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Weighing the GLP-1 Market

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Allison Nathan: GLP-1s, the term for the class of drugs that Wegovy and Zepbound belong to, are being hailed by some as miracle drugs for the treatment of obesity, a chronic disease that affects over 1 billion people globally. But will these drugs really have the impact that some investors and economists, not to mention patients, hope? I'm Allison Nathan, and this is Goldman Sachs Exchanges.

Every month, I speak with investors, policymakers, and academics about the most pressing market-moving issues for our Top of Mind Report from Goldman Sachs Research. On this episode, I share parts of my conversations with two experts featured in our latest report that explores just how large the addressable market for GLP-1s actually is. Dr. Fatima Cody Stanford, an obesity medicine physician and

scientists at Massachusetts General Hospital and Harvard Medical School, and Jonathan Gruber, professor of Economics and chairman of the economics department at MIT.

Dr. Stanford and I first discuss how GLP-1s work, what makes them so much more effective than other weight-loss medications, and, despite this higher efficacy, why she doesn't view them as a silver bullet for weight loss and for the treatment of obesity. Here's our conversation.

Allison Nathan: We're speaking to you because you have so much extensive experience with obesity medicine. Let's start with just understanding obesity a little bit better. Just a basic definition of obesity and how prevalent it is is a good place to start.

Dr. Fatima Cody Stanford: So when we talk about obesity as a disease process, we have to understand that it's a complex, chronic, multifactorial disease process. And the reason why I call it a disease is because it has pathophysiology. Most of how obesity is regulated starts in the brain, and we can look at the brain as the key organ that regulates our weight. So the brain communicates with

our adipose, or fat tissue, and it also communicates with our gut to regulate our weight status.

A lot of people are really unaware that this is how our body regulates weight. And so when we're looking at this rise in anti-obesity medications, a lot of that knowledge has come from us understanding the pathophysiology of obesity and recognizing that the pathophysiology comes from an anorexigenic pathway of the brain, what we call our POMC, or our pro-opiomelanocortin pathway of the brain, which tells us to eat less, and our orexigenic pathway of the brain, what we call our pathway that tells us to eat more. This is communicating with our adipose, our adipose which is an organ, or fat. I don't call people fat because actually fat, or adipose, is an organ that can be dysregulated, causing dysfunction within the body. And so some of us have dysregulation, and that's what leads to disease and disease processes.

Allison Nathan: We are focused on the GLP-1 medications. What role might they or are they playing in tackling obesity?

Dr. Fatima Cody Stanford: GLP-1s are a very

interesting inflection point in addressing obesity. Right now, I think we're paying attention to the GLP-1s because they do really address that key pathway of the brain that regulates food intake and storage. Many of us that struggle with excess weight, if we can just increase our anorexigenic pathway, we're not going to eat as much. And if we block the other pathway, that means that we're going to make sure that, hey, we're just not as hungry.

What a lot of people also don't know -- and this is what I really want to get across -- is that each of us has GLP-1 already inside of us. Now, I'll repeat that again. All of us have GLP-1, which is glucagon-like peptide-1, already inside of us. For those of us who happen to be leaner at baseline, we just happen to have more of it. And so those of us that happen to have more happen to have the ability to not be preoccupied with this idea of wanting to eat or thinking about food often. And for those of that don't have that ability, we can administer these GLP-1 agonists to help.

Allison Nathan: By the way, out of curiosity, can you test for that? Can you determine how much GLP-1 you have in your body?

Dr. Fatima Cody Stanford: No, we don't. But you know what, Allison? You're onto something. I think that you can just talk to people, right? So when I do that initial visit with the patient, I can ask them, you know, like, "What are some of your thoughts?" And they're telling me they're always thinking about food, or they're preoccupied or consumed with thinking. I don't have to do a test.

Allison Nathan: Got it. Okay. If we look at the efficacy of these drugs in terms of weight loss and treating obesity, give us some stats in terms of how effective these drugs are and in comparison to other types of obesity agents.

Dr. Fatima Cody Stanford: So first of all, let's give a little bit of the history of anti-obesity medications in the country. We have had agents approved by the FDA to treat obesity as long ago as 1933. So I want that to resonate for people. We think that this era of treating with medications just started in 2021 or 2022. 1933. So this has been around, right, for quite some time; meaning, agents for obesity.

However, some of those agents, several of those agents

were proven to be not effective. In 1933, DMP was approved for the treatment of obesity. It was withdrawn due to hypothermia, which means that you overheat, tachycardia, your heart beats too fast, fever, tachypnea, and death. Methamphetamine was approved back in 1947 for the treatment of obesity. In 1959, phendimetrazine, diethylpropion, and phentermine were approved for the treatment of obesity. In 1960, benzphetamine and N-Ethylpropylamine were approved for the treatment of obesity. And then of course, because it is the '60s, we see rainbow pills being approved because why not? It's the sixties. 1968, rainbow pills were withdrawn because of insomnia, palpitations, anxiety, increased heart rate, blood pressure, and -- guess what? -- death. Methamphetamine was withdrawn in 1979 due to high risk for abusiveness and addiction. In 2012, lorcaserin and phentermine-topiramate was approved by the FDA. And then in 2014, liraglutide, that was the very first GLP-1 approved for the treatment of obesity. That's the daily injection approved now age 12 and above. And bupropion and naltrexone were approved. And then finally, semaglutide being approved in 2021 and tirzepatide, which is the dual against Lilly's drug, combination of a GLP-1, GIP, which is a glucose insulinotropic polypeptide, was approved on

These drugs all work in different pathways, but notice they all work on the central nervous system but in different pathways of the brain. The reason why we think that GLP-1 efficacy is higher is because it really works on the food intake pathway. On average, when you're looking at the total body weight loss, liraglutide, which was that first-generation GLP-1, we're only seeing about 6.5% total body weight loss. Phentermine and topiramate actually outperforms liraglutide with about 10% total body weight loss. Semaglutide, which is the Ozempic/Wegovys of the world, Ozempic is the trade name for the treatment of diabetes, Wegovy is the trade name for the treatment of obesity. We're seeing about 14.9% total body weight loss. Tirzepatide, which is the dual agonist, 22.5% total body weight loss.

So we didn't really see this higher level efficacy until we got into the second-generation GLP-1s, which was semaglutide, when we finally crossed that 10% threshold. And then we didn't really see that 20-plus percent until we got into the dual agonists.

Allison Nathan: So those are averages. How does it vary in terms of effectiveness for different types of patients?

Dr. Fatima Cody Stanford: You have what I call non or minimal responders. It's interesting. I had a patient that was on high dose semaglutide, which is a 2.4-milligram dose. Had lost one pound. Like, one total pound at the highest dose. Now, her hemoglobin A1C did improve dramatically, so she did respond with regards to better blood sugar control over the year of her treatment, but she lost one pound. Which means she is a non-responder with regards to weight regulation.

And if you look at the studies, Wilding study, which is this semaglutide study, Jastreboff's study, which is the tirzepatide study, you do see scatter plots. Meaning, you have these low responders and you have these high responders. And then you obviously have the average, right? So there is this wide variation, which is why I never use words that you're going to hear me say right now -- game changer, miracle drug -- because for the people that are losing one pound, you can imagine it doesn't feel like it's a game changer or a miracle drug.

If you look at the data from the studies, somewhere between 10 to 15% are minimal to non-responders. In practice, I'm seeing closer to about 20%. And I think that may just have something to do with the variation, and my demographics have a very diverse cohort of individuals that are I would say even more diverse than what we see in the clinical trials.

Allison Nathan: So you're not calling this a game changer. Can you give us a little bit more color in terms of why that is?

Dr. Fatima Cody Stanford: First of all, we have to look at all of the treatment strategies. Not everyone needs a GLP-1 agonist. I have patients that have lost 45-50% total body weight on some of those older agents. And for those patients that could utilize lifestyle change, why not use lifestyle for the people that lifestyle works for? Surgery by itself is still the most efficacious tool for treating severe obesity and for treating metabolic disease, meaning Type II diabetes. For patients that have Type II diabetes, surgery can place them in remission from Type II diabetes within the first four to five days in 80-plus percent of patients. There is no medication that can do that. It just isn't. Even

the GLP-1s, even the best that are out there, even the triple agonists that have been published on.

Then let's bring this back to the GLP-1s. It is a great tool and a great resource that can be utilized for a variety of patients, yes. But then you also have to think that not everyone wants to be on a medication. Just because it's a tool that can be utilized doesn't mean that everyone will want to use it, and we have to think about readiness to change for patients. So not everyone that walks through the door that has obesity that even meets qualifications for these medications, that even has the tools and resources -- meaning, the insurance status to cover these -- will say, "Hey, I'm ready to go on a medication that I'm ready to use long term for the treatment of my disease."

Boomers, for example, aren't rushing the floodgates to get put on an injectable medication. And then you have to think about those that wouldn't meet criteria. So do they have contraindications? Do they have a history of medullary thyroid cancer? Do they have a history of multiple endocrine neoplasia type 2? Do they have any history of pancreatitis? Do they have any of these other things that would automatically disqualify them for use for

these medications?

Allison Nathan: How big of an obstacle of you observed lack of insurance coverage is to patients taking the medication?

Dr. Fatima Cody Stanford: Major. If you have diabetes and you have Medicare, your medications for diabetes, including the GLP-1s, are covered under Medicare. CMS recently decided they were going to cover semaglutide for heart disease because the FDA has an indication now for the prevention of heart disease. We have been trying to get CMS to recognize obesity as a chronic disease that warrants chronic therapy for over 12 years by passing the Treat and Reduce Obesity Act. But as of today, if you have obesity and want GLP-1s and you have Medicare, that is not covered. So patients, if they're hitting Medicare age, the medicine is being ripped away from them, and that's not by choice; it's by force.

In the private insurance market, Massachusetts has been leading the way in terms of coverage. Meaning, when I first got here to Massachusetts, only about half of the private insurers or the employer-sponsored insurers were covering

anti-obesity medications. But what that did was put pressure on the other private insurers because people were leaving those plans to go to the plans that were covering. So 100% of the employer-sponsored insurers in Massachusetts now cover anti-obesity medications, which is great.

But if you're not on those plans -- let's say you work for a national company that is not having that pressure -- treatment strategy is governed by what insurance covers. GLP-1s are a promising tool, but once you start looking at all of the issues, the addressable market dwindles down from the 1 billion people worldwide with obesity.

Allison Nathan: So lack of insurance coverage is a major obstacle to wider GLP-1 usage. I spoke to MIT's Jonathan Gruber to understand just how much expanding Medicare to cover these drugs for the treatment of obesity would cost the US government and what could be done to bring those costs down. Here's what he had to say in a recent conversation.

You have played a very important role in several key US health reforms in recent years. How equipped is the US

healthcare system to grapple with the rising popularity of GLP-1 drugs, which are very expensive today?

Jonathan Gruber: I think that the US healthcare system, absent government intervention and oversight, is not well equipped to deal with it. Let's take the price of GLP-1s today, $15,000. The evidence says once you're on them, you have to take them forever to keep the weight off. $15,000 a year forever adds up. And what we, with Brian Deese and Ryan Cummings, estimate is if 40% of all Americans with obesity take GLP-1s, that would, on net, cost the government about $800 billion a year, which is about the size of the Medicare program. That is enormous.

That is net of the savings. It would actually cost the government a trillion dollars a year, but the government would save about $200 billion a year in the fact that there would be less diabetes and other illnesses associated with obesity. Therefore, the net would be about $800 billion a year in government costs.

Allison Nathan: That's interesting. Let me just dig into that a drop, though, because is that really a realistic calculation if you consider that not every person in America

with obesity is well suited for these drugs?

Jonathan Gruber: You know, Allison, when you do a calculation like this, your best hope is to be no more biased one way or another. So what we did is we said, look, there's a lot of uncertainty. First of all, there's uncertainty of how many, if you made every person with obesity eligible, how many would take it? We assumed 40% would, not 100%. On the other hand, there's another 30% of Americans which are not obese but who are overweight who might also want to take GLP-1s. My friends in Palo Alto tell me that everyone out there is already on these drugs. So we could be very conservative in terms of the number of people who are eligible for these drugs and want to take them.

Allison Nathan: But high prices motivate competition. That is how the market works.

Jonathan Gruber: A valid criticism of our estimates is that we are wrong to use the current price, that competition is going to come along and drive that price down, and I sure hope so. But the problem with that is that, in our current system of patents and our system

where companies will often do lawsuits and things to extend their patents beyond the period where they're supposed to last, competition is slow to work as a mechanism. I'm not saying it can't, and it might. But it is slow to work.

Right now, not enough people are getting these drugs because insurers are so afraid of the costs, they're excessively restricting them. So in the meantime, waiting for competition to bring prices down, there are people who could benefit from these drugs who aren't getting them.

Allison Nathan: And so what actions could policymakers take to make these drugs more cost effective?

Jonathan Gruber: I think that we have to recognize that every other developed country in the world has realized what the US hasn't, which is that the purely free market in health care doesn't work. I'm an economist. I believe in the free market. I don't think the government should regulate what we pay for apples or for cars, but those are markets that work. Health care is a market that doesn't.

When the market works well, keep the government out, okay? But market failures are when markets don't deliver the outcomes that's best for society. An example of a market failure is when, if I want to buy a car, I can shop across lots of car dealers, there's lots of information on the web about what cars cost. That's not true if I want to get my heart attack treated. I can't say in the back of the ambulance, "Hey, take me to this other hospital. I want to see if that one's cheaper." I don't know what it's going to cost, so there's imperfect information.

There's imperfect competition, which is, if I want to buy a car, I can go to Route 1 here in Massachusetts and there's six car dealers within 100 yards of each other. If I have a heart attack on Nantucket, there's one hospital. They can charge whatever they want. I have nowhere else to go.

So for all these reasons, markets in health care in the US do not benefit from the same kind of market forces that make them function so well in other contexts. That doesn't mean there's not a role for markets. That means that markets in that context work best within the strictures of some more government intervention. Every other country recognizes that and regulates both the price and the use of

things like GLP-1s, and we should as well.

Allison Nathan: Can you just talk a little bit more about what price regulation would look like?

Jonathan Gruber: If we were running this in a rational way, the way other countries do, we would have a government organization in charge of adjudicating two issues. One is who should be eligible for these drugs? The second should be what should the price be? And the price should be based on the social value of the drug. Now, that is a tough question that raises things like how do you value people's wellbeing from losing weight and not having diabetes?

There is an organization called ICER, the Institute for Comparative Effectiveness Research, was a nonprofit organization that does these kinds of calculations. They have said that, for the populations that would benefit most from these drugs, they are worth about $7,000 a year. So they would argue that, at about half the current price, the cost would be justified based on the benefits of this narrow population. But that's not the only population that should take the drugs. The question is, for a broader population,

how would that number be? But the point is these calculations can be done and they should be done.

Allison Nathan: Can you give us a flavor of how you go about finding the social value of something?

Jonathan Gruber: It's super interesting and super hard and something which people need to pay more attention to because it's going to be a major issue as we eventually grapple with healthcare costs in this country. A medical treatment has two effects. It can lengthen life, and it can improve quality of life while alive. Now, the lengthening life part is the easier part. Economists have estimates of the value of a year of life. They come from things like how much more you have to pay people to take risks and how much people will pay to be protected from death.

The harder part is how do you think about the value of not having diabetes? Typically, what we do is we gather survey data from individuals. And we ask let's say I could introduce a drug that would allow you to lose 25 pounds, what's that worth to you? Let's say you wouldn't get diabetes, what's that worth to you? And they use that to

get a sense of people's inherent valuation of the benefits of these drugs. There is no right answer. And this is the number one thing we have to learn with health care is there is never a right answer to anything, but it is a much more rational way to do it than to just price it at whatever this broken market will bear.

Allison Nathan: The age-old argument against this, of course, is that it's enormously expensive for companies to develop drugs, and by setting a lower price you're taking away incentives for drug companies to innovate. What do you make of that argument?

Jonathan Gruber: Drug development in the US has been unbelievably economically successful and medically successful. That said, we have to remember that there is a trade-off. It's economics after all. And the trade-off is that the dollars that go to these companies, some of which go to R&D, some of which go to advertising and other things, the extent they come from the public sector, that freezes out things the public sector can do. And one thing the public sector can do very successfully is R&D.

Remember, every single drug that's invented is based on

basic science paid for by the US government through NIH. So if you basically say we're going to spend hundreds of billions of dollars more for the government to cover Wegovy and, by doing so, since we seem unwilling to raise taxes in this country, we're going to have to cut discretionary spending, then we're going to cut research and development. That actually lowers innovation.

So I did a calculation with Rena Conti and Richard Frank. And we found that taking a dollar out of what the government's spending on drugs and giving it to NIH does much more for drug innovation than leaving that dollar in the hands of the drug companies because the research that NIH does benefits everybody, it's public. The drug companies doing private research just benefits them.

I have a book with Simon Johnson called *Jumpstarting America.* And the point of our book is that private R&D is important, but public R&D is as important, if not more important. And we as a country used to spend 2% of our entire GDP on public science, on providing basic scientific innovations that led America to be great. That's now down to less than 0.6% of GDP. And we are 14th in the world in public R&D.

So my answer to that age-old thing is, sure, your profits should not go to zero. And I'm not even saying prices need to be as low as they are in Europe. But the bottom line is, to the extent that the prices you're charging are bankrupting the ability of the government to do basic science, that's a trade-off we shouldn't do.

Allison Nathan: So you think there should be some process of setting a price that makes sense for society, but do you think that's at all likely?

Jonathan Gruber: If you'd asked me three years ago, I would have stammered, hemmed, and hawed. But now, we have a framework with the Inflation Reduction Act, which actually puts in the ability for Medicare to negotiate the price of a limited set of drugs. That's the first time we've taken that step as a government. And I think that's a good sign that maybe we can take this battle.

We should also think about other innovative mechanisms. The Nobel Prize-winning economist Michael Kremer for many years has been suggesting prize-based incentives where you say, look, we really want to solve this disease.

We know it's expensive to solve it. We'll pay $1 billion to whoever solves it, but then you got to make the drug available for marginal cost. It worked for pneumococcal vaccine, which was developed with a prize set up by the Gates Foundation. And it spurred on the innovation. And companies were willing to take the chance. So there's no reason that can't work. Companies will react to incentives.

It's an incredibly hard battle, but we've tried everything else and it hasn't worked. And it's time to tackle this. I understand the politics is challenging, but we're a nation that's tackled bigger challenges before and we can do this, too.

Allison Nathan: While the cost of expanding insurance coverage for GLP-1s may be large, Goldman Sachs's chief US political economist Alec Phillips says in our report that this isn't necessarily an argument against expanding coverage. Phillips notes that, until 2006, Medicare didn't cover prescription drugs at all, but Congress expanded coverage for the benefit of the senior population. And similar arguments for expanding coverage to GLP-1s exists today. In fact, Goldman Sachs's senior global economist Joseph Briggs believes that the widespread adoption of

GLP-1 drugs and the associated improvement in health outcomes could have meaningfully positive impacts on US economic growth since a healthier workforce is a more productive one.

Ultimately, GLP-1 drugs may not be the silver bullet for weight loss that many people had hoped, and many hurdles may constrain their market size for the time being. But if policymakers and drug makers are able to invest, innovate, and bring down prices, the economic impact could be meaningful.

I'll leave it there for now. If you enjoyed this show, we hope you follow us on Apple Podcasts, Spotify, or Google Podcasts or wherever you listen to your podcasts and leave us a rating and comment. And if you'd like to learn more, visit GS.com where you can find a copy of this report and also sign up for Briefings, a weekly newsletter from Goldman Sachs about trends spanning markets, industries, and the global economy.

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