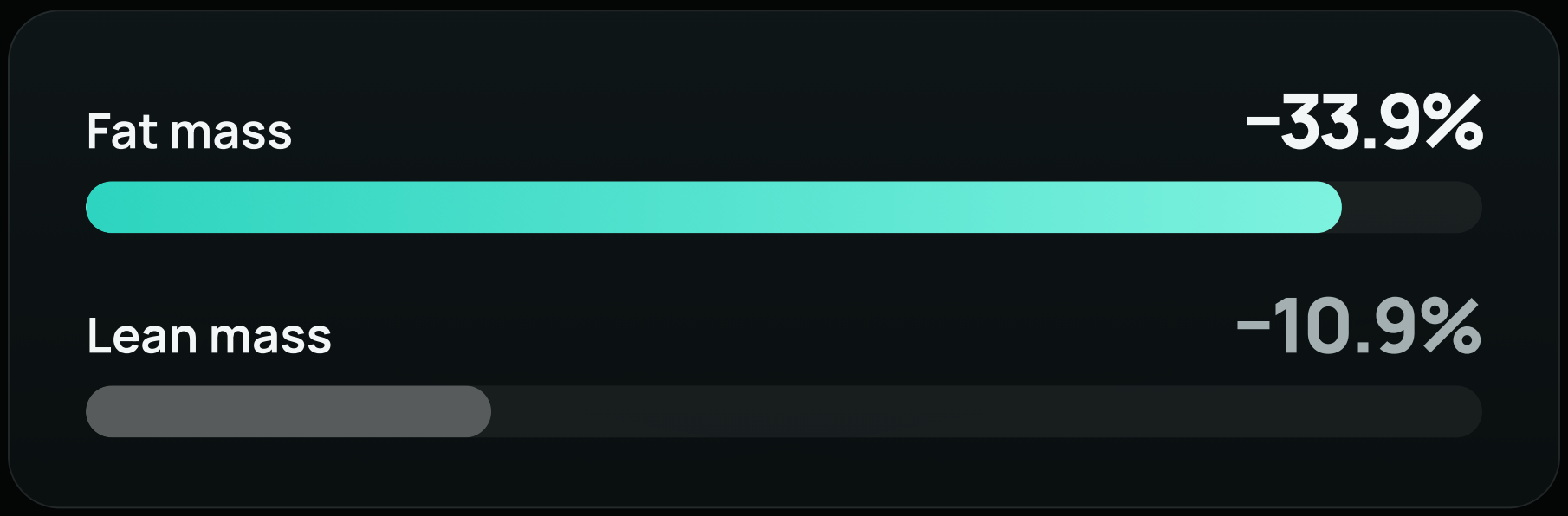
In the original obesity trial (2,539 adults), the top dose averaged **−20.9%** versus −3.1% on placebo. Nausea and other stomach effects were the most common complaints.

Sources: Aronne LJ, et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. NEJM 2025 (SURMOUNT-5). Jastreboff AM, et al. NEJM 2022;387:205-216 (SURMOUNT-1).

MUSCLE OR FAT?

What the weight is made of

Researchers didn’t guess. They put **160 people** from the big obesity trial through DXA scans, the X-ray that splits your body into fat, lean tissue and bone, at the start and after 72 weeks.



So roughly **three quarters of every pound lost was fat**, and the split held up in older adults too. Lean mass isn’t only muscle; it also counts water and organs. That’s why lifters pair it with heavy training and plenty of protein.



MARK

Real or rumor? Mostly rumor. The scans say it's mostly fat.

Source: Look M, et al. Body composition changes during weight reduction with tirzepatide in the SURMOUNT-1 study. Diabetes Obes Metab 2025;27:2720.

BLOOD SUGAR

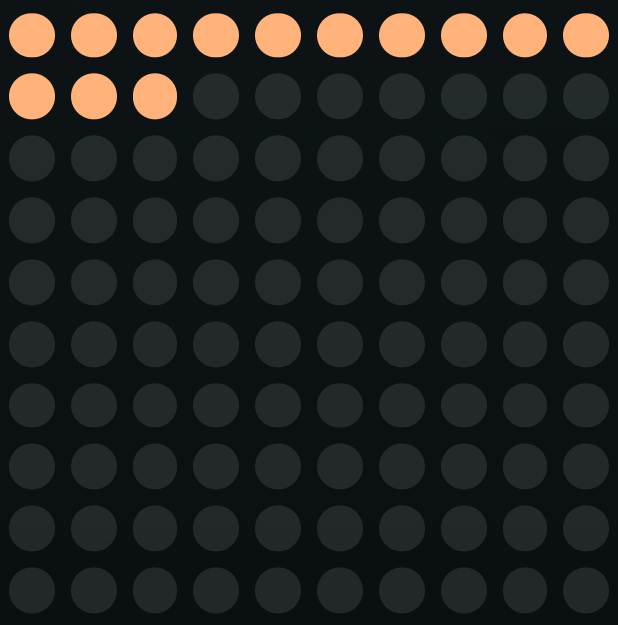
Three years, one number

About **1 in 3 American adults** has prediabetes, and most don’t know it. Lilly followed 1,032 adults with obesity and prediabetes for over three years.

PLACEBO

13 in 100

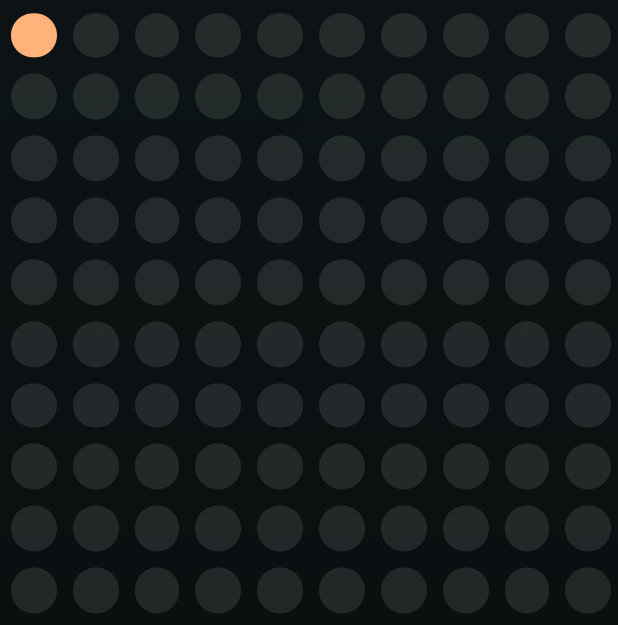
developed type 2 diabetes



TIRZEPATIDE

~1 in 100

developed type 2 diabetes



A drop of **more than 90% in risk** (1.3% vs 13.3%). When people stopped, some of that protection started to fade.

Sources: Jastreboff AM, et al. Tirzepatide for Obesity Treatment and Diabetes Prevention. NEJM 2024. CDC, About Prediabetes and Type 2 Diabetes.

THE HEART

From halftime to final score

Heart disease is still the **number one killer** of Americans. In 731 adults with obesity and a stiff, struggling heart, followed for about two years:

−38%

Worsening heart failure or heart death

Inflammation marker CRP also fell about 40%; on placebo it barely moved.

DEATHS FROM ANY CAUSE

−16%

vs dulaglutide, in 13,000+ people with diabetes and heart disease

HEART ATTACKS, STROKES, HEART DEATHS

−8%

vs an older shot already proven for the heart

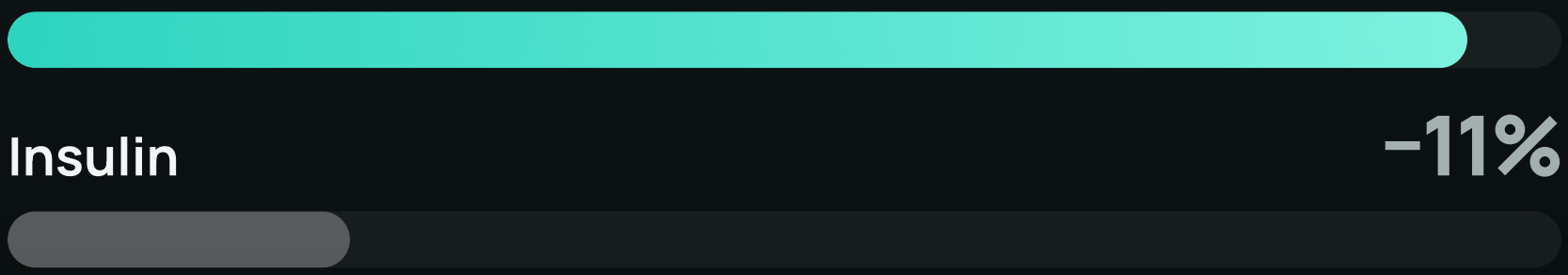
Sources: Packer M, et al. Tirzepatide for Heart Failure With Preserved Ejection Fraction and Obesity. NEJM 2024 (SUMMIT). SURPASS-CVOT, EASD 2025. CDC NCHS data brief 548.

THE LIVER

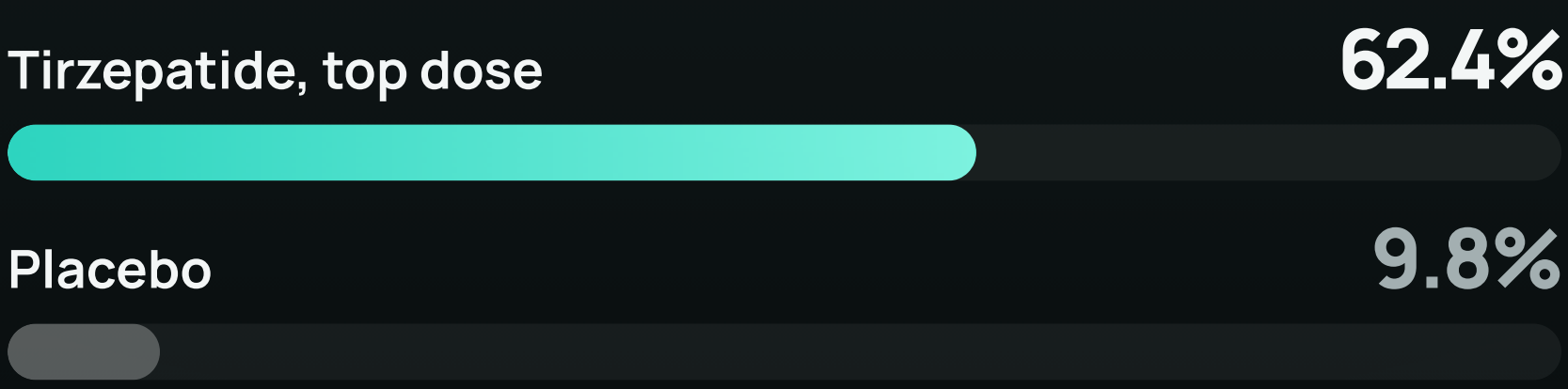
Fat that hides inside organs

Fatty liver affects about **1 in 4 American adults**. Two trials looked inside: one by MRI, one by biopsy.

MRI · liver fat after a year



Biopsy · liver inflammation resolved (52 weeks)



Up to **8 in 10** cut liver fat by at least 30%, and deep belly fat shrank too.

Sources: Gastaldelli A, et al. SURPASS-3 MRI. Lancet Diabetes Endocrinol 2022. Loomba R, et al. NEJM 2024 (SYNERGY-NASH). NIDDK, NAFLD & NASH.

SLEEP

How many times did you stop breathing?

About **30 million American adults** have sleep apnea. Lilly put 469 adults with obesity and apnea in sleep labs for a full year, some on CPAP, some not.

Breathing stops per hour, change

Tirzepatide **−25 to −29**

Placebo **about −5**

DEC 20 2024

Approved for sleep apnea, Dec 20, 2024

For moderate-to-severe sleep apnea in adults with obesity. The first medicine ever approved for it.

Sources: Malhotra A, et al. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. NEJM 2024 (SURMOUNT-OSA). FDA press announcement, Dec 20, 2024. American Academy of Sleep Medicine.

WHAT'S NEXT

Knees could be the next story

Researchers measured it: **every pound off your body takes about four pounds off your knee**, with every step.

~200

Pounds off the knee, every step

Someone at 250 lb who loses a fifth of their weight, as people did on the top dose.

IN PROGRESS

STOP KNEE-OA

A University of Melbourne trial, with Lilly's support, is testing tirzepatide against placebo for 72 weeks in people with obesity and knee arthritis, tracking knee pain and who ends up needing a new knee. First results are expected around 2027.

Sources: Messier SP, et al. Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis. Arthritis Rheum 2005;52(7):2026-32. ClinicalTrials.gov NCT06191848.

SOURCES

Every number, traced

01 **SURMOUNT-5.** Aronne LJ, et al. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. NEJM 2025.

02 **SURMOUNT-1.** Jastreboff AM, et al. Tirzepatide Once Weekly for the Treatment of Obesity. NEJM 2022;387:205-216.

03 **SURMOUNT-1, 3 years.** Jastreboff AM, et al. Tirzepatide for Obesity Treatment and Diabetes Prevention. NEJM 2024.

04 **SURMOUNT-1 DXA.** Look M, et al. Diabetes Obes Metab 2025;27:2720.

05 **SUMMIT.** Packer M, et al. Tirzepatide for Heart Failure With Preserved Ejection Fraction and Obesity. NEJM 2024.

06 **SURPASS-CVOT.** Tirzepatide vs dulaglutide, cardiovascular outcomes. EASD 2025.

07 **SURPASS-3 MRI.** Gastaldelli A, et al. Lancet Diabetes Endocrinol 2022.

08 **SYNERGY-NASH.** Loomba R, et al. Tirzepatide for MASH with Liver Fibrosis. NEJM 2024.

09 **SURMOUNT-OSA.** Malhotra A, et al. Tirzepatide for Obstructive Sleep Apnea and Obesity. NEJM 2024. FDA announcement, Dec 20, 2024.

10 **Knee load.** Messier SP, et al. Arthritis Rheum 2005;52(7):2026-32. STOP KNEE-OA, NCT06191848.

11 **Pharmacology.** Mounjaro / Zepbound prescribing information; Lilly medical information; NCBI StatPearls; Drucker DJ review.

12 **Public health.** CDC (prediabetes; NCHS data brief 548); NIDDK (NAFLD & NASH); American Academy of Sleep Medicine.

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