

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

Hey everyone, it's Ariel Hohwani and I'm Chuck Mendenhall and I'm Pete T. Carroll and together we are 3Pac.

Join us on the brand new Spotify Live app immediately after all of the biggest fights in combat sports.

And also during the weigh-ins because that's when the real drama happens.

So what are you waiting for? Follow the Ring of MMA show right now on our exclusive Spotify podcast feed.

And come join the best community in MMA.

Bruce, we're out of here.

Today's episode is about a medical revolution.

A new class of weight loss drugs that could change America, our health care, our bodies, and the way that we think about weight and willpower.

For a long time, many people thought about obesity or weight, fatness, thinness, fitness, body type.

We thought about these things as the outcome of behavior, of deliberate choices, right?

As the result of a set of good decisions versus bad decisions.

Are you eating the right stuff? Are you working out enough?

We have not historically thought about weight the way we think about a disease or a genetic disorder.

Something that people have very little control over.

In fact, you think about the phrase weight loss pill, historically it's been kind of a pejorative, right?

It has a terrible reputation from the pills of the 1980s, 1990s.

But in the past 18 months, there has been an extraordinary revolution in weight loss medication.

A few years ago, doctors realized that a medication originally prescribed for diabetes called semaglutide was having a very obvious effect on a lot of patients.

That obvious effect was that they were losing a ton of weight without terrible side effects.

And so semaglutide kicked off this wave of new weight loss therapies with brand names like Wigovie and Ozempic.

And we're going to tell you how those medications actually work in just a second.

I'm not going to tell you an extremely accomplished doctor, researcher will tell you.

But the upshot is that we seem to be in one of those rare and special moments in medical science where a real breakthrough makes its way to the general population.

Now, weight is a big deal in America.

And it's not just obesity, which affects two and five Americans today.

It's our obsession with image, how we look, how the way we look reflects something internal, who we are, our virtues, our habits, ourselves.

So I'm interested in a question beyond the health care question.

What happens when you take a country obsessed with self-image as Americans are and tell them that the mystery of weight loss has now been reduced to a daily injection?

You change a lot more than body mass index.

I think you change society.

Today's guest is Susan Z. Yanowski.

She is the co-director of the Office of Obesity Research and the program director of the Division of Digestive Diseases and Nutrition at NIH.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

We talk about the stakes of anti-obesity medication, why diet and exercise don't work for so many people, how these weight loss drugs could help American healthcare and strain American insurance and revolutionize America's sense of willpower, responsibility and diet.

It's a big episode and I hope you enjoy it.

I'm Derek Thompson. This is Plain English.

Dr. Susan Yanowski, welcome to the podcast.

Thanks, Derek. It's great to be here.

I am so interested in this issue.

We just had an episode earlier this week where we talked a little bit about the basics of obesity in America.

That conversation was more about what we're learning about diet and nutrition.

This conversation can be more focused on this extraordinary medical revolution that we seem to be at the dawn of in obesity pills that I think can change so much about health and culture in America. But I want to make sure that we reiterate the stakes here.

How serious a problem is obesity in America and is it getting worse?

Sure. Well, more than 40% of adults in the U.S. and almost 20% of children and teens have obesity. And of course, we're concerned about this because obesity increases the risk for lots of conditions like type 2 diabetes, heart disease, some kinds of cancer.

And in addition, non-alcoholic fatty liver disease, this is now one of the leading causes of liver transplantation.

And I think that the COVID-19 pandemic where we've seen that obesity increases risk for more severe disease and death has really driven home the need for effective treatments.

Why is it so hard for so many people to lose weight and sustain weight loss through diet and exercise alone?

Sure. Well, behavioral treatments, they're really the foundation for any kind of treatment of obesity, even when you use other interventions like medications or surgery.

And many people can do well with behavioral treatments alone, but actually more than half of people with obesity can't lose enough weight or maintain enough weight loss to get health benefits.

For example, we had a very successful program called the Diabetes Prevention Program where some of the top behavioral scientists in the country gave people lifestyle treatment.

We had very, very motivated patients. We were trying to get them to lose 7% of their body weight.

Well, only about half could do that, even with these best treatments.

There are going to be people who can't lose enough weight to improve their health, and those are the people who are going to possibly need extra therapies like weight loss medications.

And I really want to make sure that we create the tension here, because we know that lots of people who are overweight or are obese, that they do want to lose weight.

But it seems to me it's almost like the body doesn't want to lose weight. The body fights back against diet efforts over time, which is one reason why it's hard for diets to work, and it's even harder for them to sustain the work that they do.

Just really briefly, before we get into this medical revolution, can you help me understand why this is the case, why it seems like the body wants to, quote unquote, defend its weight, and it's so hard to keep weight off for so many people?

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

Yeah, you know, it's very interesting when you talk about what people with obesity go through and the struggles they go through. There are lots of people, most people who have obesity, who are very successful in other areas of their life, right?

They're successful in school, at work, in their communities, with their families. And it's just in this area of being able to control their body weight that they have these struggles.

And I think people who haven't experienced it themselves or haven't had a family member who's struggled with this, often they think, oh, it's just a matter of willpower.

You ought to be pushing away from your plate. But we know it's not that simple at all.

And about, no, in 1994, so quite a while ago, Jeff Friedman and his colleagues at Rockefeller discovered leptin. And this is a hormone that's actually secreted by fat, and it signals the brain and other tissues about energy source, you know, how many calories you've got.

And it showed that fat isn't really just an inert blob. It's actually an endocrine organ, and it sends signals to the brain that tell you about, you know, how adequate your energy stores are.

You know, your body can think you're starving when you're losing weight, and you're thinking about and obsessed about food all the time. You may actually be less physically active. You're more tired.

So we found out that this leptin deficiency in humans is very rare.

But it was really important because I think it really led us to understanding there's an underlying biology behind appetite regulation and energy expenditure and metabolism, and that they can have an impact on development of obesity.

You're making me feel better about the fact that we just earlier this week had an endocrinologist on the show to talk about some of the causes of obesity, and one of his points was that we can't think of it through a simplistic energy balance model of calories out, calories in, which seems to be happening with obesity and weight gain in many cases, is that there are hormonal changes, potentially as a result of diet, what people eat, but potentially as a result of environmental factors.

And those hormonal changes are partially responsible for people feeling much hungrier than average or people feeling like after they go on a diet for a while, their metabolism changes, starts to become more efficient.

And then they want, they need to eat even less food because the changes in their bodies.

And so you should have had to think of this as multi-dimensional.

It's not as simple as just, well, you know, eat less, exercise more. There are things happening inside of the body that are so much more complex that should cause us to rule out the question of, oh, this is just willpower.

This is just make the decision to eat less, make the decision to exercise more. It's as easy as A plus B.

But before we get to this class of breakthrough obesity drugs, I want to at least stop briefly at bariatric surgery, because I've heard you say on another podcast that most people who are obese want to lose 15% or more of their weight.

And those outcomes are typically only attained in the long run through bariatric surgery. Why has bariatric surgery been able to succeed where diet and exercise have failed?

Yeah, that's a great question.

Bariatric surgery does seem to really change. I don't know if you want to use the term set point or it, but people actually, it does change hormones.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

It changes. We know now that...

You know what, actually, doctor, could you, I should have done this in my question.

Yeah.

Can you define bariatric surgery first and then continue to explain why it seems to work?

Sure. Bariatric surgery, now some people are calling it bariatric and metabolic surgery because of the impact. It can also happen metabolism.

There are several kinds of bariatric surgery, but generally the ones that are used today either decrease the size of the stomach or they actually do some intestinal rearrangement in what's called a gastric bypass procedure.

And people who get this kind of surgery, generally they're people who have severe obesity.

Often they have other kinds of health problems like diabetes or high blood pressure.

And it's really the most effective treatment we've had to date for helping people not only lose weight but sustain the weight loss.

And we have lots of information also that this kind of surgery actually improves multiple health conditions.

For example, people who start out with type 2 diabetes, many of them can actually have a remission of that diabetes and have a normal blood sugar after the surgery.

Their blood pressure may go down.

There's some indication that perhaps obesity related cancers, the incidence of those are lessened.

So it really, we know that bariatric surgery for appropriate people has a lot of benefits.

However, there are also risks of bariatric surgery.

So I think one thing is a lot of people who need it or would benefit from it aren't actually referred to it, referred to doctors for it.

So it's probably underutilized.

But the other thing we really like to do is be able to have a lot of these benefits of bariatric surgery on health without actually having to undergo procedures that are going to alter your GI tract.

All right, you are accelerating us toward the main subject today, which is weight loss medication.

And when I think of weight loss pills, when I hear those words, weight loss pills or weight loss medication, weight loss therapy, as a non-expert, I feel like this category has a terrible reputation. I think about just junk pills from the 1980s and stuff that doesn't work or has some terrible side effect that will show up in the body later.

Before we get to the new crop of medications, can you help me understand why it's been so hard to design an effective and safe weight loss drug before now?

Yeah, you are absolutely correct that anti-obesity medications have a history of safety problems.

And often, like if I'm giving a talk on this topic, I start out with some medications that were used in the 20s that led to deaths.

You know, people in the 60s, they had rainbow pills where they were giving people diuretics and thyroid hormones and amphetamines all to try to get people to lose weight.

But a number of these had safety problems.

They ended up leading to withdrawal from the market.

For example, there was a drug called Cybutramine that was approved, one of the drugs approved for long-term treatment of obesity that was found to increase risk of cardiovascular disease.

Many people remember FenFen, where it turned out that FenFloramine, which was one of the drugs

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

in FenFen, actually caused valvular heart disease.

So I think there's been a good deal of skepticism about these medications.

But another thing is that the amount of weight lost with the medications approved before 2021, it's also really been modest.

Ranging from about 6 to 20 pounds more than you'd find with placebo, that's a lot less than most patients want and that many physicians want.

So I think given modest efficacy and the history of safety problems, there hasn't been a big uptake of these medications.

In fact, in 2019, the government accountability office actually did a study where they looked at how many people across the country.

There's 70 million Americans who have obesity, but only at that time about 660,000 reported using prescription weight loss drugs.

Only about 3% of Americans who were trying to lose weight reported taking them.

And in part, it was not only because of their modest effectiveness, but also because a lot of insurers don't reimburse for obesity treatment.

And most patients who are on these medications had to pay for them out of pocket.

So if they're not working or they have intolerable side effects, then not many people are going to be on them.

This all takes us to semaglutide. Tell me, what is semaglutide and why is it such a game changer in anti-obesity medication?

Sure, semaglutide is one of a class of drugs called incretin medications.

It's a leukogon-like peptide receptor agonist, and these are hormones that are secreted by the gastrointestinal tract.

I do want to say that NIH-supported research was actually fundamental to developing these medications.

So these hormones, they're proteins. They are secreted by your gut, essentially, after you eat food.

And they stimulate insulin secretion in response to the food and also in response to high blood sugar.

So they lower blood sugar, and they were approved quite a while ago for treatment of type 2 diabetes.

And as actually as part of the initial FDA approval process, the agency ordered long-term outcome studies,

and we know now that some drugs in this class, including semaglutide, actually reduce risk for heart attack

and other cardiovascular complications that are leading killers of people with diabetes.

And I think for obesity, as you mentioned, you know, the checkered history and finding out we don't want to hurt people, right?

One of the first things we learn in medicine is first, do no harm.

So finding out that at least in people with diabetes, drugs in this class may actually protect the heart, I think, is really, really important.

And they're actually doing studies of these medications right now in people who have obesity and who don't have diabetes to see if that's also the case for them.

I'm so interested in the history of discovery when it comes to these breakthroughs.

And one thing that I read that I thought was utterly fascinating, and I think you reiterated it just

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

now,

is that this drug was not initially intended in terms of clinical trials to directly treat obesity.

It was intended to treat type 2 diabetes.

What happened? Did the company just discover that patients were having the secondary effect of losing a lot of weight?

And they said, oh, wait, maybe we should have entirely different clinical trials in order to test this drug, some agglotide, for weight loss?

Yeah, I think that is what happened.

I mean, most people who have type 2 diabetes also have obesity.

So when you're looking for drugs to treat diabetes, you would like to see medications that not only improve their blood sugar,

but also don't cause weight gain.

For example, insulin treats your blood sugar, but it also can cause weight gain as do some other medications.

So when they were found to cause weight loss in the doses that they were used for diabetes, they were tested at higher doses as anti-obesity medications.

And there are actually two of these GLP1 receptor drugs that are approved in higher dose than those that are used for diabetes.

Those are loraglotide and semaglotide.

And we know how these work for diabetes.

We have a little bit less information on how they're impacting obesity,

but we know that it slows stomach age emptying and delays digestion.

And so that this can allow people to feel full faster and longer and eat less.

But there also seems to be an effect of these medications in the brain that impacts appetite and food reward.

And so people report, particularly with medications like semaglotide,

that they're not thinking about food all the time, that it's not driving their life.

And again, I think some people are worried, oh, these are going to be a quick fix.

People aren't going to have to do the work to lose weight.

Again, we are looking at obesity as a moral failing.

And we used to have people who had high cholesterol.

We were trying to get them to eat these very, very low fat, low cholesterol diets.

And when we developed effective medications that could work with the person and with their doctors that are making lifestyle changes,

we didn't hesitate to use them.

It's so utterly fascinating.

You're making me think about the idea that I've always been very interested,

not only in nutrition in terms of what it does to our bodies,

but in the way that people think about food.

And something you said was just so generative for me.

The idea that people who struggle with weight loss or struggle with body image,

you might encourage them to say, meditate more, find some way to trick the brain

or train the brain to think about food less.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

And here is this drug accidentally discovered through a diabetes 2 medication that actually has the medical effect of getting people to think about feeling hungry less as a hormonal effect.

It just raises, I think, so many deep questions about willpower and even free will, just like where our thoughts come from, the fact that this drug can change the way that people think about food.

I think it's just so utterly fascinating.

I want to talk about a conference that you were at last year.

I really want you to help us understand just how astonished scientists are by this new class of anti-OBC medications.

You're in San Diego last November at a conference where Novo Nordisk, a pharmaceutical company based in Denmark, is presenting new clinical results of semaglutide. And as I read in an essay in Nature, the results were just riotous.

People said that it was like being at a Broadway show.

Take us inside that room or that conference center.

What are scientists saying in response to what seems to be the sort of transformative breakthrough in science?

Yeah, well, I think particularly the excitement about this medication at the conference I was at, which was at the Obesity Society, was that they were going to be showing results of semaglutide treatment

in adolescence with obesity, with severe obesity.

And teens with obesity, they have been among the most difficult group to have benefit from various kinds of treatment,

whether it's lifestyle treatment, they can respond to surgery.

But again, doing surgery in a teenager is a very big deal and something we'd like to avoid.

And we really worry about teens who have severe obesity because they're going to be carrying this for so much of their life.

And teenagers who develop obesity are also at really high risk for things like diabetes development, fatty liver disease, kidney problems, heart problems, even at a very young age.

So people who treat adolescence with obesity have been trying pretty much everything they can to help them.

And until now, you could have teenagers on a medication that maybe you could get a 5% weight loss and that was considered pretty good.

Behavioral treatments, they seem to work for a little while, but weight tends to be regained.

So at this conference, the room was pretty much standing room only because people really wanted to hear the results of this trial of semaglutide.

They were using it in 200 teens with severe obesity.

And they found that it actually reduced the weight of these kids at a year by about 35 pounds, whereas the other adolescents who were getting placebo actually had a 5 pound weight gain.

So they were able to lose about 15% of their initial body weight, which is about three times as much weight loss as you'd previously seen with non-startle therapies for kids.

And I think that that's a reason, you know, there was a panel discussion later about these

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

medications.

How are they going to be used? What can we do to help?

Because if we actually have some treatments that can be successful for people who have severe obesity, it really is a game changer.

Are there other drugs in this category of game-changing anti-beasty drugs besides semaglutide that we should be thinking about and thinking about this revolution that we're at the cusp of?

Well, yeah, there's a lot going on right now.

Also on the horizon, there's another increased drug called terzepatide.

And this actually targets two receptors, that GLP1 receptor, and also one secreted by other cells in the intestine called GIP,

which is glucose-dependent insulinotropic polypeptide, a real mouthful.

It's also injected under the skin once a week.

And I should mention that these drugs, these GLP1 receptor agonists are administered as an injection under the skin.

It was approved just in May of last year for treatment of type 2 diabetes.

But again, it was found to have really robust effects on weight.

And last June, I was at a conference, the American Diabetes Association conference, where they presented results of their clinical trials and people with obesity who didn't have diabetes. They had a remarkable effect.

58% was more than 20% of their body weight.

And so if you had their average weight for the study to start was about 235 pounds, so that would be about a 46-pound weight loss.

So these results were, I mean, in a way, or at least in one clinical trial, almost more astonishing, just mathematically,

than the ones that got the standing ovation in San Diego.

Yeah. Now, these were in adults.

And so, you know, semaglutide in adults also has about a 15% weight loss.

This was even more.

And again, I think the thing that got people excited was that this is an amount of weight loss that you are, it's approaching what you see with bariatric surgery.

And, you know, about 10 years ago, I actually held a symposium at NIH called Bariatric Surgery Without the Surgery,

where we talked about what we'd really like to do is understand the mechanisms by which bariatric surgery works and then be able to give it to people with less invasive types of treatment.

So starting to see this come to fruition, I think, again, it's really exciting for those of us in the field. Surely there are side effects here.

Because, I mean, as much as I would hope there to exist a miracle drug that had absolutely nothing wrong with it,

surely some people must be experiencing something negative.

Yeah. All medications have side effects or adverse effects.

And these are no different.

And I think that, you know, for any kind of medication, you have to look at risk.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

In this case, you know, risks of the medication versus benefits. If you're finding that the medication has an impact on health and how a person feels and functions. So with these medications, for example, I'll go with somaglotide, which has actually been around for quite a while in the maraglotide. The side effect profile is pretty well known. Common side effects include nausea and vomiting. And this generally gets better over time. And the way they try to manage this is by starting with a very low dose and then gradually increasing the dose to a therapeutic dose. There's been some concern about pancreatitis with GLP1 receptor agonists. It's really, in the somaglotide studies, it does not look like there was much of an increase in pancreatitis. It's, again, something that people follow, but isn't really going to be something that is going to impact most people. One that you do see quite a bit is gallbladder disease or gallstones. And, you know, with some people needing to actually have their gallbladder removed. And this isn't surprising because any kind of large weight loss can lead to gallstones. You see this with bariatric surgery. You see it on people losing weight rapidly with very low calorie diets. So, so far, using these medications for obesity, and again, you know, you want to see how does this work when it's actually being used not in a few thousand people, but millions of people. The side effect profile seems to be pretty well known. I want to reserve the balance of our conversation for thinking about how we get these drugs into the population. Like, invention is wonderful, but without deployment, without implementation, it doesn't matter that much. Eventually, we want as many people as possible who are appropriate for this therapy to benefit from it. So, I want to talk about the present. And then after that, I want to talk a little bit about, you know, speculating about the future and how a generation of drugs like this at scale could change so many things about not just American health, but also American culture. So first to the present, what do these treatments cost? Let's talk about semaglotide specifically. What does it cost now? And how easy is it to get in America right now or even get your insurance to pay for? Sure, semaglotide, I believe the cost is about \$1,200 a month. It probably has a little bit of range around that. And not all insurers do pay for it. For example, Medicare actually excludes, specifically excludes, paying for obesity medications. For medical assistance, which is the type of insurance that are often used by people who are in poverty.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

That actually is a state-by-state decision as to whether they will pay for it.
And many private insurers don't pay for obesity medications.
I can tell you, I worked for the federal government and as of January 2023, for the first time, the federal employees health benefits program is paying for obesity medications.
So I think things are changing, but they're still out of reach for many people.
And I think that one of the things we need to do, again, I talk about obesity being a stigmatized condition.
And so if people think that it's a failure of willpower, it's a moral failing, or that you're not going to be doing the hard work of limiting your diet and increasing your physical activity.
So I think that this actually can play a role in willingness to provide obesity treatment.
And recognizing that obesity, it's a complex chronic disease.
It affects almost every organ system.
And if you can successfully treat obesity instead of the individual conditions that could have a positive impact on health.
Yeah, it seems like a good point to bring in just the fact of health disparities in America.
There's disparities in inequality when it comes to health access.
There's obviously income disparities as well.
And one concern that comes to mind is that if you have a drug that ensures won't yet cover or won't yet help to subsidize, it sounds like the federal government is changing a little bit on this.
Maybe there'll be a leading indicator, maybe not.
You're talking about a drug that's cost \$24,000, \$25,000 a year.
It's the rich that are going to be able to afford this.
And that might create more health disparities because it's the rich that can afford the medication that helps them reduce their obesity faster than the low income.
How much does that concern you?
Yeah, again, I can address policy and what policy changes ought to be made.
But I'm very happy to talk about and make sure people are thinking about the health disparities that occur with obesity.
For example, in the U.S., certain racial and ethnic minority groups have much higher rates of diabetes and obesity.
For example, more than half of non-Hispanic black women in the U.S. have obesity.
And as you mentioned, people living in poverty, regardless of race or ethnicity, they're also at higher risk.
We talked in the beginning about childhood obesity.
And that, unfortunately, with COVID seems to be increasing at an even more rapid rate.
Many of these children will have obesity and it's health consequences in adults.
And as more women have obesity and diabetes during their pregnancy, what that does is that it can actually affect the environment in the uterus
and then set their children up for increased risk of type 2 diabetes and obesity.
So you then start having a vicious cycle.
So we really, as we look towards these more effective treatments, we need to address the social and economic factors that contribute to developing obesity.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

And again, at NIH, this is really a high priority for us, is addressing the health disparities that are leading people not to get the treatments that they need.

Ideally, by addressing some of these, what we call social determinants of health, we can even help prevent obesity from developing.

Yeah, I want to make a point that you might not be able to respond to because it sort of touches on policy.

But I promise I'll give you an off ramp to talk a little bit about some of these preventative factors. I was reading that Morgan Stanley did an economic model of the future obesity medications over the next decade.

And the result was that some agatide and other copycat drugs could essentially be a \$30 billion market by 2030.

\$30 billion is roughly 10% of all U.S. drug spending.

And it could be even more than that because if doctors think of obesity the same way that they have come to think of hypertension or high cholesterol.

That is, if you have it, they might suggest some behavioral changes, but if those don't work in a few weeks, months, they can say, well, we do have a pill that's very successful.

If they medicate obesity at the same rate that they've medicated, hypertension, high cholesterol, you're talking about an obesity drug market that isn't \$30 billion.

It's closer to \$90 billion.

Now you're talking about almost one-third of total U.S. drug spending.

It seems to me from a policy standpoint that there's going to be an enormous amount of pressure on insurers to look at these results and start to help subsidize the cost of anti-obesity medication.

And maybe some of their accountants will say, well, look, it's going to cost a lot up front, especially before the patent wears out on things like WeGoV, which is I think the brand name of some agatide. But it's going to pay off in the long run because we're not going to see the long-term cost of obesity in the people that benefit from taking these drugs.

But that brings us right back to the fact that it's so important to not only think about obesity as something that we now have a pill for, but to think of it as the fact that the pill is not going to be evenly distributed.

People aren't going to have equal access to it as long as it costs \$1,000 a month.

We need to continue thinking about the social and economic factors that contribute to obesity.

So what are some of the things that you think we can do even as we have our eye focus on this incredible medical revolution coming down the pike?

What are some things that we can do to address those social and economic factors?

Right. Again, I can't speak to policy and to what I would do if I were in charge of things.

But I think it is really important, as you said, first of all, when looking at these medications to look at what is it doing to help?

What is it doing to help people feel and how they function?

But in addition, I think we need to look at how we can get in there very early and prevent obesity.

That is probably going to require some policy changes.

And I can tell you one of the things we're doing at NIH is we actually have a program with a called time sensitive program and policy evaluation.

So let's say a government wants to get in there and do a soda tax or wants to look at changes in the

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

food system.

It's really important to know what actually is working so that you can put your efforts and your money behind programs and policies that are going to move the needle.

So we actually will fund research to get in there before a policy is instituted, get in there rapidly, let people collect data, and then see what kind of impact that has on their outcomes, be they weight or food purchase behavior.

And so we can use that to have people go to the policymakers and say, here, we have some data. This is what's most likely to be helpful.

I want to talk a little bit about how this changes the future. It seems to me that if you tell the American public, here's a weight loss drug and it actually works.

It seems to be extraordinarily effective. It programs your body and your metabolism to lose weight in a way that we've never seen before without surgery.

You're going to change the world. You're going to change the world in some ways that are just obviously fantastic and some ways that are a little bit more complicated.

On the obviously fantastic side, it seems like it's the same with statins or medications that reduce cholesterol and reduce the likelihood of heart disease.

It's just clearly wonderful to see a mortality rate for certain kind of diseases that might be downstream of obesity come down in the decades after these kind of medications come online.

There's nothing bad about that.

At the same time, in a society that so values thinness, it seems inevitable to me that more people are going to try to use these drugs to escape weight stigma even if they're not obese.

They want to lose 10 pounds. They're not overweight or they're barely a little bit over average in terms of their BMI.

They just want to lose weight. They want to do it easily and they want to keep eating ice cream and bread because they like ice cream and bread.

They take these pills and they don't necessarily need them but they can afford them.

It changes the way that society thinks about thinness and body types because we have taken this incredibly complex matrix of considerations in terms of what you eat and how much you eat and whether you work out and how long you work out and how much willpower you have and how responsible you are and you reduce all this extraordinary array of factors to a pill.

That changes the world, it seems to me.

I wonder, does any of it concern you in terms of how the mainstreaming of weight loss pills like this might change the way that society values and even stigmatizes body type?

Obesity is already a stigmatized condition and what we don't want these medications to do is to increase stigma for anybody,

which I think is one of the reasons we really need to be focusing on this as health, changing people's health and helping them to live more healthy lives.

I think that that's something we really need to get that message out.

Obesity, it's not a matter of willpower, it's not a moral failing, it's a biological condition with certainly having environmental contributors.

Once people have developed obesity, there are physiologic changes that make it really, really hard for them to lose that weight and keep it off long term.

So I think we really need to get that message out.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

The other thing I think we want to get out is that this is not a magic bullet or a magic pill. You mentioned that people say, I want to be able to eat ice cream and eat bread and take a pill. What these medications may do is help people to make those healthy changes and then die in physical activity.

They're not going to allow people to eat whatever they want and not exercise and be healthy. And in fact, things like physical activity, regardless of your weight, can improve health.

So I think we want to move the conversation away from appearance and towards health.

The other thing is these medications aren't going to work for everybody.

And I don't want to see people who can't lose weight with semaglutide or terzepatide thinking again that there's something wrong with them, that if they were only a better person, that it might work.

Obesity is a very heterogeneous condition.

And what we really want to do is be able to understand more about the mechanisms about why some people develop obesity, why some people have trouble losing weight with a given treatment so that we can actually help match appropriate treatments to appropriate patients.

I don't know if you can answer this question, but it's just something that I thought of during your last comment.

We still do have a responsibility ethic, I think, in this country around health and diet and weight loss. My sense is you go to a doctor and you say, I'd like to lose weight and you have the means to pay for something like UgoV, semaglutide, terzepatide.

The doctor is going to say, initially, I would think, let's start with changes to diet and increases in exercise.

But I wonder if that's going to change or if that should change if in a world where we have a fleet of medications that are so much more effective for long-term weight loss than diet and exercise.

Whether it changes the way we think about diet and exercise.

I'm not trying to trick you into saying or even trying to represent the idea that I think a balanced diet is bad or exercise is bad.

I think that eating well is good and I think that exercising is good.

But it seems like we're entering a new paradigm here because there's an option on the table that was never previously on the table.

I don't even know if there's a question in there. It's more just like a thought that occurred to me. Do you have a response to it?

Yeah, I think it's not in either or. It's a both and.

So I think it would be a mistake for a doctor to say, here's this medication without also addressing the fact that to improve health, you also need to have a healthful diet and you need to be physically active.

But that doesn't mean I think we're moving away from saying, OK, we're going to wait six months to see if you don't lose weight with this behavioral weight loss treatment program before we add medication.

That's something that, for example, they don't do with high blood pressure anymore.

You have high blood pressure and they will start treatment with an effective medication.

So I think we need to move away from seeing these medications as, OK, when you've failed everything else, we add this.

[Transcript] Plain English with Derek Thompson / America Isn't Ready for the Weight-Loss-Drug Revolution That's Coming

But I think that we don't want to, again, these aren't magic bullets and I don't think that they can be used in isolation.

They have to be used with lifestyle change.

Right. Exercise is useful for cardiovascular health or aerobic health beyond its contribution to weight loss.

I think it's sneaky powerful that we are used to talking about weight loss in this country with a eat less, exercise more paradigm.

And that paradigm, maybe disagree, might be ending. It's not that eat less, exercise more are a bad idea.

It's that it's an unsuccessful roadmap to sustaining long term weight loss and that instead we have a pill or an injection coming online that's going to change the way that we think about regulating weight.

I just think that's a I think it's going to have powerful, weird side effects on the way that people think even about the concept of like willpower versus biology.

You know, you mentioned a couple times that there's a broad assumption in this country, I think that having the body you want is largely a matter of willpower.

You know, people who have incredible bodies, men and women say, you know, here's how I did it. I worked really hard.

It takes a lot of, you know, sit ups to get this six pack or eight pack.

You can just choose to eat less and do more sit ups.

But the fact that these drugs work the way they work, the fact that they work through somewhat mysterious biological mechanisms does seem to reinforce this idea that for many people body weight is determined in large part by things beyond sheer willpower.

They're determined by this somewhat spooky interplay.

It's spooky because it's only mildly under half understood this this complex and half understood interplay between insulin production and blood sugar and brain receptors.

It does, I think that this this obesity pill revolution, I think it does also revolutionize the way that I kind of think about, you know, the biological bases of appetite and will.

I hope it really does change the conversation about obesity and moves it out of that sphere of being, you know, a moral, a moral failing if you can achieve a normal body weight and into understanding like so many body processes that there's

a lot going on and that anything we can do to help people safely and effectively become healthier is something that we should be embracing.

That's a wonderful place to end.

Dr. Yanovsky, thank you so much for talking me through this and even for entertaining my slightly more confused and philosophical musings.

This was really fantastic and I learned a lot.

It was a pleasure.

Thank you for listening.

Plain English is produced by Devin Manzi. If you like the show, please go to Apple Podcasts or Spotify, give us a five star rating, leave a review and don't forget to check out our Tiktok at plain English underscore that's at plain English underscore on Tiktok.

Thank you.