

Wegovy and the Topsy-Turvy World of Weight-Loss Drugs

Ozempic kicked off a craze for weight-loss drugs, but Eli Lilly and Novo Nordisk may not dominate obesity the way they have dominated diabetes.

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Key Takeaways

- GLP-1 drugs, developed by Eli Lilly and Novo Nordisk in the mid-2000s to treat type 2 diabetes, reinvigorated the moribund market for anti-obesity drugs when they proved effective at inducing weight loss.
- The fen-phen craze of the mid-1990s showed how much demand there could be for effective anti-obesity medications. The potential market, and market opportunity, has only grown since then.
- Given the range of options for people who need or want to lose weight, the dominant position Eli Lilly and Novo Nordisk have in diabetes treatments is not likely to extend into the obesity market.

Eli Lilly and Novo Nordisk have dominated the market for diabetes medicines for a century. They were the first companies to commercialize insulin, and the only companies to have built a business around it, with the scale to consistently develop and sell new therapies. It was a solid, steady business. But Novo Nordisk's introduction of Ozempic, a type 2 diabetes drug that turned out to be surprisingly effective at treating obesity as well, sparked a craze that has fundamentally altered the competitive landscape for these companies.

Diabetes is a disease whereby the body does not produce adequate amounts of insulin, a hormone that helps turn food into energy and manages blood-sugar levels. For diabetics, insulin is often a life-saving therapy. Lilly started manufacturing insulin in the 1920s, Novo Nordisk in the 1930s. Today they are the two largest providers of insulin. Novo has a 33% market share, Lilly 25%.

The market for diabetes drugs has high barriers to entry. Getting a drug approved by regulators is difficult and expensive. Most trials fail; getting a drug to market can cost US\$1-2 billion. And it's not enough to just create a new, effective treatment. Existing diabetes treatments work quite well. A new drug must be effective and offer something that currently available drugs don't, whether that's better efficacy, a new delivery method, or a more convenient dosing schedule.

Lilly and Novo's competitors fall into two categories. The first are other large pharmaceutical companies. Their strategy tends to be opportunistic rather than focused on the category. If they have a drug in the diabetes market whose patents expire, they pull back and don't continue to build up their expertise the way Lilly and Novo have. Therefore, large competitors haven't been very active. In the last 30 years, only Sanofi and Boehringer Ingelheim have entered the market. The second set of competitors are

smaller biotech firms that may have a promising drug candidate, but don't have the resources to see its development through to approval. They can't afford the costs of late-stage clinical trials, manufacturing, marketing, and sales and so they often end up partnering with or being acquired by larger companies.

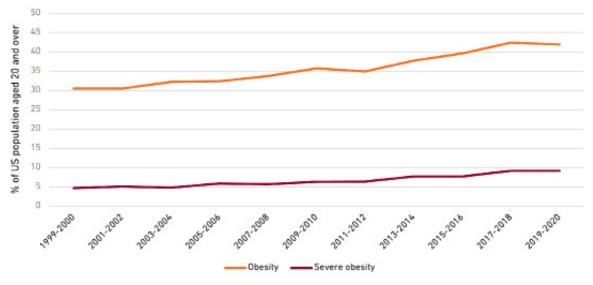
In the mid-2000s, both Novo Nordisk and Eli Lilly developed a new class of treatments that mimicked a human hormone called glucagon-like peptide-1, or GLP-1, which regulates blood sugar. These new drugs were not synthetic insulin; instead, they prompted the body to create insulin. They were designed for type 2 diabetics who were not dependent upon insulin (diabetics who are using insulin can't switch). The goal was to delay the progression to insulin dependence. They also had the advantage of being more convenient to use than earlier therapies, with a less-frequent dosing schedule and also no need for people to check their insulin levels with finger prickers.

With effective drugs, obesity could become as large a market as diabetes, if not larger. And both Lilly and Novo found themselves with drugs that quite possibly could meet that demand.

This new class of drugs had another feature that differentiated them from previous diabetes drugs: they induced weight loss. In a Phase 3 study of the active ingredient in Ozempic, for instance, patients taking the drug lost 10-12% of their body weight after 68 weeks compared to those patients taking a placebo. What this meant is that these drugs could serve both diabetics and people who were overweight. This was significant. The obesity market is smaller than the diabetes market, but only because there's never really been a truly effective obesity treatment. The demand for such a product would be significant. Obesity rates have tripled

Gaining Weight

The number of overweight Americans has been rising steadily.



Source: National Health and Nutrition Examination Survey, 1999-2019.

since 1975; more than 40% of Americans are considered obese and about 10% are considered severely obese. With effective drugs, obesity could become as large a market as diabetes, if not larger. And both Lilly and Novo found themselves with drugs that quite possibly could meet that demand.

Obesity Is Different

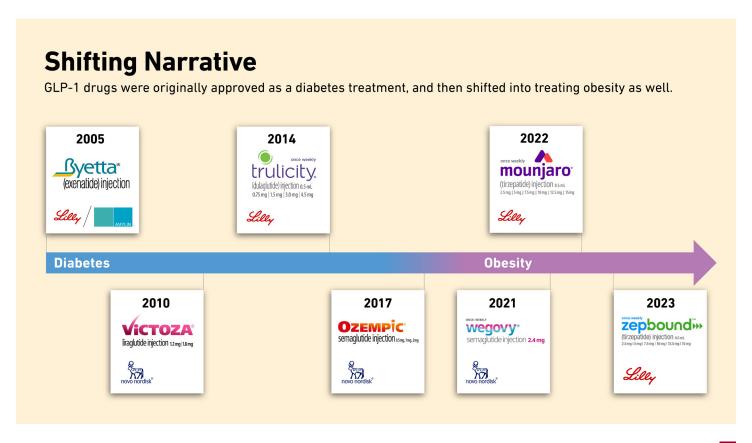
Obesity and diabetes are related to such an extent (the former is a common precursor to developing the latter) that the medical industry has come up with the term "diabesity" to describe them. But the landscape for obesity treatments has been different. Targeted obesity treatments go back 1,000 years, but traditionally obesity hasn't been considered a disease the way diabetes is. There are myriad treatment options, ranging from diet and exercise to weight-loss programs to even surgery. The pharmaceutical industry has long chased after the prospect of finding a drug that could induce weight loss, but the products never seemed to match the need. For example, in 2014 the FDA approved a Novo weight-loss drug called Saxenda that's been moderately successful: patients lost about 5% of their body weight compared to a placebo. But that is not the kind of number that sparks a craze.

The fen-phen craze of the mid-1990s however showed the spike in interest that an effective obesity drug could create. In 1992 a University of Rochester professor showed that a combination of two drugs, fenfluramine and phentermine, could induce patients to lose about 16% of their body weight. That single study sparked

a huge demand for the drugs. Fen-phen clinics popped up around the country. The treatment was featured on the cover of Time Magazine. By 1996, doctors were writing 6.6 million annual prescriptions for the drugs, among an obese population in the US of about 50 million; insurers wouldn't cover the combination and patients were paying about US\$450 a year. However, the drugs were causing serious heart-valve problems in some patients and in 1997 the FDA had the combination removed from the market (phentermine is still available as a single agent.)

The most prescribed weight-loss drug today is still phentermine, a sign of how little had changed when it comes to pharmaceutical approaches to obesity. There have been new brands that have made it to market with various combinations of older active ingredients, but none have been commercially successful. Insurers have been reluctant to cover obesity as a health condition, and the lack of insurance coverage has been a headwind for pharmaceutical companies. For instance, Medicare is barred by law from covering obesity drugs solely for weight loss, and the reason was that obesity was not seen medically as a significant condition. Another problem has been the lack of success. Between 2008 and 2017 about 80% of people with an anti-obesity drug prescription stopped taking it after three months, dissuaded by a combination of limited effectiveness and the cost.

Because of all that, the launch in 2021 of Wegovy, which comprises the same ingredient as Ozempic though at a higher dose, was like an explosion. It fundamentally changed the moribund obesity market. Using Wegovy, patients lost about 16% of their body weight, just like fen-phen. Wegovy had fen-phen-style efficacy



without the fen-phen-style side effects, and garnered fen-phenstyle demand. Soon enough Hollywood stars were suddenly slimming down, the drugs were making headlines, and "Ozempic" became a metonym for the entire class of weight-loss drugs. It was fen-phen all over again. But insurers have been reluctant to cover obesity as a health condition, and the lack of insurance coverage has been a headwind for pharmaceutical companies.

These new anti-obesity drugs were far more effective than previous treatments, and because of that Novo worked to expand insurance coverage for the drug in the US and to a lesser extent overseas. Covered patients rose from virtually zero before the GLP-1 drugs hit to the market to about 50 million currently. Also, the ones labeled for diabetes treatment already are broadly covered by insurance, and these treatments have also proven effective at combating other ailments. Wegovy's new label says it's effective at reducing major heart complications for people who are obese and have already had heart problems. That gives insurers another reason to cover the drug's use.

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Interestingly, even when insurance won't cover an obesity treatment directly, there are ways around that. Novo's Ozempic and Lilly's Mounjaro (both for diabetes) can be used in place of Wegovy and Zepbound (both for obesity), respectively, given that they are essentially the same drug. A doctor and patient can submit proper paperwork, even if exaggerated, to get Ozempic and Mounjaro approved by the insurance company (or Medicare/Medicaid) off-label for obesity. On the basis of price, it's a bit of a

trade down for the manufacturers. Ozempic is about 25% cheaper in the US than Wegovy on a list price basis and about half the price on a net price basis. This is likely similar for Lilly's products. But even at lower prices it can be a benefit to the companies. Zepbound and Wegovy are less broadly covered by insurance than Mounjaro and Ozempic, so fudging the insurance claims for patients without obesity coverage still results in a sale.

A Challenging Opportunity

There is a widespread expectation that in the coming years the obesity market will become as big as, or bigger than, the diabetes market. Today diabetes is a US\$74 billion market while obesity is an US\$8 billion market, but the latter is growing faster. Sales of obesity treatments, have grown 72% a year for the last four years and are projected to grow 26% a year for the next five years. The biggest chunk of that is coming from the US, the largest market for both diabetes and obesity treatments. Sales of diabetes treatments, by contrast, have risen 12% a year for the last four years and are projected to grow only 4% a year for the next five years.

The forecast that the obesity market will continue to see rapid growth is unchallenged, but it may already be at a fen-phen level. Today there are about 110 million obese adults, 2.4 times as many as in the 1990s. Annualized prescriptions for obesity medication are at about 22 million today—more than three times the 6.6 million fen-phen prescriptions from the 1990s. It's not clear that the market can engineer not only another fen-phen craze but build one substantially larger. Yet that is what most outsiders are predicting, expecting the obesity market to see sales hit US\$75-100 billion by 2030. Those estimates would mean the market would grow at a 37-43% annual rate, uninterrupted, for seven years. That is a tall order. Still, the opportunity for GLP-1

1,400,000 Average prescriptions written per month 1.200.000 1,000,000 800,000 600.000 400.000 200,000 2Q20 3Q20 4Q20 1Q21 2Q21 3Q21 4Q21 1Q22 2Q22 3Q22 4Q22 1Q23 2Q23 3Q23 4Q23 1024 ■ Trulicity Byetta Victoza Ozempic Rybelsus Mounjaro Wegovy Zepbound

GLP-1's Popularity Surge
The number of prescriptions for GLP-1 drugs has more than tripled in the last four years.

Source: JP Morgan Pharmaceuticals weekly TRx update, sourced from IQVIA.

drugs could extend beyond obesity. They have shown potential to address a range of maladies, sleep apnea for instance, and be a substitute for other kinds of treatments, like bariatric surgery (we wrote about this in September). As we mentioned, Wegovy's label indicates it is effective at reducing some heart conditions arising from obesity.

The dominance that Eli Lilly and Novo Nordisk built up in diabetes may not translate into obesity.

However, the dominance that Eli Lilly and Novo Nordisk built up in diabetes may not translate into obesity. For one thing, their success in opening the obesity market with GLP-1 drugs has invited a rush of competitors. There are currently 54 potential anti-obesity drugs in development. Twenty seven are in Phase 1 testing, the initial level of testing a drug on volunteers, 20 are in Phase 2, and six are in Phase 3 (including two from Lilly and one from Novo), the last stage before a company would seek regulatory approval. It seems likely that at least some of them will eventually make it to market.

Competition will be an issue, too. There are about 1.8 million prescriptions written for obesity on a monthly basis; about 960,000 are for Wegovy and Zepbound combined, and the balance are for phentermine, according to IQVIA. As a generic drug, phentermine is an option for patients who can't get their insurance company to cover Wegovy or Zepbound. It also is much cheaper, about US\$5-15 per prescription compared to Wegovy at around US\$900 per prescription. There will be other competitors as well. At last check, there were nine filers for generic versions of Ozempic/Wegovy. And of course, there is always the least costly alternative: diet and exercise.

Developing newer drugs that can command higher pricing will be a key challenge for Novo and Lilly. Novo Nordisk is banking on an improved version of a GLP-1 it calls Cagrisema, expected to launch in 2026 and cost \$8,000 a year. Lilly launched Zepbound in November 2023 and it got off to a strong start, capturing 12% share of total obesity prescriptions (TRx) in the US as of Jan. 19, 2024, taking share from phentermine generics, Saxenda, and Wegovy. However, since then its market share has comprised about 15-20%, showing that prescription volume has not grown substantially.

A Reshaped Market

On the surface, it would seem like Eli Lilly and Novo Nordisk are still in an enviable position. But for a variety of reasons, they may struggle with pricing power for the next several years, and beyond that they face an even larger challenge: the patent cliffs for their most popular drugs.

An irony for Eli Lilly and Novo Nordisk is that their success in diabetes and obesity has put them in a position where they are dependent on GLP-1 drugs. As of the first quarter of 2024, Novo and Lilly had a roughly 75%/25% split, respectively, of the US

obesity market, by dollar value, and the US market comprises about 80% of the global market. For Novo, GLP-1 represents 70% of revenue and all of its growth. For Lilly, GLP-1 drugs comprised 43% of its first-quarter revenue. Any sagging demand for their GLP-1 products will be felt acutely on the bottom line.

There is already some evidence that the hype over GLP-1 drugs is outstripping the actual demand. Prescription growth for GLP-1 drugs has slowed significantly. New prescriptions for Wegovy in the US have slowed from roughly 50% growth year-over-year in December to 30% year-over-year growth in February to no growth in April and May. Also, while Lilly and Novo have brand value in Zepbound, Ozempic, and Wegovy, that too will be undercut if competitors bring rival obesity drugs to market and negotiate with insurance companies on price. Therefore, pricing power for these companies is likely to see a long, steady decline in the coming years.

Prices are already trending down. For Ozempic, prices have fallen about 5% per year in recent years, according to Novo. That's largely due to a change in payor mix (companies typically first negotiate with payors where they can get the highest prices, like private insurance). Also, Ozempic and Mounjaro's rapid expansion in volume is resulting in payors getting bigger volume rebates.

At the same time, Lilly and Novo will be facing patent expirations on their own products. Ozempic and Wegovy lose their exclusivity in 2031 and 2032, respectively. By 2030, those two drugs are expected to represent 70% of Novo's revenue. The price and volume pressure that will ensue at that point from branded and generic competitors will be a substantial challenge for the company.

The next decade will see this market buffeted by all these swirling dynamics. Rising sales will bring more competition and give buyers more options. But Wall Street analysts continue to discount price erosion as a significant problem and expect Eli Lilly and Novo Nordisk can continue to launch new products at higher prices. That isn't how markets this competitive work. The likelihood of everything continuing in a straight line upward is low; there are too many things that can go wrong: volume demand could be overestimated; pricing comes down; new entrants break the Lilly-Novo duopoly; or insurance companies push back against coverage. We suspect that something, somewhere will have to give.

Contributors

Co-Deputy Director of Research David Glickman, CFA, contributed research and viewpoints to this piece.

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