



PATH TO PEPTIDES GLP-1 AND YOUR HEART

WHAT A 2-MILLION-PATIENT STUDY REVEALED

Diabetes drugs are showing surprising heart benefits. The research is massive — and hard to ignore.

An Educational Overview of Emerging Scientific Research

FOR RESEARCH AND EDUCATIONAL PURPOSES ONLY

A STUDY OF OVER 2 MILLION PATIENTS FOUND THAT GLP-1 DRUGS WERE LINKED TO LOWER RISK OF 42 DIFFERENT HEALTH CONDITIONS — INCLUDING HEART ATTACK, STROKE, AND HEART FAILURE.

That's not a typo. Medications originally designed to manage blood sugar are now at the center of one of the most exciting areas of heart research in years. Here's what the science shows — and why cardiologists are paying close attention.

WHY THIS MATTERS

Heart disease is the **leading cause of death** worldwide. In the United States alone, someone has a heart attack every **40 seconds**.¹ Despite decades of progress in treatments, heart disease still kills more Americans than cancer, accidents, and respiratory disease combined. That's why any medication that shows significant heart benefits gets serious attention from researchers. And GLP-1 drugs are delivering some of the most compelling cardiovascular data scientists have seen in years.

THE SCIENCE: HOW GLP-1 DRUGS MAY PROTECT THE HEART

GLP-1 receptors aren't just in your gut and brain. They're also found in your heart and blood vessels.² Think of GLP-1 receptors like locks on a door. When the right key (a GLP-1 drug) turns that lock, it triggers helpful changes inside the cell.

Scientists believe GLP-1 drugs may protect the heart in several ways:

Reducing inflammation: Chronic inflammation damages blood vessels over time. Research shows

GLP-1 drugs lower key markers of inflammation throughout the body.³

Improving blood vessel function: These drugs appear to help blood vessels relax and expand more easily, which improves blood flow and lowers blood pressure.⁴

Reducing arterial plaque: Early studies suggest GLP-1 drugs may slow the buildup of fatty deposits in arteries — the root cause of most heart attacks.⁵

Weight loss: Losing excess weight reduces strain on the heart. But researchers believe the heart benefits go beyond weight loss alone.⁶

Did You Know? In the landmark SELECT trial, semaglutide reduced major cardiovascular events by 20% in people with obesity — even those who did NOT have diabetes. That was the first time a weight loss drug showed this kind of heart protection.⁶

WHAT THE RESEARCH SAYS

THE SELECT TRIAL (2023)

This was the game-changer. Published in the New England Journal of Medicine, the SELECT trial studied over **17,600 adults** with obesity and existing heart disease — but without diabetes.⁶

Participants who received semaglutide had a **20% lower** risk of major heart events (heart attack, stroke, or cardiovascular death) compared to those on placebo. This finding led the FDA to approve semaglutide specifically for reducing cardiovascular risk in adults with obesity.⁷

THE SUMMIT TRIAL — HEART FAILURE (2024)

The SUMMIT trial, published in the New England Journal of Medicine in December 2024, studied tirzepatide in **731 patients** with heart failure and obesity.⁸

Results showed tirzepatide reduced the combined risk of worsening heart failure or cardiovascular death by **38%** compared to placebo. Participants also reported significant improvements in their ability to exercise and in their quality of life.

THE 2-MILLION-PATIENT STUDY (2024)

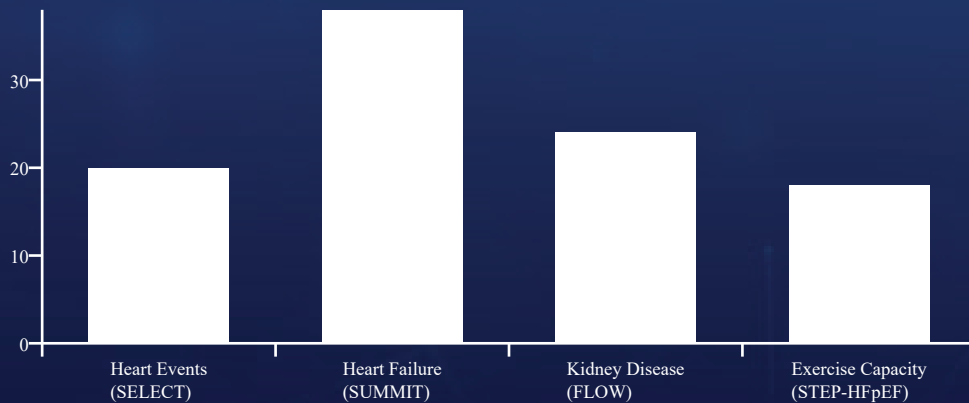
Published in Nature Medicine, this massive study analyzed electronic health records from over 2 million patients who had taken GLP-1 medications.⁹

The findings were striking: GLP-1 drug use was associated with reduced risk across 42 different conditions spanning 10 organ systems. Heart-related benefits included lower rates of heart attack, stroke, heart failure, and atrial fibrillation.

KEY CARDIOVASCULAR FINDINGS

| Study | Patients | Key Finding | Published |
|--------------------------|------------|--|--------------|
| SELECT | 17,604 | 20% lower major cardiovascular events | NEJM 2023 |
| SUMMIT | 731 | 38% lower worsening heart failure risk | NEJM 2024 |
| Nature Medicine Analysis | 2,000,000+ | 42 conditions with reduced risk | Nat Med 2024 |
| FLOW (kidney) | 3,533 | 24% lower kidney disease progression | NEJM 2024 |
| STEP-HFpEF | 529 | Improved exercise capacity + symptoms | NEJM 2023 |

RISK REDUCTION SEEN IN MAJOR GLP-1 CARDIOVASCULAR TRIALS (%)



THE BIG PICTURE: BEYOND THE HEART

The cardiovascular findings are part of a bigger story. The 2-million-patient study found GLP-1 drugs were associated with benefits across nearly every organ system studied — including the brain, kidneys, liver, and lungs.⁹

Scientists are now debating whether GLP-1 drugs reduce disease risk only because they cause weight loss, or whether they have direct protective effects on organs. Growing evidence supports the idea that both mechanisms are at work.¹⁰

As one researcher put it: these drugs may be doing something fundamentally important at the cellular level — reducing inflammation and stress in ways that protect multiple organs at once.

WHAT TO KNOW

Key Takeaways:

- GLP-1 drugs like semaglutide and tirzepatide show significant heart benefits in large trials.
- The SELECT trial led to the first FDA approval of a weight loss drug for heart protection.
- Benefits appear to go beyond weight loss — direct effects on blood vessels and inflammation may play a role.
- A study of 2M+ patients linked GLP-1 drugs to lower risk across 42 different health conditions.
- These are prescription medications — always work with your healthcare provider.
- Research is ongoing. Larger and longer studies will continue to clarify these findings.

WHAT TO KREFERENCESNOW

1. American Heart Association. Heart Disease and Stroke Statistics — 2024 Update. *Circulation*. 2024;149(8):e347–e913.
2. Drucker DJ. The cardiovascular biology of glucagon-like peptide-1. *Cell Metab*. 2016;24(1):15–30.
3. Rakipovski G, et al. The GLP-1 analogs reduce atherosclerotic plaque in ApoE-deficient mice. *J Am Coll Cardiol*. 2018;72(7):785–796.
4. Nystrom T, et al. Effects of glucagon-like peptide-1 on endothelial function. *Am J Physiol Endocrinol Metab*. 2004;286(6):E918–E922.
5. Marso SP, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2016;375(4):311–322.
6. Lincoff AM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389(24):2221–2232.
7. FDA. FDA approves first treatment to reduce risk of serious heart problems specifically in adults with obesity. March 2024.
8. Packer M, et al. Tirzepatide for heart failure with preserved ejection fraction and obesity. *N Engl J Med*. 2024;391(25):2379–2389.
9. Wang W, et al. GLP-1 receptor agonists and health outcomes: umbrella review of 2 million patients. *Nature Medicine*. 2024.
10. Sattar N, et al. GLP-1 receptor agonists: cardiovascular benefits beyond glucose and weight. *Lancet Diabetes Endocrinol*. 2024;12(1):39–47.

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This document is intended solely for educational purposes to increase awareness of emerging scientific research. It does not constitute medical advice and should not be used to make healthcare decisions.

Regulatory Status: Semaglutide (Ozempic/Wegovy) and tirzepatide (Mounjaro/Zepbound) are FDA-approved for type 2 diabetes and/or chronic weight management. Semaglutide (Wegovy) is FDA-approved to reduce cardiovascular risk in adults with obesity. Other cardiovascular applications described in this document are based on published research and may not yet be reflected in FDA-approved labeling.

All healthcare decisions should be made in consultation with qualified medical professionals.

This publication is part of an ongoing educational series designed to promote scientific literacy and awareness of developments in health research.



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PATH TO PEPTIDES

GLP-1 AND THE BRAIN

CAN DIABETES DRUGS PROTECT AGAINST DEMENTIA?

One study showed a 45% lower dementia risk. Then a major trial failed. The full story is more interesting than either headline.

An Educational Overview of Emerging Scientific Research

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A STUDY OF OVER 100,000 PATIENTS FOUND THAT PEOPLE TAKING GLP-1 DRUGS HAD UP TO A 45% LOWER RISK OF DEVELOPING DEMENTIA. THEN A MAJOR CLINICAL TRIAL FOUND NO BENEFIT. SO WHICH IS IT?

The answer may be more nuanced — and more hopeful — than either headline suggests. The science of how GLP-1 drugs interact with the brain is still unfolding, and what researchers are learning is fascinating.

WHY THIS MATTERS

Alzheimer's disease affects over 6.9 million Americans and is the 7th leading cause of death in the United States.¹ By 2060, that number is expected to nearly double.

Despite decades of research and billions of dollars invested, there are still very few effective treatments. The drugs that do exist (like lecanemab) only slow decline modestly and come with serious side effects.²

That's why any hint that an existing, widely-used medication might protect the brain gets major attention. And GLP-1 drugs have generated some very intriguing signals.

THE SCIENCE: GLP-1 RECEPTORS IN YOUR BRAIN

Here's something that surprised even scientists: your brain is loaded with GLP-1 receptors. They're especially dense in areas critical for memory and learning — the hippocampus, cortex, and hypothalamus.³

Think of it this way: GLP-1 isn't just a "gut hormone." It's also a brain chemical. Your body naturally makes GLP-1 in both your intestines AND in specific brain cells. The brain version helps with learning, memory, and protecting neurons from damage.⁴

Researchers believe GLP-1 drugs may protect the brain through several pathways:

Reducing brain inflammation: Chronic inflammation in the brain (called neuroinflammation) is a major driver of Alzheimer's and Parkinson's disease. GLP-1 drugs appear to calm this inflammatory response.⁵

Improving insulin signaling: The brain needs insulin to function properly. Alzheimer's is sometimes called "type 3 diabetes" because brain insulin resistance appears to play a role. GLP-1 drugs may help restore healthy insulin signaling in brain cells.⁶

Protecting neurons: Lab studies show GLP-1 drugs can protect brain cells from the toxic effects of amyloid plaques — the protein clumps that build up in Alzheimer's disease.⁷

Did You Know? Alzheimer's disease is sometimes called "type 3 diabetes" by researchers because problems with insulin signaling in the brain appear to play a key role in the disease. That's one reason diabetes drugs caught neuroscientists' attention.

WHAT THE RESEARCH SAYS

THE GOOD NEWS: LARGE OBSERVATIONAL STUDIES

Multiple large studies have found promising associations between GLP-1 drug use and lower dementia risk:

A study of over 120,000 patients with type 2 diabetes, published in *Alzheimer's & Dementia*, found GLP-1 drug users had a 35% lower risk of developing Alzheimer's and a 45% lower risk of vascular dementia compared to those taking other diabetes medications.⁸

A 2024 meta-analysis combining data from multiple studies confirmed the pattern: GLP-1 drug users consistently showed lower rates of cognitive decline and dementia diagnoses.⁹

THE SETBACK: THE EVOKE TRIAL

In late 2024, the EVOKE trial — a randomized controlled trial of semaglutide in 1,840 patients with early Alzheimer's disease — reported that the drug did not slow cognitive decline compared to placebo over 2 years.¹⁰

This was disappointing. But researchers were quick to point out an important detail: the trial studied people who already had Alzheimer's. It's possible that GLP-1 drugs work as prevention, not treatment.

THE KEY QUESTION: PREVENTION VS. TREATMENT

Think of it like sunscreen. Sunscreen protects your skin if you apply it before sun damage happens. But it can't reverse a sunburn that's already there.

Many researchers now believe GLP-1 drugs may work the same way for the brain — protecting healthy neurons from damage over years or decades, rather than repairing neurons that are already damaged.¹¹

New trials are now being designed to test this "prevention" hypothesis by studying GLP-1 drugs in people at risk for dementia but who haven't been diagnosed yet.

| Study Type | Population | Key Finding |
|----------------------------------|--------------------------|------------------------------------|
| Observational (120K patients) | Type 2 diabetes patients | 35-45% lower dementia risk |
| Meta-analysis (2024) | Combined studies | Consistent lower cognitive decline |
| EVOKE Trial (RCT) | Early Alzheimer's | No benefit for existing disease |
| Preclinical studies | Animal models | Reduced brain inflammation |

BEYOND ALZHEIMER'S: PARKINSON'S DISEASE

The brain research doesn't stop at Alzheimer's. A Phase 2 trial found that the GLP-1 drug exenatide (Byetta) showed neuroprotective effects in Parkinson's disease patients. After 1 year of treatment, patients on exenatide maintained better motor function than those on placebo.¹²

A larger Phase 3 trial (called NeuroPAS) is now underway to confirm these findings. If successful, it would be the first drug shown to slow the progression of Parkinson's disease — not just treat symptoms.¹³

WHAT TO KNOW

KEY TAKEAWAYS:

- GLP-1 receptors are found throughout the brain, especially in memory regions.
- Large studies link GLP-1 drug use to 35–45% lower dementia risk.
- The EVOKE trial found no benefit for people who already had Alzheimer's.
- Scientists believe these drugs may work as prevention, not treatment.
- Research in Parkinson's disease is also showing promising early results.
- This is an active area of research — no brain-related uses are FDA-approved.
- Talk to a healthcare provider about any questions regarding brain health.

REFERENCES

1. Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures. *Alzheimers Dement*. 2024;20(5):3708–3821.
2. van Dyck CH, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388(1):9–21.
3. Cork SC, et al. Distribution and characterisation of GLP-1 receptor expressing cells in the mouse brain. *Mol Metab*. 2015;4(10):718–731.
4. During MJ, et al. Glucagon-like peptide-1 receptor is involved in learning and neuroprotection. *Nat Med*. 2003;9(9):1173–1179.
5. Holscher C. Potential role of glucagon-like peptide-1 in the treatment of Alzheimer's disease. *CNS Drugs*. 2012;26(10):871–882.
6. de la Monte SM, Wands JR. Alzheimer's disease is type 3 diabetes — evidence reviewed. *J Diabetes Sci Technol*. 2008;2(6):1101–1113.
7. McClean PL, et al. The diabetes drug liraglutide prevents degenerative processes in a mouse model of Alzheimer's disease. *J Neurosci*. 2011;31(17):6587–6594.
8. Norgaard CH, et al. Treatment with GLP-1 receptor agonists and risk of dementia. *Alzheimers Dement*. 2022;8(1):e12268.
9. Cao Y, et al. GLP-1 receptor agonists and cognitive decline: systematic review and meta-analysis. *Diabetes Obes Metab*. 2024;26(3):1037–1048.
10. Novo Nordisk. EVOKE/EVOKE+ Phase 3 trial results for semaglutide in early Alzheimer's disease. Press release. 2024.
11. Holscher C. Brain insulin resistance: role in neurodegenerative disease and potential for targeting. *Expert Opin Investig Drugs*. 2020;29(1):1–3.
12. Athauda D, et al. Exenatide once weekly versus placebo in Parkinson's disease. *Lancet*. 2017;390(10103):1664–1675.
13. ClinicalTrials.gov. NeuroPAS: Phase 3 trial of exenatide for Parkinson's disease. NCT04232969.

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All healthcare decisions should be made in consultation with qualified medical professionals.

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