

AlphaSense

Obesity Treatments: An Outsized Opportunity

By Sara Mallatt Stahl, Director of Healthcare Research

September 2023

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Executive Summary

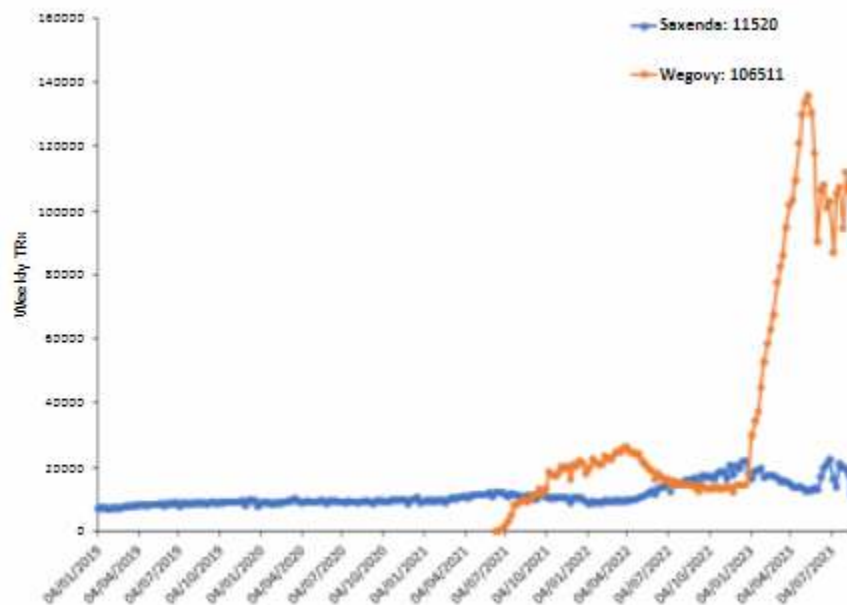
With the help of the AlphaSense platform, including first-person insights from the Stream expert transcript library, we will explore new GLP-1 based medications, which are revolutionizing obesity care. Obesity now affects more than 42% of U.S. adults and 750 million people globally. Novo Nordisk's Wegovy and Ozempic, along with Eli Lilly's Mounjaro, lead the field, achieving 15%-20% weight loss in clinical studies. Skyrocketing demand for the new class of obesity drugs is outstripping supply, despite limited insurance coverage and high out-of-pocket costs. Consensus estimates project the global obesity market to reach \$75 billion by 2028, with insurers' willingness to cover obesity drugs the biggest question mark. As the popularity of new obesity treatments grows, debates are raging about the potential impact on other business models, both within healthcare and without.

Skyrocketing Demand

Sales of a new generation of obesity drugs manufactured by Novo Nordisk are so robust, [the company is now worth more than the entire economy of its native Denmark](#). That's just one of the latest headlines underscoring the frenzy surrounding new obesity drugs on the market and in development from Novo Nordisk, Eli Lilly and others.

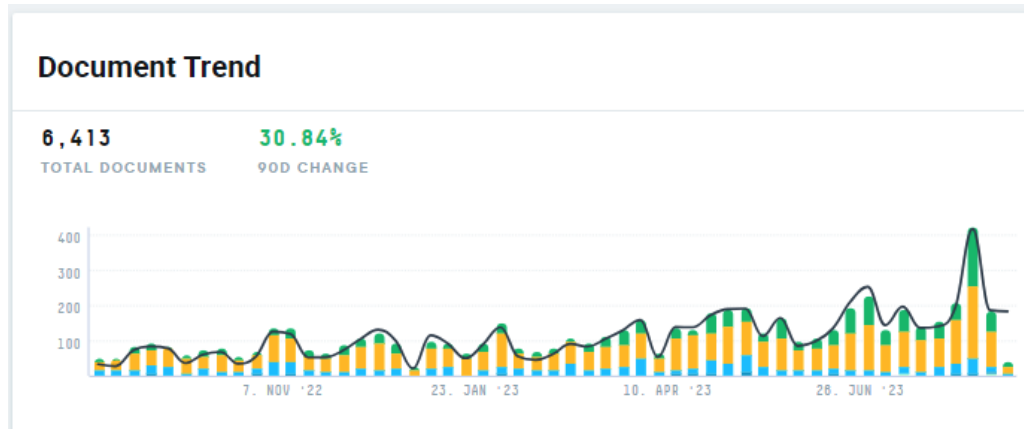
Weekly U.S. prescriptions of Novo's new Wegovy obesity treatment increased 450% y-o-y during 2Q23 and are dwarfing weekly prescriptions posted by Novo's previous-generation Saxenda obesity drug.

Weekly U.S. Prescription Volumes
NVO's Wegovy vs. Previous-Generation Saxenda



Source: [JP Morgan August 2023](#), IQVIA National Prescription Audit

Documents mentioning obesity drugs within AlphaSense have increased more than 30% during the past six months as the surging popularity of these drugs continues to raise questions about their market potential, risks, rewards and threat to other business models.



Source: AlphaSense

Let's dig into these issues with the help of the AlphaSense platform, including first-person insights from the Stream expert transcript library.

Massive Market Opportunity

As celebrities and social media influencers extol the cosmetic benefits of the new class of obesity drugs, it is easy to lose sight of the fact these drugs address a global epidemic. Obesity affects more than 764 million people globally and is associated with more than 200 serious health conditions including heart disease, diabetes, cancer and sleep apnea, according to [Novo Nordisk's Q2 2023 investor presentation](#).

"For some of these patients with [high] BMIs and cardiovascular disease... it's almost a death sentence. They're not going to live past 50 or 60."

– Expert Transcript | [Cardiologist](#)

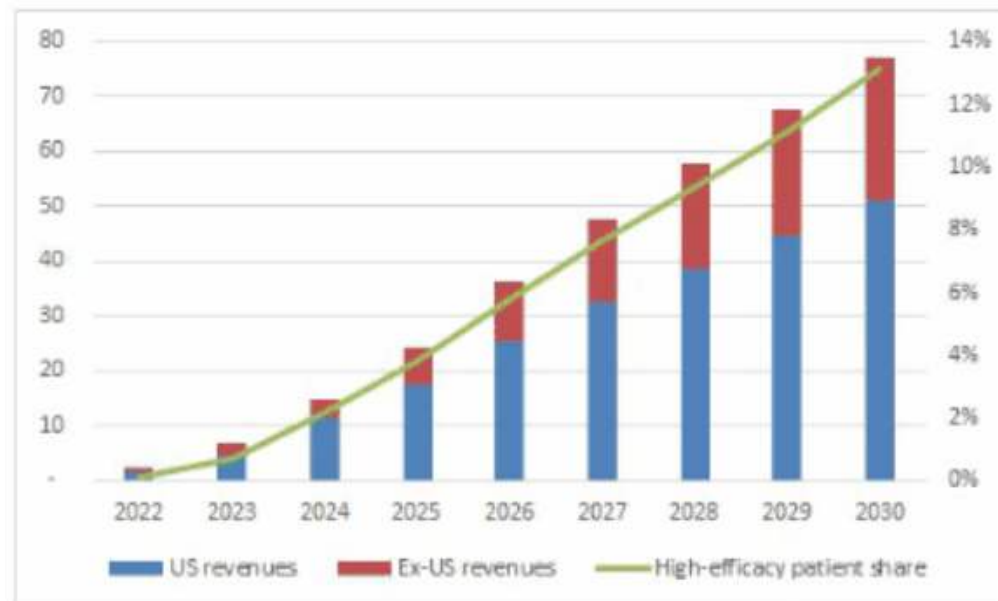


Source: [Novo Nordisk 2Q23 investor presentation](#)

In the United States, nearly 42% of adults were considered obese during 2017 - 2020 (up from 31% during 1999 - 2000), according to the [Centers for Disease Control and Prevention](#), while the estimated annual medical cost of obesity in the United States is around \$173 billion. The standard of care for obesity is diet and exercise, but a [meta-analysis](#) of 29 long-term weight loss studies indicate durable results are largely elusive.

Suffice it to say the market opportunity for obesity drugs is, well, huge. [UBS](#) recently reported consensus estimates for the global obesity market to reach \$75 billion by 2028. Meanwhile, [Morgan Stanley](#) in July projected the global obesity market to reach \$77 billion in 2030, raising estimates from \$54 billion previously.

Global Obesity Market Growth Outlook



Source: [Morgan Stanley, July 2023](#)

Breakthrough Benefits

Ozempic, Wegovy and Mounjaro are some of the most recognizable names on the prescription drug market. One endocrinologist expert stated that:

“I’ve never in my entire career dealt with any medication that has captured the fancy of so many of my patients. I’m literally accosted on the street by friends and family who are asking if they’re candidates [for obesity drugs].”

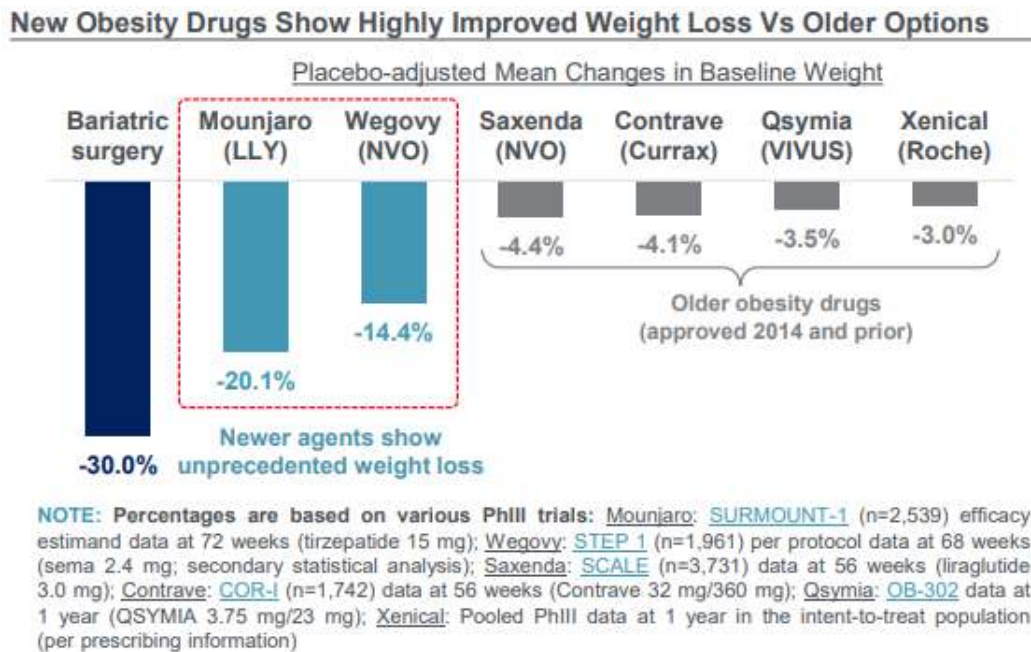
– Expert Transcript | [Endocrinologist](#)

So what are these new obesity treatments, and how do they help people lose weight? They are glucagon-like peptide-1 agonists, or GLP-1s, and they mimic the GLP-1 gut hormone, which regulates how full you feel after a meal and slows down the emptying of the stomach so you stay full longer. The GLP-1 hormone also regulates insulin secretion, which improves blood sugar control. In fact, GLP-1s were initially developed to treat type-2 diabetes, with the first GLP-1 (Alnylam Pharmaceuticals and Lilly’s Byetta) hitting the market in the mid-2000s.

As GLP-1s evolved, researchers discovered they could facilitate meaningful weight loss in diabetic patients. This led to the pursuit of GLP-1s to treat obesity in the broader population. The result: drugs showing roughly 15% - 20% loss in total body weight compared with just 3% - 4% in previous-generation obesity treatments.

“[GLP-1s have] really revolutionized obesity medicine.”

– Expert Transcript | [Endocrinologist](#)



Source: [Piper Sandler, May 2023](#)

Novo Nordisk and Eli Lilly Leading the Way

Ozempic is the brand name of Novo's semaglutide and was the first of the new wave of GLP-1s to hit the market. Ozempic received FDA approval for type-2 diabetes in [late 2017](#) but is frequently used off-label for weight loss. Novo's Wegovy is also semaglutide but with a higher maximum dose than Ozempic and [was granted FDA approval for weight loss in 2021](#).

"I have patients that have been on [Ozempic] for years now, and they have done really well, really life-changing effects... They're moving more. They have decreased their blood pressure pills, their heart failure pills, and overall feeling really well."

– Expert Transcript | [Endocrinologist](#)

Mounjaro, the brand name of Lilly's tirzepatide, received [FDA approval in 2022](#) for type-2 diabetes but is used off-label for weight loss. Tirzepatide is expected to receive FDA approval for weight loss later this year. [Recent trial results](#) indicate better performance for Mounjaro than Wegovy in both weight loss and blood sugar control, which is widely credited to Mounjaro's status as a double agonist that mimics two gut hormones: GLP-1 and gastric inhibitory peptide (GIP).

“[Tirzepatide] is a fantastic drug. I think it’s superior to what we have from older GLP-1s.”

– Expert Transcript | [Endocrinologist](#)

Some Downsides Too

GLP-1 medications are not without limitations. They are expensive, require weekly injections and typically cause loss of muscle mass. In addition, patients commonly report gastrointestinal side effects such as nausea, vomiting, diarrhea and constipation. Yet, many patients are undeterred, according to several Stream experts.

“I have patients [where] the nausea was [so] severe I was ready to stop the [GLP-1] drug, but the patients look at me and [say], ‘No, please don’t stop. This drug is not bad. I can tolerate it.’ I feel like with any other medication, if patients have even minor side effects, they will stop right away.”

– Expert Transcript | [Endocrinologist](#)

Patients also typically regain weight once they discontinue GLP-1 use.

“Pretty immediately the patients regain weight when you stop the [GLP-1] medication. They feel hungrier, they feel cravings.”

– Expert Transcript | [Endocrinologist](#)

For some patients, GLP-1s have little to no effect. (In the [SURMOUNT-2 trial](#), at least 5% weight loss was not achieved among 13.6% - 18.4% of tirzepatide patients, depending on the dose.)

Supply Woes

Soaring demand has led to widespread supply [shortages of Wegovy](#) and [Mounjaro](#) and even Novo’s previous-generation [Saxenda](#). Consequently, in May, Novo reduced the supply of Wegovy starter doses to limit new patients, and both Novo and Lilly are expanding obesity drug manufacturing capacity.

Supply shortages have persisted despite limited insurance coverage for GLP-1s and high out-of-pocket costs.

Average Monthly Retail Price of GLP-1 Agonists

| | |
|----------|-----------|
| Ozempic | \$1015.97 |
| Wegovy | \$1718.50 |
| Mounjaro | \$1179.85 |
| Saxenda | \$1608.12 |

Source: [Pharmacy Times, May 2023](#)

Telehealth companies are capitalizing on GLP-1s' lucrative economics by launching weight-loss programs directly to consumers, many using cash/pay models.

"[There are] a lot of concerns ... around tapping into supply of GLP-1s in a cash-pay model. Is that pulling the medication towards only more well-off folks who want to lose weight for cosmetic reasons?," a telehealth executive expert said.

– Expert Transcript | [Lead. Ro \(Prior\)](#)

[One recent study](#) suggests telehealth companies accounted for nearly half of all 2022 insurance claims for GLP-1 prescriptions.

Supply-demand dynamics have also given rise to compounding pharmacies mixing their own versions of Ozempic. U.S. patients are also seeking GLP-1s from other countries.

"Unfortunately, there is almost like a black market for compounding pharmacies right now,.. There are patients getting their drugs from Canada. There are patients traveling [to] Mexico... Patients are willing to go far beyond our borders to get the medications they need for a reasonable price," an endocrinologist expert said.

– Expert Transcript | [Endocrinologist](#)

Payer Resistance

Insurers are questioning whether the potential long-term benefits of obesity drugs justify immediate expenses. Specifically, the drugs' high price tags and need for ongoing use are giving payers pause, as is uncertainty about patient adherence.

"If it's going to be tens of thousands of dollars [per] patient per year in perpetuity, [insurers'] concern is, 'Okay, I'm going to pay for this, and then the patient discontinues the drug and wham-o, bam-o I've got the same problem I had before.'"

– Expert Transcript | [Healthcare Consultant](#)

Medicare is not covering GLP-1 drugs for obesity nor are most state Medicaid programs. Meanwhile, private payers are pulling back, with [one recent study](#) suggesting GLP-1 coverage for obesity among private payers declined roughly 50% during Dec '22 - June '23 from an already-low level.

Drug developers are hoping to increase payer acceptance with data showing obesity treatments also address comorbidities. At the forefront is Novo's [SELECT trial](#), which showed Wegovy reducing the incidence of heart attack, stroke and cardiovascular death by 20% in non-diabetic obese patients with cardiovascular disease.

“The [SELECT trial] data exceeded expectations.”

– Expert Transcript | [Cardiologist](#)

Novo's stock shot up 17% on the news as [Morgan Stanley](#), [Barclays](#) and other analysts opined the SELECT trial could support broader payer coverage. However, insurers interviewed for [this news story](#) were less optimistic as was a Stream expert employed by a large commercial payer.

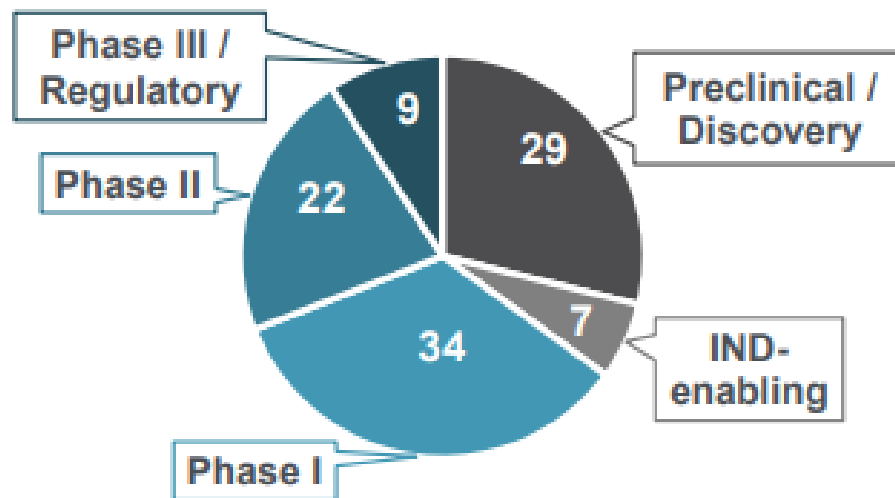
“In the short-term... insurance won't cover [Wegovy]...There hasn't been a big push that says, 'You all need to start covering it.' Until that happens, there's not going to be any changes.”

– Expert Transcript | [Lead, Humana](#)

Robust Pipeline

Drug developers are flocking to the obesity treatment landscape, attracted by the addressable market and opportunities to improve upon existing therapies. According to [Piper Sandler](#), these companies represent more than 60 assets in clinical stages and almost 40 more in pre-clinical or discovery stages.

Obesity Landscape by Development Stage



Source: [Piper Sandler, May 2023](#)

New GLP-1 Combinations

The majority of development programs focus on innovating within the GLP-1 class by pursuing combination therapies that target the GLP-1 hormone as well as one or two additional gut hormones.

Lilly's tirzepatide GLP-1/GIP dual agonist is the leading combination, with FDA approval expected by year end. Tirzepatide, as noted earlier, has shown superior results to Novo's single agonist semaglutide, and Lilly recently published trial data for retatrutide, a triple agonist that targets GLP-1, GIP and glucagon.

"We're all very excited knowing [retatrutide] is possibly coming down the pipe. It seems that the side effect profile is very similar to [the single agonist] GLP and [dual agonist] GLP/GIP, but the weight loss is much more."

– Expert Transcript | [Endocrinologist](#)

Zealand Pharma and partner Boehringer Ingelheim recently published trial results for survodutide, a GLP-1/glucagon dual agonist. Stream experts were generally upbeat about survodutide but were left with questions about the drug's dosing, safety for diabetics, and differentiation in the market.

"The weight loss [survodutide is] showing with this initial trial is pretty impressive... [but it] has some baggage based on my understanding of glucagon and insulin in regard to glycemic control. From a diabetic standpoint, I'm a little reluctant to change. I need more data."

– Expert Transcript | [Endocrinologist](#)

Meanwhile Amgen has a phase 2 trial underway for its GLP-1/GIP dual agonist, which has the distinction of requiring monthly rather than weekly injections.

Oral GLP-1s

Developers are in hot pursuit of oral GLP-1 versions, which promise greater patient acceptance and lower manufacturing costs than injectables. Lilly is developing orforglipron, an oral GLP-1/GIP, while Pfizer is developing danuglipron, an oral GLP-1. Both aim to compete with Novo's Rybelsus semaglutide, which is approved for diabetes and is the sole oral GLP-1 on the market, though it is less efficacious than injectables. Stream experts were generally more optimistic about Lilly's competitive position than Pfizer's.

"[Lilly's orforglipron] seems to rival the currently available injectable options. If it can accomplish that with an oral medicine, I think it has the potential to be a very successful medication."

– Expert Transcript | [Endocrinologist](#)

Non-GLP-1 Approaches

Developers are also pursuing alternatives to GLP-1-based therapies, which could help patients who have difficulty tolerating GLP-1s or do not respond to them.

These drugs could also be used in combination with GLP-1s to improve outcomes, which likely explains [Lilly's recent acquisition of Versanis Bio](#), whose lead asset aims to reduce the negative effects GLP-1s have on muscle mass. Meanwhile [Novo is purchasing Inversago Pharma](#), which is focused on treating obesity by blocking the body's cannabinoid receptors.

Obesity Drugs in Phase 2 or Beyond

| | Lead company | Asset | Target | Administration | Next key catalyst for the asset |
|---------------------------|---|--|---|----------------|--|
| Approved drugs | Novo Nordisk | Saxenda | GLP-1 receptor agonist | Subcutaneous | |
| | Novo Nordisk | Wegovy | GLP-1 receptor agonist | Subcutaneous | |
| Phase 3 and beyond assets | Eli Lilly | Tirzepatide | GLP-1/GIP receptor co-agonist | Subcutaneous | FDA decision expected by the end of 2023 |
| | Novo Nordisk | Oral semaglutide | GLP-1 receptor agonist | Oral | US regulatory submission expected 2H23 |
| | Novo Nordisk | CagriSema | Amylin receptor, GLP-1 receptor co-administration | Subcutaneous | Phase 3 in obesity expected completion late 2024/early 2025 |
| | Eli Lilly | Orforglipron | GLP-1 receptor agonist | Oral | ATTAIN-2 primary completion expected June 2025 |
| | Innovent | Mazdutide (4mg or 6mg mazdutide in Chinese patients) | GLP-1/glucagon receptor agonist | Subcutaneous | GLORY-1 trial started November 2022 |
| | Eli Lilly | Retatrutide | GLP-1/GIP/glucagon receptor triple agonist | Subcutaneous | TRIUMPH-4 primary completion expected October 2025 |
| Phase 2 | Boehringer Ingelheim/ Zealand Pharma | Survodutide/BI 456906 | GLP-1/glucagon dual receptor agonist | Subcutaneous | Initiation of phase 3 trials by Boehringer Ingelheim expected soon |
| | Novo Nordisk | PYY1875 | PYY analogue | Subcutaneous | Phase 2 data expected 2Q23 |
| | Pfizer | Danuglipron | GLP-1 receptor agonist | Oral | Expected phase 2 readout 2H23 |
| | Allimmune Inc | Pemvidutide | GLP-1/glucagon dual receptor agonist | Subcutaneous | Topline results for the full 48 week trial expected in 4Q23 |
| | Innovent | Mazdutide (9mg in Chinese subjects) | GLP-1/glucagon receptor dual agonist | Subcutaneous | Phase 2 study (Chinese subjects) 9mg mazdutide 24 week results May 10th, 2023, study will extend treatment to 48 weeks |
| | Amgen | AM-133 | GLP-1 receptor agonist/GIP receptor antagonist | Subcutaneous | Primary completion October 2024 |
| | Versanis (acquired by Eli Lilly) | Bimagrumab | Activin A, Activin Receptor type 2B | IV infusion | BELIEVE phase 2b study (bimagrumab+semaglutide) primary completion expected September 2025 |
| | Carmot Therapeutics Inc. | CT388 | GLP-1/GIP dual receptor agonist | Subcutaneous | Primary completion September 2023 |

Source: [Goldman Sachs Global Investment Research](#), August 2023

Challenges, Opportunities for Other Business Models

Debates are raging about the effects the new obesity treatments are likely to have on other business models. Bariatric surgery has already come under pressure, according to Intuitive Surgical Inc.'s [Q2 earnings](#) call which revealed obesity drugs had tempered use of the company's surgical robots for U.S. bariatric procedures.

“It scares me sometimes that [obesity medication could] be so pervasive that it eliminates the need for my specialty.”

– Expert Transcript | [Bariatric Surgeon](#)

Meanwhile, weight loss industry giants [Weight Watchers International](#) and [Wellful](#) (parent of Nutrisystem meals) have responded to the new environment by using acquisitions to become telehealth obesity drug prescribers.

Shares of companies making diabetes devices (e.g. Dexcom, Tandem, Insulet) and sleep apnea devices (e.g. Resmed, Inspire Medical Systems) have come under pressure on speculation that sales will be squeezed by obesity drugs.

“The [insulin] pump market will probably diminish as these drugs enter the market... I am seeing so many of my patients, type 2s, coming off insulin.”

– Expert Transcript | [Endocrinologist](#)

Other healthcare categories considered at risk are those positively correlated with obesity, including cardiovascular disease, cancer, orthopedics and general surgery procedures such as

hernia repair and gallbladder removal. Conversely, obesity drugs could fuel demand for some aesthetic procedures, likely benefitting InMode, Cutera and Bausch Health Companies.

“It’s really going to be an exciting time since so many people are going to be... accessing [obesity] medicines. That’s going to leave them with excess skin or residual fat... Those medicines [are] really great news for companies that are into body contouring and skin tightening.”

– Expert Transcript | [Plastic Surgeon-in-Chief](#)

Beyond healthcare, [Morgan Stanley](#), [BNP Paribas Exane](#) and other analysts are speculating about obesity treatments’ implications for food and beverage companies.

Big Picture

Widen the lens further, and questions arise about what other business models may be helped or hurt by potentially tens of millions of people spending less on food and healthcare while living longer, more active lives. What are the implications for recreation, travel, entertainment, retail, technology, agriculture, transportation, even energy? Although we are still in early innings, it is likely not too soon to think big about obesity treatments.

Ready to dive deep into the expert transcript library? [Start your free trial of AlphaSense today.](#)