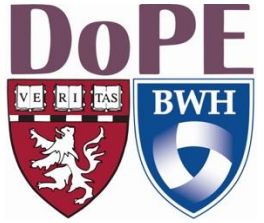




**PORTAL**  
*Program on Regulation,  
Therapeutics, And Law*



Maine Prescription Drug Affordability Board | February 24, 2025

# GLP-1 Receptor Agonists: Past, Present, and Future

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**Brigham and Women's Hospital**  
Founding Member, Mass General Brigham

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- Consulting for the non-profit Alosa Health (academic detailing)

# Outline

- History of GLP-1 agonists
  - Supporting clinical data & FDA approvals
- Treatment cost eligible population
- Coverage of GLP-1 agonists
  - Medicare & Medicaid
  - Other payers
- So what are the options?

# 2005-2015: Just another diabetes drug?

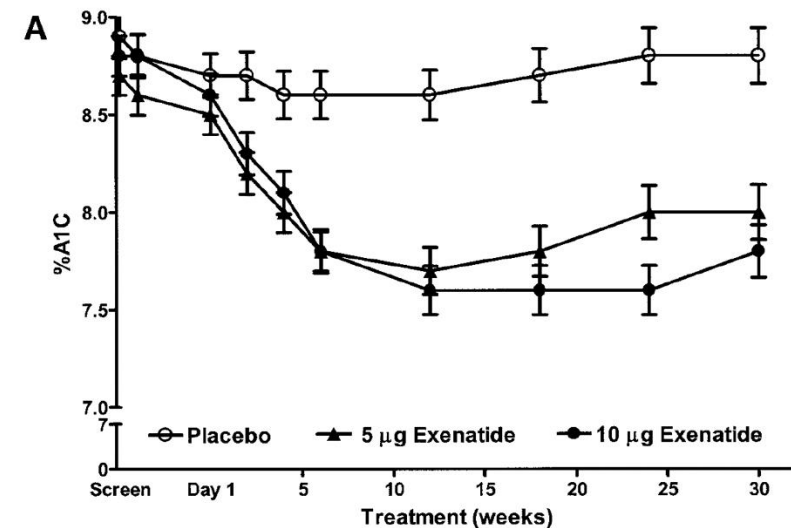
- First **daily injectable** GLP1 agonists approved for diabetes based on ability to lower A1c compared to placebo
  - 2005: exenatide (Byetta)
  - 2010: liraglutide (Victoza)
- Mainstay diabetes therapies remained metformin, sulfonylureas, and insulin.

## Effects of Exenatide (Exendin-4) on Glycemic Control Over 30 Weeks in Sulfonylurea-Treated Patients With Type 2 Diabetes

JOHN B. BUSE, MD, PHD<sup>1</sup>  
ROBERT R. HENRY, MD<sup>2</sup>  
JENNY HAN, MS<sup>3</sup>  
DENNIS D. KIM, MD<sup>3</sup>

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ALAIN D. BARON, MD<sup>3</sup>  
FOR THE EXENATIDE-113 CLINICAL STUDY GROUP\*

**S**ulfonylureas, a class of commonly prescribed antidiabetic drugs, are generally safe and efficacious in monotherapy and in combination with other oral agents and insulin in patients with type 2 diabetes. However, hypogly-



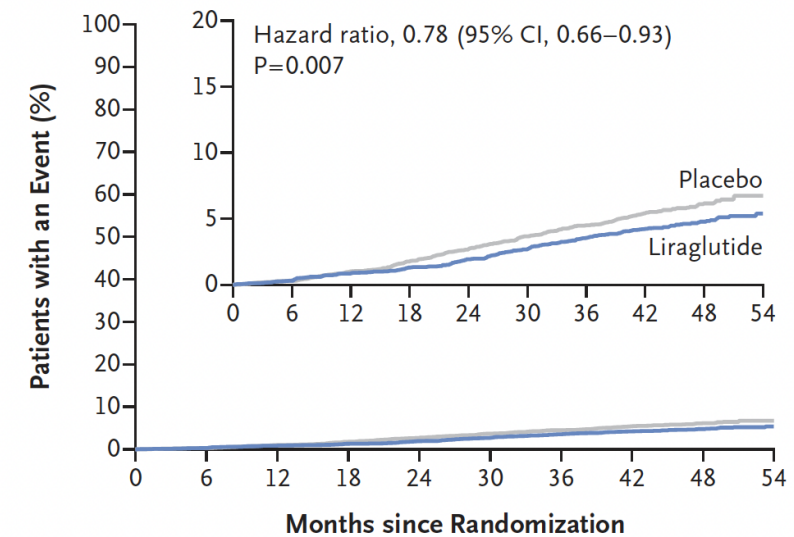
# 2016-2020: A really good diabetes drug!

- **Weekly injectable GLP1s**
  - 2014: dulaglutide (Trulicity)
  - 2017: semaglutide (Ozempic)
- Evidence that **GLP1 agonists lowered risk of cardiovascular events and death** (in patients with diabetes)
  - Jun 2016: LEADER (liraglutide)
  - Sep 2016: SUTAIN-6 (semaglutide)
  - Jun 2019: REWIND (dulaglutide)
- By 2019, GLP1-RAs (and SGLT2 inhibitors) became **preferred 2<sup>nd</sup> line treatments** (after metformin) for patients with diabetes and cardiovascular disease.

## Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, M.D., Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., Stuart Pocock, Ph.D., Neil R. Poulter, F.Med.Sci., Lasse S. Ravn, M.D., Ph.D., William M. Steinberg, M.D., Mette Stockner, M.D., Bernard Zinman, M.D., Richard M. Bergenstal, M.D., and John B. Buse, M.D., Ph.D., for the LEADER Steering Committee on behalf of the LEADER Trial Investigators\*

### B Death from Cardiovascular Causes



#### No. at Risk

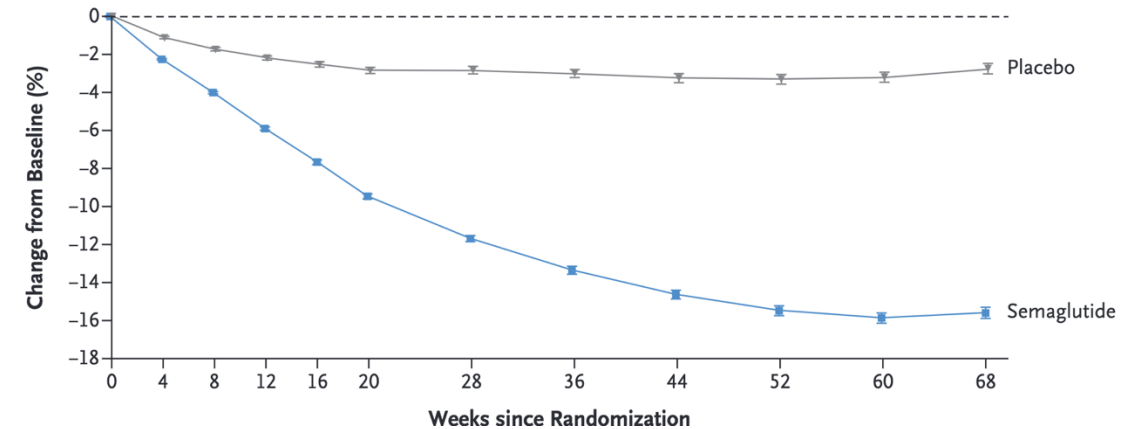
Liraglutide	4668	4641	4599	4558	4505	4445	4382	4322	1723	484
Placebo	4672	4648	4601	4546	4479	4407	4338	4267	1709	465



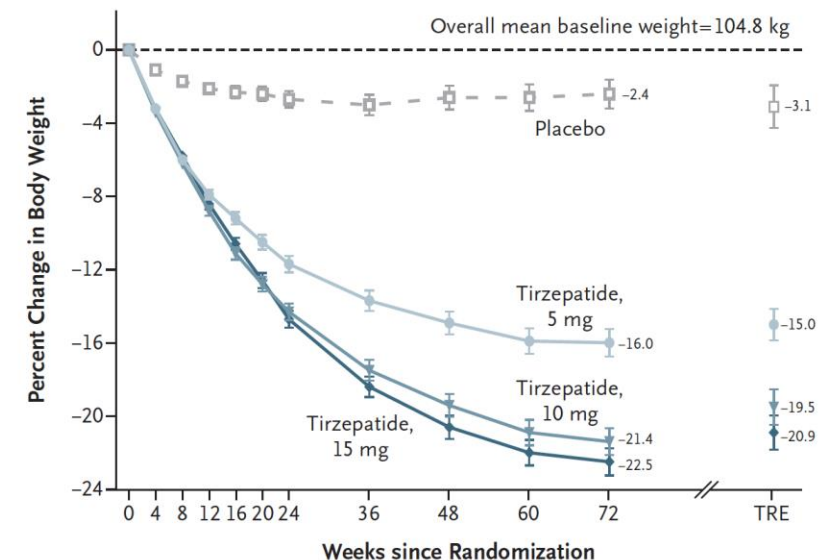
# 2021\*-2023: The anti-obesity era

- Even the first diabetes trials of GLP1 agonists demonstrated weight loss.
- FDA approvals for weight loss in patients without diabetes
  - \*2014: liraglutide (Saxenda)
    - ~8% body weight loss
  - 2021: semaglutide (Wegovy)
    - ~15% body weight loss
  - 2023: tirzepatide (Zepbound)
    - ~20% body weight

A Body Weight Change from Baseline by Week, Observed In-Trial Data



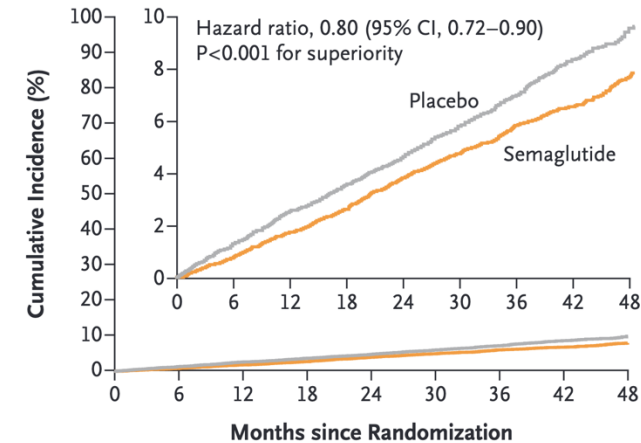
B Percent Change in Body Weight by Week (efficacy estimand)



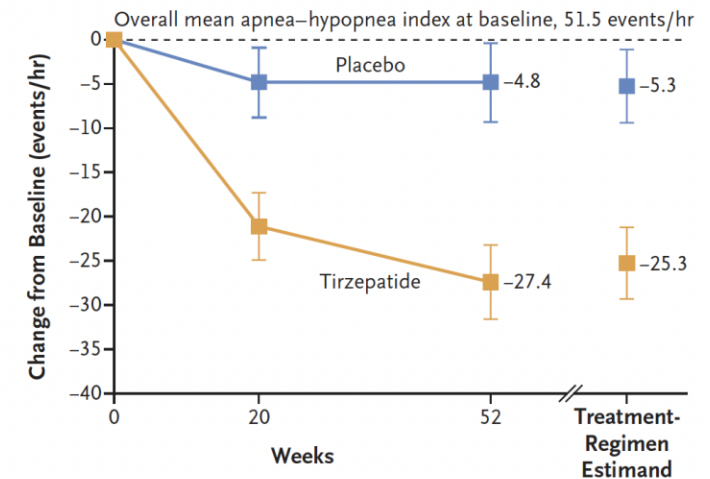
# 2024-present: More than just weight loss...

- **2024 FDA Approvals**
  - Semaglutide to **reduce cardiovascular risk** in patients with obesity + established cardiovascular disease
  - Tirzepatide for moderate-to-severe **obstructive sleep apnea** + obesity.

A Primary Cardiovascular Composite End Point



A Change in Apnea–Hypopnea Index in Trial 1 (efficacy estimand)

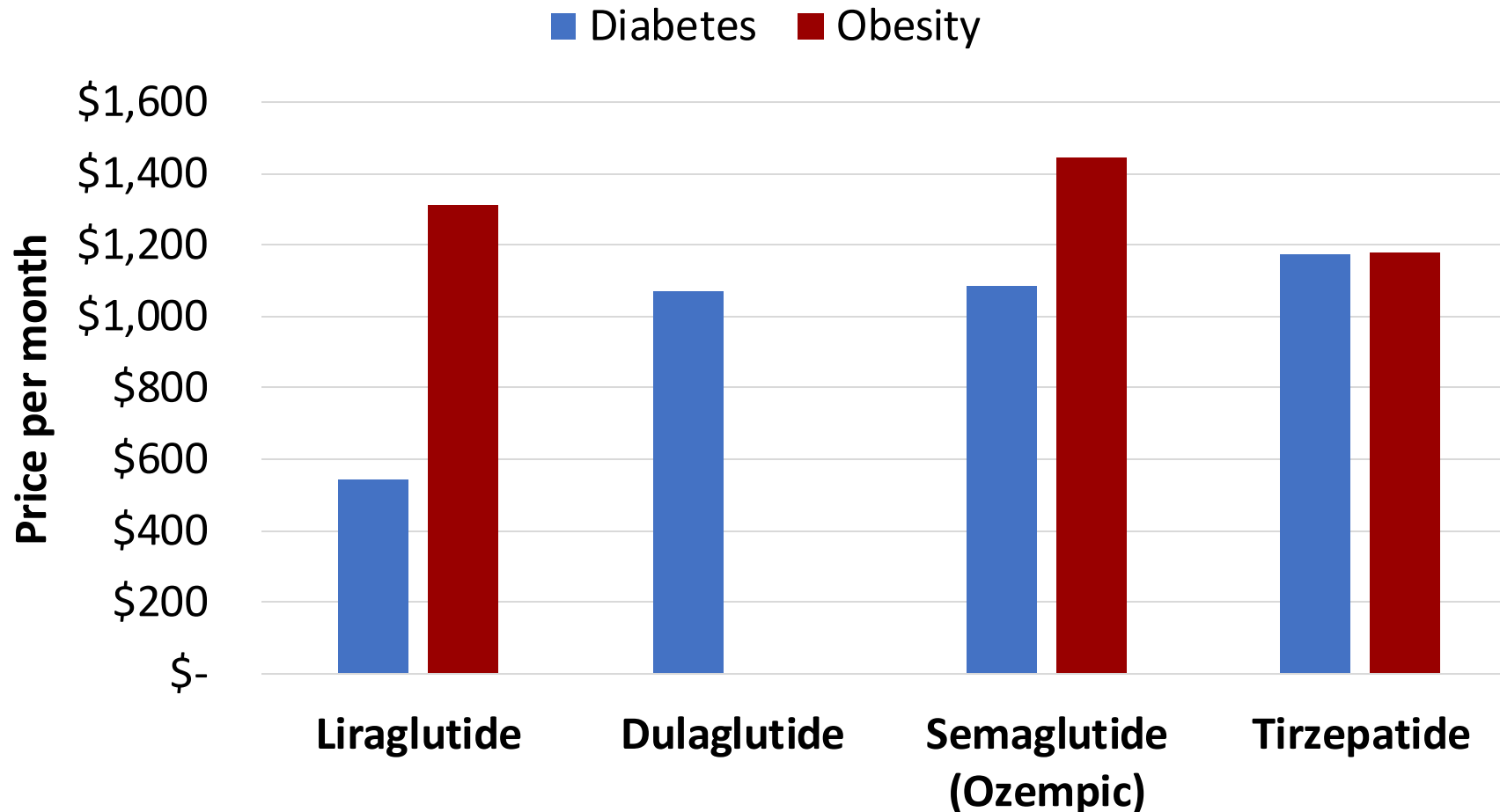


# Current FDA approved indications

	Liraglutide	Dulaglutide	Semaglutide	Tirzepatide
<b>Trade Names</b>	Victoza (diabetes), Saxenda)	Trulicity	Ozempic (diabetes), Wegovy	Mounjaro (diabetes), Zepbound
<b>Manufacturer</b>	Novo Nordisk	Eli Lilly	Novo Nordisk	Eli Lilly
<b>Admin Schedule</b>	Daily	Weekly	Weekly	Weekly
<b>Diabetes approvals</b>				
Glycemic control	X	X	X	X
Cardiovascular risk	X	X	X	
Kidney disease			X	
<b>Obesity approvals</b>				
Weight management	X		X	X
Cardiovascular risk			X	
Sleep apnea				X



# Cost of GLP-1 Receptor Agonists

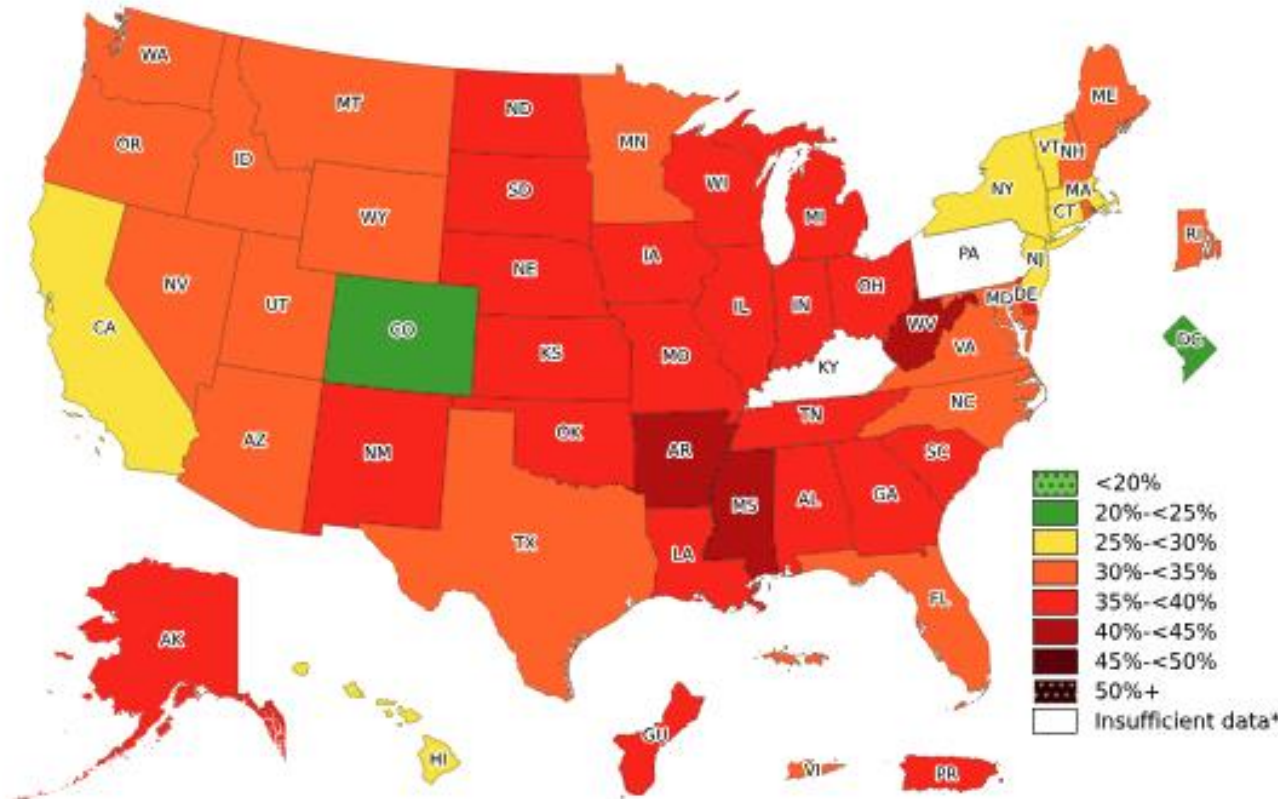


## What about Rebates?

Estimated negotiated rebates in 2022 were:

- ~50-60% for diabetes versions
- ~40% for obesity versions (*before tirzepatide*)

# The problem: High prevalence of obesity



40 states with >30% prevalence of obesity

# Coverage in Medicare & Medicaid

## Medicaid

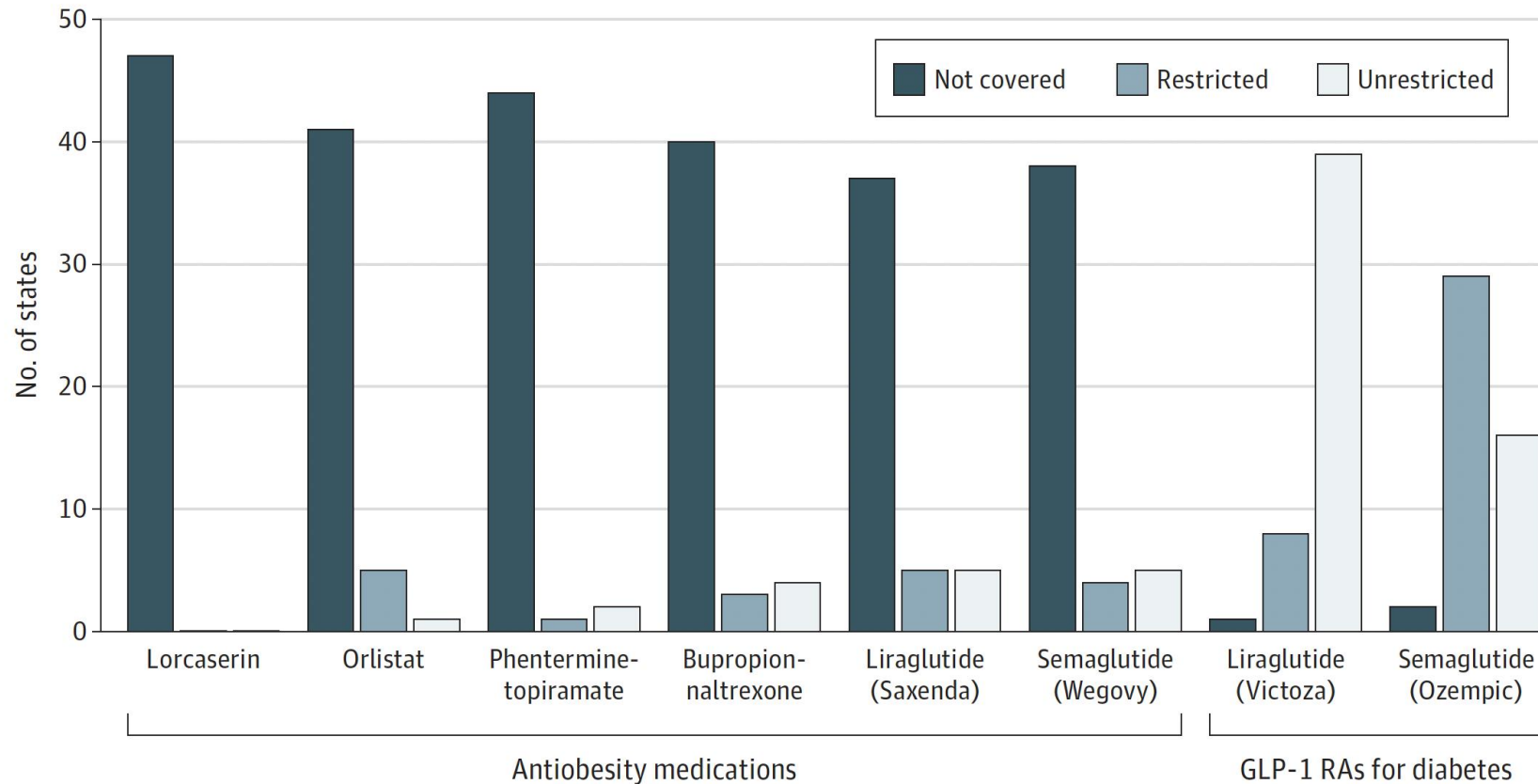
- Since 1991, the Medicaid Drug Rebate Program entitles states to receive substantial manufacturer discounts on prescription drugs, but in return must cover essentially all FDA-approved drugs.
- Certain drug classes were exempted from this coverage requirement, including “agents when used for anorexia, weight loss, or weight gain.”
- **Coverage for anti-obesity medications is optional**

## Medicare Part D

- When enacted in 2003, Medicare Part D statutorily excluded coverage of the same list of drugs that are optional for coverage in Medicaid.
- **Coverage for anti-obesity medications is not allowed**

# State Medicaid coverage of GLP1s in 2023

Figure 1. Coverage of Antiobesity Medications in Medicaid States With Preferred Drug Lists in 2023<sup>a</sup>



# Expanding Medicare Coverage

March 2024

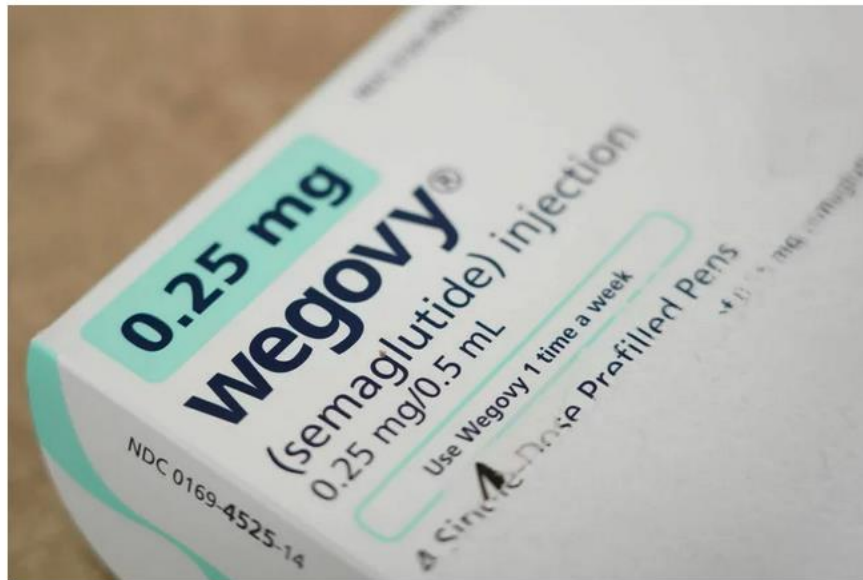


TREATMENTS

## Medicare plans can now cover Wegovy for patients at risk of heart disease

UPDATED MARCH 22, 2024 · 12:18 PM ET

By Yuki Noguchi, Carmel Wroth



November 2024



HEALTH CARE

## Weight loss drugs could soon be covered by Medicare and Medicaid

NOVEMBER 26, 2024 · 5:13 PM ET

HEARD ON ALL THINGS CONSIDERED

By Sydney Lupkin

*“CMS now proposes to **reinterpret the statute to permit [Medicare Part D] coverage** of anti-obesity medications for the treatment of obesity when such drugs are indicated to reduce excess body weight and maintain weight reduction long-term for individuals with obesity...this reinterpretation would also apply to the Medicaid program. As a result, anti-obesity medications...**could not be excluded from Medicaid coverage.**”*

# Impacts of Expanding Medicare Coverage

## OBSERVATIONS: BRIEF RESEARCH REPORTS

### Estimating New Eligibility and Maximum Costs of Expanded Medicare Coverage of Semaglutide for Cardiovascular Risk Prevention

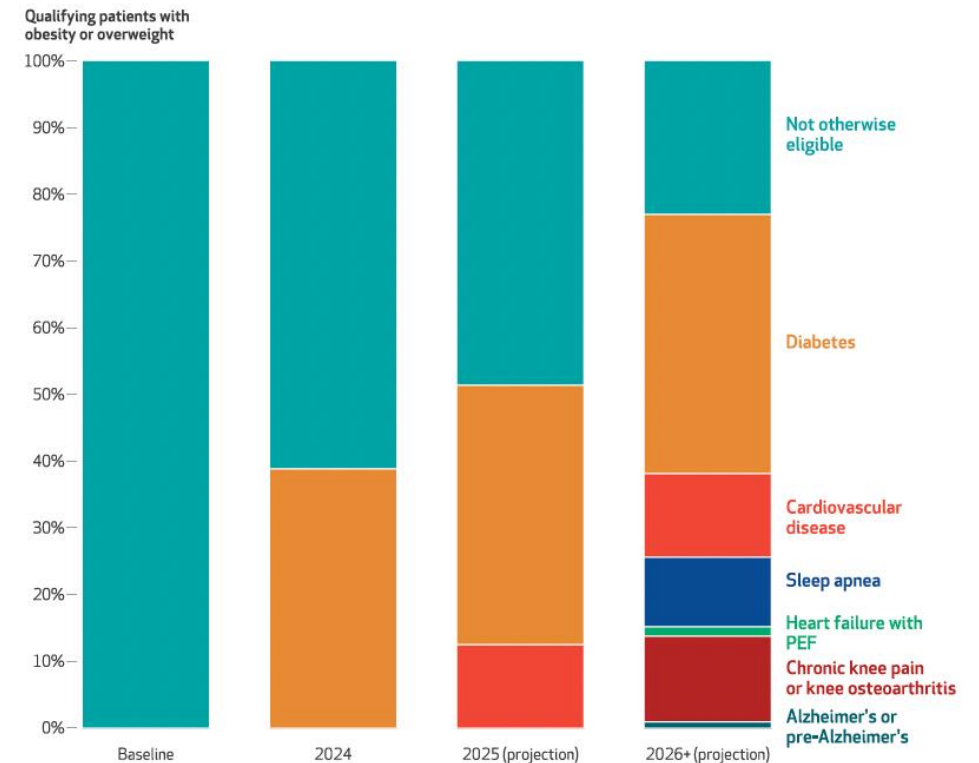
- **28%** of Medicare beneficiaries with obesity/overweight **already eligible** due to diabetes
- At least **14% newly eligible** based on cardiovascular disease
  - Higher if more liberal definition

By Benedic Ippolito and Joseph F. Levy

## Expanding Medicare Coverage Of Anti-Obesity Medicines Could Increase Annual Spending By \$3.1 Billion To \$6.1 Billion

EXHIBIT 4

Percent of qualifying patients with obesity or overweight, as of 2024, who have other conditions for which glucagon-like peptide-1 receptor agonists (GLP-1s) could be approved by 2026 and beyond





# Medicare price negotiation

- **January 2025:** Semaglutide selected for second round of price negotiation under the Inflation Reduction Act
  - Includes both diabetes (Ozempic) and obesity (Wegovy) versions
  - Negotiated price and mandatory Part D coverage will take effect in 2027
- Unclear how this will affect prices & coverage of other GLP1 receptor agonists

## *Medicare to Negotiate Lower Prices for Weight-Loss Drugs*

The government is expected to pay lower prices for Ozempic and Wegovy starting in 2027. The Trump administration will decide whether to expand coverage for millions of Americans.

Listen to this article · 6:33 min [Learn more](#) [Share full article](#) [28](#)



Hollie Adams/Reuters

# Other payers also struggling with coverage



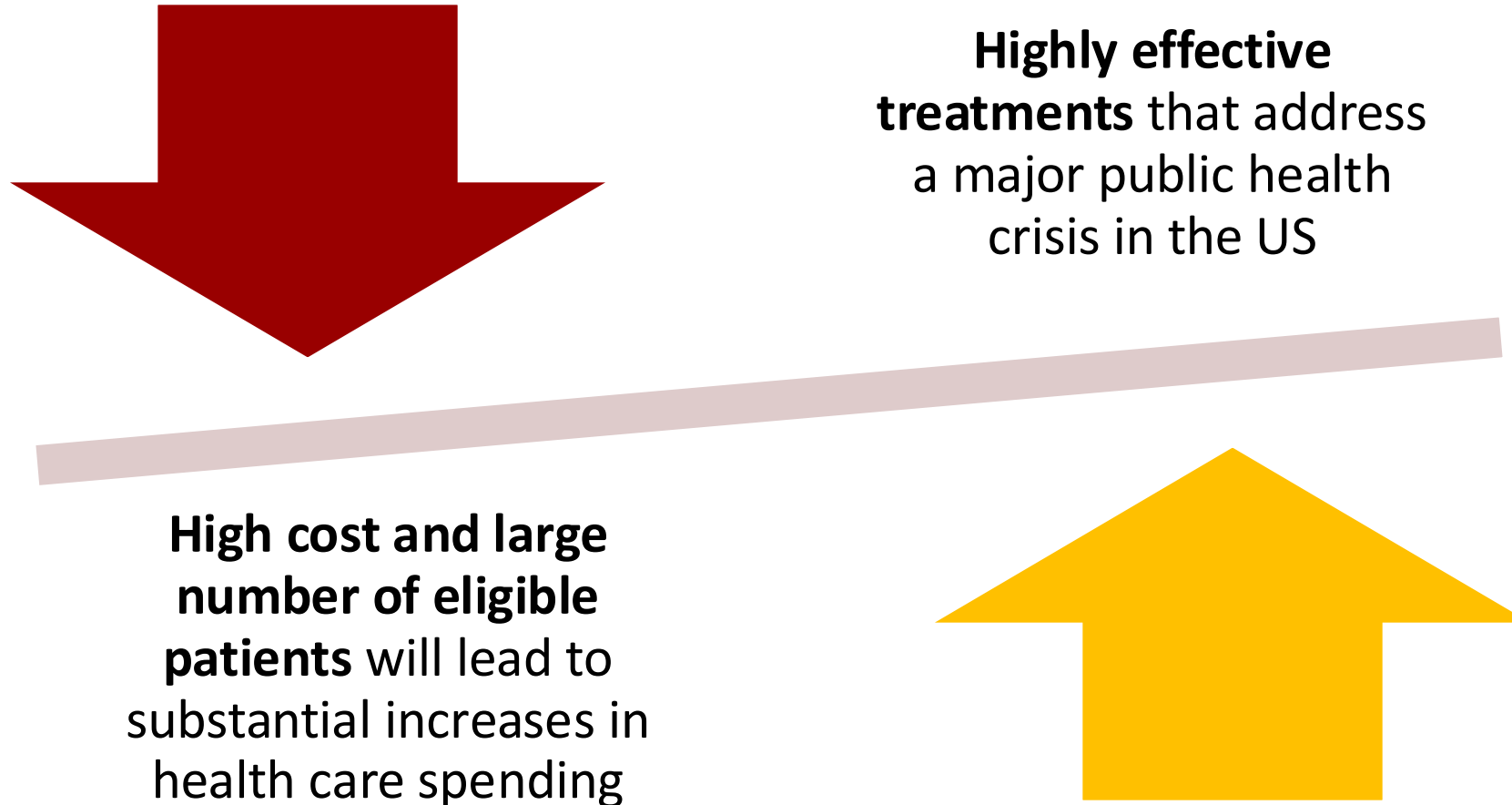
MARCH 7, 2024

## Statement Regarding GLP-1 Coverage

At the January 25, 2024, State Health Plan Board of Trustees, the board voted to remove GLP-1 and GIP-GLP-1 agonist medications from State Health Plan coverage for the purpose of weight loss effective April 1, 2024. These medications will still be covered for members managing diabetes. Read on for more information. Scroll to the bottom of this page for RFI Responses.

*“It is estimated that continuing to cover this class of medications for weight loss would result in a premium increase of **\$48.50 per subscriber per month**, doubling the premium for all individual subscribers, even those not taking these medications.”*

# The fundamental dilemma



# Some people are paying for GLP agonists out-of-pocket

## Direct-to-consumer Pharmacies

Self-pay only

Exclusively through *Lilly Direct*<sup>®</sup>

Single-Dose Vial

✓ Supply available

Doses: 2.5 mg, 5 mg


\$399<sup>\*</sup>

per month for 2.5 mg<sup>†</sup>

or

\$549<sup>\*</sup>

per month for 5 mg<sup>†</sup>



Insurance is not accepted, FSA/HSA cards accepted at checkout. Injection supplies will be available from our pharmacy provider for a nominal fee at checkout.

Rome. JAMA. 2024.

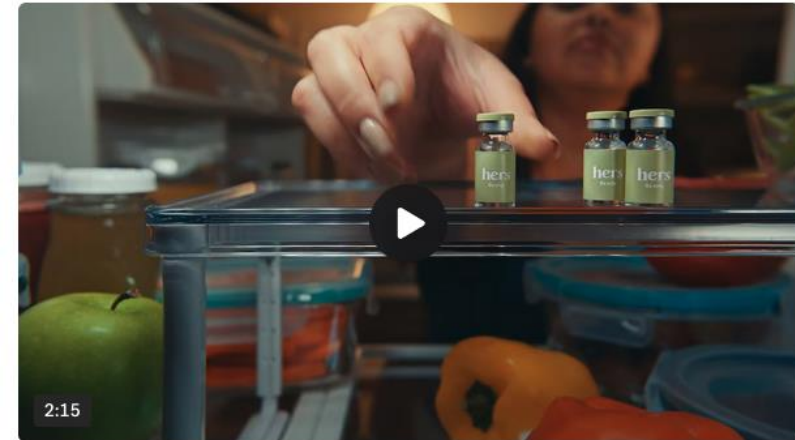
## Compounded versions while branded versions were in shortage\*

### Super Bowl ad for Hims & Hers' weight loss drug sparks backlash

Hims & Hers sells a compounded weight loss medication.

By [Jennifer Leong](#) and [Katie Kindelan](#) [GMA](#)

February 11, 2025, 5:20 PM



This photo provided by Hims & Hers shows Hims & Hers 2025 Super Bowl NFL football spot.  
Hims & Hers via AP

\*Shortages officially ended for tirzepatide (Dec 2024) and semaglutide (Feb 2025)

# So what are the options for payers?

## Not cover the drugs

- Patients who can afford them could pay cash

## Cover, but with high cost-sharing

- Concerns about equitable access; not applicable for Medicare (\$2000 cap) or Medicaid

## Cover for limited populations

- Focus on those most likely to benefit (e.g., severe obesity or obesity with comorbid conditions)

## Other coverage restrictions

- Concurrent or prior behavioral weight management programs
- Trial of less expensive anti-obesity medications (E.g. MassHealth requires phentermine)

## Negotiate lower prices (or higher rebates)

- Leverage competition between 2 manufacturers (Novo Nordisk & Eli Lilly)

# Questions & Discussion

- Thank you!