Dear friends and family,

I'm writing to tell you about the new weight-loss drugs, which appear to be nothing short of MIRACULOUS, especially Mounjaro (tirzepatide), which has fewer side effects and results in the greatest weight loss (see chart in the WSJ article below).

I know more than half a dozen people on it and they're all thrilled, having lost large amounts of weight with few side effects. One friend has lost 90 pounds in nine months – I can hardly recognize him! The *worst* outcome among my friends is a still-amazing 22-pound loss in five months.

And there may be incredible additional benefits as well – see the article below in The Atlantic and the New Yor Times, Did Scientists Accidentally Invent an Anti-addiction Drug? and People on Drugs Like Ozempic Say Their 'Food Noise' Has Disappeared. Another friend told me that Mounjaro has been the best antidepressant he's ever taken.

One friend said he was on Ozempic and lost 11 pounds in two months, but it caused all sorts of uncomfortable digestive issues/bloating, so he switched to Mounjaro two months ago and has lost weight even more rapidly – another 22 pounds – *and* has no side effects.

The drugs work by simply suppressing appetite. If you go out to a restaurant and are served a big plate of something, instead of eating all of it, you'll only eat half. You don't have to change your diet – you just eat everything you normally do, but less of it.

My friend who's lost 22 pounds loves good food and wine and is so happy that he hasn't had to give any of it up – he just eats less. In particular, he said he no longer has food cravings, so, for example, when he watches a movie at home, he no longer eats a ton of snacks.

The friend who's lost 90 pounds wrote: "The drug is liberating because it stops the noise that existed in my head about food. I still enjoy food, but I don't think about it all the time."

Most of my friends say they've been able to work with their doctors to get the $1,200 monthly cost covered by their health insurance (it's a once-a-week, self-administered injection), but those who pay for it out of pocket say they can find discounts that reduce the price by 50%.

I've just created a new personal e-mail list to which I'll send articles and commentary about these new drugs. To subscribe to it, simply send a blank e-mail to: weightlossdrugs-subscribe@mailer.kasecapital.com

I've heard six main objections to these drugs:

a) They can cause severe bloating, gassiness, burping and diarrhea.

My response: This is common among those taking Ozempic and Wegovy, but is much less common with Mounjaro, which is a major reason why all of my friends are on this drug (it also results in greater weight loss).

b) What about more serious side effects?

My response: Anyone who takes any of these drugs should do so while being monitored by a doctor because there are indeed a number of serious, though rare, known side effects, which are listed on the Mounjaro website.

For example, one friend stopped taking Mounjaro after he read that one possible side effect is tumors, even cancer, of the thyroid.

But I Googled "Does being overweight increase your risk of cancer?" and the first hit is the CDC saying "that being overweight or having obesity are linked with a higher risk of getting 13 types of cancer. These cancers make up 40% of all cancers diagnosed in the United States each year." Every drug has a long list of potential side effects – just Google "ibuprofen side effects" or "aspirin side effects".

The vast majority of people who take Mounjaro have few or no side effects – and lose *a lot* of weight, which has *huge* long-term health benefits.

c) We don't know their long-term effects.

My response: The oldest of the drugs, Ozempic, was approved for diabetes six years ago and, to my knowledge, those taking it have had no issues. And we do know the *horrific* long-term effects of being significantly overweight, so I think the risk-reward is heavily skewed toward taking the drugs.

d) They have to be taken for life (for most people, if they stop, the weight comes right back).

My response: So? Millions of people are on countless drugs for life. My dad, after developing A-fib last year and having two ablations, is on a drug for the rest of his life to control his A-fib. Ditto for the statin I just started taking to reduce my high cholesterol and the resulting plaque and calcium that's built up in my heart. And ditto for people taking drugs for diabetes, high blood pressure, coronary artery disease, asthma, kidney disease, depression, etc.

e) They're too expensive.

My response: They are indeed if you have to pay the full list price of ~$1,200 per month. But most of my friends are able to get their doctor to prescribe it so insurance covers it and those that have to pay out of pocket are able to get roughly 50% discounts. One friend told me he's able to get Mounjaro for $400 per month from a compounding pharmacy.

I also think the price is going to come down sharply as more companies introduce more of this category of drugs, including pills.

f) It's somehow cheating (I only hear this from skinny people, usually accompanied by an air of superiority).

My response: Every study shows that almost nobody is able to lose a lot of weight and keep it off in the long run. It's just too hard to significantly and permanently modify exercise and, far more importantly, dietary habits.

One friend who lost 40+ pounds in two months on Mounjaro and then stopped taking it because he bought into this "cheating" narrative. He wrote: "I decided it's time to stop taking the easy way out of not exercising. I just gotta exercise and not eat so much cake!" Sure enough, he quickly gained back every pound.

I think my friend (who's my age) is making a *big* mistake that markedly increases his chances of major health problems in coming decades and will likely shorten his life by 5-10 years.

For more on this, see this podcast: I Lost Weight on Ozempic. Here's What the Debate Gets Wrong. Why one doctor believes obesity should be treated like any disease – with medication.

Here are links to articles (full text below) from the front page of the June 16 New York Times, Barron's, three from the Wall Street Journal, The Atlantic, two more from the NYT, the NYT podcast mentioned above, and a 60 Minutes segment:

- New Obesity Drugs Come With a Side Effect of Shaming (NYT)
- At Last, Weight-Loss Drugs That Actually Work. They Could Be the Blockbusters of the Decade. (Barron's)
- Ozempic and other injections meant to treat chronic medical conditions are in high demand among elites looking to lose a little weight. 'This is the Hollywood drug.' (WSJ)
- The 'King Kong' of Weight-Loss Drugs Is Coming (WSJ)
- No More Shots: Pill Versions of Ozempic-Like Drugs Are Coming (WSJ)
- Did Scientists Accidentally Invent an Anti-addiction Drug? (The Atlantic)
- People on Drugs Like Ozempic Say Their 'Food Noise' Has Disappeared (NYT)
- What New Weight Loss Drugs Teach Us About Fat and Free Will (NYT)
- What Ozempic Reveals About Desire (NYT)
- I Lost Weight on Ozempic. Here's What the Debate Gets Wrong. (NYT)
- Recognizing and Treating Obesity as a Disease (60 Minutes)

Best,

Whitney

PS—Here are emails from two of my readers:

Gerry N.:

> I first discovered the drug from reading one of your columns last year. My doctor was skeptical at first but when you wrote a follow-up column going into the research details, he went ahead and prescribed Mounjaro for me.

The results have been amazing: I've lost 50 pounds in six months, my triglycerides have come down by 60%, and my A1C went from 6.2 to 5.7 in just three months.

I am fortunate that my health insurance pays for it with a small co-pay and there are now 6 dosage strengths available versus just three at the drug's introduction. My BMI has gone from 33% to just under 26. Another 15 pounds is my goal and I'll be at the recommended weight for my height and age.

More astounding are the psychological benefits. I used to eat every meal like it was my last. Mounjaro just tells my brain I'm not hungry so I eat less and I don't snack any more. Those dreaded evenings in front of the TV eating anything that was around are over! While I was always active, I used to just eat more – simply offsetting the calories I was burning. My energy level is way up and I feel great.

Also, I was on Ozempic for a while before this and in spite of the claims most folks have about losing 25 pounds, I didn't lose any weight whatsoever. Mounjaro has been a life-changing drug for me.

Given the improvements in mental and physical health for so many people across the world, governments, insurers and the pharmaceutical industry need to start approaching this class of drugs as a miracle breakthrough for the problem of obesity, not a luxury for those that can afford it. Please keep pounding the table on this issue – we will be way better off as a result.

Your investment advice is spot on and I love your weekly newsletters but honestly, I will always be grateful that it was your column that convinced my doctor to prescribe Mounjaro for me – that payoff alone is priceless.

Rick A.:

I read about Mounjaro, researched it, and concluded it would be good for me.

I'm a semi-retired 59-year-old man who was always been very lean, athletic, and in shape most of my working life, but became overweight by 40 pounds. I'm on blood pressure medication, gout medication, and few others.

Every time I went to my doctor, he told me the same thing: you have to lose weight so don't eat potatoes or rice, reduce carbs, work out, and no drinking. I tried to lose weight, but after two weeks I felt bad mood swings and always went back.

So my doctor prescribed a very low dose (2.5mg) of Mounjaro about five months ago.

Today I'm down 32 pounds. I feel great, think clearer, and am much more active. Everyone tells me I look great – they actually ask me if I had plastic surgery. I no longer take any medication. No more mood swings. My wife tells me I don't snore anymore.

> There are so many benefits I have received from this once-a-week injection. I truly feel so many people are in the same position as I was: overweight and cannot seem to get normal weight loss measures to work.
>
> From health, personal appearance, mental aspects, and personal thoughts about one's self, I think the upcoming approval for Mounjaro for weight loss will be a great benefit to society.

PPS—This is what I included in my investing daily on June 27:

A heartbreaking 1.13 million Americans have died of COVID since the deadly virus struck a little more than three years ago.

Over the same time, nearly as many Americans have died of another deadly disease that causes high rates of diabetes, heart disease, 13 types of cancer, osteoarthritis, high blood pressure, sleep apnea, dementia, various forms of mental illness, body pain, and poor physical functioning.

Worse yet, it is immediately obvious who is suffering from this disease and there are terrible stigmas associated with it. Those suffering from it are widely assumed to be ugly, lazy, lacking willpower and moral character, having bad hygiene, and being less intelligent. Not surprisingly, therefore, sufferers feel anxiety, depression, and shame.

By now you've probably guessed that the disease I'm talking about is obesity.

More than 70% of Americans are overweight, almost half of whom qualify as obese.

This leads to a myriad of lifelong health problems, culminating, for many, in early death: An estimated 300,000 Americans and between 2.8 million and 4.7 million people worldwide die each year from being overweight or obese.

These horrifying numbers rival COVID's, yet the responses to these deadly epidemics couldn't be more different.

When the virus hit, pretty much every government, scientist, and person on earth reacted with alarm and took dramatic measures to reduce the impact of the pandemic.

And it worked! In record time, vaccines were developed and made widely available, for free, which saved millions of lives.

In contrast, we've basically done nothing as the obesity epidemic has spread across America and around the world...

In fact, things have rapidly been going from bad to worse in recent decades. According to this 2019 *New York Times* article, You're Not Getting Much Taller, America. But You Are Getting Bigger:

> Meet the average American man. He weighs 198 pounds and stands 5 feet 9 inches tall. He has a 40-inch waist, and his body mass index is 29, at the high end of the "overweight" category.
> The picture for the average woman? She is roughly 5 feet 4 inches tall, and weighs 171 pounds, with a 39-inch waist. Her B.M.I. is close to 30.
>
> That's a not at all how Americans used to look. New data show that both men and women gained a whopping 24 pounds on average from 1960 to 2002; through 2016, men gained an additional eight pounds, and women another seven pounds.

The story is similar around the world.

However, things may be about to change radically for the better thanks to three weight-loss drugs – Ozempic and Wegovy (semaglutide), made by Novo Nordisk (NVO), and Mounjaro (tirzepatide), made by Eli Lilly (LLY).

Numerous studies show that people taking these drugs lose 15% to 22% of their body weight and keep it off. For a 240-pound person, that's a life-changing/extending/saving 36-53 pounds! And there are even more promising drugs under development (see article below).

I know more than half a dozen people on Mounjaro (which appears to be the best of the current drugs, with the greatest weight loss and fewest side effects) and they're all thrilled. One friend has lost *90 pounds* in nine months – I can hardly recognize him! The *worst* outcome among my friends is a still-amazing 22-pound loss in five months.

But in a scandalous side of the story, these drugs aren't widely available. It is very difficult to get health insurers to pay for them, and few people can afford their $1,200 monthly cost.

As a result, they're disproportionately being used by the wealthy, despite the fact that it's lower-income people who need these drugs the most, because they're more overweight and have inferior access to health care to treat all of the terrible consequences of obesity.

Can you imagine the outcry if this is how we had handled the COVID vaccines?

In future e-mails, I'm going to do a deep dive into these drugs, but for today, I'll just highlight two recent pieces of good news...

Experimental drug could offer more weight loss than any drug now on the market, study finds. Excerpt:

> An experimental drug from Eli Lilly has the potential to provide greater weight loss benefits than any drug currently on the market.
>
> The experimental drug, retatrutide, helped people lose, on average, about 24% of their body weight, the equivalent of about 58 pounds, in a mid-stage clinical trial, the company

> said Monday from the American Diabetes Association's annual meeting in San Diego. The findings were simultaneously published in The New England Journal of Medicine.
>
> If the results are confirmed in a larger, phase 3 clinical trial – which is expected to run until late 2025 – retatrutide could leapfrog another Lilly weight loss drug, tirzepatide, which experts estimated earlier this year could become the best-selling drug of all time. Tirzepatide is currently approved for Type 2 diabetes under the name Mounjaro; FDA approval of the drug for weight loss is expected this year or early next year.
>
> The new findings, according to Dr. Shauna Levy, a specialist in obesity medicine and the medical director of the Tulane Bariatric Center in New Orleans, are "mind-blowing."
>
> Levy, who was not involved with the research, said the drug seems to be delivering results that are approaching the effectiveness of bariatric surgery. "It's certainly knocking on the door or getting close," she said.

No More Shots: Pill Versions of Ozempic-Like Drugs Are Coming. Excerpt:

> In the works for people flocking to Ozempic to shed lots of pounds: Weight-loss medicines that come in a pill.
>
> Drugs such as Ozempic that have surged in popularity for weight loss must be injected. Yet many people despise needles, prompting drugmakers to explore formulations that could be swallowed.
>
> The chemistry isn't simple. But if researchers can pull it off, the tablets could appeal to the sizable number of people who fear needles, while also costing hundreds of dollars less than their injected cousins.

Lastly, I've just created a new personal e-mail list to which I'll send articles and commentary about these new weight-loss drugs. To subscribe to it, simply send a blank e-mail to: weightlossdrugs-subscribe@mailer.kasecapital.com

New Obesity Drugs Come With a Side Effect of Shaming

Wegovy and other drugs expose a social tension between a quest to medicate illness and a stigmatizing belief that obese people lack sufficient willpower to lose weight.

Eileen Isotalo, who went on her first diet at age 14, lost 50 pounds after consulting a weight management clinic at the University of Michigan and being prescribed Wegovy.

By Gina Kolata

Ms. Kolata interviewed numerous patients at a weight management clinic in Ann Arbor, Mich. for this article.

June 14, 2023

https://www.nytimes.com/2023/06/14/health/obesity-drugs-wegovy-ozempic.html

Eileen Isotalo was always able to lose weight, but always gained it back. Now 66, her first diet was with Weight Watchers at age 14. She went on to try one diet after another and bought so many books on weight loss that she thinks she has more than the public library.

In desperation, she finally went to a weight management clinic at the University of Michigan. She had sleep apnea and aching knees, but could not curb her appetite.

“It’s just this drive to eat,” said Ms. Isotalo, a retired interior design coordinator. “It’s almost like this panic feeling when you start craving food.”

“My mental shame was profound,” she said.

Now, though, since she started taking Wegovy, one of a new class of drugs for obesity that was prescribed by her doctor at the clinic, those cravings are gone. She has lost 50 pounds and jettisoned the dark clothes she wore to hide her body. Her obesity-related medical problems have vanished along with much of the stigma that caused her to retreat from family and friends.

But like others at the clinic, she still struggles with the fear others will judge her for receiving injections to treat her obesity rather than finding the willpower to lose weight and keep it off.

Yet the drug, she said, “changed my life.”

Wegovy and drugs like it make this “a very exciting time in the field,” said Dr. Susan Yanovski, co-director of the office of obesity research at the National Institute of Diabetes and Digestive and Kidney Diseases.

About 100 million Americans, or 42 percent of the adult population, have obesity, according to the Centers for Disease Control and Prevention. For the first time, people with obesity, who faced a lifetime of medical jeopardy, can escape the ruthless trap of fruitless dieting and see their obesity-related health problems mitigated, along with the weight loss.

But there is still the taint.

“There’s a moral component to it,” Dr. Yanovski said. “People really believe that people with obesity just need to summon their willpower and they think that taking a medicine is the easy way out.”

Unlike other chronic diseases, obesity is on full public display, Dr. Yanovski said. “No one looks at you and knows you have high cholesterol or high blood pressure,” she said.

Obesity, she added, “is one of the most stigmatized conditions out there.”

Wegovy's maker, Novo Nordisk, reports that doctors in the United States have written about 110,000 prescriptions for the drug.

Wegovy and a similar but less effective medication, Saxenda, are the only ones in their class of drugs so far to be approved for the treatment of obesity — others like Ozempic and Mounjaro are diabetes drugs but also spur weight loss.

Novo Nordisk, Wegovy's maker, reports that doctors in the United States have written about 110,000 prescriptions for the drug. Citing a huge demand, the company recently put its advertising for Wegovy on hold.

"We can't make enough," said Ambre James-Brown, a Novo Nordisk spokeswoman. Supplies are so limited that the company is only selling the drug in the United States, Norway and Denmark, the company's corporate headquarters. Its high list price of $1,349 a month puts it out of reach for most whose insurance will not cover it. But increasingly many insurers do.

The drugs have arrived at a time when researchers have documented the risks of obesity and the futility of prescribing only diet and exercise as a treatment. Decades of studies have consistently shown that very few people can lose excess weight and keep it off with lifestyle changes alone.

People with obesity are at risk for a variety of serious medical conditions, including diabetes, hypertension, high cholesterol, sleep apnea and nonalcoholic fatty liver disease, a leading reason for liver transplants in the United States.

Losing weight can make some of these complications vanish.

Katarra Ewing of Detroit will readily tell anyone who asks that she takes Wegovy, which helped her lose 90 pounds. But she said some longtime friends fell away after she lost weight.

Yet the belief persists — fed by diet gurus, influencers and an industry selling supplements and diet plans — that if people really really tried, they could shed pounds.

So those who take a drug like Wegovy often end up in uncomfortable situations that are influenced by the common view that obesity is a lifestyle choice.

At the University of Michigan clinic there are those like Ms. Isotalo whose reluctance to admit to taking Wegovy stems from her conviction that those who take it are often thought to be cheating.

Another patient, though, Katarra Ewing of Detroit, readily tells anyone who asks that she takes the drug. She tried diets, but it was Wegovy that allowed her to lose 90 pounds.

She came to the weight management clinic after her all-night shift at a Ford factory, ebullient and vibrant, wearing a vivid green sweater. She has more energy now that she lost the weight, her mood is brighter, her high blood pressure gone.

But she discovered an unintended social consequence to weight loss, as many longtime friends fell away.

“Only my genuine friends are left and that’s a very small number,” Ms. Ewing said.

Obesity medicine specialists say they are not surprised — they see the same thing after people lose weight with bariatric surgery.

Relationships shift because obesity is such a defining condition. People of normal weight may feel superior to a friend with obesity and that helps define a relationship — until the friend loses weight. Other friends who themselves have obesity may use the condition as a bonding factor in the relationship. Now that is gone.

Another issue is the drugs' reputation as vanity medications, which has been amplified by comedians' punchlines at the Oscars and in other high-profile settings.

But when Samuel Simpson came to the weight management clinic, he considered losing weight to be a matter of life or death.

Mr. Simpson was terrified he'd face the fate of his mother, brother and sister, all of whom had obesity and diabetes. They all developed kidney failure that ultimately killed them, each dying at the age of 59.

Amy Rothberg, the medical director of Rewind, a company that counsels diabetic patients, and a professor of medicine at the University of Michigan. "I don't think it's a matter of willpower," she told one patient.

His first appointment with Dr. Amy Rothberg at the clinic was nearly two years ago, when he was 58. He had obesity and diabetes. Although he was taking high doses of insulin to lower his blood sugar, his kidneys were starting to fail.

“I was so afraid,” he said. “Was I going to end up on dialysis like everyone else? I’d be history.”

He began with a diet and then Dr. Rothberg added Mounjaro, a drug by Eli Lilly that appears to be even more powerful than Wegovy in eliciting weight loss, but is, so far, only approved for people with diabetes.

Now he’s lost 44 pounds, 20 percent of his original weight, and his diabetes is in remission. The weight loss, he said, “turned my life around.”

He will tell those who ask how he lost the weight,

“I’m not like the roadside preacher but when someone asks me how I did this I will tell them,” he said.

Art Regner had a different issue. A garrulous color commentator for the Detroit Red Wings hockey team, he said he was not ready to resort to medication. But when he came to Dr. Rothberg’s clinic he was chagrined. He’d regained 22 of the 76 pounds he lost by dieting.

Dr. Rothberg, who is also the medical director of Rewind, a company that counsels diabetic patients, suggested Wegovy or Mounjaro. But Mr. Regner felt he should have enough willpower to do it on his own. He knows his blood sugar is high and is aware of the consequences of diabetes.

Dr. Rothberg gently explained to him that it was not his fault he kept regaining weight every time he lost some.

“I think biology is conspiring against you,” she said. “I don’t think it’s a matter of willpower.”

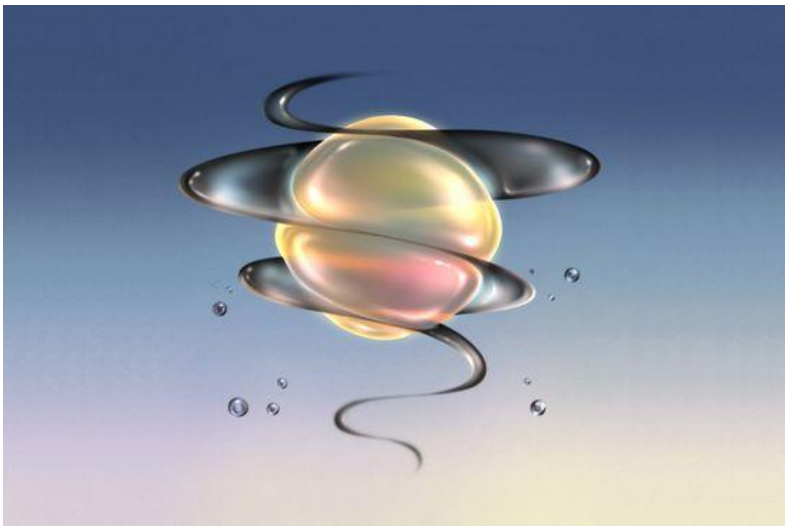
Mr. Regner was not swayed. “I believe in myself,” he said. “I wake up in the morning and look in the mirror and say, ‘Are you going to do it or aren’t you?’”

At Last, Weight-Loss Drugs That Actually Work. They Could Be the Blockbusters of the Decade.

By Bill Alpert

Barron's, Aug. 12, 2022

https://www.barrons.com/amp/articles/buy-eli-lilly-novo-nordisk-stock-price-picks-weight-loss-drugs-51660319418



This is not a typical weight-loss story.

After all of the diet, supplement, and workout fads we've endured, we're about to have drugs that are safe and effective. They're our best hope yet for stemming the obesity epidemic that threatens the lives of 100 million Americans and half a billion people worldwide.

No one has ever seen the kind of weight loss achieved by these new drugs, known as incretins. In scientific studies, they have let people safely shed more than 20% of their weight. Incretins could become the best-selling drugs in pharmaceutical history for their competing developers, Novo Nordisk (ticker: NVO) and Eli Lilly (LLY). The companies' stock market valuations reflect high hopes. But those hopes are merited.

If every hefty American got treated at these drugs' current prices, the annual market for incretins would be a trillion dollars. Insurers can't afford that, of course, and access to the new drugs is highly restricted. But there's plenty of room for prices to come down and still reward Novo and Lilly shareholders. The drugs will be widely used if studies can show they prevent diabetes, heart disease, and other costly ills.

Novo Nordisk and Lilly—rivals for a century—originally developed incretins to treat Type 2 diabetes. The drugs also turned out to promote weight loss. When Novo got U.S. approval last year to market the injectable drug semaglutide for obesity, under the brand name Wegovy,

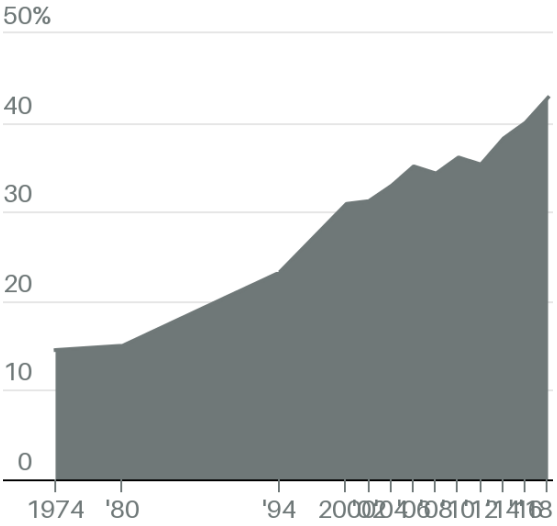
demand was so strong that Novo stock rose 50% over the following year, to hit a peak this year near $122 and an earnings multiple some 70% above most of its pharma peers.

Lilly is hot on its heels with tirzepatide, which is also administered via a weekly injection. It enabled people to lose an average of 21% of their weight in a study reported in June. While not yet approved for weight loss, tirzepatide is one reason that Lilly is Wall Street's favorite drug stock. At its recent price around $300, Lilly trades at 34 times the consensus forward 12-month earnings forecast, or twice the average multiple of its sector.

The Problem

The share of Americans considered obese has nearly tripled since 1974.

U.S. Obese Adults, Ages 20-74



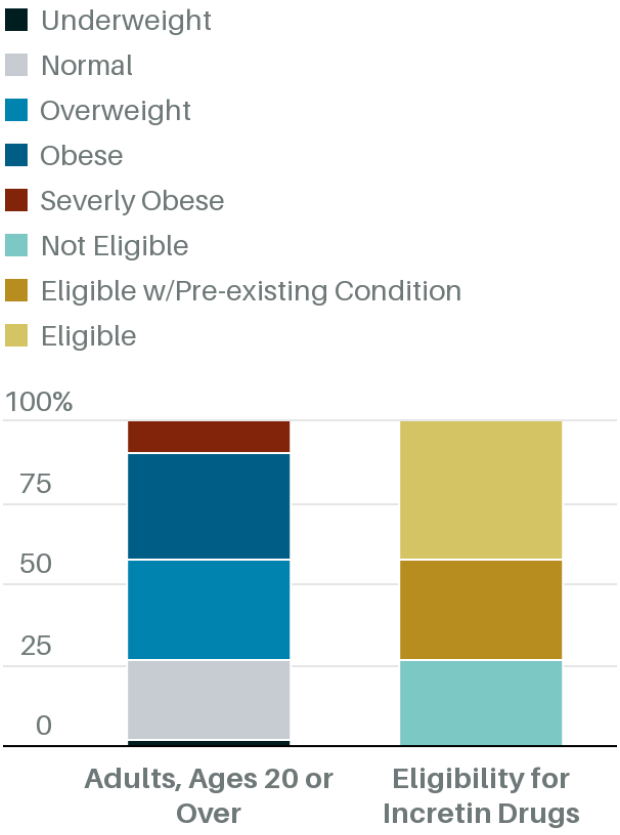
Source: National Center for Health Statistics

Investors' esteem for the stocks has climbed on estimates that annual sales of incretins for diabetes and obesity could top $50 billion or $60 billion by the start of the next decade, split by a duopoly of Lilly and Novo. For perspective, a drug is often considered a blockbuster if it generates $1 billion a year in sales. The AbbVie (ABBV) product Humira is currently the world's top-selling drug, with over $20 billion in annual sales.

The sales will be well deserved, as incretins appear to be the best shot at dealing with the dangerous weight problem of developed nations like the U.S. The percentage of American adults who are obese—or dangerously heavy for their height—has risen from 13% to 43% in the past 60 years. That's more than 100 million people in just the U.S. The average American male now weighs 200 pounds, up from 166 in 1960. The average female is 171 pounds, up from 140.

Who Can Get the Drugs?

Incretins are for adults who are either obese or simply overweight but have preconditions like high blood pressure.



Sources: company reports; J.P. Morgan; National Center for Health Statistics

There are many ripple effects from that. Obesity increases the risk of diabetes, cardiovascular disease, and cancer, while interfering with sleep, work, and other daily activities. Excess weight may result from factors like the elimination of physical labor and the availability of cheap calories, but stemming the epidemic will require more than diet and exercise.

Taking on the weight of the world could make Novo and Lilly into two of this decade's best drug stocks. But for all the promise of incretins, investors should temper expectations until a couple of issues get clarified. The first concerns Novo Nordisk, whose foreseeable future is a highly concentrated bet on semaglutide products like Wegovy—without many other sure blockbusters in the pipeline. By contrast, Lilly's pipeline is a diversified bet on many compounds, with intriguing prospects for treating Alzheimer's disease, autoimmune disorders, and cancer.

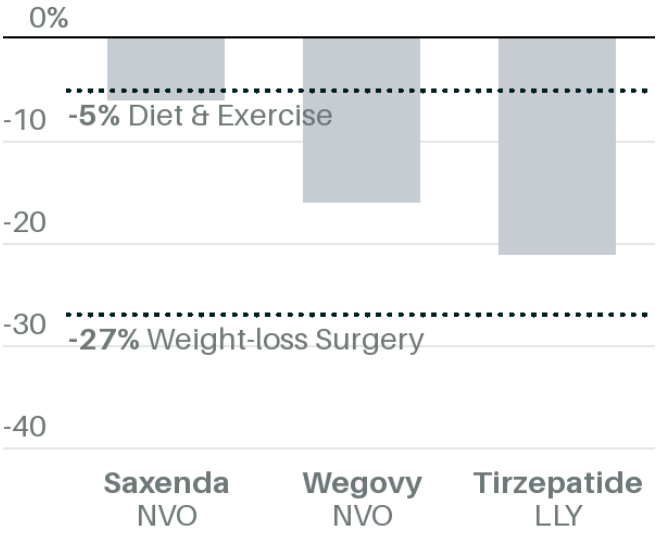
Both companies must surmount a second challenge: getting their potent, but expensive, weight-loss drugs covered by insurers and government programs. Incretins may alleviate obesity, but

they don’t cure it. Experience so far with the drugs suggests that patients will need to take them in perpetuity. Healthcare payers aren’t ready to assume that cost.

And the Winner Is...

In tests, the new drugs have been significantly more effective than diet and exercise, and tirzepatide has approached the results of surgery.

Average Percentage Weight Loss



Note: All drugs at highest doses.
Sources: company reports; J.P. Morgan

“Many insurers do not cover anti-obesity medicines,” says Maria Cecilia Asnis, an endocrinologist who runs the medical weight-loss program at Stamford Health in Connecticut. “List price is also a barrier. People are going out of the country to get these medications.”

Patients without coverage can face monthly costs of $1,000 to $1,500 for Novo’s Wegovy, says Asnis, who receives no remuneration from any drug company. Even after the discounts typically negotiated by health plans, Wegovy can cost payers about $10,000 a year. There’s evidence that rescuing people from their weight will save them from diabetes and heart problems, and the associated health costs. But Novo and Lilly must complete clinical trials to prove those benefits and persuade insurers that spending tens of billions on incretins will be offset by preventive savings.

Researchers first took notice of incretins 35 years ago, when they found that a hormone called glucagon-like peptide-1, or GLP-1, was released in the gut after food intake. GLP-1 boosts insulin levels and reduces appetite, but its natural form lasts just minutes in the blood. The pharmaceutical industry sought longer-lasting products that mimic GLP-1’s effects as injectable treatments for Type 2 diabetes.

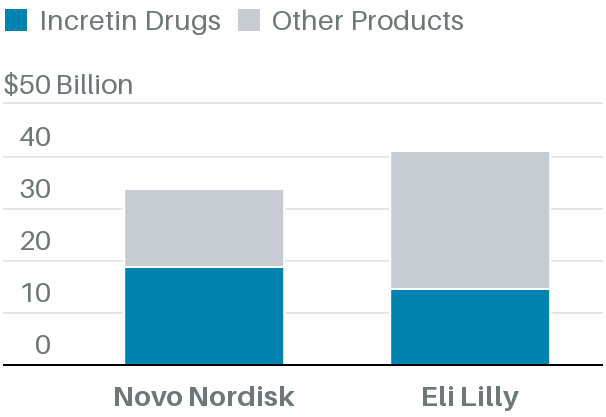
AstraZeneca (AZN) launched the first in 2005. Its sales were overtaken by Novo's Victoza in 2010 and Lilly's Trulicity in 2014.

Diabetes patients taking the GLP-1 drugs lost weight. Novo started testing the compound in Victoza among people who weren't diabetic but suffered from obesity, or who were overweight and had a weight-related condition like high blood pressure. Doctors define obesity by a height-to-weight ratio known as the body-mass index, in which a BMI of 30 or more is considered obese. For a 5-foot-10-inch person, that would be about 210 pounds.

Two Companies, Two Strategies

Novo Nordisk represents a more concentrated bet on incretins. Eli Lilly is more diversified.

2025 Projected Drug Sales



Note: Estimated Incretin sales are for both diabetes and obesity.
Source: UBS estimates

After showing that the drug helped patients lose 5% to 8% of their weight, Novo got U.S. Food and Drug Administration approval in 2014 to market the first incretin for weight loss, under the brand name Saxenda. Like all approvals since, the FDA indicated that the pen-injection should be used as part of a program of diet and exercise.

Incretin drugs kept getting better.

In 2017, Novo introduced Ozempic, a once-weekly injectable treatment for diabetes, based on the GLP-1 variant semaglutide. While normalizing glucose levels in diabetes patients, Ozempic also enabled them to lose more weight than any approved GLP-1. As part of the body's complex regulation of food metabolism, there are GLP-1 receptors in many organs, including the brain. Semaglutide was better than other GLP-1s at reaching brain receptors to temper food cravings.

Lisa Robillard certainly noticed when she took part in a weight-loss study among people who were heavy but not diabetic. Robillard went on her first diet when she was 10. That's when her grandmother took the grade-schooler to a Weight Watchers meeting. Nothing helped. Through work, marriage, and motherhood, Robillard was able to control many things, but not her weight. By the time she turned 50, climbing stairs left her winded. She says she feared she wouldn't live to see her son grow up.

She was contemplating weight-loss surgery in 2018 when an internet search turned up an experimental drug trial for Novo's semaglutide. Robillard started once-weekly injections, and within the first couple of months it was clear she hadn't gotten the placebo.

"I wasn't craving sugar or thinking about food," she recalls. "I was leaving food on my plate, and my brain was saying, 'You're full. Stop eating.' " Over the course of the trial, Robillard lost 56 pounds. The 1,300 people who got Novo's drug in the study lost an average of 17% of their body weight, with improvements in their blood pressure, cholesterol, and inflammation levels. No serious safety issues arose.

Novo got U.S. approval to market semaglutide as a weight-loss drug in June 2021, branded as Wegovy. Prescriptions quickly shot past 10,000 a week, then 20,000. Then, in December, the company announced that problems at its outside manufacturer were crimping supplies. While fixing production, Novo pulled back its marketing of Wegovy. It expects to resolve the problems by the end of this year.

As its answer to semaglutide, Lilly developed a compound called tirzepatide that targets GLP-1 receptors, but also boosts another nutrient-stimulated hormone known as GIP. In a head-to-head trial against semaglutide among patients with Type 2 diabetes, Lilly reported that its "twincretin" drug controlled glucose better than Novo's drug—and caused patients to lose much more weight.

One of those patients was Mary Bruehl, an Oklahoma lawyer who had developed diabetes, hip problems, and fatty-liver disease after many years of carrying too much weight. Over the course of the study, her glucose levels normalized and she lost a remarkable amount of weight—dropping from more than 200 pounds to near 130.

Bruehl's time on tirzepatide coincided with the Covid pandemic office closures. She says that when she returned to the office, slimmed down, people treated her so differently that it actually made her angry. She sought counseling to deal with this unexpected result of her weight loss.

Mary Bruehl dropped from more than 200 pounds in a clinical study of Eli Lilly's tirzepatide compound. Here, at her home in Norman, Okla.

Eli Lilly's head of diabetes product development, Jeffrey Emmick, says the company began a parallel development track for just obesity as soon as the company saw diabetes patients averaging better than 20% weight loss. "That exceeded our expectations," he says.

This past April, Lilly reported the first of its weight-loss trials for tirzepatide. Patients on the highest dose averaged a 21% weight loss, after 72 weeks. The drug got FDA approval as a diabetes treatment in May, under the brand Mounjaro. Lilly had planned to apply for a weight-loss indication around late 2023, after more weight-loss studies. But on its latest earnings call, executives said they would talk to the FDA about whether an earlier submission might be considered, combining data from the diabetes trials with the just-reported obesity study.

Stamford Health's Dr. Asnis says that her medical weight-loss practice has developed a long wait list as word of the new drugs gets out. She treated no more than 30 patients for weight loss in 2019. This year, she expects more than 1,000. Before incretins, weight-loss drugs could cause heart problems and weren't terribly effective anyway. "The advantage of these medications," Asnis says of the incretins, "is that they are not only cardiac safe. They are cardiac beneficial."

That doesn't mean the Novo and Lilly drugs lack side effects. Many patients experience nausea or diarrhea as dosage rises. Asnis says those problems taper off, or can be managed with anti-nausea medications. Only a handful of the thousands she has treated have stopped taking

incretins because of side effects. A more common reason for patients to discontinue the drugs, she says, is the lack of insurance coverage. Every prescription requires prior authorization. For some patients, she has had to write essays.

To persuade insurers and public officials to pay for obesity treatment, both Novo and Lilly are carrying out studies to show that treating weight prevents other ills like sleep apnea, diabetes, and stroke. “Our job is to generate broader data that will allow the decision makers to make the right decision,” says Novo’s head of development, Martin Holst Lange. “Can we show weight loss is associated with improvements in outcomes and decreased healthcare consumption?”

Novo is well along in a study of 17,500 overweight people to see if treatment with Wegovy reduces the rate of heart attacks, strokes, or sudden cardiac death. Lilly will be recruiting for similar studies. “If a person walks into a doctor’s office and has five or six things going on—four may directly relate to obesity,” says Lilly’s medical director for obesity, Dr. Nadia Ahmad. “But the approach of the healthcare system and the payment system is to treat the complications. We’re saying treat obesity first.”

Patients and the healthcare system will certainly benefit as Novo and Lilly continue to play leapfrog with product innovations. Novo launched a once-daily tablet form of semaglutide for diabetes, as Rybelsus, in 2019 and has oral incretins in Phase 1 testing for obesity. It has an injectable combination called CagriSema beginning Phase 3 trials this year that it thinks will outperform Lilly’s tirzepatide.

Lilly, meanwhile, has a triple-incretin candidate nicknamed GGG in Phase 2 trials, as well as an oral incretin.

Wall Street is optimistic about the incretins. At the start of June, J.P. Morgan's Richard Vosser upgraded his rating on Novo stock from Neutral to Overweight, after doubling his sales forecast for the company's incretin products. He thinks that Wegovy and CagriSema will outsell rival Lilly products and add up to $27 billion of the $40 billion total revenue he predicts for Novo in 2030. He says that Novo's $100 stock could hit $127 next year.

One who disagrees is UBS' Michael Leuchten. A few weeks after Vosser's upgrade, Leuchten dropped his rating on Novo from Neutral to Sell. He thinks that Lilly's incretins will outperform and outsell Novo's, leaving less upside in the latter's sales than its premium-priced stock requires.

He agrees that Novo sales of incretins will rise—but it alarms him that the company could be getting nearly 60% of its sales from semaglutide-based products in a few years. To escape that much concentration, Leuchten thinks Novo will have to spend more on research.

Lilly could get the greater part of the diabetes and weight-loss markets for these products, and still not have the incretins rise above 40% of its total revenue, according to UBS analyst Colin Bristow. Incretins could bring in about $22 billion of the $52 billion that Bristow projects for Lilly in 2030. He believes that Lilly's incretins will remain best in class, but sees that reflected in Lilly's stock price and rates the shares Neutral.

As both Lilly and Novo bring improved drugs to market, investors will have many opportunities to decide whether the UBS analysts are being too cautious. And as the health and social costs of obesity spread and are counted, the incretin market may prove bigger than anyone expects.

Ozempic and other injections meant to treat chronic medical conditions are in high demand among elites looking to lose a little weight. ‘This is the Hollywood drug.’

By Sara Ashley O'Brien

Oct. 12, 2022 8:00 am ET

https://www.wsj.com/articles/ozempic-weight-loss-diabetes-drug-11665520937

At least once a day, Nancy Rahnama’s clinical nutrition practice in Beverly Hills, Calif., gets a call from a patient looking for a diabetes drug that they’ve heard can help them lose weight fast.

“They specifically say, ‘How much is it to get Ozempic?’” Dr. Rahnama said.

Ozempic, which is taken by injection in the thigh, stomach or arm, was approved by the Food and Drug Administration in 2017 to help lower blood sugar in people with Type 2 diabetes. One Ozempic injection pen typically lasts about a month and costs about $900 before insurance, though coverage can be hard to come by.

The brand is not approved by the FDA for weight loss. But recently, Ozempic and other drugs of its kind have become the subject of conversations about weight loss, thinness and so-called biohacking in Hollywood, the tech industry and beyond.

Ozempic, made by Novo Nordisk A/S, is one of several brand-name drugs on the market containing an antidiabetic ingredient called semaglutide. Semaglutide stimulates insulin production and also targets areas of the brain that regulate appetite, according to the FDA. The federal agency has approved semaglutide for weight loss under the brand name Wegovy, which Novo Nordisk sells at a higher price than its cousin Ozempic.

Elon Musk, the Tesla and SpaceX CEO who has more than 100 million followers on Twitter, tweeted this month that he was taking Wegovy in combination with fasting to lose weight. Mr. Musk could not be reached for comment.

In late September, Andy Cohen, the Bravo host and “Real Housewives” executive producer, tweeted: “Everyone is suddenly showing up 25 pounds lighter. What happens when they stop taking #Ozempic ?????” Through a representative, Mr. Cohen declined to be interviewed.

‘Everybody I know is on it.’

— Patti Stanger, star and executive producer of the reality show ‘The Millionaire Matchmaker’

Ozempic isn’t meant to be taken as a get-thin-quick treatment. Doctors use medical discretion to prescribe it to people who are obese or overweight—an off-label use given the drug’s similarity to Wegovy. However, in some cases, patients who meet neither of those criteria are still getting their hands on Ozempic.

“This is the Hollywood drug,” said Patti Stanger, star and executive producer of the reality show “The Millionaire Matchmaker” who has also tweeted about Ozempic, in an interview.

“It’s nationwide,” Ms. Stanger said. “I have friends in Miami, I have friends in New York who are doing it.”

Cat Marnell, a writer in New York City, said she first heard about Ozempic over the summer, while gossiping with friends about celebrities. “It’s definitely a dinner conversation in the Hamptons,” she said.

“Everybody I know is on it,” Ms. Stanger added, noting that she paused her own semaglutide treatment due to side effects, but plans to soon restart with some changes to dosing. She first heard about Ozempic from Shamsah Amersi, a Santa Monica-based gynecologist, but consulted with her functional-medicine doctor for a prescription.

Dr. Amersi, whose clientele includes celebrities, said she prescribes the drug to some people who have exhausted other avenues for weight loss, including women who have underlying hormonal issues that may contribute to difficulties losing weight.

“I tell my patients to use this to retrain the way we eat,” Dr. Amersi said.

A New Class of Drugs

People have long sought a way to lose weight by taking a drug, and pharmaceutical companies have long aimed to capitalize on that demand. Yet drug researchers have struggled for years to find medicines that accomplish that goal. Ozempic and Wegovy belong to a new class of drugs, called GLP-1s, that some studies indicate may significantly reduce weight when combined with other lifestyle changes—at least in certain people.

Ozempic’s embrace among relatively healthy people isn’t supported by scientific evidence, however. Wegovy itself isn’t approved to treat all those seeking weight loss. The drug’s 2021 weight-loss approval was for people who are obese or overweight with a coexisting condition related to weight, such as high blood pressure, Type 2 diabetes or high cholesterol. It is priced at $1,350 for a month’s supply, which includes four injection pens. (Novo Nordisk has also introduced a once-a-day semaglutide pill called Rybelsus. A 30-day supply, without insurance coverage, costs $850.)

Wegovy, which is FDA-approved for weight loss, is sold at a higher price than its cousin Ozempic.

Cost might be one reason people seeking to lose weight are flocking to Ozempic, rather than Wegovy. Supplies might be another. Wegovy was on the market for barely six months before Novo Nordisk announced it was in short supply, in December 2021. The company has attributed the shortage to an issue with its contracted manufacturer. Both Wegovy and Ozempic are on the FDA's shortage list, which makes information publicly available about drug supply issues.

Under the terms of their approvals, neither drug should be taken for casual weight loss.

Though Ozempic and Wegovy contain the same active ingredient, Novo Nordisk's executive director of medical affairs, Jason Brett, says they are not interchangeable. He cited differences including dosage amounts and escalation schedules for the drugs. Because the drugs are intended for people with chronic conditions, they are not meant to be used as short-term treatments.

"From our standpoint, we don't promote or suggest or encourage any off-label usage at all," Dr. Brett said, further noting that "we're not looking at weight loss for cosmetic purposes or episodic weight loss for people who don't fit those criteria from the FDA-approved label indications."

Doctors are generally able to prescribe medications off-label as they see fit, a fact that FDA spokeswoman Chanapa Tantibanchachai pointed to in an emailed statement.

Ms. Tantibanchachai continued: "It is important to note that the FDA approval (or clearance) of a medical product for one intended use does not assure its safety and effectiveness for other uses."

Ozempic and Wegovy are not the only new GLP-1s used off-label—some doctors say Mounjaro, a different formula approved by the FDA in May for diabetes treatment, is also being prescribed for weight loss. Maker Eli Lilly & Co. said the drug is only promoted "consistent with its FDA indication and label for Type 2 diabetes," per a spokeswoman.

'Everyone Wants a Quick Fix'

Rupal Mathur, an internist in Houston whose practice specializes in weight loss, said three of her patients developed pancreatitis while taking Wegovy or Mounjaro and had to come off the medications. Other side effects Dr. Mathur warns patients about, and which are also listed on the

labels for these drugs, include gastrointestinal issues such as gallbladder disease. Those with a family history of thyroid cancer are advised against taking the drug.

Allison Schneider, director of media relations for Novo Nordisk, said, “to date, the safety data from trials and post-marketing safety surveillance have not identified any risks that outweigh the benefit of treatment,” adding that the company is continuing to monitor the drug’s safety.

Dr. Mathur said the drugs are meant to be taken long-term and that people who withdraw from them may gain back weight they have lost.

The drugs have only been studied in people who met certain criteria, including a minimum BMI threshold, she added.

“Ozempic is really hard on the stomach,” said Julie Fredrickson, a startup investor who has been open about losing weight on the drug. Ms. Fredrickson, who lives in Montana and considers herself a biohacker, was first prescribed the medication in 2020 to help her shed unwanted weight she gained as a result of other prescription drugs she takes for a medical condition. She said she lost nearly 25 pounds in six months.

Since posting about her experience online, more than two dozen women have asked her how they could qualify for it, she said, adding that some have asked to discuss the injection over Signal, an encrypted messaging app, for privacy reasons.

Ms. Fredrickson, who bought stock in Novo Nordisk around the time she began taking Ozempic, said that after she stopped taking Ozempic, she regained much of the weight she had lost. She cautioned that due to other medications she takes, it is hard to pinpoint the cause. She has since restarted Ozempic.

The rise of off-label use is being monitored by organizations such as the American Diabetes Association and Mutual Aid Diabetes, whose representatives expressed concern about shortages affecting patients. Robert Gabbay, chief scientific and medical officer for the American Diabetes Association, said he has seen some of the patients in his own practice struggle to fill prescriptions at their local pharmacies.

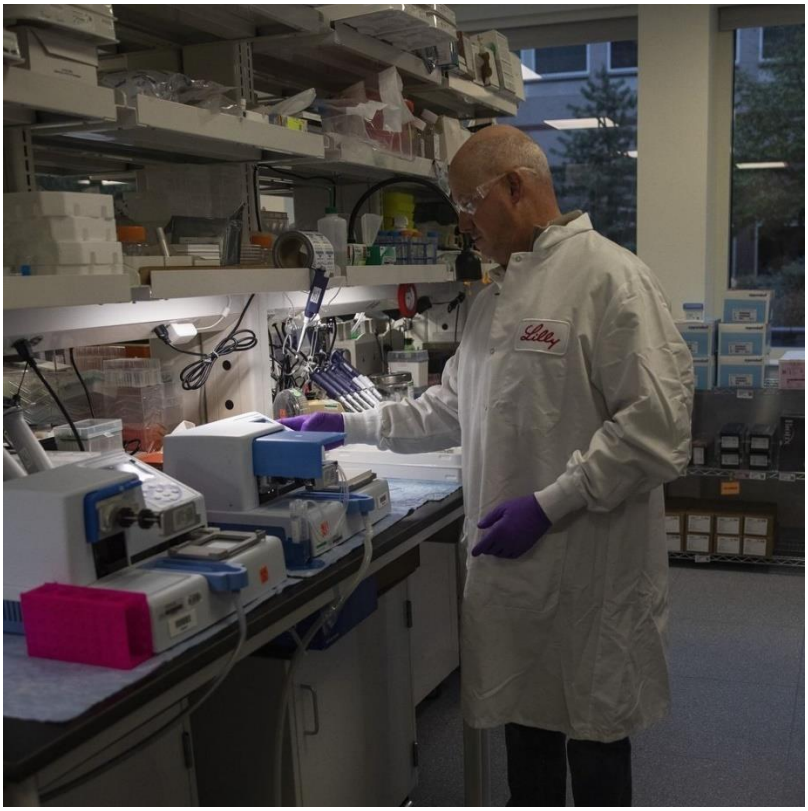
While Ozempic’s website clearly states that it is “not a weight-loss drug” but may help those who take it lose weight, third-party companies are using its name to advertise virtual-weight loss programs and discounted prescriptions. People are turning to social media for tips about how to get the drug.

“Everyone wants a quick fix,” said Lisa Moskovitz, a registered dietitian and CEO of NY Nutrition Group. She believes some doctors are prescribing Ozempic too liberally—and in some cases, she said, giving samples to patients who can’t afford to continue taking the drug once the free doses run out.

“When you stop taking it, you lose that feeling of fullness, that benefit of not being as hungry,” Ms. Moskovitz said. “And now your hunger signals and cues can become a lot stronger.”

The ‘King Kong’ of Weight-Loss Drugs Is Coming

Eli Lilly’s Mounjaro could outpace Ozempic as the most powerful treatment on the market. To develop it, the drug company needed to overhaul long-held but failing practices.



Todd Suter, senior principal biologist, at a lab at Eli Lilly headquarters in Indianapolis.

By Peter Loftus

April 3, 2023 10:31 am ET

https://www.wsj.com/articles/ozempic-mounjaro-weight-loss-drug-wegovy-eli-lilly-66f2906

People who are overweight are flocking to the drug Ozempic to slim down. Looming is an even more powerful weight-loss treatment.

The drug Mounjaro helped a typical person with obesity who weighed 230 pounds lose up to 50 pounds during a test period of nearly 17 months.

No anti-obesity drug has ever safely made such a difference. In the coming months, it is widely expected to get the go-ahead from U.S. health regulators to be prescribed for losing weight and keeping it off, and some patients are already using it unapproved for that purpose.

The advance of Mounjaro, which is already on the market to treat Type 2 diabetes, has excited doctors and patients who have been waiting decades for effective treatments, while helping turn

its maker, Eli Lilly & Co., into the most valuable standalone pharmaceutical company in the U.S. with a market value of more than $300 billion.

It's a product of Lilly's recent, sometimes painful overhaul of how it develops drugs. After several costly drug failures, Lilly abandoned some of its long-held practices, including waiting for multiple committees to weigh in before advancing a drug. The company had also been prioritizing its existing successful drug franchises at all costs, sometimes at the expense of promising new treatments.

That now discarded approach would have stifled the development of Mounjaro. Some people inside Lilly discouraged pursuing the drug in the mid-2010s because it might compete with a Lilly product that was already selling well. Overriding these concerns, Lilly pushed its labs to move fast, pursue ambitious projects and worry less about the business ramifications, even if that would mean cannibalizing sales of high-selling products with years of lucrative patent protection left. Lilly scientists were able to chase Mounjaro, and they worked quickly.

"Every program we do, we look at what our competitors have done, who's done it the fastest, and then we set a goal to go even faster," said Daniel Skovronsky, Lilly's chief scientific and medical officer. "Speed becomes our No. 1 incentive, which is hard because it's a cultural change."

Comparing Weight-Loss Drugs

	OZEMPIC	WEGOVY	MOUNJARO
AVG PERCENTAGE BODY WEIGHT LOSS*	Studies not designed to assess weight loss	Up to 17%	Up to 22.5%
APPROVED USE	Type 2 diabetes	Obesity	Type 2 diabetes
YEAR INTRODUCED IN U.S.	2017	2021	2022
MOST COMMON SIDE EFFECTS	Nausea, vomiting, diarrhea, abdominal pain	Nausea, diarrhea, vomiting, constipation	Nausea, diarrhea, decreased appetite, vomiting
GENERIC NAME	semaglutide	semaglutide	tirzepatide
MANUFACTURER	Novo Nordisk	Novo Nordisk	Eli Lilly

*Figures are from separate studies that tested different dose levels for varying durations.

Source: The companies and the New England Journal of Medicine

Since it shifted its approach, in stages over the past decade, Lilly's overall R&D output has been among the industry's most prodigious. The company has had new prescription drugs approved in the U.S. or other countries since 2014 for conditions such as cancer, migraines and Covid-19. It has cut their development timelines to an average of six years from 11.

The revamp has produced medicines that could make big differences in diseases that have long frustrated researchers and debilitated patients.

Mounjaro helped people who have difficulty losing pounds despite dieting cut their weight by up to 22.5% over 72 weeks during testing. In comparison, Ozempic and its sister drug, Wegovy, made by Novo Nordisk AS, which share the same active ingredient, induced weight loss of up to around 17% in studies.

Also up for approval from Lilly is an experimental Alzheimer's drug that slowed the disease's progress in a key study. The experimental Alzheimer's drug, if approved, could reach $12 billion in yearly sales, according to analysts.

Mounjaro could be one of the highest-selling drugs of all time with annual sales exceeding $25 billion. Novo's Ozempic and Wegovy brought in close to $10 billion last year, with prescriptions rapidly growing.

'We gotta get out of this'

Lilly, founded in 1876 in Indianapolis, was the first drug company to sell insulin and distribute the polio vaccine globally. Starting in the 1980s, it became known for groundbreaking psychiatric drugs including the antidepressant Prozac.

By the early 2010s, however, the company's labs were striking out. Experimental drugs for heart disease, schizophrenia, depression and Alzheimer's failed in large, expensive clinical trials. Big-selling products such as the antipsychotic Zyprexa began facing competition from lower-cost generics. Company shares sank.

A museum of the history of the Eli Lilly company at Lilly's Indianapolis headquarters.

"Oh man, we gotta get out of this," John Lechleiter, then Lilly's chief executive, recalled thinking on a walk home from work in 2009 after the stock hit a decades low.

To innovate, Lilly would need to let go of its single-minded focus on protecting its existing lucrative drug franchises, maximizing their sales until patents ran out and then chasing further sales with new products that weren't all that different from the ones they replaced.

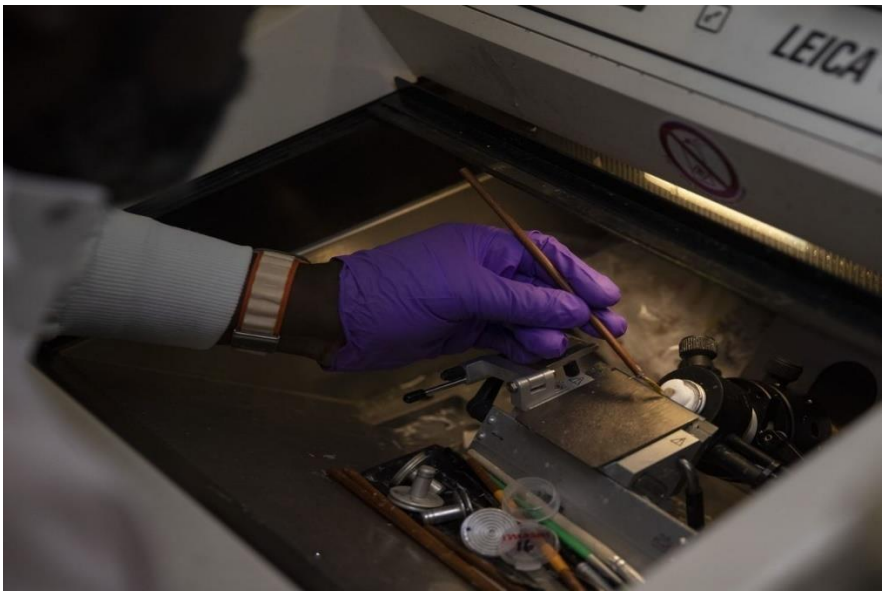
The company also needed to move faster. One internal committee after another second-guessed every recommendation to advance a promising drug candidate. "The decisions got revisited every step of the way," recalled J. Anthony Ware, who led product development at Lilly before retiring in 2017.

The committees were intended to ensure thorough vetting, but in practice became a limiting process that squeezed out bold ideas, according to Dr. Skovronsky.

Dr. Skovronsky, who joined Lilly after it acquired his brain-imaging firm in 2010, was accustomed to moving quickly because money was tight at the startup. Lilly lacked the same urgency, Dr. Skovronsky said, and the slowness made it miss out on huge opportunities.

Lilly's scientists, for instance, were among the first to see potential for a new type of breast cancer drug targeting proteins known as CDK4 and CDK6 that play a role in tumor growth. It took them too long to get internal funding for clinical trials, however, handing competitors Novartis AG and Pfizer Inc. the advantage of bringing their therapies to market first. Lilly's drug, Verzenio, was approved by the FDA in 2017, after Pfizer's Ibrance in 2015 and Novartis's Kisqali earlier in 2017.

Daniel Skovronsky, Lilly's chief scientific and medical officer, has spearheaded efforts to move more quickly in drug development.



A Lilly scientist analyzes an animal specimen.

Lilly also missed out on cancer immunotherapies, ceding the treatments to rivals such as Merck & Co. and Bristol-Myers Squibb Co. Their drugs have saved many skin and lung cancer patients and are now among the industry's biggest sellers.

Dr. Skovronsky was frustrated with Lilly's slow pace. "Let me understand this," he recalled saying at a committee meeting setting timetables for getting experimental drugs to market. "Our goal is to be slower than average, and we're failing at that goal? This can't be the way to do things."

In 2015, Lilly's board of directors asked Dr. Skovronsky, then senior vice president of clinical and product development, to help analyze Lilly's research flops over the prior 10 years and figure out how to do R&D better.

A big reason for the failures, Dr. Skovronsky found, was that Lilly's business-unit heads, focusing on sales potential, were making decisions about which drugs to promote to late-stage studies. The result: The company advanced into the large, expensive studies candidates that had mixed results in earlier testing. Dr. Skovronsky found that drugs that had earlier mixed results often failed the later studies.

The business-unit officials overplayed "what would really be great for sales representatives and underplayed what would be great science and great for patients," he said.

Dr. Skovronsky recommended Lilly pursue drug projects where it best understood the science, and lean less on commercial sales estimates. Lilly was not very good at predicting a drug's sales over time anyway, he concluded, but could better predict the scientific probability of a drug's success.

Lilly jettisoned research on diseases where it was tougher to deliver an advance, including osteoporosis and psychiatric conditions, and doubled down in areas where it had expertise: diabetes, oncology and Alzheimer's disease.

"We had to hunker down in a lot of ways to free up resources for other priorities," said Chief Executive David Ricks, who led Lilly divisions including its China and U.S. businesses during this period, before becoming CEO in 2017.

‘We had to hunker down in a lot of ways to free up resources for other priorities,’ Chief Executive David Ricks said, describing the process of jettisoning some projects to focus on areas where Lilly had the most expertise.

Lilly, founded in 1876 in Indianapolis, was the first drug company to sell insulin and distribute the polio vaccine globally.

Lilly also tried to become more open to outsiders to help bring in fresh ideas. In 2018, it promoted Dr. Skovronsky to the chief scientific officer role. When Lilly acquired cancer-drug developer Loxo Oncology in 2019, it put Loxo’s leaders in charge of Lilly’s cancer research.

Along with its successes, Lilly has had setbacks, including pulling a new cancer drug from the market in 2019 after a study found it wasn’t helping patients. Last year, U.S. drug regulators rejected a proposed new cancer therapy co-developed by Lilly and a Chinese biotech company because of concerns about the medicine’s testing in China. Then, in January, the U.S. Food and Drug Administration hit the brakes on speedily approving Lilly’s experimental Alzheimer’s therapy, saying it would wait for more study data before making a decision. Still, these types of setbacks are happening less frequently than before.

‘King Kong’

The new obesity drug grew out of long-running efforts at Lilly to promote the body’s production of insulin, the hormone used to control blood-sugar levels. Lack of insulin or insufficient insulin are hallmarks of diabetes.

In 2014, Lilly introduced a drug that helped people release more insulin when they eat. The drug, named Trulicity, did that by mimicking a hormone in the gut called GLP-1 that naturally mobilized the release of insulin. Scientists also found it suppressed appetite and made people feel full when they eat.

Patients with the most common form of diabetes needed to inject Trulicity once a week, not every day like older medicines. And not only did the drug significantly reduce blood sugar levels, it helped patients lose some weight.

Doctors and patients began flocking to the new drug. Analysts projected it would be a big seller for Lilly, perhaps reaching $2 billion in annual sales. And the company could look forward to patents protecting those hefty sales for years.

When Lilly scientists proposed, in 2014, pursuing a drug that promised to lower blood sugar more than Trulicity and cut weight by even larger amounts, company leaders hesitated.

“It was controversial among senior colleagues at Lilly,” recalled David Moller, a former company head of diabetes research. “There were those who thought Trulicity was the best we could do.”

Scientists at the Lilly Innovation Center in Cambridge, Mass., in 2017, where researchers developed new medical devices to deliver insulin.

Lilly scientists expressed hope their drug candidate could do much more than that. The experimental drug combined a synthesized GLP-1 gut hormone like the one in Trulicity with a cousin called GIP, which the scientists theorized could produce even more insulin and suppress appetite further.

Two weeks after starting to get the compound, chubby laboratory mice given the compound lost 20% to 25% of their weight.

Drug effects in mice, such as weight loss, often don’t carry over to humans. Despite the unknowns, Lilly went ahead and greenlighted the experimental drug for human testing. “It was the largest degree of weight loss I had ever seen in a mouse model of obesity. It felt pretty compelling,” Dr. Skovronsky said.

Initially, the plan was to get the drug candidate through clinical testing and approved for marketing as a diabetes treatment in 2024, Dr. Skovronsky said. Then Lilly reorganized to move more quickly.

To stop the second-guessing of decisions, Lilly established independent internal units operating like biotech companies—with less bureaucracy and faster decision-making—to manage each of its high-priority drug projects. Lilly dubbed the new project "GIP Bio," said Ruth Gimeno, a biologist who joined from Pfizer in 2011 and now serves as Lilly's vice president of diabetes, obesity and cardiometabolic research.

GIP Bio had its own board of directors, made up of senior researchers and executives from Lilly's diabetes business unit. They were given a budget, and charged with making quick decisions on their own. After a Lilly researcher proposed a last-minute change to the design of the second phase of human testing, the GIP Bio board met within 24 hours and approved the change so the study could start on time, Dr. Gimeno said.

Results from the study in people echoed the findings in overweight laboratory mice. The drug candidate, which Lilly was then referring to by the chemical name tirzepatide and later branded as Mounjaro, not only cut blood sugar levels sharply in people with diabetes but also helped them lose much more weight than older diet drugs could achieve.

Lilly released the Phase 2 tirzepatide results publicly in October 2018 at a diabetes conference in Berlin.

Mounjaro and Ozempic at a medical clinic in Spokane, Wash.

Julio Rosenstock, a veteran diabetes doctor, took the microphone to share his reaction. Dr. Rosenstock, senior scientific advisor at clinical-trial site operator Velocity Clinical Research and a clinical professor of medicine at University of Texas Southwestern Medical Center in Dallas, wasn't involved in the study but has worked with Lilly on other studies. He said he had nicknamed Ozempic, the drug from Lilly's rival Novo Nordisk, the "gorilla" because it had been

the most potent GLP-1 containing drug to that point. “But tirzepatide is really a King Kong,” Dr. Rosenstock said.

Just as the Phase 2 testing was getting off the ground, Lilly started spending money to prepare for the third and final phase of testing required to gain regulatory approval. Typically, companies wait before starting the last-stage studies because they can cost several hundred million dollars. Lilly decided it was worth the risk for certain high-priority drugs, however, because that could hasten their speed to market.

The Phase 3 studies began in late 2018. The decision to go ahead with the investments ultimately cut about nine to 12 months off the development timeline, Dr. Skovronsky said.

In May 2022, the FDA approved Mounjaro for the treatment of Type 2 diabetes. Lilly expects to complete the application for Mounjaro’s use treating obesity after results of another study are available by the end of April, which could lead to approval later this year or early 2024.

Though doctors consider it to be safe, Mounjaro does have side effects, with the most common being nausea and other gastrointestinal issues. Similar side effects have been reported for Ozempic and Wegovy.

Lilly is studying the drug for additional uses like treating a liver disease, and is monitoring whether the weight loss it induces has downstream benefits including heart health.

“To me, tirzepatide in my career may be the most important drug Lilly’s been a part of,” said Mr. Ricks, the chief executive, who has worked at Lilly for more than 25 years. “It is one of the rare ones that has a chance to move the life expectancy of the population.”

Now, Lilly is developing a drug that adds a third component, called glucagon, to GLP-1 and GIP, to see if that induces even greater weight loss. Phase 3 studies are set to begin this year. The drug could be up for FDA approval in 2026, well before Mounjaro’s key U.S. patent expires in 2036.

My comments:

It's great news that these miraculous, lifesaving/life-improving drugs are being developed in pill form and at lower cost.

It scandalous that they are currently disproportionately being used by the wealthy when it's lower-income people who need these drugs the most, both because they're more overweight (see: What to know about obesity and poverty) and have inferior access to healthcare to treat all of the terrible things that result from obesity: diabetes, heart disease, higher rates of 13 types of cancer, osteoarthritis, high blood pressure, sleep apnea, dementia, mental illness such as clinical depression and anxiety, etc. (see: Health Effects of Overweight and Obesity).

No More Shots: Pill Versions of Ozempic-Like Drugs Are Coming

Tablets could appeal to people who want to lose weight but despise needles

By Peter Loftus

June 25, 2023

https://www.wsj.com/articles/no-more-shots-pill-versions-of-ozempic-like-drugs-are-coming-ca286ca2

In the works for people flocking to Ozempic to shed lots of pounds: Weight-loss medicines that come in a pill.

Drugs such as Ozempic that have surged in popularity for weight loss must be injected. Yet many people despise needles, prompting drugmakers to explore formulations that could be swallowed.

The chemistry isn't simple. But if researchers can pull it off, the tablets could appeal to the sizable number of people who fear needles, while also costing hundreds of dollars less than their injected cousins.

The hunt for tablet versions of the injectable weight-loss medicines is among the hottest areas of drug research, attracting industry heavyweights like Eli Lilly, Novo Nordisk and Pfizer and fueled by a potential multibillion-dollar market.

Farthest along is a tablet form of semaglutide—a main ingredient in the injections—developed by Novo Nordisk.

Ozempic has gained popularity for its potential to help people lose significant weight.

The experimental pill helped people who took it daily for 68 weeks as part of a study lose up to 17.4% of their body weight, Novo Nordisk said in May. The reduction was similar to what testing found for Ozempic's cousin, the drug Wegovy.

Later this year, Novo Nordisk plans to ask U.S. and European drug regulators to approve the tablet. Novo already sells a tablet form of semaglutide, Rybelsus, to treat Type 2 diabetes, though some people use it off-label for weight loss.

Novo Nordisk's Ozempic and Wegovy therapies and Lilly's Mounjaro have emerged as viral sensations—touted by celebrities and discussed on Facebook and TikTok—because of their potential to help people lose significant weight.

These types of drugs, first approved to treat diabetes, work by mimicking gut hormones that play a role regulating blood sugar and, it has turned out, appetite. A key gut hormone is called glucagon-like peptide-1, or GLP-1.

Peptides are large molecules, which are easier to package and deliver as an injection**.** Drugmakers also have made their GLP-1 drugs into injections so they avoid the journey of pills, which travel through the digestive tract because they are swallowed**.** The digestive tract can degrade peptides, minimizing their benefits.

But manufacturing the peptides and the devices, known as pens, to inject them is expensive and complex. Injectable drugs must be stored at certain, often cold, temperatures. And they strike fear in a small but still significant group.

"Some people are just needle-phobic," said BMO Capital Markets analyst Evan David Seigerman.

Analysts project the anti-obesity medicine market will be so large that drugmakers have launched efforts to find tablets that would appeal to those who don't want to be injected.

Seigerman estimated that pill forms of weight-loss drugs could make up about 15% of the total market, which he predicts will reach $100 billion in annual sales worldwide in coming years.

Drugmakers have designed the oral versions of the gut-hormone drugs to overcome digestive-tract degradation by either using a higher dose than the injected drugs or by using a non-peptide form of gut hormone.

Given the chemistry, pill forms aren't likely to surpass the weight loss that can be achieved with the current once-weekly injections, doctors and analysts said. Some tablets might even deliver inferior weight loss. And some patients might prefer the convenience of a once-weekly injection over a daily pill.

"I'm just guessing people will say, 'You know that once a week sounds much simpler,'" said Dr. Robert Kushner, an obesity-treatment specialist at Northwestern University Feinberg School of Medicine.

Yet the pills could prove attractive to a segment of patients if priced less, according to analysts and doctors.

Wegovy injector pens

A pill being developed by Structure Therapeutics could be priced at about $500 a month if it succeeds in testing and is approved by regulators, Seigerman estimated, roughly half the cost of the injected drugs. Structure Chief Executive Raymond Stevens said it was too early to discuss a specific price, but the company's goal is to price the drug to make it accessible to patients.

“If these oral medications are more affordable or more accessible, that could be where they could fill that gap,” said Dr. Ania Jastreboff, director of the Yale Obesity Research Center in New Haven, Conn.

Eli Lilly is developing a non-peptide GLP-1 pill called orforglipron. The once-daily pill, taken for 36 weeks, helped volunteers lose up to 14.7% of their body weight in a mid-stage clinical trial of more than 270 people with obesity, researchers reported Friday at the annual meeting of the American Diabetes Association in San Diego.

That was a loss of about 35 pounds for a person in the study who had the average starting weight of 240 pounds.

The company has said its GLP-1 pill is unlikely to help people lose as much weight as its injected drug Mounjaro, which adds a second gut hormone, GIP, to GLP-1.

In one study, patients taking Mounjaro lost up to about 22.5% of their body weight. If the experimental pill can match the GLP-1-only injected drugs, however, it could be an option for some patients.

Pfizer is developing anti-obesity pills including danuglipron, which showed promise in a mid-stage study reported earlier this year.

In testing, the pill versions of the weight-loss injections come with similar gastrointestinal side effects such as nausea for some patients. The companies have said the events are generally mild to moderate and typically occurred when doses were increased.

Did Scientists Accidentally Invent an Anti-addiction Drug?

People taking Ozempic for weight loss say they have also stopped drinking, smoking, shopping, and even nail biting.

By Sarah Zhang

The Atlantic, May 19, 2023

https://www.theatlantic.com/health/archive/2023/05/ozempic-addictive-behavior-drinking-smoking/674098

All her life, Victoria Rutledge thought of herself as someone with an addictive personality. Her first addiction was alcohol. After she got sober in her early 30s, she replaced drinking with food and shopping, which she thought about constantly. She would spend $500 on organic groceries, only to have them go bad in her fridge. “I couldn’t stop from going to that extreme,” she told me. When she ran errands at Target, she would impulsively throw extra things—candles, makeup, skin-care products—into her cart.

Earlier this year, she began taking semaglutide, also known as Wegovy, after being prescribed the drug for weight loss. (Colloquially, it is often referred to as Ozempic, though that is technically just the brand name for semaglutide that is marketed for diabetes treatment.) Her food thoughts quieted down. She lost weight. But most surprisingly, she walked out of Target one day and realized her cart contained only the four things she came to buy. “I’ve never done that before,” she said. The desire to shop had slipped away. The desire to drink, extinguished once, did not rush in as a replacement either. For the first time—perhaps the first time in her whole life—all of her cravings and impulses were gone. It was like a switch had flipped in her brain.

As semaglutide has skyrocketed in popularity, patients have been sharing curious effects that go beyond just appetite suppression. They have reported losing interest in a whole range of addictive and compulsive behaviors: drinking, smoking, shopping, biting nails, picking at skin. Not everyone on the drug experiences these positive effects, to be clear, but enough that addiction researchers are paying attention. And the spate of anecdotes might really be onto something. For years now, scientists have been testing whether drugs similar to semaglutide can curb the use of alcohol, cocaine, nicotine, and opioids in lab animals—to promising results.

Semaglutide and its chemical relatives seem to work, at least in animals, against an unusually broad array of addictive drugs, says Christian Hendershot, a psychiatrist at the University of North Carolina at Chapel Hill School of Medicine. Treatments available today tend to be specific: methadone for opioids, bupropion for smoking. But semaglutide could one day be more widely useful, as this class of drug may alter the brain’s fundamental reward circuitry. The science is still far from settled, though researchers are keen to find out more. At UNC, in fact, Hendershot is now running clinical trials to see whether semaglutide can help people quit drinking alcohol and smoking. This drug that so powerfully suppresses the desire to eat could end up suppressing the desire for a whole lot more.

The history of semaglutide is one of welcome surprises. Originally developed for diabetes, semaglutide prompts the pancreas to release insulin by mimicking a hormone called GLP-1, or glucagon-like peptide 1. First-generation GLP-1 analogs—exenatide and liraglutide—have been on the market to treat diabetes for more than a decade. And almost immediately, doctors noticed that patients on these drugs also lost weight, an unintended but usually not unwelcome side effect. Semaglutide has been heralded as a potentially even more potent GLP-1 analog.

Experts now believe GLP-1 analogs affect more than just the pancreas. The exact mechanism in weight loss is still unclear, but the drugs likely work in multiple ways to suppress hunger, including but not limited to slowing food's passage through the stomach and preventing ups and downs in blood sugar. Most intriguing, it also seems to reach and act directly on the brain.

GLP-1 analogs appear to actually bind to receptors on neurons in several parts of the brain, says Scott Kanoski, a neurobiologist at the University of Southern California. When Kanoski and his colleagues blocked these receptors in rodents, the first-generation drugs exenatide and liraglutide became less effective at reducing food intake—as if this had eliminated a key mode of action. The impulse to eat is just one kind of impulse, though. That these drugs work on the level of the brain—as well as the gut—suggests that they can suppress the urge for other things too.

In particular, GLP-1 analogs affect dopamine pathways in the brain, a.k.a. the reward circuitry. This pathway evolved to help us survive; simplistically, food and sex trigger a dopamine hit in the brain. We feel good, and we do it again. In people with addiction, this process in the brain shifts as a consequence or cause of their addiction, or perhaps even both. They have, for example, fewer dopamine receptors in part of the brain's reward pathway, so the same reward may bring less pleasure.

In lab animals, addiction researchers have amassed a body of evidence that GLP-1 analogs alter the reward pathway: mice on a version of exenatide get less of a dopamine hit from alcohol; rats on the same GLP-1 drug sought out less cocaine; same for rats and oxycodone. African vervet monkeys predisposed to drinking alcohol drank less on liraglutide and exenatide. Most of the published research has been conducted with these two first-generation GLP-1 drugs, but researchers told me to expect many studies with semaglutide, with positive results, to be published soon.

In humans, the science is much more scant. A couple of studies of exenatide in people with cocaine-use disorder were too short or small to be conclusive. Another study of the same drug in people with alcohol-use disorder found that their brain's reward centers no longer lit up as much when shown pictures of alcohol while they were in an fMRI machine. The patients in the study as a whole, however, did not drink less on the drug, though the subset who also had obesity did. Experts say that semaglutide, if it works at all for addiction, might end up more effective in some people than others. "I don't expect this to work for everybody," says Anders Fink-Jensen, a psychiatrist at the University of Copenhagen who conducted the alcohol study. (Fink-Jensen has received funding from Novo Nordisk, the maker of Ozempic and Wegovy, for separate research into using GLP-1 analogs to treat weight gain from schizophrenia medication.) Bigger and longer trials with semaglutide could prove or disprove the drug's effectiveness in addiction—and identify whom it is best for.

Semaglutide does not dull all pleasure, people taking the drug for weight loss told me. They could still enjoy a few bites of food or revel in finding the perfect dress; they just no longer went overboard. Anhedonia, or a general diminished ability to experience pleasure, also hasn't shown up in cohorts of people who take the drug for diabetes, says Elisabet Jerlhag Holm, an addiction researcher at the University of Gothenburg. Instead, those I talked with said their mind simply no longer raced in obsessive loops. "It was a huge relief," says Kimberly Smith, who used to struggle to eat in moderation. For patients like her, the drug tamed behaviors that had reached a level of unhealthiness.

The types of behaviors in which patients have reported unexpected changes include both the addictive, such as smoking or drinking, and the compulsive, such as skin picking or nail biting. (Unlike addiction, compulsion concerns behaviors that aren't meant to be pleasurable.) And although there is a body of animal research into GLP-1 analogues and addiction, there is virtually none on nonfood compulsions. Still, addictions and compulsions are likely governed by overlapping reward pathways in the brain, and semaglutide might have an effect on both. Two months into taking the drug, Mary Maher woke up one day to realize that the skin on her back—which she had picked compulsively for years—had healed. She used to bleed so much from the picking that she avoided wearing white. Maher hadn't even noticed she had stopped picking what must have been weeks before. "I couldn't believe it," she told me. The urge had simply melted away.

The long-term impacts of semaglutide, especially on the brain, remain unknown. In diabetes and obesity, semaglutide is supposed to be a lifelong medication, and its most dramatic effects are quickly reversed when people go off. "The weight comes back; the suppression of appetite goes away," says Janice Jin Hwang, an obesity doctor at UNC School of Medicine. The same could be true in at least certain forms of addiction too. Doctors have noted a curious link between addiction and another obesity treatment: Patients who undergo bariatric surgery sometimes experience "addiction transfer," where their impulsive behaviors move from food to alcohol or drugs. Bariatric surgery works, in part, by increasing natural levels of GLP-1, but whether the same transfer can happen with GLP-1 drugs still needs to be studied in longer trials. Semaglutide is a relatively new drug, approved for diabetes since 2017. Understanding the upshot of taking it for decades is, well, decades into the future.

Maher told me she hopes to stay on the drug forever. "It's incredibly validating," she said, to realize her struggles have been a matter of biology, not willpower. Before getting on semaglutide, she had spent 30 years trying to lose weight by counting calories and exercising. She ran 15 half marathons. She did lose weight, but she could never keep it off. On semaglutide, the obsessions about food that plagued her even when she was skinny are gone. Not only has she stopped picking her skin; she's also stopped biting her nails. Her mind is quieter now, more peaceful. "This has changed my thought processes in a way that has just improved my life so much," she said. She would like to keep it that way.

People on Drugs Like Ozempic Say Their 'Food Noise' Has Disappeared

For some, it's a startling side effect.

By Dani Blum, June 21, 2023, New York Times

https://www.nytimes.com/2023/06/21/well/eat/ozempic-food-noise.html

Until she started taking the weight loss drug Wegovy, Staci Klemmer's days revolved around food. When she woke up, she plotted out what she would eat; as soon as she had lunch, she thought about dinner. After leaving work as a high school teacher in Bucks County, Pa., she would often drive to Taco Bell or McDonald's to quell what she called a "24/7 chatter" in the back of her mind. Even when she was full, she wanted to eat.

Almost immediately after Ms. Klemmer's first dose of medication in February, she was hit with side effects: acid reflux, constipation, queasiness, fatigue. But, she said, it was like a switch flipped in her brain — the "food noise" went silent.

"I don't think about tacos all the time anymore," Ms. Klemmer, 57, said. "I don't have cravings anymore. At all. It's the weirdest thing."

Dr. Andrew Kraftson, a clinical associate professor at Michigan Medicine, said that over his 13 years as an obesity medicine specialist, people he treated would often say they couldn't stop thinking about food. So when he started prescribing Wegovy and Ozempic, a diabetes medication that contains the same compound, and patients began to use the term food noise, saying it had disappeared, he knew exactly what they meant.

As interest has intensified around Ozempic and other injectable diabetes medications like Mounjaro, which works in similar ways, that term has gained traction. Videos related to the subject "food noise explained" have been viewed 1.8 billion times on TikTok. And some of the people who have managed to get their hands on these medications — despite persistent shortages and list prices that can near or surpass a thousand dollars — have shared stories on social media about their experiences.

When food noise fades

Wendy Gantt, 56, said she first heard the term food noise on TikTok, where she had also learned about Mounjaro. She found a telehealth platform and received a prescription within a few hours. She can remember the first day she started taking it last summer. "It was like a sense of freedom from that loop of, 'What am I going to eat? I'm never full; there's not enough. What can I snack on?'" she said. "It's like someone took an eraser to it."

For some, the shortages of these medications have provided a test case, a way to see their lives with and without food noise. Kelsey Ryan, 35, an insurance broker in Canandaigua, N.Y., hasn't been able to fill her Ozempic prescription for the last few weeks, and the noise has crept back in. It's not just the pull of soft-serve each day, she said. Food noise, to Ms. Ryan, also means a range of other food-related thoughts: internal negotiations about whether to eat in front of other people, wondering if they'll judge her for eating fried chicken or if ordering a salad makes it look like

she's trying too hard. Ozempic is more of a way to silence the food noise than anything else, she said.

"It's a tool," she said. "It's not like a magic drug that's giving people an easy way out."

What causes food noise?

There is no clinical definition for food noise, but the experts and patients interviewed for this article generally agreed it was shorthand for constant rumination about food. Some researchers associate the concept with "hedonic hunger," an intense preoccupation with eating food for the purpose of pleasure, and noted that it could also be a component of binge eating disorder, which is common but often misunderstood.

Obesity medicine specialists have tried to better understand why a person may ruminate about food for some time, said Dr. Robert Gabbay, chief scientific and medical officer of the American Diabetes Association. "It just seems to be that some people are a little more wired this way," he said. Obsessive rumination about food is most likely a result of genetic factors as well as environmental exposure and learned habits, said Dr. Janice Jin Hwang, chief of the division of endocrinology and metabolism at the University of North Carolina School of Medicine.

Why some people can shake off the impulse to eat, and other people stay mired in thoughts about food, is "the million-dollar question," Dr. Hwang said.

How does medication suppress food noise?

The active ingredient in Ozempic and Wegovy is semaglutide, a compound that affects the areas in the brain that regulate appetite, Dr. Gabbay said; it also prompts the stomach to empty more slowly, making people taking the medication feel fuller faster and for longer. That satiation itself could blunt food noise, he said.

There's another theoretical framework for why Ozempic might quash food noise: Semaglutide activates receptors for a hormone called GLP-1. Studies in animals have shown those receptors are found in cells in regions of the brain that are particularly important for motivation and reward, pointing to one potential way semaglutide could influence cravings and desires. It's possible, although not proven, that the same happens in humans, Dr. Hwang said, which could explain why people taking the medication sometimes report that the food (and, in some cases, alcohol) they used to crave no longer gives them joy.

Researchers are continuing to investigate how semaglutide works, how it may influence aspects of the brain like food noise and the potential it has for other uses, like treating addiction.

Ms. Klemmer said she worried about the potential long-term side effects of a medication she might be on for the rest of her life. But she thinks the trade-off — the end of food noise — is worth it. "It's worth every bad side effect that I'd have to go through to have what I feel now," she said: "not caring about food."

What New Weight Loss Drugs Teach Us About Fat and Free Will

Jan. 31, 2023

By Julia Belluz, New York Times

Ms. Belluz is a health journalist. She is writing a book about nutrition and metabolism.

https://www.nytimes.com/2023/01/31/opinion/ozempic-weight-loss-drugs.html

In the girl's home in Hertfordshire, England, you need a key code to enter the kitchen, where all the cupboards are under bolt and chain and the garbage bin is locked shut. Without these measures, the child — whose name cannot be published because she's currently in foster care — wouldn't be able to stop eating, even scraps of raw meat or leftover pasta wasting away in the garbage.

"She is constantly alert to any possibility of gaining access to food," her foster father told me, like a calorie-seeking missile. Her brain doesn't register that she's eaten. So she lives with a constant, raging hunger, an all-encompassing obsession about her next meal or snack, one that distracts from her other interests — in dolls, horse riding and drawing.

Age 12, the girl is thin, birdlike. If her foster parents didn't police her every morsel, she'd be much larger, like many people who share her disorder, Prader-Willi syndrome. Patients with Prader-Willi can eat so much that in extreme cases, their stomachs burst open, causing death.

The disorder is a rare and devastating genetic cause of obesity. But it also exists on the far end of a spectrum of eating behavior common to us all, as I was told recently by Tony Goldstone, an Imperial College London endocrinology researcher and physician who works with patients with Prader-Willi. "People think they only eat because they want to eat, or they're cognitively deciding to eat," Dr. Goldstone said. "But much of it is not taking place at that conscious level."

We tend to believe body size is something we can fully control, that we're skinny or fat because of deliberate choices we make. After talking to hundreds of patients with obesity over the years and to clinicians and researchers who study the disease, let me assure you: Reality looks a lot less like free will. The advent of new and effective obesity drugs offers a stark illustration of this little-appreciated fact of physiology. The debates the medicines prompted also show how little we appreciate about obesity.

Biological systems, influenced by our environments and our genes, control the flow of energy through us: Energy goes into us in the form of food and is used up or is stored in our bodies, primarily as fat. These systems, stemming from interactions between the brain and body, are in large part involuntary. They tick along, like our reproductive drive or the mechanisms that steady our body temperatures.

The Hertfordshire child with Prader-Willi "has an abnormality in the energy balance thermostat in her brain and she's not responding," Dr. Goldstone said. But she's experiencing just a variation on the kinds of hunger and satiety signals we all live with.

It's relatively easy to comprehend that our environment influences our eating behavior and how much weight we gain. "Living next to a farmers market or in a food desert will have a far greater influence on whether a person makes healthy food choices than how much self-discipline they have," Dan Brierley, a University College London neuroscientist studying obesity, told me. Many of us now live in places overflowing with cheap, ultraprocessed calories, which may help explain soaring obesity rates.

But not everyone has obesity today. That's because how we respond to our environment is also subject to internal controls — invisible nudges guiding us at every meal. Researchers observed this more than 100 years ago and only recently began to truly unpack how these systems work. The new class of diabetes and obesity drugs — such as semaglutide (sold under the brand names Ozempic and Wegovy) and tirzepatide (Mounjaro) — evolved from that research.

The cascade of discoveries leading to these injectable medications, considered the most effective ever approved for obesity, can be traced back to 1840, when doctors started sharing case studies of patients who, for reasons that seemed outside of their conscious control, overate to the point of severe obesity. On further examination, many had tumors in their brains. The tumors impinged on their physiology in mysterious ways that changed what and how much they ate.

Animal studies that followed hinted at a new understanding of what was going on: Body weight and eating behavior were regulated, not the product of conscious control alone, and the brain somehow orchestrated the process.

Genes also appeared to play a role. Scientists had long observed that obesity ran in families, but it wasn't clear how much heredity or the environment explained that. A famous 1990 study of identical twins born in Sweden showed that pairs who were separated at birth and adopted had weights more similar to each other than to their adoptive families.

In the mid-1990s, scientists peered inside this complex machinery, to see at the molecular level how brains and genes shape appetite and weight. Early studies in mice revealed that the rodents produce a factor that sends a signal to the brain about how much body fat they had stored on them. Some mice with obesity lacked that factor and couldn't stop eating. Researchers at Rockefeller University in New York identified the factor in 1994: It was a hormone, which they named leptin, coded by a gene known as LEP.

Later, Cambridge University researchers discovered leptin's role in humans, after finding patients with extreme forms of childhood obesity, caused by LEP mutations. Just as in mice, leptin is produced by body fat and transported into the bloodstream, where it circulates to the brain. There it sends a message about how much energy is stored on the body in the form of fat. When leptin levels drop, or people have genetic abnormalities that don't allow them to produce leptin or register leptin's signal, the brain reads that there's not enough fat on the body; people get hungry and eat more.

While leptin regulates energy balance over time horizons like weeks, there are many other signals that drive our nutritional choices from meal to meal (just as there are now more than 1,000 known gene variants implicated in obesity). One well-known player is the hormone

glucagon-like peptide-1, or GLP-1, which Wegovy and Ozempic mimic. Primarily produced by the gut, it tells the brain when we've had enough to eat.

The ability to sense such fullness — and hunger — varies, the result of genetic differences in brain circuits that control appetite. This manifests in a range of experiences, from people with Prader-Willi to that annoying friend who forgets to eat and is effortlessly skinny all his life (and therefore, perhaps can't understand why anybody struggles with weight).

The new drugs are the first to manipulate the hormonal regulatory systems governing energy balance. The drugs simulate the action of our native GLP-1 but with longer-lasting effects, amplifying the fullness signal inside the body. People who struggle to feel sated suddenly don't, effectively giving "someone the willpower of those lucky enough to have won the genetic lottery," said Dr. Brierley.

Many people who have taken the medicines for obesity described to me how their experience of hunger had fundamentally changed. Patricia McEwan, who has injected Ozempic for nine months, said she planned to stay on the drug for life because it "shut off the intrusive constant thoughts about food" that had consumed too much of her mental space since childhood. Before Ozempic, Ms. McEwan thought her overeating was driven by her emotions and lack of willpower. After Ozempic, she understood that how she responded to food was the product of her physiology.

There are open questions about how GLP-1-based drugs will work long term in individual patients and what impact, if any, they'll have on the surging global obesity rate. The data we have suggests people's weight loss can plateau after a while and side effects are common, as is weight regain when patients go off the medicines.

There have been many reports about insurance hurdles or supply shortages that interrupt or block people's access to obesity drugs in the United States, and it's unclear how low-income people will get access to them. Meanwhile, the energy balance model of appetite regulation is being complicated by evidence that we have other kinds of nutrient appetites — for protein, for example — and there's very little understanding of how the medicines will affect these.

At the very least, though, the way the drugs work can teach us that people who are larger did not necessarily choose to be, just as people who are smaller did not — and are not morally superior. This "isn't a free pass, either to individuals who do have the capacity to choose better, nor does it take the heat off of food industries," said a University of Sydney nutritional biologist, Stephen Simpson, but it's "evidence that obesity isn't a personal lifestyle choice."

Learning about this science helped me see my own weight changes in a new light. When I became pregnant with my second child, I very quickly developed a voracious appetite. I felt a pain from hunger I'd never experienced, would obsess about my next snack or meal in ways I don't usually and ate quantities I would have found unimaginable (even unbearable) a few weeks prior. I also gained weight rapidly.

Suddenly in my second trimester, the increased appetite and the weight gain eased. But the preoccupation with food I'd just experienced recalled my earlier years, when I struggled with

obesity. Now I could see the changes were not the result of a sudden shortage of willpower. My brain was telling my body to get more energy to support the growing fetus.

How women's brains and bodies manage this during pregnancy and breastfeeding is still mysterious, a phenomenon that's also been observed in lactating mice who tend to eat three times their usual calories. Some people with obesity are plagued by the kind of hunger I had in pregnancy all the time. It's also not their choice.

What Ozempic Reveals About Desire

June 4, 2023

By Maia Szalavitz, New York Times

Ms. Szalavitz is a contributing Opinion writer who covers addiction and public policy.

https://www.nytimes.com/2023/06/04/opinion/ozempic-weight-loss-addictions-desire.html

Mary Boyer, a 41-year-old tech worker, started taking the drug Mounjaro last October to treat obesity. She has since lost more than 40 pounds, going from 267 when she started to 221 when she weighed herself recently. “I’m losing, like, a pound and a half a week pretty steadily,” she said.

For decades, she was preoccupied with dieting, hunger and cravings. Now that obsession is gone. “I just straight up lost my sweet tooth,” she said. She still sometimes turns to pizza or tacos to stanch emotions, but less often. “What happens now is either I get them and I have a little bit and I’m satisfied or I’m just like, ‘You know, I don’t really need that,’” she said.

Mounjaro — like the better-known Ozempic — is one of a new class of diabetes and obesity drugs that work differently from earlier medications in ways that are not yet fully understood. Unlike stimulants, which can be addictive, these drugs may fight addictions and not just those related to food. Newer, stronger versions are on their way.

Discovering how the new weight loss medications alter appetite and the compulsive behavior that can be associated with it could offer new insight into the nature of pleasure and addictions. Adjusting brain systems that regulate desire may also affect the stigma that society pins on people with conditions that can lead to loss of control. When drugs can significantly ease weight loss or addiction recovery, it’s hard to argue that the problem is moral rather than medical.

The new weight loss drugs are called GLP-1 receptor agonists. They do much of their work in the brain, reducing the way that hunger centers attention on seeking food. This affects one of our two primary types of pleasure, which Kent Berridge, a professor of psychology and neuroscience at the University of Michigan, has labeled “wanting.” The positive side of wanting is feeling empowered and focused on getting what you desire; the negative side, of course, is craving that goes unsatiated.

The second kind of pleasure, which Dr. Berridge calls “liking,” is linked with the satisfaction and comfort of having achieved your goal. While there is less downside here, if people felt forever satisfied, they’d probably lack motivation to do much. The psychiatrist Donald Klein eloquently distinguished the two joys as the “pleasures of the hunt” and the “pleasures of the feast.”

Dr. Berridge and his colleagues showed how wanting and liking rely on distinct but connected circuitry. In his theory of addiction, he argues that wanting escalates as drug use increases, while liking plateaus or diminishes, leaving people frantically seeking something that no longer

provides much, if any, satisfaction. Although he was previously skeptical of food addiction, recent research has convinced him that some people respond to food the way others crave drugs.

The blisses of eating, of sex and of drugs feel different. But the brain processes many emotions via the same circuitry. The wanting circuits tend to rely on the neurotransmitter dopamine, while liking is more associated with the brain's natural opioids. Having these common currencies of emotion allows our brains to modulate what we want, depending on what it perceives as our most pressing needs.

When this circuitry works harmoniously, wanting and liking are tuned down after a need is satisfied. This is why, for most people, once they are full, more food is unappealing. The result is that pleasure is relative and context dependent — and sadly, what makes them happy now may not do so later, whether it's a drug, a new outfit or a relationship.

These facts have inspired the design of drugs to fight addictions. Some, like methadone and buprenorphine, satiate opioid craving by providing a consistent level of a drug similar to the one that is wanted, without the chaos that can prevent people with addiction from living well.

When people take these medications consistently in appropriate doses, they are not impaired or high because they have become tolerant of those effects. Their brain receptors are now accustomed to certain levels of opioids and are occupied and activated when taking the medications. Consequently, people can get on with their lives, with a 50 percent or greater reduction in their risk of dying from overdose.

Other medications, like naltrexone, do the opposite and prevent opioid receptor activation. This, however, means that they can interfere with non-drug-related liking pleasures also mediated by these receptors, like those associated with socializing. Not surprisingly, patients overwhelmingly prefer drugs that satiate desire rather than reduce pleasure.

A third group of medications — antipsychotics, which block some dopamine receptors in the wanting circuitry and are used to treat schizophrenia — has also been tried for addiction. But these medications aren't selective. For some people, they reduce the thrill of the chase so dramatically that motivation is minimized and life feels empty. Some of the newer antipsychotics seem to cut alcohol craving; however, they may also worsen stimulant addictions and are notorious for causing weight gain.

GLP-1 drugs act differently. They modulate the motivational dopamine systems but apparently not in a way that dampens desire overall. According to Randy Seeley, a professor of surgery at the University of Michigan School of Medicine who has been funded by drug companies for some of his research, they lower the body's set point, or the weight it has determined it should be.

"Millions of years of evolution have told you that at some point food is the most important thing and at some point it's not," said Dr. Seeley, explaining how the brain makes choices about whether food or something else, like sex, should be desirable at any given time. He added, "It's not a system that was designed to just accede to your force of will."

Because these drugs act so specifically on a person's set point, Dr. Seeley suspects that, despite the parallels between food and other addictions, the drugs may not work to treat substance problems. Food and fluid intake are heavily regulated by the brain through many complex mechanisms because they are critical to survival. But it's not yet clear if these systems can also create signals that say no to more drugs and, if so, how this varies among individuals.

So far, the data on using GLP-1 drugs for substance addictions is mixed. Some studies showed positive results in animals and humans, but others found no effect.

Dr. Nora Volkow, the director of the National Institute on Drug Abuse, is funding research on these medications for drug addictions. She said that they might work "by interfering with that urge to have more." It will be fascinating to learn whether it's possible to alter or even create a set point that signals that "enough" drugs have been taken. People with alcohol problems seem to lack such an off switch, while those who drink moderately report clearly knowing when to stop.

Dr. Berridge noted that while neuroscientists know a lot about how to change the intensity of cravings, they don't yet understand what controls the focus of desire. This could be how GLP-1 drugs work, by reducing the value that motivational systems place on getting more food now, thereby cutting hunger. In other words, they don't block pleasure but shift attention. And this could help tame many types of obsessions. Some people who are taking these drugs already report ending compulsive shopping and nail biting.

But perhaps one of the greatest benefits of the widespread availability of drugs that make losing weight or kicking addictions easier is the reduction of stigma. People with obesity or drug addictions are often seen as selfish, shamefully lacking in willpower and lazy. Both are derided for apparently abandoning themselves to indulgence, even though research shows that they are more likely to be trying to ease emotional pain.

Seeing people change with ease on medication after years of struggle could help the public recognize that these are truly medical issues. Simply by working the way they do, GLP-1 medications suggest that the difference between addicted people and others is chemistry, not choices.

Alternatively, some advocates for fat acceptance worry that such drugs will actually add stigma, increasing pressure to change rather than encouraging society to value those of all sizes. Others are concerned about the persistence of the idea that making change without hard work is cheating, like taking steroids to gain muscle.

It is long past time to stop shaming people with disorders of appetite in a futile attempt to tame our own fears of loss of control. Whatever condition is being treated, we all deserve the easiest possible path to recovery. Understanding how wanting, liking and attention are regulated by the brain could lead to better self-control for many, across diagnoses.

I Lost Weight on Ozempic. Here's What the Debate Gets Wrong.

Why one doctor believes obesity should be treated like any disease – with medication.

Podcast: https://www.nytimes.com/2023/01/19/opinion/obesity-disease-weight-loss.html

Transcript: https://www.nytimes.com/2023/01/19/opinion/obesity-disease-weight-loss.html?showTranscript=1. Excerpt:

From New York Times Opinion, I'm Lulu Garcia-Navarro. And this is "First Person." There's a whole debate right now about the use of medication for obesity. But I think there's been something crucially missing in how it's being discussed.

Let me start by saying I've been fat since puberty. Not just a few pounds here and there, I've been clinically obese for most of my adult life. I've done everything to deal with it, fat camps when I was young, then crash diets, medical spas. I've had operations.

About 40 percent of American adults have clinical obesity. And as anyone who is a person of size will tell you, there's a lot of shame and guilt around being fat. Most everyone sees it as an issue of willpower or motivation, and so did I. Then about two years ago at my old job, I had a life changing conversation with Dr. Fatima Cody Stanford. She's a professor at Harvard Medical School and an Obesity Medicine Specialist at Massachusetts General Hospital. It was a conversation about Covid vaccines and obesity. And during the interview, she told me this on air:

> Unfortunately, we have these preconceived notions, because we haven't recognized obesity for the disease that it is, that people that have obesity did this to themselves. And that is, indeed, a fallacy.

The fact that obesity is a disease was new to me. And still, many primary care doctors don't treat it that way, even as new weight loss drugs have been entering the market. You might have heard about some of them like semaglutide, which is marketed under the names Ozempic and Wegovy. That's what I was prescribed soon after I first talked to Dr. Stanford. And it's been very effective for me.

But even as these drugs become more popular, there's a fierce cultural debate happening about who should take them and when. Dr. Stanford's entire career has been at the forefront of the evolving science around obesity. She treats patients, conducts obesity research at Harvard, and we should note, advises a number of pharmaceutical companies, including the one that makes Ozempic. So we put some of these questions to her. Today on "First Person," Dr. Stanford on obesity, stigma and Ozempic.

Recognizing and Treating Obesity as a Disease

By Lesley Stahl

January 1, 2023 / 7:29 PM / 60 Minutes

https://www.cbsnews.com/news/weight-loss-obesity-drug-2023-01-01/

(You can watch the 13:23 segment on YouTube here.)

Almost half of American adults have obesity, a condition that was a fraction of that just 40 years ago and scientists don't agree on what's caused the dramatic increase. What everyone does agree on is that it's a major health crisis, because obesity can cause type 2 diabetes, hypertension, stroke and more than a dozen cancers.

Now there's a medication that leads to dramatic weight loss. But it's wildly expensive. Hollywood celebrities take it to flatten their tummies, but few can afford the thousands of dollars it costs a year.

And very few insurance companies will cover it, even though in 2013 the American Medical Association, some would say, finally recognized obesity as a disease.

Dr. Fatima Cody Stanford: It's a brain disease.

Lesley Stahl: It is?

Dr. Fatima Cody Stanford: It's a brain disease. And the brain tells us how much to eat and how much to store.

Dr. Fatima Cody Stanford, an obesity doctor at Mass General Hospital and associate professor at Harvard Medical School, says common beliefs about obesity are all wrong

And diet shows like "The Biggest Loser" are snookering people.

Lesley Stahl: If you diet, you lose weight, right?

Dr. Fatima Cody Stanford: For many of us, we can go on a diet. Something like "The Biggest Loser," right? You go and you restrict people. You make them work out for 10 hours a day and then you feed them 500 calories. For most people, they will acutely lose weight. But 96% of those participants in "The Biggest Loser" regained their weight because their brain worked well. It was supposed to bring them back to store what they needed or what the brain thinks it needs.

Lesley Stahl: So willpower?

Dr. Fatima Cody Stanford: Throw that out the window. My last patient that I saw today was a young woman who's 39 who struggles with severe obesity. She's been working out 5 to 6 times a week, consistently. She's eating very little. Her brain is defending a certain set point.

A set point, says Dr. Stanford, is a range of weight your brain is in charge of maintaining by controlling how much food you eat and how much of it you store. One theory is that it's an evolutionary survival mechanism that helped retain fat during famines.

Dr. Fatima Cody Stanford

Lesley Stahl: So we had COVID. Lots and lots of people gained weight. Did those people have a new set point that's higher now?

Dr. Fatima Cody Stanford: Absolutely. So when you have a chronic stressor and you get to a certain weight and maintain that weight for, let's say, at least 3 to 6 months, then you recalibrate that set point to a different set point.

Lesley Stahl: I've always heard that it's the fast food. That it's the Diet Cokes, that kinda thing, that is the instigator. Is that true?

Dr. Fatima Cody Stanford: So I think we have to look at the different causes of obesity as a big pie. And that's one factor. But notice how I'm using this part of the pie, right?

Dr. Fatima Cody Stanford: But the number one cause of obesity is genetics. That means if you were born to parents that have obesity, you have a 50-85% likelihood of having the disease yourself even with optimal diet, exercise, sleep management, stress management, so when people see families that have obesity, the assumption is, "Ugh. What are they feeding those kids? They're doing something wrong." Actually do you know this? 79-90% of physicians in the United States have significant bias towards individuals that are heavier. Now, doctors listening to me may say, "Oh, it's not me." Hold your horses, because has that patient come to you and told you, "Look, Doc, I'm eating well." "Look Doc, I'm exercising." And the doc says to them, "Are you sure? I don't believe that that's really what you're doing."

Lesley Stahl: Wait, are you saying that doctors don't understand obesity? Doctors?

Dr. Fatima Cody Stanford: Doctors do not understand obesity.

In one of her published studies, Dr. Stanford found that most medical schools don't teach that obesity is a disease and in fact don't even offer courses on it, even though it's the second leading cause of preventable death in the country after smoking.

Nicole Sams, mother of five from Rhode Island, spent years going to doctors who all had the same message.

Nicole Sams: "Well, you just have to go see a dietician." And I did. I did everything I was told to do: I went to a dietician; you know, I sat, had the rubber foods come in front of me, "Oh, you'll only eat this portion," I'm like "Oh."

Nicole Sams

Maya Cohen went on her first diet when she was 13. At her heaviest, at 5 feet tall, she weighed 192 pounds.

Lesley Stahl: Did you feel that people looked at you and said "Why doesn't she stop eating? She's eaten her way to that"?

Maya Cohen: You know you look at someone and you internalize, "Oh, they must think I'm eating too much." So it's just, after a while you just personally think that, "Okay. Everyone's telling me that I'm — that this is a flaw in my character;" therefore, it must be true. And so you start believing this.

Dr. Caroline Apovian: Don't you think if people walking down the street with obesity, stigmatized as they are, shunned, don't you think if they could lose weight and keep it off they would?

Dr. Caroline Apovian, co-director of the Weight Management and Wellness Center at Brigham and Women's Hospital in Boston who sees both Maya Cohen and Nicole Sams, is relieved that at last she has a highly effective medication to offer her patients that's safe, according to the FDA.

Dr. Caroline Apovian

It's part of a new generation of medications that brings about an impressive average loss of 15% to 22% of a person's weight and it helps keep it off. Drs. Apovian and Stanford have been advising companies developing drugs for obesity, including the Danish company Novo Nordisk, an advertiser on this broadcast. It makes the drug Wegovy that you inject yourself once a week with, something like an epipen. It's not easy to get. The drug is currently in short supply. And it costs more than $1,300 a month.

Lesley Stahl: People in Hollywood can afford these expensive injections. And they're taking them.

Dr. Fatima Cody Stanford: Right.

Lesley Stahl: And they're not necessarily people with obesity.

Dr. Fatima Cody Stanford: Yeah. We have a national shortage on these medications. If those that have the means, are able to get them yet the people that really need them are unable to. Then that creates a greater disparity, right? The haves and the have nots.

The vast majority of people with obesity simply can't afford Wegovy and most insurance companies refuse to cover it partly because, as AHIP - the health insurance trade association – explained in a statement, these drugs "have not yet been proven to work well for long-term weight management and can have complications and adverse impacts on patients."

- **Doctors explain how Wegovy and Ozempic work**
- **Novo Nordisk Statement to 60 Minutes**

Dr. Caroline Apovian: What we've seen so far is really nausea, vomiting, you know that's why these drugs are dosed slowly and starting with low doses.

Lesley Stahl: Oh, and build up?

Dr. Caroline Apovian: And build up.

Dr. Apovian says most of the side effects go away over time.

Dr. Caroline Apovian: We are frustrated every single day when we see patients who desperately need to lose weight to reduce the diabetes, reduce the hypertension, stroke, heart disease, and we can't give them this fabulous, robust medication that is very effective and safe. And we can't give it to them because insurance won't cover it. I receive emails about denials-- that state that we're denying this because "the doctor has not counseled the patient on behavior change as part of this." That's where the stigma of obesity comes in, the idea that the patient can do it with diet and exercise. You would never do that to a patient with hypertension or heart disease or Type 2 diabetes, tell them that you "Just don't eat sugar, you'll be fine."

Novo Nordisk also makes a drug for type 2 diabetes called Ozempic, which most insurers and employers do cover. What frustrates the doctors is that Ozempic and Wegovy are exactly the same drug, though Wegovy for obesity is usually prescribed at a higher dosage.

When Maya Cohen wanted the medication for obesity…

Maya Cohen: My insurance company told me that they consider it a "vanity drug."

Lesley Stahl: A "vanity drug."

Lesley Stahl: So that suggests that the insurance company does not consider obesity a disease--

Maya Cohen: Correct.

Maya Cohen

Nicole was also denied coverage. On its website, her health plan, through the state of Rhode Island, puts anti-obesity medications in the same category as drugs for erectile dysfunction and cosmetic purposes.

There are about 110 million Americans eligible for an anti-obesity medication, making it a costly investment for insurance, but if they covered it, overall government and private health care spending would probably come down. Just take diabetes, that is, in many cases, caused by obesity. Diabetes costs more than $300 billion a year, most of which is covered through Medicare and Medicaid. But University of Chicago health care economist Tomas Philipson points out that there's actually a law that prevents Medicare from covering weight loss drugs.

Lesley Stahl: You would think that that insurance program for older adults would see an enormous benefit to these drugs?

Tomas Philipson: Yeah, a third of Medicare spending is diabetes, you know, which is highly with-- tied to obesity. And Medicare kind of sees all the health care expenses when you get older when you have heart disease, et cetera, from your obesity. I think what ultimately will drive it is that they have evidence that this is actually gonna lower total Medicare costs.

Tomas Philipson

When Dr. Apovian told both Maya Cohen and Nicole Sams that their obesity was not a weakness of willpower, they were blown away.

Nicole Sams: I looked at her and I said, "I don't believe you. What do you mean, 'It's not my fault?' It is my fault." Because it's what I heard for my entire life.

Maya Cohen: I went home that day like-- a boulder had come off my shoulders. Like, "Okay, there's finally hope. There's hope."

Lesley Stahl: Did you cry?

Maya Cohen: I did. A lot. (LAUGH)

Dr. Caroline Apovian: All those years of thinking that somehow you have no willpower and it's your moral failing and you're a glutton and why did you eat so much and-- feeling shame. It's the shame.

Lesley Stahl: Yeah, yeah. It's the shame.

Dr. Caroline Apovian: It's the shame.

Maya was ultimately able to get the medication covered by her insurance because she has type 2 diabetes. She's lost more than 50 pounds. Dr. Apovian says she does have to continue dieting and exercising and, like most patients, will be taking the drug indefinitely to maintain her weight. Nicole doesn't have type 2 diabetes.

Lesley Stahl: Nicole, we called your insurance company and they gave us a statement.

Nicole Sams: Okay.

Lesley Stahl: "Earlier this year the State of Rhode Island, in consultation with its pharmacy benefits manager, decided that health insurance for the State of Rhode Island employees would cover the entire class of anti-obesity drugs."

Nicole Sams: Oh-- really?

Lesley Stahl: "This coverage change goes into effect January"--

Nicole Sams: Okay.

Lesley Stahl: --"2023"

Maya Cohen: I'm so happy for you.

Nicole Sams: Yes. This is great. This is great. (CLAPS) Wow. Wow.

In its statement, the health insurance trade association said, "obesity is a complex disease and the evidence and clinical guidelines related to obesity treatment… are evolving rapidly. Health insurance providers will continue to review the clinical evidence."