

What you should know about...

Weight Management, Diabetes and GLP-1s

Mike Margevicius RPh
Pharmacy Director, CarelonRx



Understanding the broad impact of obesity



Obesity has replaced tobacco as the top driver of preventable diseases and death, including:

- **Diabetes**
- **Cardiovascular disease**
- **Musculoskeletal disease**
- **Cancer**

Obesity trends¹:

- Over 42% of adults in US are obese.
- By 2030, 50% will be obese and 25% severely obese.
- 33% of children are overweight or obese (risk of obesity 2-3X higher with one obese parent, 15X higher with two).

Mortality trends:

- All-cause mortality increases 30% for each 5-point increase in BMI.²
- Disease-specific mortality increases with increasing weight.²
- Life expectancy after age 40 decreases 4.2 years for men and 3.5 years for women with BMI ≥ 30 ³

¹ Centers for Disease Control and Prevention, National Center for Health Statistics: *Prevalence of Overweight, Obesity, and Severe Obesity Among Adults Aged 20 and Over: United States, 1960–1962 Through 2017–2018* (January 29, 2021): [cdc.gov/nchs/data/hestat/obesity-adult-17-18/obesity-adult.htm](https://www.cdc.gov/nchs/data/hestat/obesity-adult-17-18/obesity-adult.htm).

² Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, Qizilbash N, Peto R, et al.: *Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. The Lancet* (March 18, 2009): [thelancet.com](https://www.thelancet.com).

³ Bhaskaran K, Dos-Santos-Silva I, Leon DA, Douglas IJ, Smeeth L, et al.: *Association of BMI with overall and cause-specific mortality: a population-based cohort study of 3.6 million adults in the UK. The Lancet* (October 30, 2018): [thelancet.com](https://www.thelancet.com).

The cancer impact of obesity

Cancer and obesity

>15

Cancers associated with obesity

4-8%

Cancers attributable to obesity

17%

Increased risk of cancer-specific mortality due to obesity

Cancers associated with obesity

- Post-menopausal breast
- Colorectal
- Ovarian
- Pancreatic
- Multiple myeloma
- Prostate
- Thyroid

Cancer rate increase

Breast cancer: 11% increased risk for each 5 kg of weight gain

Colon cancer: BMI over 30 doubles risk of cancer for people under 50

Esophageal: 51% increased risk due to obesity

Endometrial: 59% increased risk due to obesity

Cancer mortality

Obesity associated with 13% increased recurrence of early-stage cancer

Obesity associated with 14% higher all-cause mortality and 17% cancer-specific mortality.

Interventions

A range of options are available to treat obesity



Behavioral Modification

Moderation leads to a balanced approach to eating and exercise.

- Modest weight loss (4-10%)¹
- Reduction in DM2 progression (DPP) with 5% weight loss
- Maintenance of weight loss requires continued support and intervention



Bariatric Surgery

Bariatric surgery allows people with morbid obesity to achieve lasting weight loss.

- 25-30% weight loss
- DM2 remission
- Lower cardiovascular and all-cause mortality²
- Reduced cancer rates (30%)³
- Weight re-gain 5 to 10% of body weight at 10 years starting year 2



GLP-1/GIP Drugs

Originally developed to treat diabetes, these drugs have been making headlines for their weight-loss effects.

- 15-20% weight loss
- Reduced mortality and cardiovascular mortality in DM2 patients
- Reduced major cardiovascular events in obese members with high risk but without DM2
- Weight loss not durable after stopping (yet)

1 Metabolic surgery for treating type 2 diabetes mellitus: Now supported by the world's leading diabetes organizations. Effectiveness of primary care-relevant treatment for obesity in adults: a systematic evidence review for the U.S. preventive Services Task Force. *Ann Intern Med.* 2011;;155(7):434.

2 Comparative Effectiveness and Safety of Bariatric Procedures for Weight Loss: A PCORnet Cohort Study *Ann Intern Med.* 2018;169(11):741. Epub 2018 Oct. 30.

3 Bariatricsurgery and the Risk of Cancer in a Large Multisite Coho *Ann Surg.* 2019;269(1):95.

GLP-1 Drugs are Brought to you By...

The Gila Monster

- Glucagon-like Peptide (GLP-1)
- Mimic hormones to control cravings
- Increase insulin production
- Help slow the movement of food from the stomach to the small intestine – feel fuller



The latest with GLP-1s

- GLP-1s are moving beyond diabetes and weight management into other indications, such as secondary prevention indication, heart failure, and sleep apnea.
- Wegovy was the initial drug to expand beyond weight loss and diabetes.
- Zepbound will be the next to expand to other indications, with others on the horizon.
- The FDA continues to review and approve for new indications.

Diabetes (Type 2)

- Ozempic
- Rybelsus
- Mounjaro
- Victoza
- Trulicity

Weight loss

- Wegovy
- Saxenda
- Zepbound

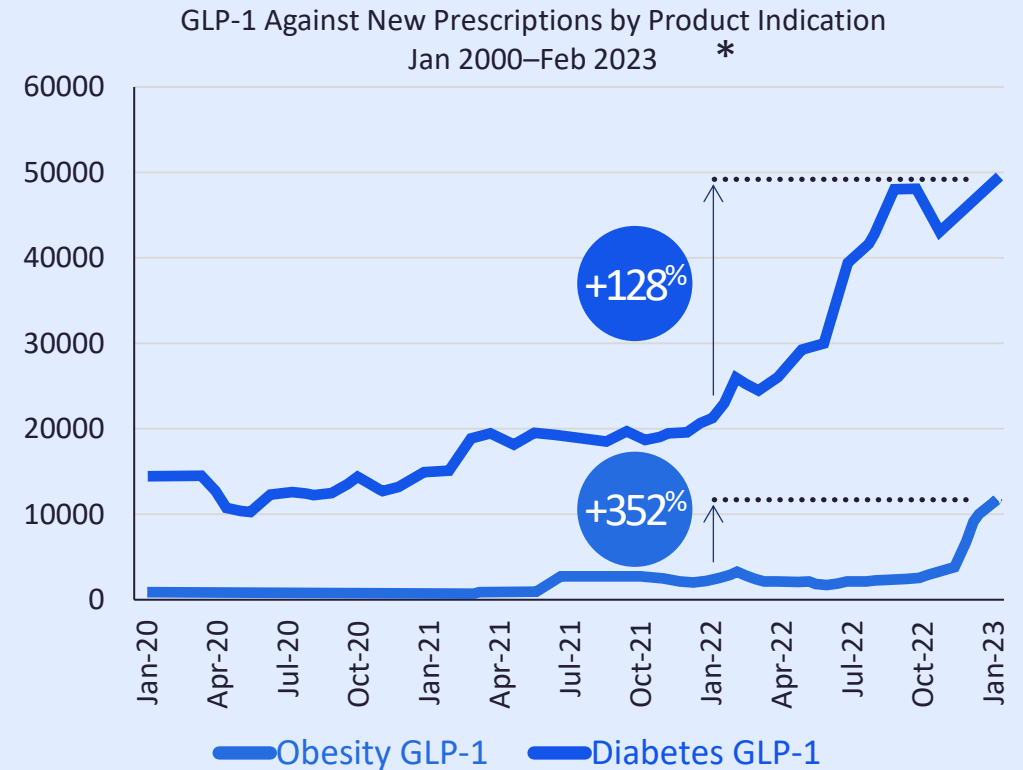
Cardiovascular

- Wegovy



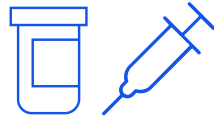
Making Sense of GLP-1 Drugs

- Rapid escalation Post-Covid 19 Pandemic
- Increase in both diabetes and weight loss
- Triple-digit growth in prescription volume
- New criteria added for both weight loss and diabetes in May, 2023
- Utilization has slowed by Q1 2024
- Changes in effect for all members



Making Sense of GLP-1 Drugs

- GLP-1 (glucagon-like peptide) drugs were created as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes
- Fast-track status by FDA for treatment of adults with obesity, or overweight with weight-related comorbidities



Diabetes (Type 2)

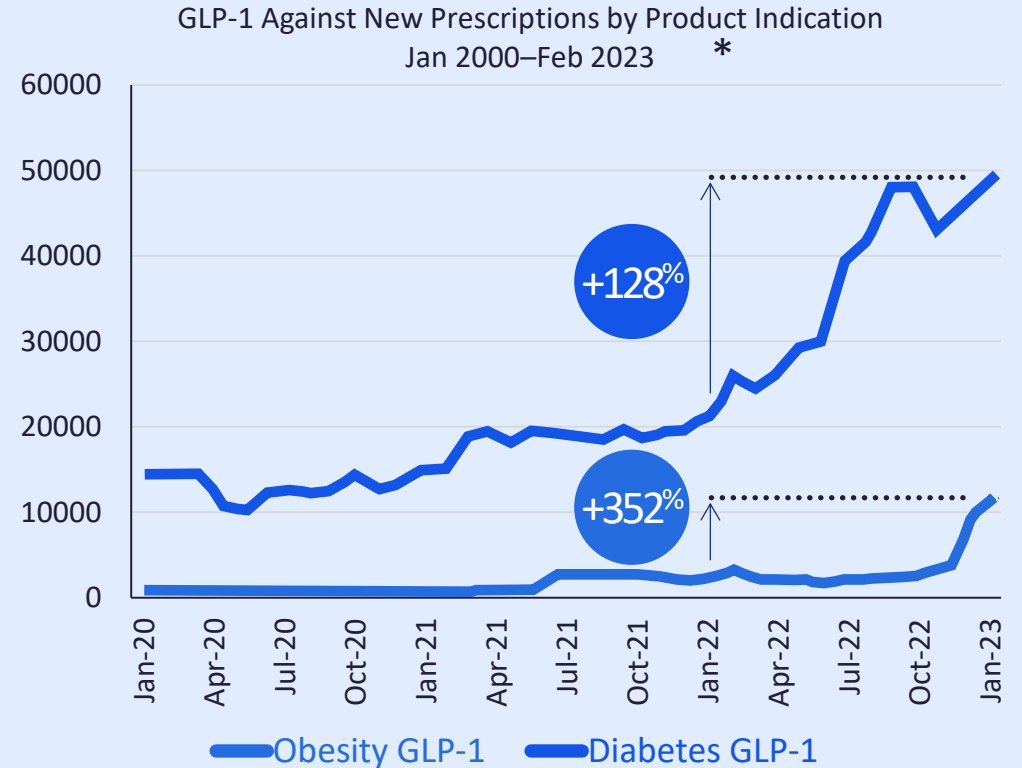
- Ozempic
- Rybelsus
- Mounjaro
- Victoza
- Trulicity

Weight loss

- Wegovy
- Saxenda
- Zepbound

Other Indications

- NASH/MASH
- Anti-inflammatory
- CV/Heart Failure



*IQVIA National Prescription Audit, Feb 2023; IQVIA Institute, Mar 2023. updated 1/24/24

GLP-1 Outlook Summary

New Indications for GLP-1 drugs (in order of potential trend impact):

1. Wegovy – *Cardiovascular indication (FDA approved)*
 2. Zepbound – *Obstructive Sleep Apnea indication*
 3. Wegovy – *MASH (liver) indication*
 4. Wegovy – *Heart Failure indication*
- Ozempic Chronic Kidney Disease (CKD) indication could draw use away from other diabetes drugs like SGLT-2s (i.e., Jardiance)
 - Rybelsus as a first oral GLP-1 for weight management. It would provide easier administration and may offset ongoing drug shortages.
 - Other new weight loss pipeline drugs will mainly compete with existing agents.



If drug shortages continue, the impact of new drugs could be higher if they provide access where patients were unable to get drug due to the shortage.

GLP-1 pipeline – New indications for existing products

	Chronic kidney disease in diabetics	Peripheral arterial disease	Alzheimer's disease	Diabetic retinopathy	Weight management	Obstructive sleep apnea in obesity	Heart failure	CV event reduction	NASH/MASH in overweight/obese
Existing diabetic drugs seeking other indications:									
Ozempic	✓ 2024	✓ 2025	✓ >2025	✓ TBD					
Rybelsus			✓ 2026		✓ 2024			✓ 2025	
Weight loss drugs seeking broader indications:									
Zepbound	✓ >2026				✓ Approved 11/23	✓ 2024/25	✓ 2024/25	✓ 2027/28	✓ 2025/26
Wegovy							✓ 2024	✓ Approved 3/24	✓ 2025

New GLP-1 drugs in development for weight management

New products with weight loss indication awaiting approval:

Product	Projected Approval	Other Indications
Rybelsus (oral)	2H 2024 – 1H2025	
Orforglipron (oral)	2H 2025 – 1H 2026	-
CagriSema	2026	-
Survodutide	2026 or later	NASH/MASH in overweight/obese
Retatrutide	2H 2026 – 1H 2027	Chronic kidney disease in diabetics
Danuglipron (oral)	TBD – Phase 3 Pending	

Studies on value of weight loss drugs

Do the outcomes justify the cost and risks?



- Health-benefit price benchmark for semaglutide is **\$7,500 to \$9,800** per year, representing a discount from the wholesale acquisition cost of **44% – 57%**.
- Majority of ICER panelists found semaglutide combined with lifestyle modification represents “low” long-term value for money overall and “low” long-term value for money compared to legacy weight loss products like Qsymia.
- The lifetime cost of Wegovy is **\$274K** and medical offsets are \$62K for a net lifetime cost of **\$213K**.

Despite increased production, ongoing demand and off-label use for weight loss has led to GLP-1 class shortages*

Drug	Supply Status
Diabetes medications	
Ozempic	No shortage - All doses available
Trulicity	0.75 mg and 3 mg are available, limited availability of 1.5 mg (through May 2024) and 4.5 mg (through 2Q 2024)
Victoza	Limited supply through June 2024
Mounjaro	2.5 mg available. Limited supply of all other strengths through 2Q 2024
Weight Loss Medications	
Saxenda	Limited supply expected to continue indefinitely
Zepbound	2.5 mg available; limited supply of all other strengths through 2Q 2024
Wegovy	1.7 mg & 2.4 mg are available; other strengths have limited availability

Sources: Novo Nordisk: *Updates about Wegovy® (May 2, 2024)*: (novonordisk-us.com); U.S. Food and Drug Administration: *FDA Drug Shortages* (accessed June 4, 2024): accessdata.fda.gov/scripts/drugshortages/default.cfm; and ASHP: *Drug Shortage Lists* (accessed June 04, 2024): ashp.org.

What's happening in pharmacy: Other hot topics....

- ADHD Medication availability
- Flu Vaccine and Covid Vaccine Update – 2024/2025
- Gene Cell and CAR-T Therapies
- Biosimilars and Humira



Questions & Comments

