

Whitney Tilson's e-mails about the new weight-loss drugs

From: Whitney Tilson

Sent: Saturday, October 21, 2023 1:14 PM

Subject: This Drug Could Be the Next Ozempic. Bootlegs Are Already Selling Online.; What To Know About Retatrutide: Unapproved Drug Boasts Greater Weight Loss Than Ozempic, Mounjaro, Wegovy; Friends' comments

1) STOP THE PRESSES! This WSJ exclusive story highlights that a drug Lilly has under development, retatrutide, which results in even greater weight loss than Mounjaro (see article below⁰⁰²⁹, is available right now for a fraction of the cost. I think this will literally be a life-saver for millions of people: [This Drug Could Be the Next Ozempic. Bootlegs Are Already Selling Online](#). Excerpt:

A potential blockbuster weight-loss drug still years away from U.S. regulatory approval is already being sold online, another example of a thriving gray market for unapproved weight-loss medications, according to a Wall Street Journal review.

The Journal found hundreds of merchants offering the new drug, which is being developed by Eli Lilly and is called retatrutide. Most appear to be Chinese sellers shipping directly to U.S. consumers from sites such as Made-in-China.com. Some of the sites, including ones that appear to be based in the U.S., have marketed their products via posts on Facebook, LinkedIn and Reddit. A handful have run paid ads on Instagram and Google. A fitness influencer has offered it for sale via his newsletter.

In August, the Journal reported that more than 50 websites were selling knockoff semaglutide and tirzepatide, the active ingredients in Ozempic and Mounjaro respectively. The Food and Drug Administration issued warning letters to two websites for “unlawful sale of unapproved and misbranded drugs” after the Journal’s article. One, GorillaHealing.com, no longer lists those two drugs on its website, but does offer retatrutide. Last week, three days after the warning letter was posted publicly, the top result in a Google search for “buy retatrutide” was a GorillaHealing.com ad.

If anyone knows of a safe and inexpensive way to get retatrutide, please let me know and I’ll pass the info along...

2) Here’s a Forbes article about it: [What To Know About Retatrutide: Unapproved Drug Boasts Greater Weight Loss Than Ozempic, Mounjaro, Wegovy](#). Excerpt:

A new weight loss drug from Eli Lilly has shown promising results, with participants in a new study averaging a loss of 24% of their body weight, the highest weight loss percentage from any drug in its class.

Eli Lilly, the manufacturer of Mounjaro, published results from two separate studies on Monday showing promising signs for a new injectable weight loss drug.

The drug, called retatrutide, helped patients lose an average of 24% of their body weight over the course of 48 weeks on the highest dosage, according to a mid-stage study published in the New England Journal of Medicine.

Participants lost an average of 58 pounds over the course of 11 months—every participant on the highest dose lost at least 5% and a quarter lost 30% or more of their weight.

In the second study published in the Lancet, researchers found retatrutide not only saw significant weight reductions in people with type 2 diabetes, but it made improvements in glycemic control as well.

Participants lost an average of 17% of their body weight in nine months, which is remarkable as it's typically more difficult for type 2 diabetics to lose weight compared to others with obesity or who are overweight.

The drug's side effects are similar to other medications in its class—like Ozempic, Mounjaro and Wegovy—which are mostly gastrointestinal and include mild to moderate nausea, constipation, vomiting and diarrhea.

3) I emailed four friends (all men) who are on Mounjaro the following questions:

I'm curious how your diet has changed since you've been on Mounjaro. I understand that you're eating less, but has the mix changed? I've been hearing stories about how people on these drugs feel like they have a license to eat anything they want, so they actually eat MORE crap food... Is there any type of food you eat a lot more of? Less of? What about alcohol? Soft drinks?

I'm trying to think of the investment implications. If tens of millions of Americans start taking these drugs, is that good or bad for gyms? Good for dating sites and bad for makers of artificial hips and knees, I assume?

Here were their replies...

Friend 1

Definitely causes you to eat less. I seemed to fizzle out on meals much quicker and my wife says I also ate a lot slower. Another thing I noticed is that diet soda became unappealing to me. In the past, I would drink one or two diet sodas a day. On Mounjaro, I noticed I had little interest in having them or could barely finish one in a day. My wife and I don't drink a lot of alcohol these days as we are doing IVF. I did notice that I would get really sick on alcohol if I had more than a drink or two. This almost made me scared to drink...which isn't necessarily a bad thing I guess.

As far as its impact on gyms, I would assume average gym-goers might not feel as compelled to use the gym for "aesthetics". Most people who are serious about diet and exercise know caloric-restriction is only part of the equation to being in shape. I imagine not ALL the weight lost by Mounjaro is fat and that some lean mass is lost too (especially in the absence of strength

training). And yes, I agree that it would likely be great for dating sites and probably less so for medical sales.

I have been off of Mounjaro for a three weeks now as I figure out if it is financially sound going forward. Have gained a few pounds back but haven't had any wild food binges or "rebound side effects". If I can figure out how to get it cheaper and fit it back into my budget, I would love to get back on it and continue my weight loss efforts. Still have a little ways to go! Thanks for flying us into this miracle drug. Sure did make it easy to lose weight while it was affordable!

Friend 2

I unfortunately have not stayed on the medications regularly. I started gaining back weight and found that the initial results didn't seem to sustain.

I gained back about half the weight I lost — I am discussing options with my doctor.

I mostly just ate less when I was on them, not so much different foods.

Friend 3

My eating has improved because I crave sweets less. I bet this is highly variable based on personality and biology.

There is definitely a group of people who take these drugs, don't exercise, and eat poorly. But there's also a group that gets motivated by the positive results, and eats better and exercises more, unfortunately I do not have a sense as to the size of each group.

Friend 4

This is a super interesting question. Keep in mind I wasn't a junk food eater but I viewed my ability to go on these drugs a blessing so I want to make sure my diet became super clean. I was a big eater though. Big portions of healthy food are still too many kcals. I am really happy that I paid super close attention to my diet because I wouldn't have the same amount of success and confidence to know that I could keep off the weight. I also learned so much from Rich and Betty over the years at FiteMeHealth that I had the knowledge and tools to be successful. [If you want to contact Rich, his email is rich@fitsmehealth.com]

In short, I eat now like some who had bariatric surgery. I eat smaller portions and make sure I get lots of protein to maintain/build muscle and have a lot of nurturing dense food. It has been a continual learning process for me.

So to dive in...

What doesn't work;

- Food that is too rich or greasy; very much upsets my stomach. This could be a tuna salad made with too much mayo, something that has too much butter (like I ordered an avocado toast and the place butters the bread – it was greasy, I couldn't eat it) or the thought of eating something like a foie gras just makes my stomach churn now. Ok. I don't eat that with any regularity but the thought of something that rich is unappealing now.

- Too much sugar; I have found that some sugar is ok – especially natural and with fiber (dates especially), but the drug is a diabetes drug and is meant to help regulate blood sugar. I have found if I had a full desert (bowl of ice cream, slice of cake) it is too much. I don't feel well/right. A taste is sufficient (small amounts). I was at a benefit on Monday, they served a molten chocolate cake for dessert. That would fall into the too rich and too much sugar. It had 4 raspberries and like a Tbs of whipped cream. I ate the raspberries and whipped cream. It gave me some sweetness and was the right amount that I felt fine.
- Red meat – anything that can take a long time to digest is hard on my stomach now. I have always found red meat harder to digest then other animal protein. That is really the case now. The drug causes our stomach to empty slower, so stuff that is hard to digest and sits in my stomach longer doesn't work for me. Other protein; poultry, fish, tofu are all fine.
- Too much fiber – I know this is an issue for very few people, but if I am say at 50+ grams of fiber in a day, that can also be hard on my GI system. This is a real balance for me and has taken me time to figure out as the drug can either constipate or cause diarrhea so I need fiber, but too much is hard on my stomach. In this regard, I don't eat broccoli like I used to because I have found it harder to digest. Fear not, I have switched to eating more spinach (more on that below).
- Larger meals – the drugs do make you eat less, but larger meals, if you are not mindful make you feel too full for too long and uncomfortably so. Given many people's largest meal is at dinner, I have found it can impact my sleep if I ate too much for me on the drug too late.
- I know is this a me-ism, but too many/types of probiotics as messed with me – like many things overall keeping it simple is better. So I do yogurt (Siggi's or Fage 0%) and Kim Chi. I had added in other fermented food (sauerkraut/cabbage/fermented carrots and ginger), Kefir, etc. and it messed with my stomach. That may not even be because of the drug. So I have gone back to work I know works for me; yogurt and kim chi (not together 😊)

What does work:

- Smaller meals throughout the day; say every 3-4 hours. Even if I break up an ordinary lunch into 2 meals say at 12 and 3pm that works. I know this can vary widely based on what people actually eat, but I have found 400-500 Kcal meals for me to be a sweet spot. When I cross into 600+ kcal meals they are either too large or take too long to digest. Snacks 200-300 kcals. I was eating on average 1600 kcals a day on Mounjaro while losing. My RMR was 2350 or so (I was also exercising a lot – still am). So that was 3 meals and snack in the afternoon. We are now ramping down my dose and I am eating closer to 2200-2500kcals by focusing on high nutrient and kcal foods, but still low volume (nuts, salmon, maybe 1.5T of olive oil instead of 1T in dressing to up my kcals to maintain but not increase volume, add an Rx bar in around 10:30am, mixing in fun ingredients like 1T of cacao powder and 2t of collegian protein into my morning latte)
- High Nutrient foods that can be smaller in volume. This is where the spinach comes in. I can steam 5oz of spinach down into a small volume. So I can get a lot of nutrients in a small amount of volume b/c I fill up fast now.
- High calorie foods that are smaller volume; nuts and nut butters.

- Smaller prepacked protein – cans of tuna, salmon or sardines (all low sodium – of course). I have found brands that are smaller portion size (King Oscar Skinless boneless, in water, no salt Sardines – 4.23 oz, Safe Catch Wild Pacific Pink Salmon Skinless and Boneless no salt – 5oz, Vital Choice, Solid White Albacore in water, no salt added – 3.75oz). These are all approved brands on Consumer Labs. High protein, low mercury and just the right amount of protein.
- Protein bars; but for me – really Rx bars. I know the ingredients. They are the right volume and aren't sugary or too rich. I use these A LOT.
- Shakes! Blending down ingredients has made them easier to digest. Plus helps with a volume. I make both fruit based and veggie based shakes depending on what I am in the mood for. Dates come in handy for me here too as they add sweetness to the shakes
- Seeds; adding in either chia, flax or hemp seeds to meals to get protein and fiber with minimal volume
- Beans – fiber and protein and for me easy to digest, but need to be careful that I don't overdo it on fiber here so I try and limit beans to no more than ½ cup a day.
- More lacto-ovo vegetarian based diet – eggs, yogurt, beans, kefir, plant based milk . tofu all easier to digest than animal protein (I find chicken and fish ok – but I eat more vegetarian than I used too). So breakfast could be a some oatmeal, berries and 2 hard boiled eggs or 1 hard boiled egg and egg whites
- Last and certainly not least - critical to stay hydrated; water and unsweetened iced tea for me. I still drink seltzer but the bubbles can also make me feel very full on the drug.

This is what I have so far; off the top of my head. Really happy to discuss this with you. You know I love this stuff and I record everything I eat so I can retrace my journey with you...plus I am still on the journey.

As to your direct questions...

While lower weight would mean less knee/hip replacements – more exercise may mean other injuries. But if you also focus on more lower impact exercise I could see an increase in say walking shoes or brands like Hoka.

I could see a rise in smaller portion bags even for junk

One less talked about side effect is I have lost a taste for alcohol. Just no longer appeals to me. So could see that hurting consumption. I stopped consuming artificial sweeteners many many years ago – so no soft drinks here (have Betty talk to you about that – it's really fascinating)

In speaking with my personal trainer today; she has other clients on Ozempic and Mounjaro.

Agrees about dating sites, also people will want to travel more – people feel good and are looking good. They will be interested and able to travel (better for airlines if less weight re fuel). Clothing industry should be a boon as people will not only need but want new clothes, but especially maybe bathing suits and/or lingerie.

Also, while knee & hip replacement may go down, I think cosmetic surgery especially excess skin removal will go up. That is not covered by insurance, I believe.

Occurred to me this morning; what I do see a big market for is prepacked meals/protein bars/shakes etc. Lots of people when they go on these meds are not hungry at all. Literally do not eat. So they are losing weight and muscle mass, but it is also really unhealthy for them as they aren't getting their daily nutrients. So I see a big market for someone/company who can come out with a range of good tasting portable Meals for those on Mounjaro that are hitting daily requirements. Small, fiber, protein, easy to digest, vitamins, etc. This way if you aren't really hungry you could say have something the size of protein bar that gives you the nutrients your body actually needs. To function properly.

From: Whitney Tilson

Sent: Sunday, October 15, 2023 11:29 PM

Subject: Feedback from readers; Novo Nordisk stops Ozempic kidney trial after early signs of success; Weighing Down the Taxpayer; Scott Galloway

1) A nice note from a reader:

Thank you for weight loss articles!!! Bless you, Whitney Tilson. You're helping me change my life, after dealing with obesity since I was a child. 🙌🏻🙏🏻

2) Another reader wrote:

Hi Whitney,

It may have been in your newsletter or someone else's posts that GLP-1 drugs work very well at first (perhaps too well, where the fast weight loss can lead to wegovy-face gauntness), but after some years (around 6) your body will adjust and the dosage will need to be increased. Then after a couple of years that doesn't even work and the weight starts to come back. Everyone is envisioning taking these drugs for life, while really they might only work for 10 years max (at great expense to our health care plans, driving up insurance costs). Plus the gastrointestinal problems that can crop up, like slowing digestion or even life-threatening stomach paralysis. Certainly all the financial projections are the enormous profits going forward from more and more people taking these for life.

I have read some people feel they have lost so much weight they can start eating ice cream and fattening foods again, or like the stomach-stapled people start eating around it and regaining the weight (an acquaintance gained weight to qualify for stomach stapling, then celebrated how good she looked after - but then ate around it, regained weight, and ended up divorced).

Lucky for me I stopped drinking all sugar sweetened beverages 20+ years ago (65 now) when I started feeling ill from the free soda my employer provided. But if I started drinking 2 or 3 cans of soda a day, I would start gaining weight. Regardless of whether

people are inclined to be obese or not, anyone that watches TV a lot, chugs soda and sugar sweetened beverages and constantly snacks will be (or become) overweight, and then be depressed and eat more food+snacks for comfort. No body can tolerate that, at least not older bodies.

Thanks for your newsletters.

3) From a friend who's 6'5", maybe 260, who went on Mounjaro last Dec., lost 40 pounds in two months, then went off it:

As I have said to you before, I think yours and Scott Galloway's fatal flaw in touting these weight-loss drugs are that the increased risks of these drugs over the longer term are simply unknown. They have not been around long enough.

If I was morbidly obese, I would do a gastric bypass before messing up my digestion abilities.

If you remember, I was ahead of the pack here... nobody on the dive boat had heard of Mounjaro and yet I was touting it as a jump start to working out.

When I came off it I not only gained back all my weight but things were worse for me. I jettisoned to my highest weight ever and I am not entirely convinced that Mounjaro didn't have something to do with it.

Some things just strike me as an unnecessary fu*king around with ones internal ecosystem and these drugs might be devastating to all the fat skinny people looking to short cut a healthy lifestyle which I honestly was also guilty of trying to avoid myself.

I would cut bait on your endorsement of these drugs- it might very well blow up in your face and more importantly, hurt a lot of people.

I replied:

I agree that there are unknown possible future risks – that's true of anything.

But balanced against the CERTAIN outcomes of obesity (or even being significantly overweight), I think the answer is clear. But I understand how others might weigh the risks differently.

This reminds me of the debates I had with some friends about the COVID vaccines... and it never led to anyone changing their views, so I won't email you again about this.

Best,

Whitney

My friend who's lost 90 pounds on Mounjaro added:

There are a lot of naysayers out there. The Post reporting on two people who had side effects as an example. I know Rich Weil has commented on this already.

We do know that the drugs will wear off eventually, but there are already new drugs getting ready to come to market. Like other diseases, the pharma companies will look to stay ahead of this as well especially as they see they will make big money off of this.

However, what people need to realize it is DIET, EXERCISE and the new drugs to be successful long term. That is why I wanted you connected to Rich and Betty from FitsMeHealth. They teach the long term skills, even with the meds, that people with this disease need to be successful.

I eat completely differently then I used to. I eat now like someone who had bariatric surgery. Small meals. Nutrient dense. I work out a lot more. Walk everywhere. I am more active then I was. People need to learn new skills. If I ate a pizza every night but then started the drugs and eat a 1/2 pizza every night, I'll lose weight but without focusing on nutrient quality and exercise that approach will not be successful to maintain the weight loss as the current batch of drugs wears off.

Dr. Maki wrote:

I agree that people rarely change their views. I have worked hard at keeping an open mind and updating my views as new data become available. We have had GLP-1 receptor agonist drugs for some time but only a few years for Ozempic/Wegovy and Mounjaro, which produce larger amounts of weight loss. We need longer term data. Here is a summary of results from an observational study that are somewhat encouraging, albeit still only for 2-3 years of follow-up: [Weight Loss With Semaglutide Maintained for up to 3 Years](#)

Also, as is the case for drugs for other cardiometabolic conditions (e.g., diabetes, hypercholesterolemia, hypertension), long-term use will likely be required to control weight. Lifestyle therapy should remain a central part of the program long-term with counseling and support regarding diet, exercise, sleep quality and quantity, stress management, and behavioral strategies.

4) More on what I expect will be the never-ending stream of studies showing the incredible benefits of the weight-loss drugs: [Novo Nordisk stops Ozempic kidney trial after early signs of success](#). Excerpt:

Novo Nordisk (NOVOB.CO) said on Tuesday it will stop a trial studying Ozempic to treat kidney failure in diabetes patients ahead of schedule because it was clear from an interim analysis that the treatment would succeed.

Novo said the trial would be halted almost a year early based on a recommendation from the independent data monitoring board overseeing the study. Independent monitors can recommend stopping a trial early if there is clear evidence that a drug was going to succeed or fail based on interim analyses.

The Danish drugmaker said the trial was testing whether the widely used diabetes drug, which contains the active ingredient semaglutide, could delay progression of chronic kidney disease and lower the risk of death from kidney and heart problems.

Semaglutide is also the active ingredient in Novo Nordisk's powerful weight-loss drug Wegovy.

Barclays analyst Emily Field said in a note that the company's decision affirmed the view that GLP-1 receptor agonists like Ozempic have "therapeutic benefits far beyond their original intended purpose."

5) More from the "we can't afford to give these drugs to everyone who needs them" crowd: [Weighing Down the Taxpayer](#). Excerpt:

Given that 45 percent of Americans express interest in taking a safe and effective prescription weight-loss drug, and 52 million receive Medicare Part D (expected to cover 93 percent of drug costs in 2024, and funded 86 percent by taxes), adding coverage for semaglutide to Medicare could cost up to \$254 billion per year. Even if user uptake and adherence is lower than expected, the cost dwarfs the projected annual Medicare savings from covering the drug—\$18 billion, according to a supportive study...

Therefore, little preventative or insurance justification exists for adding coverage of weight-loss drugs to Medicare. While such an expansion might be popular with voters, the new taxes needed to finance it surely would not be.

Two thoughts: a) I didn't hear these arguments about the COVID vaccines (and more Americans die of obesity every year than COVID at the peak); and b) obviously the government will negotiate MUCH lower prices for these drugs as a condition for covering them.

6) I saved the best for last – here's Scott Galloway: [Seconds](#)

From: Whitney Tilson

Sent: Saturday, October 7, 2023 12:22 PM

Subject: New study on side effects of Ozempic; Unaffordable cost; We don't know why they work; Causes of the obesity epidemic; Support group; Reduced heart failure; The N.Y.C. Neighborhood That's Getting Even Thinner on Ozempic; Diet Coke; articles

Catching up on a month or two of studies, articles and commentary from my expert friends...

1) From Dr. Jason Fung:

Hey Whitney - Have a look at this new JAMA article on the risks of Ozempic (attached).

The risk of pancreatitis is 909% higher than normal, bowel obstruction is 4 times normal and gastroparesis 3.6 times normal. Those are massively high hazard ratios.

Yes, while these drugs are relatively safe, there are real, serious side effects. The drug company studies don't show this because this data base was 16 million patients and these side effects are rare, and the drug company is always anxious to show the drug in the best light.

For sick patients, with type 2 diabetes or morbid obesity, GLP1s are worth it (I prescribe a lot of them), but for the person trying to lose 5 pounds for a high school reunion, or just joined Weight Watchers and gets sold Ozempic (because WW just bought an Ozempic pill mill) these are definitely not worth it.

Dr. Kevin Maki's comments:

I agree with Jason. All drugs have side effects and associated risks. People who are clinically obese are at increased risk from the obesity. The risk/benefit balance is favorable for them. People who want to lose a few pounds to fit into a dress or look good at a reunion are taking on an unfavorable risk/benefit ratio. Pancreatitis is rare but it can be life threatening. People who want to use a weight loss drug should do so under the supervision of a qualified (and ethical) healthcare professional who can discuss the risks and potential benefits with them so that an informed decision can be made.

Rich Weil of FitsMeHealth (Rich@fitsmehealth.com) comments:

Attached are the common, less common, and possible rare side effects of the top 12 medications used OTC and/or prescribed in the United States. For the life of me I cannot remember even one article on CNN, MSNBC, NYT, or other mass media where they sensationalized the side effects of these commonly prescribed meds (with the possible exception of hydrocodone). My absolute favorite was on CNN Health: "They took blockbuster drugs for weight loss and diabetes. Now their stomachs are paralyzed." For some people, they must take these common meds for the rest of their lives. As I've mentioned before, the bias against weight loss meds comes from an extremely insidious and egregious, internalized bias against people with obesity. People think about people with obesity, "Why do they need meds to lose weight? Just eat less, exercise more, exert willpower and self-discipline, and put the fork down."

My comment: I agree with my doctor friends. Note that the study was done using semaglutide (Ozempic and Wegovy), NOT Mounjaro, which studies have shown (and many of my friends have told me) has far fewer side effects (AND results in greater weight loss) – so that's definitely the drug to use.

2) The biggest problem isn't these drugs' side effects but their COST, as this WSJ article notes: [To Pay for Weight Loss Drugs, Some Take Second Jobs, Ring Up Credit-Card Debts](#). Excerpt:

Each month Tina Marie Porter pays about \$1,000 out of pocket for Mounjaro. To make up for the extra monthly expense, the 49-year-old director of operations takes on more assignments and seeks odd jobs.

Porter belongs to a growing population of people taking extra measures to cover the full or almost-full price of popular drugs used for weight loss, after their insurance denied them coverage.

"It is life changing," said Porter, 49, of Kansas City, Mo. "But I shouldn't have to pay because my insurance won't cover it. It is making me healthier. It makes no sense."

Across the country, some consumers are paying \$10,000 a year or more to get popular drugs from Eli Lilly & Co. and Novo Nordisk. Patients report taking on second jobs, racking up credit cards and cutting back on travel or family expenses to afford Lilly's Mounjaro, a diabetes drug being used off-label for weight loss. They are also self paying for off-label use of Novo's diabetes drug, Ozempic, and sister drug Wegovy, which is approved for weight loss.

The willingness of consumers to pay thousands of dollars of their own money underscores the public's appetite for more effective weight-loss medications, especially for people who have long struggled with obesity. The injectable medications can result in patients losing roughly more than 15% of their body weight.

Consumers are paying significant sums out of pocket in large part because insurers are denying coverage for weight loss. In addition, the drugmakers are charging the full list price of a drug instead of offering any of the discounts they give to health plans.

It's outrageous that these drugs aren't covered by every insurer (including Medicare and Medicaid), but this will take time...

Rich comments:

We have always considered that people with obesity have an addiction. Work at NIH, especially Norma Volkow and Gene Jack Wang in addiction research, amongst others, have shown down-regulation of dopamine receptors in people with addiction to substances such as cocaine, alcohol, and food. Which of course means they need more of the substance to get their fix. It is not one bit surprising that people would do just about anything to acquire a medication that would help them lose weight safely and effectively. There has been research that asks people how hard they would work for food, tapping into the reward pathway and salience of food. Turns out people would go to great lengths to acquire food if they have a craving.

To be perfectly honest, none of the articles I have read on the topic of weight loss meds, since they became very popular, is the slightest bit surprising or informative to me. We, meaning, Betty and I, and most likely many of our colleagues, have known for decades

what these folks with obesity are up against. Neurobiology is extremely powerful, and when it affects appetite regulation, well, just as the article points out, people would do just about anything to acquire a substance of abuse. The possible good news here is that the news is finally coming to light that maybe the population will learn that obesity is a disease, and not a lack of willpower, self-discipline, or a character flaw. But I doubt it will matter one bit. People are not getting proper education and information through the media. CNN, and pretty much all media, do not do an effective job at educating anyone about a complex problem such as obesity and appetite regulation, and certainly not brain biology; and to make it worse, Americans in general are not able to critically think about problems such as these like a scientist. They simply do not have the education in science, medicine, or obesity management, nor the proper analytical skills to question what they are reading.

So this article, and so many like it (I loved the headline where they said people were taking the weight loss meds and their stomachs were paralyzed), do almost nothing to inform the public of the real problems we as clinicians, and investigators, are up against. Media is very good at sensationalizing problems to sell their product. The deeper truth behind the problem just isn't quite that important, and certainly not as sexy as bold, attention-getting headlines.

3) Two of my cousins (brothers) who live in Washington state are on them and are happy with the early results, but are struggling to afford staying on them. One writes:

My brother and I were able to get 3 monthly doses or 12 pens using the savings card for \$500 per box, but the card appears to expire and then it's \$1,000+ per box...ouch! I used Walgreens who made it a huge pain every time; my brother used Costco, which seemed to work better.

Any chance you could try to find out more what the trick is to get it long-term without having to jump through all the hoops every time? I'm going to try printing a new savings card and hope that it works at least three more times, grrrr...thx!

My cousins need to be careful because there are a lot of scammers out there, as this WaPo article highlights: [Inside the gold rush to sell cheaper imitations of Ozempic](#). Some "compounding pharmacies" are legit, but many are not. One friend who's lost 90+ pounds on Mounjaro over the past year writes:

There are pharmacies that apparently can compound Mounjaro, but (with insurance) I'm able to get the real drug for \$400 (about the same price as the compound version). Even my doctors who have used them caution that it's not the same as the real thing, so if you can afford it, they strongly recommend using the real script.

Rich commented:

Your cousins should call their doctor and check the web site of the drug company and call the company directly. And ask the drug companies about rebates. Those are the most effective methods. And then persistence. Don't give up, keep calling.

If they're on Mounjaro and they do not have diabetes [they don't], then the drug company may decline because they and some insurance companies have started requiring doctors to write a diagnosis of diabetes on the prescription (and pre-diabetes won't cut it). We still have some patients on Mounjaro who do not have diabetes, but it seems to be luck of the draw, there's no rationale that we can pick up on. In fact we have a patient who does not have diabetes and their insurance covered Mounjaro but would not cover Saxenda. It makes no sense. But that's where we are at the moment and I don't know how long it will be until the dust settles.

But Wegovy and Saxenda are approved for weight loss. Wegovy is the second most effective medication behind Mounjaro in our experience. There is also Saxenda, although it's a daily injection. They can try one of those. They should call their insurance company to see if they will cover one of those, and like I said, be assertive, persistent and pushy.

4) One idea: order them from overseas. As this article notes, they're MUCH cheaper everywhere else in the world (like almost all drugs – another outrage): [How do prices of drugs for weight loss in the U.S. compare to peer nations' prices?](#)

List prices are significantly higher in the U.S. than in peer nations

List prices of drugs used for weight loss in the U.S. and peer nations

	▼ Ozempic (semaglutide, injection)	Rybelsus (semaglutide, tablets)	Wegovy (semaglutide, injection)	Mounjaro (tirzepatide, injection)
U.S.	\$936	\$936	\$1,349	\$1,023
Japan	\$169	\$69	-	\$319
Canada	\$147	\$158	-	-
Switzerland	\$144	\$147	-	-
Germany	\$103	-	\$328	-
Netherlands	\$103	\$203	\$296	\$444
Sweden	\$96	\$103	-	-
United Kingdom	\$93	-	-	-
Australia	\$87	-	-	-
France	\$83	-	-	-

Note: List prices in \$USD based on web searches as of August 15, 2023. Prices are for one-month supply of Ozempic 1mg, Rybelsus 7mg, Wegovy 2.4mg, and Mounjaro 15mg. Some drugs are not available in all countries and prices were unable to be found in other countries. Some drugs are approved for diabetes and prescribed off-label for weight loss.

Source: KFF analysis • [Get the data](#) • [PNG](#)

Peterson-KFF
Health System Tracker

5) From the front page of the NYT on August 18: [We Know Where New Weight Loss Drugs Came From, but Not Why They Work](#). Rich commented:

This is a long and detailed article, very well covered. The Gila monster story made a huge splash when it was first reported. In 2006 I had the privilege of being selected for the "Diabetes Dream Team" by Becton-Dickinson (<https://investors.bd.com/node/9631/pdf>)

where five diabetes professionals took care of five patients with diabetes to show how intensive care improved diabetes. We prescribed Byetta (exenatide) to some of the patients, the first GLP-1 agonist, and patients lost weight. So GLP-1 agonists are not a new story.

I'd like to respond to just one point in this NYT article, the issue of having to exercise caution because the medication may be needed for life.

They say in the article: "Although the drugs seem safe, obesity medicine specialists call for caution because — like drugs for high cholesterol levels or high blood pressure — the obesity drugs must be taken indefinitely or patients will regain the weight they lost."

I offer no apologies for stepping on my soapbox. I don't hear anyone complaining about people having to take medications for life to control and manage hypertension, depression or other mental health problems, heart, asthma, diabetes, and many, many other medical conditions. I think the issue of caution about taking obesity medications for life stems from an intrinsic bias against individuals with obesity. People, including doctors, think, "why can't people just lose weight on their own? Why do they need medication?" People attribute the obesity to a lack of willpower, character flaw, or lack of discipline. We have known for a very long time that obesity is a chronic disease, complicated by many, many, factors, just two of which include genetics and the neurobiology of appetite regulation. I have never in my 40-year career in weight loss and diabetes met anyone who woke up one day and thought how cool it would be to struggle with their weight and develop obesity. Obesity is a chronic disease, and if there is finally a safe and effective medication that you have to take for life, and maybe just once a week, to control this disease, then why not support it? Like every other medication, there is the potential for complications, and these can be monitored. Anyone ever heard of rhabdomyolysis from statins? So it's time we stop blaming the patient and be grateful there is relief for people who have been shamed and demoralized their entire adult life, or even their whole life, by body weight.

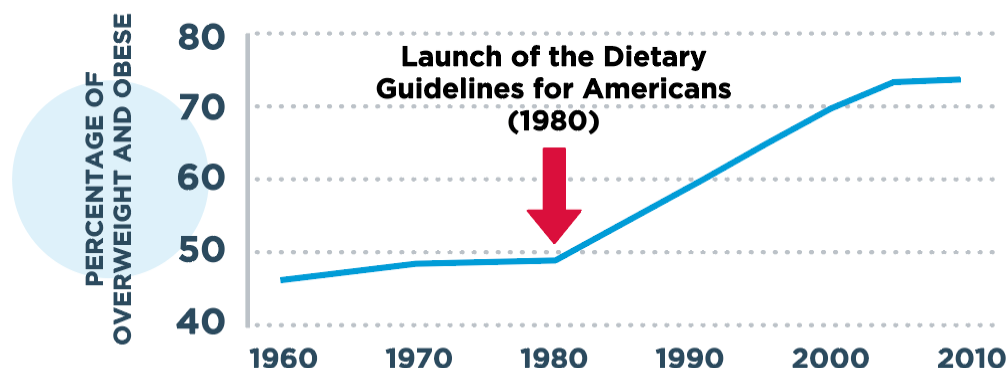
Every single participant in mine and Betty's weight loss program is so grateful for the relief and the edge they get from the weight loss meds. For the first time they leave food on their plate, have fewer or no cravings, experience satiety, and report less "noise" about food in their head. How can this possibly be a bad thing?

6) I asked my team of experts: "What's caused obesity to run amok in recent decades? Is it that food engineers at fast food chains and consumer food makers (Nabisco, Hostess, General Mills, Mondelez, Nestle, etc.) are designing foods that trigger the addiction?"

Dr. Fung replied:

Good question, Whitney. Looking at obesity in the USA, we see this.

RISE IN U.S. OVERWEIGHT/OBESITY COINCIDES WITH BEGINNING OF DIETARY GUIDELINES



The slope of the line clearly changed with the Dietary Guidelines, which were important for several reasons. First, it was the first time that the government 'backed' a specific diet.

Second, the focus was to lower dietary fat to reduce heart disease and there was no consideration of obesity which, at the time, was not a big issue. There is no evidence that lowering dietary fat reduces heart disease, as these guidelines have all been rescinded in the last few years.

However, in order to reduce dietary fat, the government encouraged 55-60% carbs, which were not broccoli, but mostly white bread, pasta and rice - not exactly slimming foods. Also, government encouraged the development of highly processed foods (to process out the fat, unfortunately by adding more sugar). So the real rise of processed foods changed significantly with the Dietary Guidelines - more sugar, more additives, less fiber, more refined carbs - all considered good, because they were low fat.

This was also an era that we thought we could make a better breast milk (formula) than breast milk. Seems stupid now, but physicians needed a massive public health campaign called 'breast is best' to convince people to go back to breast feeding.

Perhaps the dietary guidelines had nothing to do with the rise of obesity, but it seems too much to be a coincidence.

Dr. Maki added:

The prevalence of obesity in the US was fairly stable through the 1970s and then took off starting in about 1980. There have been many changes in culture and lifestyle that may have contributed. I think that changes in the food supply have likely played a role. However, there are a myriad of other issues as well. Physical activity is lower than it was in the 1960s, screen time and other sedentary behaviors are up, intakes of refined starches

and added sugars in highly processed foods with high energy density (kcal per 100 g consumed) are also up. Snacking between meals has become much more common than it was in earlier decades and where, when, and how Americans eat has evolved in ways that may promote overconsumption. Anxiety and depression are more common now than in past decades, particularly in adolescents and young adults. Food is used by many for psychological/comfort reasons when lonely, bored, or anxious. All of these factors and more may have played some role and there is no clear single cause.

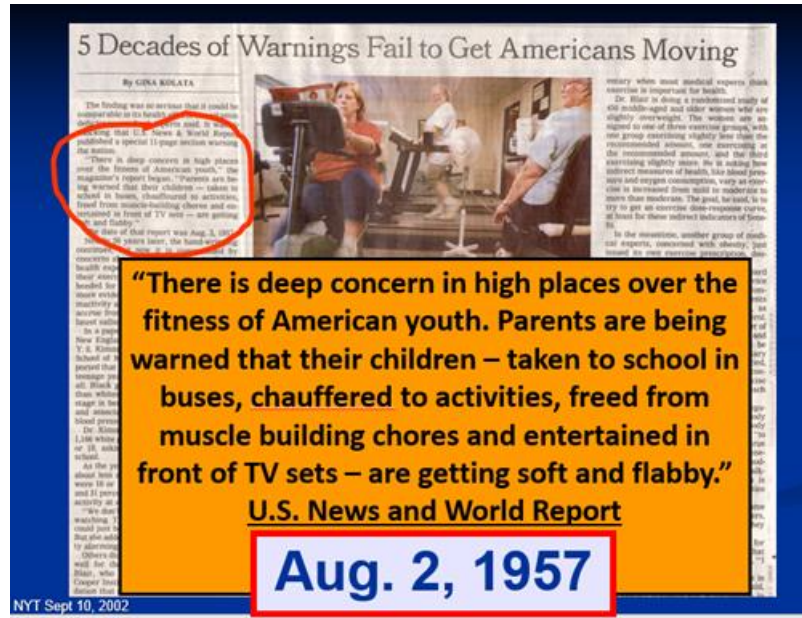
The daily energy imbalance needed to explain the obesity epidemic is very small, as outlined by Kevin Hall from the NIH and colleagues below (a persistent imbalance of only 7 kcal per day can explain average weight gain – see excerpt from this Lancet paper, [Quantification of the effect of energy imbalance on bodyweight](#)). Obesity appears to be preventable but very difficult to treat once present. Kevin Hall and his colleagues conducted assessments of participants in The Biggest Loser show and this link is to a [slide deck that outlines their findings](#). Some of the same material is covered in [this webinar](#). The summary from the slide deck is as follows:

- The body resists weight loss and promotes weight regain via slowing metabolism and increased appetite
- Long-term maintenance of lost weight requires ongoing support and persistent effort
- Increased physical activity may be especially beneficial for maintaining lost weight, in addition to its overall health benefits
- Reengineering your food environment may help facilitate maintenance of lost weight
- Less ultra-processed foods with lower energy density

In my view, pharmacotherapy will have an important role to play in obesity management, but drug therapy needs to be paired with lifestyle intervention involving a healthy diet, exercise (aerobic and resistance), adequate sleep quantity and quality, stress management, and psychological/behavioral support.

Rich Weil commented:

I show this slide frequently in our weight loss program. Published in the NYT in 2002, it shows as far back as 1957 that the problem already existed:



I once read an excerpt from a book from the mid 1880's (not 1990's) that reported gluttony and sloth were already problems, comparing residents of France to the United States. Again, that was in the 1800's. There is evidence for the problem in the early part of the 20th century, and the President's Council on Fitness started in the Eisenhower administration in the 1950's because they were concerned about the lack of fitness in our school children and the potential for an unfit for combat armed services vis a vis the Red Scare.

I have read Kevin Hall's work, and heard him speak many times. He is a brilliant guy, but a physicist, not a clinician, and I have used his calculations to estimate how much weight someone would lose based on multiple variables. When I applied it to the real world of our weight loss program population, it wasn't close. But the points from the webinar that you outline are good ones, but they don't explain the whole story. I've been at this 40 years, weight loss and preventing regain, especially in the real world, when people go to work, deal with all the problems of daily life including sick parents and children, financial stress, illness, genetics, epigenetics, and so much more, all which make obesity a serious and major multi-factorial problem to say the least. I have constructed a list of more than 32 factors that apply to a model of obesity that I teach, and the list grows.

All the reasons you post below about causes of the obesity epidemic are true, and of course there are many more variables, but as I said, this problem has been around much longer than most people think. You might even ask why BMI was developed in the 1830's through the 1850's, what was the concern then? And then the modern version in the early 1970's by Ancel Keys.

I've already mentioned it multiple times in these emails, the weight loss meds are game changers. Finally we have something that side-steps the bias that people with obesity are weak-willed, lack discipline, and have character flaws, and deals directly with the neurobiology of the brain and many other factors including appetite regulation. I take

extreme exception to individuals, including physicians and investigators, who complain that you might have to take weight loss meds for life. So what? People take all sorts of meds for life for many medical conditions, and you don't hear people complaining about that. What's the problem with taking a medication for life that treats the chronic disease of obesity? And you might only need to take it once a week. And wait for the new medication from Lilly in phase 2 that looks even better than Mounjaro.

And as I mentioned previously, none of these weight loss medication articles in the media are enlightening me, Betty, or many of our colleagues to the problems or solutions. They sensationalize the problems and make things worse.

Dr. Maki added:

Agree. People take medications to prevent heart attack and stroke for decades such as those for lipids and blood pressure. Effective weight loss will lessen the need for these. Like other chronic diseases, obesity requires medical management, including behavioral and lifestyle support, and medications will play an important role for many. While obesity is much more common now than it was in the first half of the 20th century, it was present in 10-15% of the population even then. I hope that the availability of effective drugs will help to change the views of healthcare professionals so that obesity is viewed more as a chronic medical condition rather than reflective of deficiencies of character and discipline.

7) By the way, Rich is offering a new weight loss medication support group for individuals who are taking weight loss medications or considering it:

With the popularity of the new, effective and safe weight loss medications, we have decided to start a new weight loss medication support group for individuals who are taking weight loss medications or considering it. We believe that with the wide-spread use of these medications, and the rapid and large amounts of weight loss they cause, individuals will experience emotional/psychological and physiological changes that are new and can be unnerving, especially if you have had obesity all of your life or all of your adult life. With the speed and amount of body weight changes that these medications are causing, there are many issues that need to be addressed with authoritative and accurate information, and with group support facilitated by health-care experts, especially professionals who have weight loss experience. Some of the many issues that we will cover in the group are:

1. Dealing with not feeling hungry, maybe for the first time
2. Dealing with feeling full, maybe for the first time.
3. Shopping for new clothing at a brick-and-mortar store and not online.
4. Reducing or eliminating the "noise" about food in the brain such that obsessing and cravings are no longer an issue.
5. Learning how to plan what to eat and setting new and different kinds of food plans.
6. Leaving food on your plate.
7. Losing interest in food.
8. Compliments about your new appearance.
9. Side effects of the meds.

10. Being able to physically move easier.
11. Addressing body image issues such as fitting in seats that you never thought you could fit in before; simply taking up less space; having your picture taken, and more.
12. How to navigate the insurance system and problems with acquiring the medications.
13. All the benefits of learning about lifestyle changes to complement the use of the meds. The drug companies recommend diet and exercise to complement the use of the medications, and it's been our experience that people taking the medications who lose the most weight are consistently participating in many lifestyle changes including regular exercise and attention to healthy diet choices that are an intrinsic part of our program.
14. And many more emotional and physiological issues that are new to individuals who have lost as much weight and as quickly as the new weight loss medications are causing.

We are waiting to set the start date depending on interest, but interest has been high, so we are ready to move on this in the next 2-3 weeks.

Our website is www.FitsMeHealth.com You can reach me at this email address if you have questions.

Please email me at Rich@fitsmehealth.com if this is a group you are interested in joining.

Group time: 7:15pm to 8:15pm ET

Location: Zoom

Day: Tuesday (we may start with every other Tuesday, to be determined)

Number of sessions: 12. (We can always add more if there is interest)

Fee: \$45 per session

8) The paper was published in the New England Journal of Medicine on September 21: [Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity](#). Here's the summary:

Novo Nordisk's (NVO) anti-obesity drug Wegovy also eased the symptoms of a common form of heart failure in patients who also have obesity, according to results published online in the New England Journal of Medicine. The patients who took the once-weekly injection for a year reported improvements in fatigue and shortness of breath, and found they could walk longer distances, all while losing an average of 13% of their body weight.

Dr. Maki commented: "These results are as I would have predicted. I expect the results from the SELECT trial to be presented and published in November in conjunction with the American Heart Association meeting."

Rich added:

I agree. I also would have predicted the same. Not really that much of a surprise. As an aside, it used to be we told patients with heart failure not to exercise, or do it very, very lightly. Now that's all changed. Exercise has been shown to improve heart function and quality of life in heart failure patients. With medications such as semaglutide on board, profound weight loss, and regular exercise, this combination is going to make an enormous difference in health and quality of life for many individuals, with many different medical conditions, and not just heart failure.

Dr. Maki wrote:

Spot on, Rich! I am in the middle of a project to look at the effect of weight loss on risk for chronic kidney disease (in Dr. Fung's wheelhouse). The list of conditions associated with obesity is long and I am hopeful that we will see benefits for many. A partial list includes heart attack, stroke, diabetes, kidney disease, high blood pressure, heart failure, arthritis, depression, sexual dysfunction, and urinary incontinence.

9) This NYT article triggered a discussion among my experts: [The N.Y.C. Neighborhood That's Getting Even Thinner on Ozempic](#). Rich wrote:

NYC obesity and diabetes maps by zip code, poverty, and socioeconomic status, have always shown what you expect. The poorest neighborhoods, and people of color, always had the highest rates. The upper east side of Manhattan, where there is a high concentration of wealth, always showed, and still does, low levels of obesity and diabetes. Hopefully what happens is that the medications become affordable and available to everyone, and not just those who can afford it, or have employers or insurance that covers it. This article reminds me of an expression we used decades ago that applied, in particular, to wealthy women and socialites on the upper east side of Manhattan as "social x-rays". One of the problems is that individuals who have just a few pounds to lose are taking these medications that are not indicated for them, and creating shortages for people who need them. Let's hope Medicare gets on board, and Medicaid contributes more than it already is doing, and that overall the medications become more financially accessible and available. I was interviewed recently about the meds, and the interviewer asked me if this is the end of obesity. I told him that that might be a slight stretch, but it certainly is for people who are fortunate to have access to them and continue to take them. I've never seen information about a medication reach the consumer faster than these meds.

Dr, Maki added:

I am hopeful that information about benefits regarding heart attack, stroke, and heart failure will prompt wider availability of these agents to people who are not wealthy. The largest burden of obesity-related diseases is among racial and ethnic minority groups and those with lower socioeconomic status.

Rich replied:

I've never seen the information about a medication, for weight loss or any other condition, reach the consumer as quickly as these weight-loss meds have, so maybe there is some hope that the message will get out to a wider audience. And of course, the issues we have already discussed such as availability, education of doctors and the public, use of the meds off-label or when it's not indicated, and a myriad of other issues.

Dr. Fung chimed in:

Precisely why I find it unfair that doctors and the media push Ozempic so hard while ignoring interventions like intermittent fasting that can benefit everybody, and not just the rich.

At physicians conferences the lectures dedicated to Ozempic compared to fasting are about 1 million to one, if that.

I asked: "I agree with you about the benefits of IF - I've tried it myself - but it's hard and I think only a small fraction of people could/would do it, even if doctors, leaders and the media pushed it."

Rich's partner Betty Kovacs-Harbolc (betty@fitsmehealth.com) weighed in:

I completely agree about the benefits of IF, but they have made it too complicated by having too many options. The idea that they can eat whatever they want in a 5 hour window will never work for a binge eater. Most of my clients start out confused over all of the IF possibilities. I have had the most success with getting at least a 12 hour fasting state overnight (time restricted eating). Some start at 10 or 11 pm, and eventually move up to 8 or 9. Explaining the benefits for autophagy has helped a great deal with compliance.

So did Rich:

Betty has a great deal of clinical experience with this and her comments should be carefully considered. I would add that IF is to some degree a restrictive intervention, even though it seems to be easier to follow for some people than other dietary changes, but if it's restrictive, which we have observed, then it will not be sustainable. There are times where I have counseled patients to eat only at specific times of the day to get control over food and cravings back, but again, these sorts of restrictions mostly lead to rebound. As effective as IF can be, and we have seen that to be the case, and recommended it for as long as it has been around, with success, but I don't think in the long run, that IF will be able to compete with the medications. There are simply too many mechanisms of action with the meds, including the brain and other organs, that helps regulate appetite, which is very complex. IF can't do all of that, and again, it can be viewed as restrictive for people, and once they start rebounding, that rebound turns into lapses or relapses for physiological and psychological reasons. We won't stop recommending IF, especially for patients who don't want meds, but a comparison between the two is a stretch.

10) My mom is bugging me about my Diet Coke consumption (as I sit here drinking one!), citing this study to link it to a few hypomanic episodes I've had in the last dozen years:

[Neurophysiological symptoms and aspartame: What is the connection?](#)

I asked Dr. Maki what he thought and he replied:

I have done studies with various high-intensity sweeteners for decades. I am not an expert in the neurobehavioral aspects, but I know that many of the claims made for cardiometabolic effects and obesity have been based on very weak evidence, mostly from studies in animals, and on theoretical concerns. I remain unconvinced and the results from the studies I have done do not support adverse cardiometabolic effects.

Also, one has to compare even potential adverse effects to those from added sugars, which appear particularly bad, especially when consumed in beverages. I think that limiting intake of high-intensity sweetener intake to some reasonable amount (say, 1 serving of diet soda per day) is a good way to hedge. I have a history of drinking a lot of Coke Zero and have tried cut back with flavored carbonated water as an alternative. Personally, I have observed no differences in how I feel or behave with and without high-intensity sweetener consumption and various metabolic measurements have shown no differences for me. I can say that I enjoy Coke Zero much more than carbonated water!

I can't rule out the possibility that some individuals may have adverse responses. I remain very skeptical of claims of adverse effects but keep an open mind and hedge my bets by limiting consumption. I am much more concerned about added sugars, and to a lesser extent, refined starches, than I am about reasonable levels of consumption of diet sodas.

11) Other articles of interest:

- From today's WSJ: [The Company That Defined Dieting Is Sorry It Told Us to Have More Willpower](#) [about Weight Watchers and Oprah]
- [The Disruptive Power of Weight Loss Drugs Is Being Felt Beyond Pharma](#)
- [America's Food Giants Confront the Ozempic Era](#)
- [How Stress Leads Us to Reach for Comfort Foods](#)
- [Amgen Could Get a Piece of the Obesity Market](#)

From: Whitney Tilson

Sent: Saturday, August 19, 2023 10:04 AM

Subject: Articles and comments from my experts; The Obesity Code; Rybelsus; We Know Where New Weight Loss Drugs Came From, but Not Why They Work; Ozempic Settles the Obesity Debate: It's Biology Over Willpower

Catching up on many articles over the past few weeks about the miraculous new weight-loss drugs.

For those of you who are new to this e-mail list, [here is a link to a pdf](#) to some of my commentary and past articles on this topic.

A HUGE thanks to Dr. Kevin Maki and Dr. Jason Fung, as well as Rich Weil (rich@fitsmehealth.com) and Betty Kovacs-Harbolc (betty@fitsmehealth.com) of [FitsMe Health](#), who I would recommend to anyone who's taking these drugs.

1) I just finished listening to Dr. Jason Fung's book, [The Obesity Code - Unlocking the Secrets of Weight Loss](#), and really enjoyed it. He argues that obesity isn't due to lack of self-control, but hormones and recommends eating unprocessed foods and doing intermittent fasting.

He recently emailed me this:

This article in the NY Times about diabetes, [How Do We Fix the Scandal That Is American Health Care?](#), illustrates perfectly why I've dedicated so much time to reversing type 2 diabetes, not with drugs, but with ancient time-tested treatments like intermittent fasting.

While I prescribe a lot of Ozempic and Wegovy, those treatments are not available to most people due to cost, and that doesn't seem fair to me. I spend lots of my time trying to educate people on a treatment (fasting) that has the potential to reverse type 2 diabetes, free, and available to anybody, anywhere.

I'm currently working with a subsidiary of United Health called Level2 that is dedicated to remission of type 2 diabetes through diet and lifestyle changes for exactly these reasons. Hopefully, this will eventually make a dent in the epidemic of type 2 diabetes in America, something I wrote about in [The Diabetes Code: Prevent and Reverse Type 2 Diabetes Naturally](#).

2) One of my readers emailed me:

I have been taking Rybelsus for about 8 months for diabetes. I have also lost about 25 pounds, no hunger, easily full. No side effects. Now, why is Rybelsus never mentioned in these conversations about Ozempic, etc. It is the same as Ozempic, just a daily pill rather than a weekly injection. I know FDA has not approved it for weight loss why not.

Those of us who take these drugs for diabetic control do not, at this time need to worry about gaining weight back as we will not go off these drugs. Yes, their efficiency around weight loss does diminish, but not completely.

Dr. Maki replied:

Oral semaglutide is being studied for a potential obesity indication, but at higher dosages than Rybelsus, similar to the situation for Ozempic and Wegovy. Rybelsus does produce weight loss at the usual dosage of 14 mg/d (like Ozempic) and produces weight loss similar to Wegovy at a dosage of 50 mg/d.

Dr. Fung added:

Regarding Rybelsus - I have much less clinical experience with it since it is not covered under the Ontario health plan. From the studies I've seen and the few patients I've had, it seems to work much the same as Ozempic and Wegovy. I just saw a [new study](#) in JAMA regarding this question, and it seems like the oral version is as effective as the injection.

Dr. Maki then emailed:

Thanks Jason and Whitney. Here is a MedPage summary of the results from the study on oral semaglutide: [High-Dose Semaglutide Pill Just as Effective as Wegovy for Weight Loss](#). Excerpt:

When added to lifestyle intervention over 68 weeks, patients taking 50 mg of oral semaglutide lost 15.1% of their weight compared with a loss of 2.4% among those on placebo (estimated treatment difference -12.7 percentage points, 95%CI -14.2 to -11.3), reported Filip Knop, MD, PhD, of the Center for Clinical Metabolic Research at Gentofte Hospital at the University of Copenhagen in Denmark, and colleagues.

3) In response to something in one of my earlier e-mails, Dr. Fung wrote:

I was interested to read about your cousin's experience, as it is precisely what I see clinically. Here's what he wrote:

It's going great! Started on 6/23 at 235 and about 6 weeks later I'm at 221! First two weeks definitely felt a strong feeling of fullness plus some of the side effects like stomach pain, nausea, etc. Those passed though and more recently the hunger feeling came back after three or four days instead of the full week so I actually took another 2.5mg dose early the last two weeks to try to get back on track so to speak.

This is what happens to a lot of people. You start losing a lot of weight. Great! Amazing! You think it'll last forever. But it doesn't. The body starts getting used to the effect and the nausea that causes the appetite suppression wanes. So you get hungry, and need a higher dose. Which is fine. For about **6 months - 2 years**.

Then the weight has plateaued, and is starting to come back. The hunger is coming back. Because of the drug, you don't enjoy food to nearly the same degree you used to. One of life's great pleasures has been denied to you.

Here's the next part to be cautious of. He wrote:

It's truly amazing how it works. I've been able to eat and drink pretty much whatever I want – just less of course – and still lose weight...:)

If you don't take the time to learn what the best things to eat or not eat, the best times to eat or not eat, then you will simply eat around the drug. That is, you start eating ice cream

because hey, you lost a lot of weight, and you're not getting pleasure eating food anymore, and it doesn't make you nauseated like a pork chop does. But in the long term, that leads to weight regain.

That's when people stop taking the drug. Because taking Mounjaro is not the same as taking your blood pressure or gout medication. I start a patient on a BP medication, they take it for the next 25 years without a peep of complain. I start Mounjaro, 1/3 will be off of it in a year.

If your cousin wants to REALLY succeed, then he needs to use this opportunity to clean up his eating habits. As the effect of the drug fades, the habits that are formed now will sustain his weight loss. I started prescribing a ton of GLP-1's 4 years ago. I had the same enthusiasm then. They're still great drugs, but they aren't quite miracles.

4) A fascinating article from the front page of yesterday's NYT about the history of the miraculous weight-loss drugs: [We Know Where New Weight Loss Drugs Came From, but Not Why They Work](#). It concludes:

Researchers continue to marvel at these biochemical mysteries. But doctors and patients have their own takeaway: The drugs work. People lose weight. The constant chatter in their brains about food and eating is gone.

And, while the stigma of obesity and the cultural stereotype that obese people aren't trying hard enough to lose weight endures, some experts are optimistic. Now, they say, patients no longer have to blame themselves or feel like failures when they can't lose weight.

"The era of 'just go out and diet and exercise' is now gone," said Dr. Rudolph Leibel, a professor of diabetes research at Columbia University Irving Medical Center. "Now clinicians have tools to address obesity."

5) From the front page of the WSJ earlier this week: [Ozempic Settles the Obesity Debate: It's Biology Over Willpower](#). Excerpt:

Ozempic and similar drugs are transforming the world's understanding of obesity. It isn't so much about willpower: It's about biology.

The success of the powerful new class of diabetes and weight-loss drugs shows how important chemistry is to determining a person's weight. The brain is the body's chief chemist, regulating appetite and making it difficult for many people to shed pounds and keep them off. The brain determines how much fat it wants people to carry, according to years of research bolstered by the new drugs.

The amount is like a setting on a dial, or what many researchers call a "set point" or "defended fat mass." The brain maintains the dial setting or set point by regulating how much a person eats. Ozempic, its sister drug Wegovy and another, Mounjaro, lower the

dial setting, or set point, in effect by acting on the brain to reduce hunger and make a person feel full sooner, some obesity researchers say.

The new set point lasts as long as a patient is on the drug, they say. Patients who ate a lot before they started taking one of the drugs feel less hungry and fill up more quickly—sometimes after one slice of pizza when they once ate the whole pie.

"This is not about willpower or personal choice," said Dr. Florencia Halperin, an endocrinologist and chief medical officer of Form, a virtual medical weight-loss clinic. "This is about your brain driving behaviors."

Dr. Maki:

I have been saying since the 1980s that obesity appears to be relatively preventable but very difficult to treat. We don't understand appetite regulation well and it is clear that once people gain weight that the drive to eat changes to defend that higher weight (or possibly level of body fat. When people who are obese lose weight without drug therapy, there are clearly increases in appetite and cravings. In classic studies done with conscientious objectors during the Korean war, Ancel Keys and colleagues ran studies to simulate POW conditions, with energy restriction. The participants showed profound psychological changes, including cravings, constant fantasizing about food, plans to food-related careers after the experiment, etc. That is effectively what we are asking obese people to do with lifestyle modification.

Many can lose 5-10% of body weight, but it is very uncommon for people to lose more than that and keep it off. Jim Hill and Rena Wing have a registry of people who have lost a significant amount of weight (at least 30 lb) and kept it off for an extended period (<http://www.nwcr.ws/>). They have published many papers from the registry and some of the key findings are summarized here: <http://www.nwcr.ws/Research/default.htm>.

Drug therapy with GLP-1 (and related G2 and G3 drugs) helps to change the drive to eat and reduce cravings. I am hopeful that their responsible use will lead to sustained weight loss and obesity-associated disease risk reduction. Time will tell!

Dr. Fung:

Obesity is always about biology, not willpower - my argument is that it is all hormonal.

If you increase certain hormones, then you can gain weight (insulin, cortisol) and if you change others (GLP-1, glucagon) then you can lose weight. It's not about controlling the calories. It's about controlling the hunger that leads one to overeat those calories.

Reminds me of the old question about the Titanic. What caused the Titanic to sink? Most people respond - Because it hit an iceberg. Wrong. That is the proximate, not the real answer, which is that the Titanic was sailing too fast. Same as calories. Most people ask 'What causes obesity? Too many calories.

Rich Weil:

The reality is that none of these articles contain anything new to us. Suddenly the world has awakened to the reality that obesity we are treating is a disease. Had they contacted us 40 years ago I would have told them then. In any event, Betty and I are trying our best to start a group for people who are taking the meds. These folks have unique biological and psychological problems that we can help them with. If you have any ideas about how to promote for us through your newsletter, we would be appreciative. We have offered some free workshops and a few of the people from your newsletter have attended, but this has not translated into people signing on for groups. People in our program who are taking the meds understand the importance of remaining in the program because they get the counseling, information, and support they need and are receiving from us, but educating the immediate world has proven difficult. The meds appear to be a panacea for many, and we think people taking them believe they don't need anything more, an issue we have been concerned about ever since the meds have seemingly taken over the entire field of weight loss. Anyway, any thoughts you have would be appreciated.

6) A new study: [Wegovy could prevent up to 1.5 million heart attacks, strokes over 10 years, study says](#). Excerpt:

- Novo Nordisk's blockbuster weight loss drug Wegovy could prevent up to 1.5 million heart attacks and other cardiovascular events in the U.S. over 10 years, according to a study from UC Irvine.
- The study was partly funded by Novo Nordisk.
- The results complement the initial data Novo Nordisk released last week from a large clinical trial, which found Wegovy slashed the risk of serious heart problems and heart-related death by 20%.

Dr. Fung:

These are actually the types of studies I hate, because there is a lot of extrapolation of the data, as well as conflicts of interest.

Essentially, Wegovy maker NovoNordisk paid a bunch of 'scientists' to write a study about how great Wegovy is. It's advertising disguised as a scientific study. There are 2 problems. First, it just extrapolates the data 10 years into the future, which is no different than extrapolating stock prices 10 years into the future. Not useful.

Second, it's well known that funding a study will have massive effects on the results. If a drug company funds a study, it is 400% more likely to find a positive result – see: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC156458/>

Dr. Maki:

Jason and I have different views on this issue. I will note a couple of things before providing my opinions. First, the link below shows that the senior author on the recent paper is my good friend Nathan Wong. Second, I have been on many Steering Committees for clinical trials on drugs in the cardiometabolic area and am currently Co-Investigator for an Investigator Initiated trial funded by Novo Nordisk with semaglutide – see: [Popular weight loss medication may benefit 93 million U.S. adults, UC Irvine study found – UCI News](#)

While I do believe that it is necessary to be clear about the uncertainty involved in projecting results out to longer timeframes than the trial follow-up period, I believe that doing so is reasonable. For example, most of the trials with statins showing reduced cardiovascular event rates had about 5 years of follow-up. We regularly make projections beyond five years and, in fact, ask patients to take statins for much longer periods. The reality is that we will not have 10-year trials on preventive therapies, so some degree of projection is necessary to inform clinical and policy recommendations.

Regarding the greater likelihood of pharma industry funded studies showing favorable results, in many instances, that is simply because the studies have better designs. I have been on Steering Committees that guided the design elements of numerous pharma trials. These studies are often designed by the top experts in the field who consult with the pharma companies. In contrast, many NIH-funded studies are poorly designed and frequently try to answer the wrong question, or too many questions in a single trial. When I teach courses on clinical trial design, I provide many examples of poorly designed studies funded by the NIH, VA, USDA, and other federal agencies. I have been an ad hoc member of advisory committees for federally funded studies and left frustrated with the poor decision-making on issues of study design.

The pharma industry has not been perfect. However, having worked both in academia and with the pharma industry on the development and testing of agents for cardiometabolic health, I see many more checks and balances in the pharma industry trials than for those run by academia. I do take issue with some of the marketing done by pharma companies, but I have a much more favorable view than Jason regarding the quality of pharma industry sponsored trials.

7) A new drug under development: ['Game-changing' drug that spurs weight loss without dieting in the works](#). Excerpt:

Researchers are closer to developing a drug that could one day rival celebrity-touted Ozempic, as initial experiments show that an in-the-works medication can both prevent weight gain and promote weight loss.

Scientists from the University of Texas Health Science Center at San Antonio tested the "game-changing" drug, called CPACC, on mice.

Led by professor of medicine Madesh Muniswamy, the researchers discovered that the drug curbed weight gain from foods high in sugar and fat, which are prevalent in the Western diet.

It seems to be great news for people with a sweet tooth: In theory, people could chow down on whatever they wanted without the added health risks and weight gain.

Dr. Maki:

Very early days for this agent. This is interesting from a mechanistic perspective, but new drugs are like guppies. Many are birthed but few reach adulthood.

Dr. Fung:

I agree with Kevin. When a study is done in mice, it's unlikely that we'll see anything come out of that for at least a decade, and usually never. They make nice newspaper articles, but mostly it's way too early and too many things can go wrong in between.

Rich Weil:

It has been long known that magnesium helps control blood glucose and diabetes, insulin resistance, and reduces inflammation and oxidative stress, all factors related to weight loss and weight control. In people with type 2 diabetes, there is typically a magnesium deficiency. Remember that all the GLP-1 agonists started off with weight loss by controlling diabetes, so the fact that magnesium helps with diabetes control may point to an association with weight loss too, because when you control diabetes you typically get weight loss through a number of mechanisms including decreasing insulin resistance.

Magnesium also is associated with lower weight in some studies, and it has a positive role in energy metabolism and production in the cell through ATP, cell replication, oxidative phosphorylation (which occurs inside mitochondria and releases energy for the cell which may help burn fat), protein synthesis, muscle and nerve function, all factors that could directly or indirectly affect weight loss. Magnesium is also associated with heart health.

As for mitochondria, magnesium has a major role in function of mitochondria including energy production (ATP), but glucose is not burned in the mitochondria (fat is), so any effect that magnesium has on glucose control and subsequent weight loss would more than likely be indirectly associated and not causative, and not through mitochondria. But I have not read the paper, so I cannot comment on the direct effect of magnesium on weight control, especially through mitochondria control. There may some biochemical and enzymatic reactions that they have identified that I am not familiar with. My colleague Betty would know the recommendations for magnesium supplementation.

8) Be careful: [The Wall Street Journal identified more than 50 websites selling knockoff versions of Ozempic, Wegovy and Mounjaro, popular drugs that have been used for weight loss, without a](#)

[prescription](#). I have one friend who's getting Mounjaro from a "formulary," but there are a lot of fraudsters out there. Excerpt:

Spend enough time searching for Ozempic, Wegovy or Mounjaro, and you'll find dozens of websites selling knock-off versions of the popular drugs without a prescription.

These websites are part of a robust online marketplace for what have been called weight-loss miracles, selling raw ingredients that cost far less than the brand-name drugs. They market to customers on social media, emphasizing discounts and "pharmaceutical grade" quality while stating that their products are "for research purposes" only.

The Wall Street Journal identified more than 50 websites selling semaglutide and tirzepatide, the active ingredients in Novo Nordisk's Ozempic and Wegovy and Eli Lilly's Mounjaro. Nearly all of them include disclaimers that the substances are "not for human consumption." But several also include instructions for how to prepare human doses, or sponsor online forums where people explain how to inject the substances. The Food and Drug Administration has called similar websites' research disclaimers "bogus" and says that customers shouldn't buy their products, as they haven't been tested by the agency.

9) Be careful (2): [The Risks of Taking Drugs Like Ozempic When You're Over 65](#). Excerpt:

There are few constants within the world of weight loss, but one concept holds up: No matter how you lose weight — through restrictive eating, bariatric surgery or the new, buzzy class of injectable medications like Ozempic and Wegovy — you're also probably shedding muscle.

That's particularly a concern for older adults, obesity medicine experts say. The more muscle someone over the age of 65 loses, the greater their risk of becoming frail or suffering a fracture or fall (which can be fatal in older adults). It is crucial for older adults to maintain muscle mass so that they can stay mobile and independent.

Dr. Fung:

It's a legitimate concern. Some of the [studies are showing that almost 40%](#) of the weight lost may be lean mass, more than typical for other forms of weight loss.

Ozempic causes mild nausea, which suppresses the appetite. The easiest things to eat when nauseated are the refined carbohydrates - white rice, white bread, white potatoes and sugary drinks. It's hard to eat a pork chop when you're nauseated. So, some people, especially the elderly, who take Ozempic will eat lower protein and higher refined carbs which is not great for maintaining muscle.

Dr. Maki:

The points that Jason raises about maintaining lean mass are on target and speak to the need for dietary counseling, physical activity, and resistance exercise for the best

outcomes. However, I would point out that loss of lean body mass with drugs like Ozempic should be expected to occur. The rule-of-thumb is that 25% to 33% of body weight lost is fat free mass (using a two-compartment model with fat mass and fat free mass).

Based on the available literature, I think that the greater loss of lean body mass (or fat free mass) with Ozempic and similar agents is mainly a reflection of greater weight loss, since the proportions of weight loss from lean body mass (or fat free mass) have not been consistently larger than the proportions in the control groups (lifestyle only) in the same studies. However, the absolute loss of lean mass is larger because there has been more weight loss. I would like to see more studies on this issue in a wider range of patients but, so far, I have not been overly concerned about this issue.

Rich Weil:

One of our concerns about the meds is that individuals may not get the counseling they need on lifestyle changes necessary to complement the use of the medication and prevent health problems such as the ones mentioned in the article (no matter what the age). Physicians don't have the nutrition, exercise, and behavioral training necessary to counsel patients, plus they are very busy, and they would not get reimbursed for the counseling even if they had the experience and training. It's why we're adding a weight loss medication group to our program. People like a quick fix, and we're concerned that they may see the meds as the panacea and that nothing else, such as lifestyle counseling, is necessary. People will end up with all sorts of medical and mental health problems if they don't get proper care with so much weight loss.

1. The loss of muscle with rapid weight loss is no joke. Whenever people lose weight they lose muscle and fat. The muscle loss during traditional weight loss can be as much as 35% of the weight that's lost. With rapid and profound weight loss like we're seeing now with the new meds, who knows how much muscle is lost. The studies have not been done yet. We did a study many years ago where patients were put on low-calorie diets (no meds) and assigned either aerobic exercise 3x/week, resistance exercise 3x/week, or no exercise. Participants lost about 20 pounds over a 22-week period, so roughly 1-pound per week, which is not rapid. The no-exercise group lost 28% of their weight from muscle; the aerobic group lost 20% from muscle; and the resistance group lost only 8% from muscle. Exercise, and particularly resistance exercise, is critical during weight loss.
2. Muscle is important for lots of reasons:
 - a. As we age we naturally lose muscle protein. Older folks can lose as much as 55% of muscle protein past the age of 70. Whole body protein loss can be more than 25%. Thus the imperative to consume more protein with excess and rapid weight loss.
 - b. As we age we also lose muscle fibers. By age 80 you can lose as much as 50% of your muscle fibers, and the type of fiber you lose primarily is type-2 fiber, which is muscle responsible for strength, thus you get weaker and are less self-sufficient. It can also lead to loss of stamina from the loss of type 1 muscle fibers. Quality of

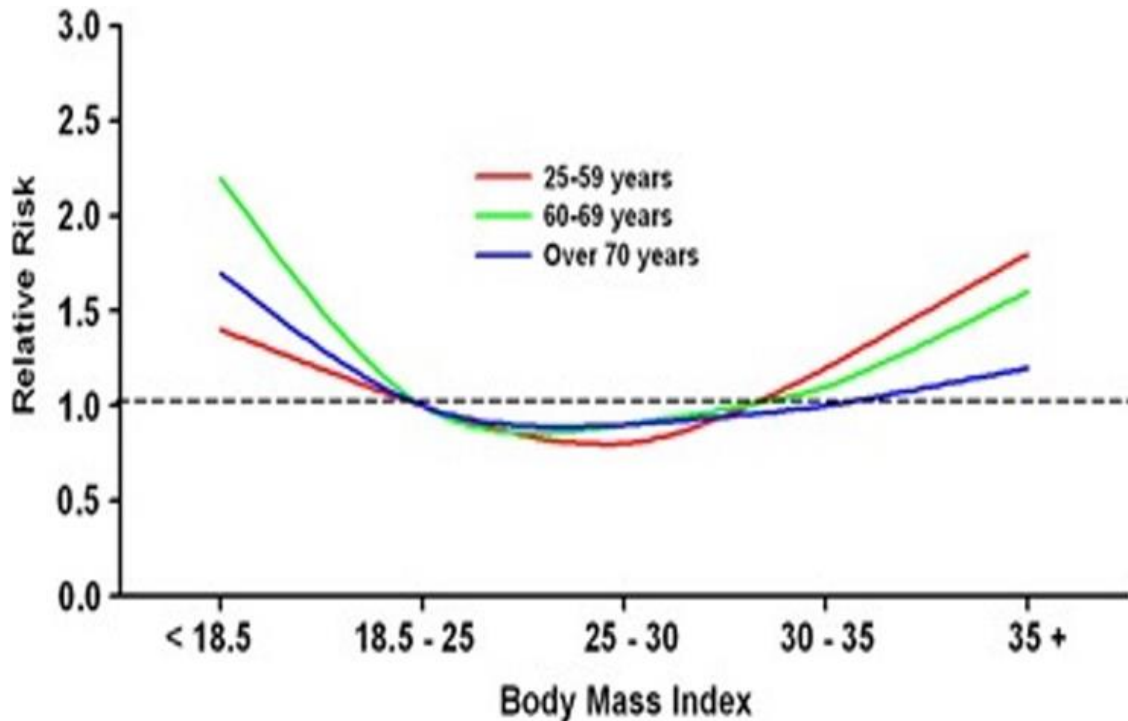
life dramatically decreases as a result of this kind of loss; activities of daily living such as carrying groceries, climbing stairs, and even simple tasks such as getting up from the toilet, are compromised. With rapid and profound weight loss the loss of muscle has the potential for dire health consequences; both physical and mental health.

- c. Metabolic rate. There is a direct, linear relationship between metabolic rate and muscle mass. The lower your muscle mass, the lower your metabolism. Lose too much weight too quickly and you risk great decreases in metabolic rate.
 - d. Muscles pull on bones when you use them, such as during resistance exercise, or even aerobic activity such as biking, walking, jogging, and other modalities. The loss of stress from the muscles pulling on bones causes bones to demineralize, and increase the risk of osteoporosis. It's the mechanical strain of the muscle and tendon pulling on the bone that keeps the bone dense and healthy. You lose bone density as a natural part of aging (osteoporosis), so it's important to do resistance exercise, and this is especially important during rapid weight loss with meds, because with so much less weight, the bones are not stressed as much due to the lower body weight during simple activities such as walking, not to mention the loss of calcium with all that weight loss. These studies have not been done yet, but it is expected that the effect of so much weight loss, and the speed at which it occurs, will have great detrimental effects on bone density.
 - e. Not only that, but loss of bone density is associated with falling, and falling is the fifth most expensive health condition in the U.S. In some cases, falling can lead to death in elderly individuals. Rapid and profound weight loss from the weight loss meds and the effect on bone density must be addressed.
 - f. Rapid weight loss is associated with loss of mitochondria in the muscle, the organelles that, among other functions, burn fat. With less mitochondria there will be less fat burning, and this puts people at risk for cardiovascular disease and high blood pressure (especially less burning of visceral fat, the fat that is deep in the abdomen and surrounds and infiltrates organs such as the liver and pancreas). It's very well known that aerobic and resistance exercise help reduce the risk of cardiovascular disease, stroke, high blood pressure, and much more.
3. Rapid weight loss is also associated with lower glucose metabolism due to loss of the special cells in muscles that burn glucose. Normal amounts of weight loss is healthy for glucose metabolism, and decreasing insulin resistance, but it's not clear what the effect of rapid and profound weight loss is on glucose metabolism. Losing too much muscle adversely affects glucose metabolism.
 4. The fatigue associated with the meds may be alleviated by regular exercise, both aerobic and resistance exercise. It's well known that regular exercise increases energy level. Too much fatigue from the meds and rapid and profound weight loss may be reduced or prevented by regular exercise.
 5. Medications taken for controlling high blood pressure and high blood glucose, such as with diabetes, will need to be reduced with all of this weight loss because if the body is lighter it won't need as much medication. This must be monitored closely. The risks of

over-medication as body weight decreases for these two medical conditions will result in low blood sugar and low blood pressure, causing people to feel dizzy, lightheaded, disoriented with loss of cognition, and even pass out (which can lead to traumatic head injury). Changes in posture may cause orthostatic hypotension, a drop in blood pressure, as they mention in the article, which can also cause people to pass out. A loss of just 3% of body weight can lower blood pressure and blood glucose, necessitating the reduction in medications that control these conditions. People are losing in excess of 25% of their body weight with these new meds.

Rich's colleague, Betty Kovacs-Harbolc, adds:

The field of weight loss and aging is lacking in studies in every area. There is some evidence that having a slightly higher BMI can be protective with age (graph below). The medications are not for the people in the slightly elevated BMI range. A higher BMI, with health issues (diabetes, hypertension, high cholesterol, metabolic syndrome), will shorten life expectancy and the quality of life. For example, we now know that one of the keys to protecting cognitive function is maintaining adequate blood flow. The WHO Risk Reduction of Cognitive Decline and Dementia guidelines state that "Crucially, while age is the strongest known risk factor for cognitive decline, dementia is not a natural or inevitable consequence of ageing." The WHO, the Lancet Commission and several studies have found that some of the modifiable risk factors for prevention, intervention, and care of cognitive decline and dementia are physical activity (esp. resistance exercise), maintaining normal blood sugars, treating hypertension, reducing obesity, maintaining normal blood cholesterol, and healthy diets. The medications are a tool to use along with diet, physical activity, and behavior modification. If someone is unable to lose weight, we need options other than eat less, and exercise more. When used correctly, the medications can assist with increasing both lifespan and healthspan.



10) [Most patients using weight-loss drugs like Wegovy stop within a year, data show.](#) Excerpt:

Only about one-third of patients prescribed a popular weight-loss drug like Novo Nordisk's (NOVOB.CO) Wegovy were still taking it a year later, while total healthcare costs for the group rose sharply, according to an analysis of U.S. pharmacy claims shared with Reuters.

The annual cost of overall care for patients prior to taking Wegovy or a similar drug was \$12,371, on average, according to the analysis. The full-year cost after starting the medication jumped by 59% to \$19,657, on average.

Advertisement · Scroll to continue

The costs for a similar control group of patients not taking the drugs decreased by 4% over the same period. The mean age of patients included in the analysis was 47 and 81% were female.

Dr. Fung:

Again, consider the typical patient.

0-6 months - start Wegovy, lose 40 pounds going from 280 lbs to 240 lbs. Feeling nauseated, not enjoying food anymore (that's how the drugs work). lots of people telling me I look great. tradeoff is worth it.

6-12 months - still at 240 pounds. still not enjoying food, one of life's great pleasures. nobody comments on my appearance anymore.

12-18 months - weight now at 245 pounds. still not enjoying food. Nobody congratulating me on my 'great health'. is this really worth it? Maybe I'll just stop.

Eating delicious food is one of life's universal great pleasures. Wegovy takes that away. That's a big difference between a blood pressure or cholesterol pill and weight loss injections. Sure, you can accept the tradeoff for 6 months, a year, 2 years even. But forever?

If you only read the clinical study, you won't get the whole picture. Surveillance studies only follow those people still taking the drug. People stopping the drug often stop going to the clinical studies, so they are 'lost to follow up' and not counted rather than being counted as somebody who quit the drug. The 'scientific' study will be biased towards showing a greater percentage of people continuing the drug, and will still show a 35 pound weight loss and call it a 'miracle drug'.

But again, the real life experience on the ground is significantly different. The academic doctor only reading studies will say "Evidence based medicine says these drugs are amazing" and concoct a theory as to why people are stopping the drug - usually saying people are ignorant or that internet gurus are trying to sell their diets. The regular doctor, seeing hundreds of patients on these drugs will understand, but those doctors never write papers or get quoted in the NY Times.

Same argument as for bariatric surgery (RYGB) - studies still suggest it's the best treatment of obesity. So why are the number of procedures not double or triple the level of 10 years ago? Those numbers don't lie. It's like watching free cash flow rather than revenue - cash doesn't lie.

11) Pivoting to the opposite of obesity, this is terrible: [AI is acting 'pro-anorexia' and tech companies aren't stopping it](#). Excerpt:

Disturbing fake images and dangerous chatbot advice: New research shows how ChatGPT, Bard, Stable Diffusion and more could fuel one of the most deadly mental illnesses

Artificial intelligence has an eating disorder problem.

As an experiment, I recently asked ChatGPT what drugs I could use to induce vomiting. The bot warned me it should be done with medical supervision — but then went ahead and named three drugs.

Google's Bard AI, pretending to be a human friend, produced a step-by-step guide on "chewing and spitting," another eating disorder practice. With chilling confidence, Snapchat's My AI buddy wrote me a weight-loss meal plan that totaled less than 700 calories per day — well below what a doctor would ever recommend. Both couched their dangerous advice in disclaimers.

Then I started asking AIs for pictures. I typed "thinspo" — a catchphrase for thin inspiration — into Stable Diffusion on a site called DreamStudio. It produced fake photos of women with thighs not much wider than wrists. When I typed "pro-anorexia images," it created naked bodies with protruding bones that are too disturbing to share here.

This is disgusting and should anger any parent, doctor or friend of someone with an eating disorder. There's a reason it happened: AI has learned some deeply unhealthy ideas about body image and eating by scouring the internet. And some of the best-funded tech companies in the world aren't stopping it from happening.

Pro-anorexia chatbots and image generators are examples of the kind of dangers from AI we aren't talking — and doing — nearly enough about.

From: Whitney Tilson

Sent: Tuesday, August 8, 2023 8:52 AM

Subject: Obesity Drug Wegovy Cuts Risk of Heart Attacks and Strokes by 20%, Study Shows

STOP THE PRESSES – this is HUGE news! [Obesity Drug Wegovy Cuts Risk of Heart Attacks and Strokes by 20%, Study Shows](#)

I'm not surprised that a drug that significantly reduces obesity would also significantly reduce one of the major things obesity causes, a major cardiac event, but the results from this [global five-year study](#) are nevertheless extraordinary.

It should dramatically increase the usage of these miraculous weight-loss drugs, both because more people will want to take them and also because payors – governments and health insurers – will find it harder to deny coverage.

I have no doubt that the similar studies underway for Ozempic and Mounjaro will show similar, if not greater, results.

Lastly, I think it's highly likely that future studies will show tremendous benefits across a wide range of ailments that result from obesity. 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.

From: Whitney Tilson

Sent: Thursday, August 3, 2023 1:19 PM

Subject: Zoom tonight at 7pm with Betty Kovacs-Harbolc and Rich Weil of FitsMe Health; My cousin's experience with Mounjaro; Employers Cut Off Access to Weight-Loss Drugs for Workers; Eating Ourselves to Death

1) The first of two Zoom calls I've arranged with Betty Kovacs-Harbolc and Rich Weil (whom I quote below) of FitsMe Health, who helped my friend lose 90 pounds over the past 11 months, is at 7pm this evening. See below for details on who they are and how to register for the call this evening or the other one on August 9 at 5:30pm.

2) After reading my emails about it, my cousin started on Mounjaro six weeks ago and is thrilled that he's already lost 14 pounds. He just sent me this update:

It's going great! Started on 6/23 at 235 and about 6 weeks later I'm at 221! First two weeks definitely felt a strong feeling of fullness plus some of the side effects like stomach pain, nausea, etc. Those passed though and more recently the hunger feeling came back after three or four days instead of the full week so I actually took another 2.5mg dose early the last two weeks to try to get back on track so to speak.

I met with my doctor last Fri and after sharing that experience he agreed to up my dose to 5mg, so I'm hoping that gets me back to a full week between doses without too many side effects.

It's truly amazing how it works. I've been able to eat and drink pretty much whatever I want – just less of course – and still lose weight...:)

Also, my brother was having some FOMO so he just started on Mounjaro as well. We figure we'll both look like you this time next summer – ha ha! But really appreciate you sharing all the info, etc. on it, as we would have never thought we would have this option otherwise, thanks!

3) A troubling article in the WSJ: [Employers Cut Off Access to Weight-Loss Drugs for Workers](#). Excerpt:

So many people have turned to drugs used for weight loss that some employers are cutting off insurance coverage to head off climbing bills.

Spending on the popular drugs, which belong to the class including Ozempic and can cost as much as \$1,350 a month for a patient, has quickly leapt into the tens of millions of dollars for insurance plans. The outlays are straining the finances of some plans, including those funded by employers.

After its costs for the drugs more than tripled over the past 18 months to about \$5 million a month, the University of Texas System said it would end insurance coverage of Novo Nordisk's Wegovy and Saxenda for its employees and others covered by its health plans effective Sept. 1.

Continuing to pay for the medicines "is unsustainable due to the current rate of prescription drug expenditures," said a university benefits newsletter.

This is outrageous. We should be EXPANDING access to these miraculous drugs to every one of the 73% of Americans who are overweight, starting with the more than half of them who are obese.

This is an epidemic that is killing 400,000 Americans every year and sickening millions more – numbers that approach COVID at its peak. And we now have vaccines! Can you imagine if the government or health plans refused to cover the COVID vaccines when they became available?!

However, at current prices, making such access this widespread would bankrupt us, which is why the government and health plans need to negotiate with the drug makers to cut prices massively, while increasing demand massively.

4) Speaking of health plans cutting coverage, I asked Rich Weil about this article and the affordability issue in general and he replied:

It's a complicated issue and one that I do not ever recall seeing in 40 years of doing this work. The meds are very effective but expensive. In some cases the medical benefit of weight loss does not cover the medical savings that you would expect from weight loss (There are complex medical reasons why this may be so). In some cases it does, and all companies need to do those analyses.

There are savings cards and coupons available from doctors and from the pharmaceutical companies themselves. In some cases it can be as little as \$25 a month for up to a year. Individuals should contact their doctors for savings cards and coupons, and they should contact the pharmaceutical companies for discounts applying to GLP-1s (Novo-Nordisk and Eli Lilly) for coupons and rebates. We've had patients get as much as \$575 back a month as a rebate. And the employers themselves should contact the drug companies to see if they can negotiate some type of deals. One thing for sure, individuals must be very assertive and proactive with their doctors and the pharmaceutical companies. The savings

may be out there if you are persistent enough. Many of our patients have good stories to tell about these coupons and rebates.

Medicare does not cover any weight loss meds, but supplemental insurance may. Again, people just need to keep pushing and be persistent. And hopefully the cost of these meds will come down, but as long as demand remains as high as it is, and shortages remain, there is not much incentive for the pharmaceutical companies to lower costs.

5) I enjoyed this podcast: [Eating Ourselves to Death](#), though there was a glaring omission: there was no discussion of the weight-loss drugs. Excerpt:

Fifteen years ago, there was a lot of talk about the obesity epidemic. In 2008, Michelle Obama started a government program called "Let's Move!" that sought to reduce childhood obesity. You might remember the First Lady teaming up with everyone from Beyonce to Big Bird to promote exercise and better eating habits. Unfortunately, the program was largely a failure. And the obesity statistics continued to rise.

74% of Americans today are either obese or overweight. And yet, we're no longer talking about it. The national conversation around health and weight has turned away from things like good nutrition, weight loss and the importance of physical fitness, and instead adopted phrases like "fat acceptance" and "healthy at any size." In some circles, there's even blanket denial that there is anything unhealthy at all about being obese.

Shaming people for being overweight is unequivocally wrong. But in our attempt to not offend, we've lost sight of the very real fact that there's a problem. Americans are heavier than ever, sicker than ever, dying earlier than ever, and... it's all preventable. So today, a conversation with

, a Stanford trained physician who left the traditional medical system behind to solve the one problem that she says is going to ruin us all: bad food.

From: Whitney Tilson
Sent: Monday, July 31, 2023 5:34 PM
Subject: The Fear I Felt When I Was Told My Daughter Looked Perfect

This op ed today's NYT mentions Ozempic: [The Fear I Felt When I Was Told My Daughter Looked Perfect](#). It had never occurred to me – but makes sense – that people who are prone to anorexia might be triggered by seeing overweight people losing weight due to the new weight-loss drugs...

From: Whitney Tilson
Sent: Sunday, July 30, 2023 10:12 PM
Subject: The Risks of Taking Drugs Like Ozempic When You're Over 65; They took blockbuster drugs for weight loss and diabetes. Now their stomachs are paralyzed; Overuse of weight-loss drugs

I asked the experts on this email list to weigh in on some recent articles that readers sent me...

1) In response to this NYT article, [The Risks of Taking Drugs Like Ozempic When You're Over 65](#), Jason Fung wrote:

It's a legitimate concern. Some of the [studies are showing that almost 40%](#) of the weight lost may be lean mass, more than typical for other forms of weight loss.

Ozempic causes mild nausea, which suppresses the appetite. The easiest things to eat when nauseated are the refined carbohydrates - white rice, white bread, white potatoes and sugary drinks. It's hard to eat a pork chop when you're nauseated. So, some people, especially the elderly, who take Ozempic will eat lower protein and higher refined carbs which is not great for maintaining muscle.

Kevin Maki added:

The points that Jason raises about maintaining lean mass are on target and speak to the need for dietary counseling, physical activity, and resistance exercise for the best outcomes. However, I would point out that loss of lean body mass with drugs like Ozempic should be expected to occur. The rule-of-thumb is that 25% to 33% of body weight lost is fat free mass (using a two-compartment model with fat mass and fat free mass).

Based on the available literature, I think that the greater loss of lean body mass (or fat free mass) with Ozempic and similar agents is mainly a reflection of greater weight loss, since the proportions of weight loss from lean body mass (or fat free mass) have not been consistently larger than the proportions in the control groups (lifestyle only) in the same studies. However, the absolute loss of lean mass is larger because there has been more weight loss. I would like to see more studies on this issue in a wider range of patients but, so far, I have not been overly concerned about this issue.

2) In response to this CNN article, [They took blockbuster drugs for weight loss and diabetes. Now their stomachs are paralyzed](#), Jason wrote:

It's certainly possible, because this is the way the drug works (slows gastric motility) but I haven't seen it yet personally, so it must be quite a rare side effect.

My best guess is that some editor decided that it was no longer newsworthy to write about 'miracle weight loss drugs' since every newspaper has done it already, so decided to write the opposite article. Sort of how they tried to make '[keto crotch](#)' a real condition a few years ago, because writing about the keto diet wasn't newsworthy anymore. I knew hundreds of people on keto and nobody complained about this.



[Keto crotch: Is it real and how to treat it](#)
People use the term "keto crotch" when they notice atypical vaginal symptoms while following the keto diet. Find out if keto crotch exists here.
www.medicalnewstoday.com

On the other hand, I just saw over the weekend my first case of acute kidney injury. Somebody was taking an SGLT2 for diabetes, got added the Ozempic and then became so severely dehydrated that their kidneys shut down, almost to the point of dialysis. Spent about a week in hospital but luckily OK now.

Kevin added:

It is not clear to me that GLP-1 RA drugs are causing gastroparesis per se, although it is conceivable that use could be a contributing factor. Almost all of the cases of gastroparesis that I have seen in people who volunteered for our research trials were individuals with diabetes (which can cause neurological dysfunction that affects the stomach), or who were taking opioids. Below is an excerpt from the [Mayo website](#) about causes. My guess is that the cases outlined in the story were people who were predisposed, and use of a GLP-1 RA agent pushed them into more severe dysfunction. Again, rare side effects (if this is really a side effect) will not show up until there is widespread use.

The cause of gastroparesis is usually unknown. Sometimes it's a complication of diabetes, and some people develop gastroparesis after surgery. Certain medications, such as opioid pain relievers, some antidepressants, and high blood pressure and allergy medications, can lead to slow gastric emptying and cause similar symptoms. For people who already have gastroparesis, these medications may make their condition worse.

Finally, Rich Weil of [FitsMe Health](#) wrote:

The article tells a very small percent of the full story, not atypical for mass media reporting.

The article reports on a sample size of a few of the worst cases, something the media is very good at finding and loves to write about. Plus, they can write colorful and ominous titles such as "now their stomachs are paralyzed". They love that stuff and excel at it. On the other hand, we can provide patients who would swear by the positive effect of taking the medications, and some of them report that the side effects, if they get them, and not

all do, are worth it to finally lose the weight that has made their lives a true misery for dozens of reasons.

Here's my take on the article:

1. Gastroparesis, or just milder delayed gastric emptying, is common, and people don't always know it. It can be silent. The GLP-1s slow gastric emptying, that's one of their main mechanisms of action. No one is hiding that fact. It's one of the things these meds do. If a patient already has a pre-existing, or underlying and undetected delayed gastric emptying syndrome, then a GLP-1 agonist may exacerbate it. If this is the case, then patients need to be worked up properly before taking the weight loss meds, and should be warned by their doctors about the possible side effects and report it to the doctor if they occur.
2. In diabetes, the autonomic nervous system is affected and this delays gastric emptying, so much so that it becomes very difficult to calculate insulin doses, and even the macronutrient content of the food being consumed.
3. The average time to a diagnosis of type 2 diabetes is 10 years. It means the disease progresses over all those years and frequently goes undetected until frank diabetes is present (diagnosed with an A1C 6.5 or above, or abnormal glucose tolerance tests). Since diabetes, and insulin resistance, are associated with overweight and obesity, and presumably these patients in the article had obesity, it's possible they already had diabetes, or pre-diabetes (maybe not even knowing it), and the autonomic nervous system was already negatively affected which increased delayed gastric emptying. Then the GLP-1 medication exacerbated an already underlying and undetected condition. Again, if that's the case, then patients being considered for these weight loss meds should be worked up properly.
4. Many medications can lead to delayed gastric emptying. Antidepressants, opioids, high blood pressure meds, and allergy meds, all can lead to delayed gastric emptying. They don't mention anything in the article about what meds, if any, these particular people were taking, or had taken in the past.
5. It's also true that the cause of gastroparesis is sometimes unknown and this is called idiopathic gastroparesis. Who knows if some of the patients in this article had this condition.
6. It's critical that patients with or without diabetes who have gastroparesis see a dietitian for proper counseling on how to eat, so why not have patients who are taking GLP-1s see a dietitian too? I can tell you that people taking these new weight loss meds now do not know what to eat since they never had normal satiety or hunger signaling, and they simply are in the dark. They leave food on the plate, they get full, the "noise" in their head about food has diminished or disappeared, cravings are less, and some have simply lost interest in food. It's unnerving. They need professional counseling from a registered dietitian like Betty on formulating a safe and effective food plan.
7. These meds are not the panacea for everyone, patients will need to work on it. Doctors have neither the training, experience, nor time, to counsel patients on these issues, and they would not get reimbursed even if they did spend the time counseling. I've been a certified diabetes educator since 1986 and have seen

hundreds of these cases, maybe thousands, and with proper counseling, the patients live healthy lives.

8. There simply is not enough research to make definitive conclusions, position statements, or physician guidance, and unfortunately, articles such as this will confuse the public and maybe scare them off from a medication that may help them emotionally, psychologically, and physically. And it offers physicians no guidance at all. Much more research is clearly needed. A sample size of a few of the worst cases reported by CNN is not medical research.

3) Jason and Kevin also expressed concern about the overuse of the new weight-loss drugs. Jason wrote:

The issue is that Ozempic is a huge net benefit for those significantly overweight or type 2 diabetes. However, I now hear stories of people using it to lose the 'last 3 pounds'. This is a 120-pound woman, who got Ozempic at a medical spa.

For those people, there is no net benefit, and the risks loom large. The problem will get worse because the exact same 'pill mills' are being opened up all over the U.S. A company gets a doctor to write a few hundred prescriptions sight unseen and the 'medical spa' then hands out Ozempic like candy. Patients get Ozempic. The crooked doctor makes a killing. The clinic makes a killing.

Weight Watchers just bought Sequence - this exact type of pill mill but instead of opioids, it's Ozempic. Hence the headline ['Weight Watchers expands into remote prescribing of hot weight loss drugs'](#).

The company Sequence basically does a phone consult, and then write a prescription, never having seen the patient. That simple business plan made Sequence worth over \$132 million in a few years. As long as you have no medical scruples, it doesn't take a lot of brains to copy the opioid prescribing game plan and make a lot of \$\$\$.

It's disgusting. Yes, I prescribe a lot of Ozempic to my patients. Yes, it's a great drug. But there is a dark side, and it's coming fast, because there's a lot of money involved here. Every crooked doctor is figuring out how to make a killing by becoming a 'remote prescriber'.

Kevin added:

Indeed. I am very concerned about improper use of such medications. These agents are very helpful for those in whom the risk/benefit ratio is favorable, but that will often not be the case for someone who wants to lose weight to fit into a dress for a high school reunion. There seems to be a never-ending supply of people with no functioning moral compass who are willing to provide what people want to enrich themselves without regard for the potential harms. I live in Florida where opioid pill mills were rampant. It is disturbing to see some of the same practices now with weight-loss drugs.

From: Whitney Tilson

Sent: Friday, July 28, 2023 5:24 PM

Subject: Introduction to Betty Kovacs-Harbolc and Rich Weil of FitsMe Health; Orientation Zoom sessions Aug. 3 at 7pm and Aug. 9 at 5:30pm

My friend who has lost 90 pounds on Mounjaro in the past 11 months introduced me to Betty Kovacs-Harbolc (betty@fitsmehealth.com) and Rich Weil (rich@fitsmehealth.com) (photos and bios below) of [FitsMe Health](https://fitsmehealth.com), who have been providing him with advice/counseling/support every step of the way.

I recently had an in-depth Zoom call with Betty and Rich, was very impressed, and would recommend them to anyone who's try to lose weight – whether via drugs, surgery or diet. They form and run weight-loss groups (email them if you're interested in joining the next one they're forming now), do educational workshops, and host free webinars and program orientations, all via Zoom.

(You're also going to hear a lot from them, in addition to Dr. Kevin Maki and Dr. Jason Fung, as all four of these experts have been kind enough to share comments on articles I send them and answer questions.)

I've always said that anyone who starts on the new weight-loss drugs should do so only under the supervision of a doctor. However, I've heard from many people that that's not feasible – their doc doesn't have the time or expertise, so basically they're on their own to manage side effects and a host of other medical and emotional/psychological issues (for example, Rich is hosting a 30-minute seminar at 6pm on Aug. 17 on "[Weight Loss Success: Managing Sagging Skin and Muscle Loss](#)"). I'm sure this is a major reason why only 1/3 of people who start on these drugs are still one them a year later.

So that my readers can "meet" them on Zoom, ask questions, and learn more, they've set up two free program orientations on August 3 at 7pm and August 9 at 5:30pm. To register and get the Zoom link, simply go to their website at <https://fitsmehealth.com/>, scroll down, and click BOOK on one of these links:



Program Orientation: An introduction and discussion with Betty Kovacs-Harbolc, MS, RDN, CDN, ND, BCC and with Richard Weil, M.Ed., CDE

August 3, 2023, 7:00 PM
30 mins | Free

BOOK



Program Orientation: An introduction and discussion with Betty Kovacs-Harbolc, MS, RDN, CDN, ND, BCC and with Richard Weil, M.Ed., CDE

August 9, 2023, 5:30 PM
30 mins | Free

BOOK

Best,

Whitney



BETTY KOVACS-HARBOLIC,
MS, RDN, CDN, BCC, ND

Betty Kovacs-Harbolc is a registered dietitian nutritionist and a board-certified coach with over twenty years of experience working with thousands of clients. She holds a Master's from New York University (NYU) in Clinical Nutrition, a Bachelor's in Foods and Nutrition and an Associate's in Business Administration. She completed her internship at the Department of Veterans Affairs Medical Center, Bronx NY.

Betty was a medical writer for WebMD, a CO-Principal Investigator for a multi-million dollar federally funded study, worked as a clinician on several large research studies, and returned as a professor to two colleges she'd previously attended. She is an educator to her peers, speaking annually at the Columbia University Obesity: Etiology, Prevention, and Treatment Course, presenting at conferences and grand rounds, and serving on advisory panels. Her career goals outside of weight loss are to bring an understanding and excitement to aging healthfully.

Betty was recognized as a leading registered dietitian in Manhattan in Quest Magazine's Annual New York Resources issue. She has appeared on WNBC news, WABC Eye Witness News, New York 1 News, and News 12, and she has been interviewed by numerous magazines and newspapers, including Woman's World, Glamour, Newsday, LA Times, Daily News, and Travelers Magazine.

— Show Less



RICHARD WEIL, M.ED., CDE

Rich is an exercise physiologist and has been the director of the weight loss program since its inception in 2004, when he and Betty Kovacs designed and created it. He has worked in weight loss programs, weight loss clinics, and diabetes centers in New York City for 37 years.

He has written dozens of articles on exercise, diabetes, and obesity, which have appeared on websites including WebMD and MedicineNet, and he has contributed to the exercise chapters of several books.

He has also appeared numerous times in print media, television, and on radio, and he speaks locally and nationally about exercise, obesity, and diabetes to health professionals and the general public. He is on the editorial board of Diabetes Self-Management Magazine, and he was previously a consultant to the Centers for Obesity Research and Education, a national, multi-center course to educate physicians and other health professionals about treating obesity.

He is a faculty member at the Institute of Human Nutrition at Columbia University Medical Center, and he has done research and published in peer-reviewed journals in a wide range of areas, including exercise and prevention of type 2 diabetes in teenagers, exercise program design, body composition in adults, telephone-based weight loss interventions, control and reduction of food cravings, associations of body mass index (BMI) to biomarkers of metabolic syndrome, use of shoe orthotics in adults with BMIs greater than 35, weight loss and idiopathic intracranial hypertension, and psychological predictors of weight loss in adults.

— Show Less

From: Whitney Tilson
Sent: Friday, July 28, 2023 5:37 PM
Subject: The Hidden Career Cost of Being Overweight -- and comments from Dr. Maki and Rich Weil

Welcome to the many new subscribers to this email list. For those who missed it, [here's a link](#) to a 60-page pdf I've compiled of my prior emails and best articles on the new weight-loss drugs.

This WSJ article, [The Hidden Career Cost of Being Overweight](#), captures (yet, I suspect, understates) the huge deleterious impact being overweight often has on someone's career.
Excerpt:

Weight stigma is rarely talked about at work, but it pervades workplaces everywhere, employees and hiring managers say. Study after study shows heavier people are paid and promoted less than thinner colleagues and are often stereotyped as lazy or undisciplined. In a spring survey of more than 1,000 human-resources executives, 11% said an applicant's weight had factored into hiring decisions. Half of managers surveyed in a separate poll said they preferred interacting with "healthy-weight" employees, according to SHRM, the human resources professional network that conducted the surveys.

I asked my expert friends for comments and Dr. Maki wrote:

Indeed. Discrimination based on weight (and, incidentally, height) is well known. Much of it is not conscious. Also, there is bias among physicians. There is a view that obesity reflects character flaws and lack of discipline. Again, much of this may not be conscious, but the result is that obesity is not managed in the same way that other risk factors for chronic diseases are handled.

Rich Weil added:

There are no surprises here. And I don't believe for a second the 11% number. It's much higher, but people just won't admit it. In the very same paragraph in that article they report on 50% of managers preferring to interact with healthy weight employees. That's more like it, although the number is probably higher than that. Other studies of bias in the workplace show that people with obesity are viewed as: less productive, poorer work habits, lower job performance, lower leadership potential, unfit for a challenging job, lower ability to do strenuous physical work, fewer interpersonal skills, less trusted, lower popularity, lack of self-discipline, less ambitious, do not take as much initiative, give up easier, less intelligent, less reliable, less conscientious, more insecure, lower self-esteem, less adaptable, more indecisive, less clean, and more disorganized.

Weight bias is rampant. It's well known that thinner people are more likely to think of people with obesity as bad, lazy, and less motivated. It gets worse. Studies show that children would rather have cancer or lose a limb than have obesity, almost 50% of adults would rather give up a full year of life than have obesity, and 30% would rather be

divorced than have obesity. In a well-known study of attendees of an obesity conference who did obesity research or were clinicians and were assessed for their weight bias, 68% considered people with obesity to be more lazy than thinner people, 20% thought they were more stupid, and 26% thought they were worthless. These are *professionals* who work in the field, and I'm sure the numbers were probably higher than that.

You wouldn't believe the things doctors say to their patients with obesity. I can't recall how many times a patient of ours came back from the doctor in tears about how they were treated or what the doctor said to them. Studies show that physicians report their patients with obesity are more annoying, less self-disciplined, and the doctors spend less time with them than with thinner people. One patient I recall told me how before he stepped on the doctors' scale, the doctor slid the weight all the way to the right, others have reported being called fat by their doctor, doctors do not have gowns big enough to fit them, chairs large enough to comfortably sit in the waiting room, or blood pressure cuffs not large enough to fit around their arm. It's a humiliating experience, and as a result, it's known that people with obesity go to the doctor less for these very reasons.

And you know what? 79% percent of people with obesity report using food to cope with weight bias on multiple occasions. Ask people with obesity in an office how difficult it is to walk by the kitchen without going in and eating the high-calorie junk food that is always in office kitchens. To sensitize people to the difficulty of giving up food like this, or just adjust eating patterns, I frequently ask people to imagine if you had alcohol addiction and everywhere you see food (street vendors, restaurants, there is even Godiva chocolate at the Barnes and Noble check-out counter) there were bottles of alcohol. How easy would it be to remain abstinent then?

People with obesity are not a protected class, but rates of discrimination against people with obesity in the workplace and elsewhere, are close to, or higher than, rates of racial discrimination.

So when I read an article like the one you sent the other day from CNN written by a journalist, not a scientist, bashing weight loss medications with the scantest of evidence, I cringe. I could go on.

From: Whitney Tilson

Sent: Wednesday, July 12, 2023 8:43 AM

Subject: A friend's comments on sugar; Europe Is Probing Whether Ozempic Use Raises Risk of Suicidal Thoughts

1) In response to the debate I had with a friend about the new weight-loss drugs, my friend who's lost 90 pounds since last August on Mounjaro wrote:

Part of the issue of sugar compared to, say, smoking is that we, as animals, are biologically programmed to crave sugar and to seek it out. As an animal, it was an important source of energy we needed to survive. Now "sugar in the wild" is way different than what people eat today that causes obesity, but our minds and bodies don't

necessarily differentiate them. So it's hard to put extreme prohibitions and taxes (as we did with cigarettes) on something that, biologically, we are programmed to seek out. It's very different from smoking, which created an addiction for something harmful.

Once obesity is properly viewed as an illness, it will help with how it is treated and start to move the needle on things. PepsiCo has announced they are working to cut sugar levels in the EU by 25% by 2025 and 50% by 2030. I don't know what they are replacing the sugar with, if anything, but for me the jury is really still out on sugar-free sweeteners. People still get "addicted" to sweet things even if that is Diet Coke. Unlike other addictions, obese people can't stop eating. An alcoholic can never have alcohol again. We really do need to re-teach people how to eat, but they have to want to change and that is hard. Plus there are so many reasons people eat: emotions, etc.

For me, I know if I have refined sugar, I want more sugar. I crave it. So I work hard to really avoid eating it. Fortunately, I am more a salt person than a sweet tooth. I still have sweet things, but now I reach for medjool dates or berries, which satisfy my craving without causing me to want more. But the vast majority of obese people do not have my means to have such healthy options always available to them. Not to mention the endless advertising of food on TV, billboards, social media – we are bombarded by it. Make it really hard for people that have food noise to tune it out, especially since we have to eat and are biologically programmed to seek out sugar (and fat for that matter).

2) This article, [Europe Is Probing Whether Ozempic Use Raises Risk of Suicidal Thoughts](#), based on reports from three people, initially struck me as ridiculous because I have no doubt that three people who took, say, aspirin in the past year also reported thoughts of self-harm...

But I didn't want to dismiss it without checking with the experts, so I emailed Kevin Maki and Jason Fung, who were kind enough to reply. Dr. Fung wrote:

It's always better to be cautious because rare side effects are not detected until a drug gets wide usage.

We know that some foods light up the reward centers of the brain, so a drug that reduces appetite may theoretically lead to dysthymia (like a mild depression) that may predispose to suicide. This is all theoretical, but better safe than sorry.

There are lots of drugs that we don't find the side effect out until way later and we don't usually know the mechanism prior: Vioxx, myocarditis with the COVID vaccine. rosiglitazone, and of course, the infamous thalidomide.

Additionally, [this study](#) in 2019 showed that bariatric surgery (RYGB) is associated with almost a doubling of suicide risk, so it wouldn't be unprecedented that GLP-1s also have a risk. It doesn't mean that these drugs won't be useful, just that we need to be cautious.

Dr. Maki added:

I agree that rare side effects do not always emerge until a drug is widely used. If a side effect occurs in 1 in 5,000 or 10,000 people and occurs with some frequency in the background in the population, it is difficult to determine whether the effect is causally related to the drug. There was a drug for obesity approved in Europe but not in the US called rimonabant, a cannabinoid-1 receptor blocker, that suppressed appetite and produced weight loss, but also increased depression and suicidal ideation. So, it is not out of the question that such effects could occur with other drugs that suppress appetite. I think we can be confident that this does not occur frequently, but it is not possible at present to completely rule out a causal association.

Thank you!

From: Whitney Tilson

Sent: Sunday, July 9, 2023 1:11 PM

Subject: A discussion of the new weight-loss drugs by two of the world's leading experts on them

I'm sending this as a separate email because I think it's so important – a discussion of the new weight-loss drugs by two of the world's leading experts on them. This is a perfect example of why I've created 20 e-mail lists dedicated to particular topics I'm interested in – I learn so much... Enjoy!

Dr. Kevin Maki engaged in a discussion with another one of my readers, Dr. Jason Fung, a "nephrologist (kidney specialist) who has prescribed these weight loss drugs for several years, as these are diabetic medications." He gave me permission to quote him by name because, as he explained:

I'm actually a pretty public figure already. I've been on the New York Times best sellers list, my book, [The Obesity Code: Unlocking the Secrets of Weight Loss](#), has over 37,000 reviews on Amazon, having been translated into 37 languages. That's my best-selling book, but the one I'm proudest of is [The Cancer Code : A Revolutionary New Understanding of a Medical Mystery](#). I have over 1 million YouTube subscribers. So being public doesn't bother me much.

In Dr. Fung's initial email to me, he wrote:

From my experience of prescribing hundreds of patients these drugs for the last 4-5 years, what generally happens is that people do indeed lose lots of weight INITIALLY. The drug (semaglutide) basically causes people to lose their appetite. In higher doses, it makes them nauseated. So they don't want to eat. They lose lots of weight and are happy.

Then, the body adjusts, and the appetite suppression/ nausea slowly fades, and the weight is generally regained unless the person has learned about proper nutrition. But most haven't, because they see it (as it seems like you do) as a 'miracle' drug that lets them lose weight effortlessly, so why bother learning about eating natural unprocessed foods and more vegetables?

The experience is almost identical to the enthusiasm around bariatric surgery circa 2009. The 'experts' all proclaimed the 'cure' for obesity. Then it became clear after about 4-5 years that people could easily regain their weight. Now, just about nobody does lap bands or bariatric surgery anymore. The body adapts, and people learned that they could easily stomach sugary drinks and highly refined foods after surgery or lap band. So they ate more ice cream and drank more soda, because they were 'cured' of obesity. Until all their weight returned.

The problem is the same as with semaglutide. If your appetite is down, you don't want to eat a steak, or pork chops or eggs. But you can drink sugary soda and ice cream and muffins (highly refined foods). So that's what you do. Forget about diet, because you have the 'cure' for obesity.

Whitney, your current enthusiasm is nice (and I'm sure the pharmaceutical companies will make a LOT of money), but ultimately I think misplaced. Will this actually help people become healthier? I doubt it, although I hate to say it, even as I prescribed this hundreds more times.

Dr. Maki replied (I've excluded their discussion of bariatric surgery, as I think this procedure goes away now that there are these new drugs):

It is certainly true that some people will lose weight and then regain some or all of it over time. However, my experiences have me feeling more optimistic than I have in the past. I have been involved in designing and running clinical trials to test weight loss drugs since the early 1990s and was not optimistic until recently, with the latest generation of GLP-1 RA and GLP-1/GIP drugs. We sold our clinics at the end of 2021, so I have been less directly involved recently, but the longer-term, open-label extension studies for development trials have shown fairly high rates of continued success. Time will tell for the newer agents. It is true that those most likely to be successful are people who change their dietary habits, engage in daily physical activity, and do other things such as weighing every day and recording the results.

Dr. Fung:

Whether the newer GLP-1 and now GLP-1/ GIP and GLP-1/GIP/ Glucagon agonists will cause long term success is an open question. However, my own clinical experience started out as optimistic and am now pessimistic. I don't always trust what the drug companies studies say, just as I would not trust a 'new study from Coke says sugar is GOOD for you'. A drug company study that says their drug is super amazing and the benefits last forever also falls in the "trust, but verify" category.

Right now, I have dozens of patients who did really, really well initially on Ozempic. They lost too much weight! Now, all of them are regaining. All of them. So, I sure do hope I'm wrong and these drugs are as amazing as they seem, but I doubt it.

Dr. Maki:

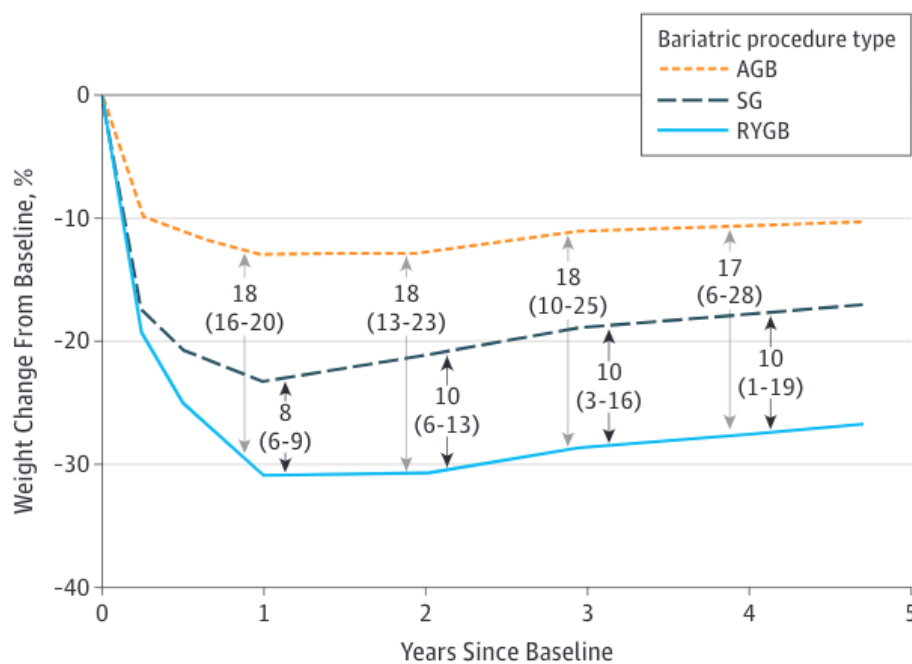
I agree that we will need more time to assess longer term outcomes with the newer GLP-1 RA and dual or triple target (GIP, glucagon) agents.

Dr. Fung:

I agree that it's great to have some frank discussion with opposing views - a great way to learn a lot. I have no dog in the game, so it matters little financially either way, both for bariatric surgery and the new weight loss drugs. I don't invest personally in any drug makers because it may influence my prescribing behavior, which cost me a LOT of money, as I knew 4 years ago that Ozempic was going to be huge with the [STEP trials](#) published in the Lancet in 2021. The Ontario formulary covered Ozempic in 2019, which is when most of us started prescribing it heavily, and results were pretty obvious within 6 months of clinical use.

Whitney, there are no studies of long term usage studies and I wouldn't trust the ones from the drug company anyway, because they will always be open label rather than randomized data, which leaves it prone to bias. That is, people who regained their weight ON Ozempic will be more reluctant to share their data, or are more likely to be lost to follow up. This leaves the company with only the people who did well. You can see that the effect clearly wanes over time:

Figure 3. Differences in Estimated Percentage of Weight Change From Baseline by Surgical Procedure Type



The thing to understand is that trial data is ALWAYS better than real life data. There were tons of doctors spouting the safety of drugs like Vioxx and Rosiglitazone based on the studies before the real life doctors forced them to admit that their products were deadly. The drug company does the trial, and it's in their huge financial interest to make it look as good as possible, so you need to take their data with a grain of salt, or at least verify that results are as good as they say they are.

I asked:

What percent of your patients taking one of the new weight-loss drugs have regained substantial amounts of weight WHILE REMAINING ON THE DRUGS?

I have seen no studies showing this, but would be curious if there's any anecdotal evidence (forgive the oxymoron).

Dr. Fung replied:

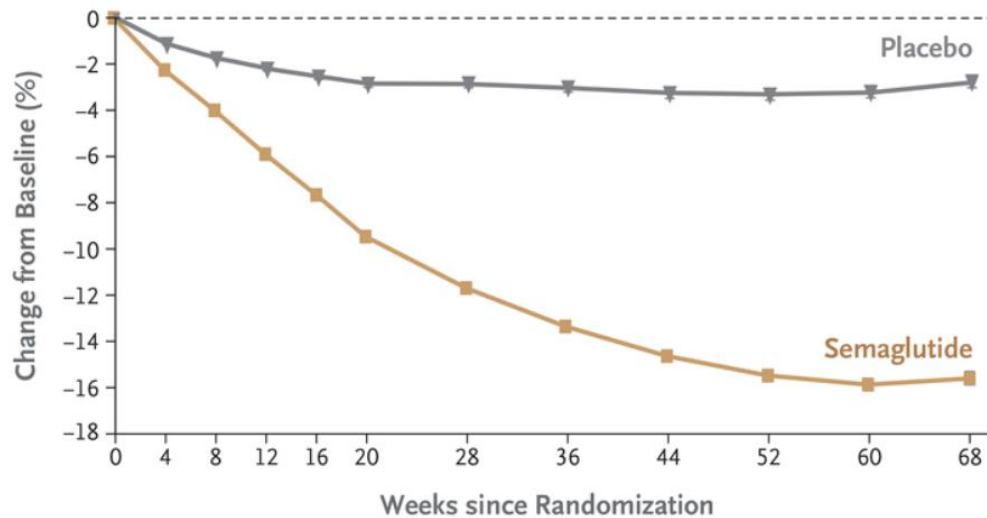
Yes, there are no studies on this. I can only give you my clinical impression from my own practice and my discussions with colleagues.

As a kidney specialist, there is evidence that Ozempic prevents progression of diabetic kidney disease, so I have all my patients stay on Ozempic regardless of weight loss or regain. Most of my patients have stayed on since 2019.

I estimate only about 10-15% have regained substantial weight on Ozempic, which we've generally managed by increasing the dose - not great, since side effects tends to go up.

Most (maybe 60-70 %) have this slow regain of weight while on the same dose, similar to what the studies show. This is the big difference between Ozempic and say cholesterol or blood pressure medications. Those medications don't have the same waning effect over time. Your statin or BP med has the same effect after 5 years of use, where the Ozempic clearly has a slow loss of effect. (from the NEJM paper, you can see the plateauing effect at 60 weeks and slight uptick):

Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk	
Placebo	655 649 641 619 615 603 592 571 554 549 540 577
Semaglutide	1306 1290 1281 1262 1252 1248 1232 1228 1207 1203 1190 1212

So here's the typical patient:

- Start Ozempic - lose 50 pounds - ecstatic, although still 50 pounds overweight. Game changing drug! Wow! Friends say I'm looking amazing.
- Year 1 - still around 50 pound weight loss - still happy. great drug, breakthrough.
- Year 2 - regained 5 pounds. Less happy. Up the dose, but side effect intolerable
- Year 3 - regained another 5 pounds. Not sure if Ozempic is still working. Is there anything newer and better?
- Year 4 - regained another 5 pounds. Not that happy. Ozempic is an OK drug. Works, but not a panacea. Not a miracle drug. (This is the stage where most of my patients are).

The studies would show that patients still have a 35-pound weight loss. An incredible result! But on the ground, the outlook considerably less rosy. All the patients are expecting that within the next 4-5 years, that all weight will be regained, and they're probably not wrong. In clinical trials, a two-year trial is really, really long, but for a 65-year-old person, two years is nothing.

Problem is that people eat for many reasons. Ozempic may take away hunger, but how many people are eating purely because they're hungry? People eat because they enjoy it, or want to celebrate, or for social reasons or because of habits, or because they're depressed etc. Ozempic can't change any of that. People tell me, they want to really enjoy their food, which they can't on Ozempic.

There's a big difference, though, between the clinical story, and the financial one. There's no doubt that these drugs will be huge money makers for decades to come. I'm only talking about the clinical outcomes.

Dr. Maki:

Thanks for your message describing your typical patient experience. Our views are not far apart. There is typically some weight regain after weight loss interventions. In our studies in the 1990s, we clearly saw that when someone switched from drug to placebo, there was accelerated weight gain and at the end of two years the drug to placebo groups looked just like the placebo throughout groups (everyone received a lifestyle intervention). For the groups that stayed on drug therapy for the full two years there was some regain, but less than with placebo.

One point that is often underappreciated is that the weight trajectory for most in North America is an upward march of about one pound per year (see graph below), albeit with large variability between individuals. Recently we have seen that the slope of weight gain per year is increasing. For example, in the US Nurses' Health Study there was an average increase of 0.6 pounds per year in body weight. However, in the US Nurses' Health Study II, that had increased to 1.3 pounds per year.

These experiences speak to the need for continued efforts to encourage healthy diet, physical activity, sleep hygiene, and stress management to "flatten the slope" for weight change over time. Of course, this is difficult, and many patients won't maintain those changes. I suspect that is particularly true for your patients with renal disease.

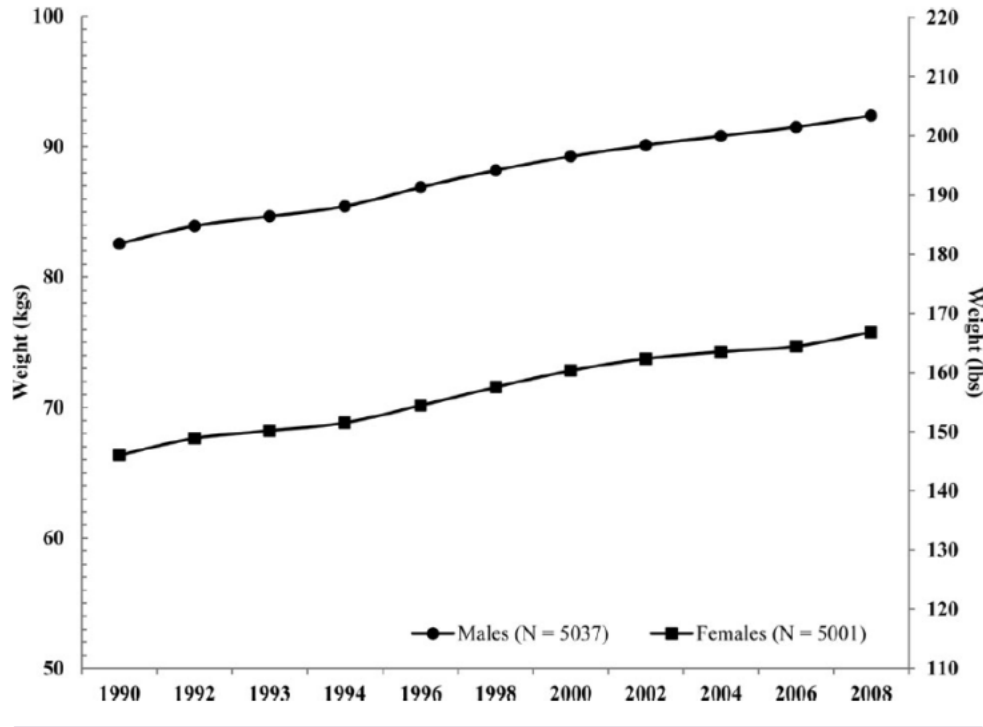


FIGURE 1 "Average" 18-year (1990–2008) weight trajectory for men and women

Obesity (2013) 21, 1923–1934. doi:10.1002/oby.20318

Dr. Fung:

Absolutely agree with you. I think we're actually pretty much of the same view. I hope, as you do, that the new drugs are game changers, and I'm probably one of the biggest Ozempic prescribers in my local area. But my early initial optimism has been significantly tempered. (But I think the drug companies will still make a lot of money).

It's just that I've seen this optimism before with bariatrics (there were even several TV shows about it on TLC channel back a few years when optimism was running high). The academic studies on RYGB, as you and I agree, were amazing. But, as Nassim Taleb has said: "In academia, there is no difference between academia and real life. In real life, there is"

Thanks for the information about the Nurses Health Study II. I didn't realize things were getting worse even faster.

Dr. Maki:

Yes...that Taleb comment is a corollary to the old expression that in theory there is no difference between theory and practice, but in practice, there is.

I hope that the newer agents are game changers, but I am always of the view that I may have to change my mind if the data lead me in a different direction.

From: Whitney Tilson

Sent: Sunday, July 9, 2023 1:03 PM

Subject: High cost of these drugs; Debate with a friend about Mounjaro; People on Drugs Like Ozempic Say Their 'Food Noise' Has Disappeared; Do the drugs cause you to lose weight via muscle or fat?

1) Regarding the cost of these drugs: they are indeed expensive 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 the cost, 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.

2) I've been having an argument with one of my friends, who writes:

Fast Facts on Diabetes

Diabetes

- **Total:** 37.3 million people have diabetes (11.3% of the US population)
- **Diagnosed:** 28.7 million people, including 28.5 million adults
- **Undiagnosed:** 8.5 million people (23.0% of adults are undiagnosed)

Prediabetes

- **Total:** 96 million people aged 18 years or older have prediabetes (38.0% of the adult US population)
- **65 years or older:** 26.4 million people aged 65 years or older (48.8%) have prediabetes

This is fucking bananas. Basically half of Americans are either diabetic or pre-diabetic. How is this not a five alarm fire?

I agreed, and wrote: "When 70% are overweight and 40% obese, I'm surprised it's not higher. We need to get all of them on Mounjaro!"

But he disagreed, writing:

No, we need to get them all off sugar. We did it with lung cancer. We did it with seat belts and car accidents. Why can't we do it with sugar? Problems are there to be fixed.

It's fucking absurd that we have half the country sick with diabetes. And fucking even more absurd that the "solution" is a pill with unknown long-term consequences that'll cost us \$1 trillion in additional healthcare care spend when the solution is free: stop eating sugar.

It's pretty damn simple. Look at incidence of diabetes around the world — or obesity — and look at the consumption of processed foods in those countries. It's a direct fucking correlation.

How is it not blatantly obvious to you that we are being POISONED by the food we eat?

I replied:

I mostly agree with you about what has happened to the modern diet and lifestyle, and the horrific health consequences. I simply think that your proposed solution has less than a 1% chance of success -- if we define it as anything like the success we've had with cigarettes -- for many reasons. Look at what happened to poor Mike Bloomberg when he tried to implement a baby step of reducing jumbo drink cups. The public has proven mostly willing to accept high taxes and huge restrictions on smoking whereas there is almost no support for measures that could be similarly effective re. changing the diets of billions of people. And at the same time, there are miracle drugs available RIGHT NOW.

Truth be told, I don't think you hate these drugs because they're unproven, might have bad long-term consequences, etc. I think you think that fatsos need to better control themselves and eat and exercise better rather than "cheat" with a drug.

Fundamentally, you don't think obesity is a disease, you think fat people are just weak and need a kick in the ass. I disagree.

Needless to say, he didn't take kindly to my assessment of the root of his opposition to the weight-loss drugs, writing:

No. I don't like these drugs because I am very concerned that we will wake up 10 years from now and find all the problems they caused.

I would much prefer if we had POLICY from the government that shifted the incentives away from these toxic sugary foods.

I want people to realize how toxic this shit is, and stop rewarding children with sugar all the time, at every fucking occasion, because, well, look at the statistics?

I replied:

You're missing the point: I AGREE with you about the cause and consequences. We simply disagree on what steps governments should take to help their populations. 50% of Americans are suffering from a deadly illness that's killing and making sick as many people as COVID every year, which has steadily been getting worse every year for the last 60 years.

In response, you want to try a series of things that just ain't gonna happen, with almost zero chance of success. I want to give as many people as possible a life-changing/saving

vaccine, even if there's a tiny risk of unknown long-term consequences, just as we did with COVID.

3) I somehow missed this article that appeared in the NYT three weeks ago, which mirrors what I've heard from many friends on Mounjaro: they no longer have food cravings and don't binge-eat anymore: [People on Drugs Like Ozempic Say Their 'Food Noise' Has Disappeared](#). Excerpt:

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.

4) One of my friends emailed me:

I believe that peer-reviewed analysis has demonstrated that the weight loss through these drugs is different than the weight loss through caloric reduction/more exercise/etc. The weight loss from these drugs skews significantly higher as a percentage of total loss towards loss of muscle weight.

I asked Dr. Kevin Maki to reply:

There have been surprisingly few studies that included assessment of changes in body composition rather than weight alone. The studies of which I am familiar showed loss of fat-free mass that is roughly similar to that observed in trials of dietary modification and bariatric surgery for weight loss. Typically, about 25% of weight loss (i.e., about 2.5 lb for every 10 lb lost) is fat-free mass, which includes some muscle, as well as connective tissue, fluid, etc. The studies with the new weight loss drugs have shown similar losses of fat-free mass as a percentage of the weight lost. However, more research is needed on this topic. Below I have excerpted a few sentences from the attached Medscape story on weight loss with Mounjaro that quotes Louis Aronne, who has been a long-time clinician and clinical trialist investigating weight loss interventions:

As with lifestyle and surgical treatments, participants taking tirzepatide had around a three times greater percentage reduction in fat mass than lean mass, resulting in an overall improvement in body composition, reported Aronne. "We want loss of fat not lean mass, and we know that we lose around one part lean to three parts fat mass when on a diet and exercise regimen," he went on to explain.

"We see exactly this [balance of lean-to-fat-mass loss] here with 33.9% total fat mass reduction in the treatment group compared with 8.2% in the placebo group."

Visceral fat mass reduction was 40% in the treatment group compared with 7.3% with placebo. "It's good to see there's more loss of visceral fat," said Aronne. Lean mass loss was 10.9%. "So around three times greater reduction in fat over lean mass loss, resulting in overall improvement of body composition," he reported.

As an aside, the reduction in fat-free mass loss can be minimized by consumption of adequate protein, physical activity, and resistance exercise. These strategies should be recommended to nearly everyone trying to lose weight.

My friend replied:

If I read the appendix to [this 2021 study](#) attached correctly, it appears to me that in this trial 41% of the weight loss consisted of lean body mass (6.92 kilos of mean lean body mass lost relative to 16.86 kilos of mean lost total weight). So would not this be consistent with a higher proportion of lost weight using Semiglutide than the lost lean mass with weight loss via restricted caloric intake or bariatric surgery driven weight loss?

Dr. Maki replied:

In this substudy (n = 95 on semaglutide and n = 45 on placebo), about 40% of the weight lost based on Table S2 in the semaglutide group was from lean body mass (total loss of fat mass + lean mass = 17.32 kg, of which 6.92 kg was lean body mass = 40.0%). That is higher than is typically observed. However, notice that in the placebo group (i.e., lifestyle changes only), 1.48 kg of the 2.65 kg loss of fat + lean mass was from lean mass. Therefore, in the lifestyle only group the fraction of lean body mass lost was 56%. That is also higher than is typical but not outside the realm of what we have observed in our studies. These results would lead to the inference that the percentage of lean body mass lost was numerically less with semaglutide than with placebo (lifestyle only).

Some loss of lean body mass (or fat free mass using a two-compartment model of fat mass and fat free mass) is appropriate with weight loss since less architecture is needed to support a lower body weight. Too much loss can be problematic because it increases risk for frailty in older individuals and lowers resting energy expenditure, which is a majority of daily caloric output. In our studies, we encourage aerobic and resistance exercise plus adequate protein intake to limit loss of lean mass.

From: Whitney Tilson

Sent: Monday, July 3, 2023 2:12 PM

Subject: Mounjaro dosage; Metformin; Obesity drugs' real costs mount as users don't know when to stop; Naps; The Ethicist

Welcome to the many folks – now up to 852 people – who've joined this, my new email list about the miraculous new weight-loss drugs.

1) A friend just started Mounjaro because he's 50 pounds overweight. He said, "I lost 30 pounds because I wanted to look good for my wedding a few years ago, but afterward it came right back." He asked: "Can you ask your friends what dosage they're on and/or did they have to increase it to get better results?"

One friend (a doctor) simply replied: 10mg.

Another, who's lost 90 pounds, wrote:

If he took his first injection, he should have started at 2.5mg. You go up in 2.5mg increments. I went up to 5mg after one month on 2.5mg. We went up because the results on 2.5mg were positive AND I have no side effects. Went to 7.5mg after 1 month at 5mg. Went to 7.5mg because I was having very positive results on 5mg and no side effects. Went to 10mg after 1 month for same reasons BUT started having GI side effects on 10mg. However, my doctor and I didn't think it was from the drug, so went to 12.5mg after 2 months on 10mg. Kept having GI side effects that weren't acceptable, so dropped back down to 10mg after 1 month on 12.5mg. Stayed on 10mg for another month, but side effects continued. So dropped down to 7.5mg, which is where I remain for now and the foreseeable future. I do have side effects, but only for one day each week and then gone. May go down to 5mg after a few more months – we'll see. Hope that helps.

So roughly...can get you more exact dates if needed.

Aug 12 – Sept 12 – 2.5mg

Sept 19 – Oct 19 – 5mg

October 26 – November 26 – 7.5mg

Dec 3 – Feb 10 – 10mg

Feb 17 – March 17 – 12mg

March 24-April 24 – 10mg

May 1 – Present – 7.5mg

2) One of readers, John P., emailed me:

This is my first time writing to you. I have a couple comments on your discussion of weight loss medications.

I tried a prescription medication (Staxyn) several years ago on a one-month free trial. It worked but I did not continue its use due to the cost of \$1300 per month. Every weight loss drug currently being used is some form of diabetes or pre-diabetes drug costing around \$1000 per month. That made me wonder if a generic diabetes drug would have the same effect. After reading the article below in National Geographic, I asked my doctor for a prescription for Metformin. In 5 months I have gone from 192 lbs to 170 lbs with no side effects and no hunger issues. I did supplement the Metformin with commercially available DHEA, to help build muscle. If this article, [Can Aging Be Cured? Scientists Are Giving It a Try](#), is correct, I have gained additional health benefits in addition to the weight loss. And the Metformin only costs \$1.00 per month.

For the record, I am 78. My general health and bloodwork were excellent before I started the Metformin and they still are. Most of my weight loss was visceral fat around my waist. I look and feel better than before I lost the weight. My waist size went from 38 to 34.

Could it be possible the big pharma companies don't want to acknowledge a cheap product that everyone needing to lose weight can afford? There's certainly no profit for them at \$1.00/month.

I asked Dr. Kevin Maki for his thoughts and he wrote:

Yes, metformin has a well-established ability to produce mild weight loss. In the Diabetes Prevention Program (paper [here](#)), participants were assigned to three groups: an intensive lifestyle intervention targeting 7% weight loss and at least 150 min/week of exercise, metformin, or placebo. The lifestyle intervention was the most effective for inducing weight loss and reducing risk of new onset diabetes. However, metformin produced slightly less than half the weight loss and lowered diabetes risk about half as much as the lifestyle intervention. Of course, the optimal strategy is to use metformin plus lifestyle modification.

Some people respond better to metformin than others. I have seen cases of zero weight loss and losses of 20+ pounds. As an aside, metformin is one of a handful of medications that is being studied for possible geroprotective effects. Compared to people who don't take it, older adults taking metformin seem to have lower risks for some types of cancer and all-cause mortality. There are biologically plausible mechanisms that might support causality for these associations, although these potential benefits remain to be demonstrated in randomized clinical trials.

3) A Bloomberg article that highlights: [Obesity drugs' real costs mount as users don't know when to stop](#). Excerpt:

Two years and more than a million prescriptions after Wegovy first went on sale, there's one taboo question for some doctors who prescribe the hit obesity drug: When can patients stop taking it?

The new medicine by Novo Nordisk and others in the same class can melt away pounds that diet and exercise don't budge. But it doesn't change the underlying issues that drive metabolism, leaving newly lean people wondering whether they will need to bear the expense and the side effects of the drugs for decades or risk relapse.

Packets of Wegovy move along a conveyor at the Novo Nordisk A/S production facilities in Hillerød, Denmark, on Monday, June 12, 2023.

The weight rebound is a growing problem in the U.S. as some insurers balk at the drug's more than \$1,000-a-month price, a situation that will be more acute in Europe's cash-strapped public health-care systems. A U.K. health agency has already recommended

capping care at two years. At stake are billions of dollars and a fundamental issue: whether obesity should be treated as a disease long after its most visible symptom has vanished.

Here is my response that I've sent around previously:

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.

4) This has nothing to do with the weight-loss drugs, but my aunt sent me a link to [this short video](#) by a guy named Vishen Lakhiani making all sorts of big claims about napping: "you'll be 34% better at anything," etc. So I asked Dr. Maki for his thoughts and he replied:

There is some truth in what he is saying in the video. However, things are a bit more complicated. Adequate sleep quantity and quality are associated with lower risks for cardiovascular disease as well as other chronic diseases. One of the functions of sleep seems to be to clear away cellular debris, including that in the central nervous system. Napping is associated with higher brain volume and less risk of dementia in older adults. Many older adults have a difficult time getting the recommended amount of sleep at night.

Napping tends to be associated with greater overall weekly sleep quantity. Therefore, it is not clear that it is napping per se, rather than adequate sleep quantity that is driving the association. Also, people's estimates of how much sleep they get are often inaccurate and newer methods such as use of smartphone apps to quantify sleep time are a real help for this kind of research. Some people nap because they don't sleep enough at night. The recommended amount of sleep is roughly 7-8 hours per 24-hour period. If someone is sleeping 6 hours at night and then takes a 20-60 min nap, that is getting the person closer to the recommended amount of sleep. There does seem to be some ability to make up for a sleep deficit on a given day with additional sleep in the subsequent day or two.

Most of what we know about sleep and chronic disease risk comes from observational research, which is subject to various types of bias and confounding. Therefore, some caution is warranted in interpretation. However, the risks are minimal, so it is reasonable to recommend napping, particularly for those who do not get the recommended amount of sleep at night.

5) A follow-up from the NYT Ethicist to the Q&A I sent around a few days ago:

Readers Respond

Last week's question was from a reader whose two best friends were taking Ozempic to lose weight. They disapproved of their decision, and wrote: "I'm conflicted about the safety and popularity of these drugs for weight loss, and so I've remained silent whenever this topic comes up. Our annual trip is coming up, and I fear I'll be forced to offer my opinion about their weight loss, especially since the trip involves time at the pool. Should I compliment them to keep the peace? Or is there a tactful way to make my differing opinion about these drugs known?"

In his response, the Ethicist noted: "It's not the job of friends to play doctor. People who have been prescribed semaglutide will have received medical advice about possible side effects. More than a few will have experienced them. You imply there's a moral problem about taking the drug, but you don't say what it is. ... Not knowing what your specific concerns are, I can't tell you how to broach them. But if what's really bothering you is the thought that your friends are taking the easy way out, well, I doubt that's a cogent position. In any case, the evidence is clear: Moralizing weight issues doesn't help solve them." (Reread the full question and answer [here.](#))



There is no better way to ruin a friendship than to discuss a friend's weight. As the letter writer did not reveal her moral objections to the drug, it's even more incumbent on her to avoid any discussion of it. Until she is able to voice her concerns coherently and in a kind and respectful manner, she needs to stay silent. — *Wendy*



I agree with the Ethicist when he says, "Moralizing weight issues doesn't help solve them." But he doesn't explicitly tell the letter writer what they need to hear: Don't comment on somebody else's weight. Period. Their weight is not your business. There should be no moral superiority attached to this topic. — *Lisa*



The Ethicist missed the mark here. The letter writer clearly has a moral objection to their friends' full-throated endorsement of, and participation in, a diet culture that has damaging repercussions far beyond those a given individual taking Ozempic may experience. When thinness becomes "easy," it also becomes compulsory in the eyes of many, leading to the further marginalization of those in larger bodies. — *Emily*



Our friends don't need us to judge them. Instead, they need us to listen and support them. If the letter writer's friends are taking Ozempic to drop 20 pounds, it is not her place to judge. The friends could want to look and feel better, which is their prerogative. Here, negativity can be misconstrued as jealousy, so perhaps the letter writer should explore those feelings. — *Kathleen*



In our family, we have a saying, derived from a long family history of eating disorders and discomfort with body image: "No body talk." We tell interlocutors that we are uncomfortable talking about people's weight and appearance. Period. Rather than criticizing her friends' choices, your reader can simply say, "No body talk," and leave it there. — *Katherine*

From: Whitney Tilson

Sent: Thursday, June 29, 2023 11:34 AM

Subject: My response to the five main objections to the new weight-loss drugs; 7 articles: Goodbye, Ozempic; Ozempic Might Help You Drink & Smoke Less; My Friend Has Become

Obese. Should I Intervene?; My Best Friends Are Taking Ozempic. Can I Share My Disapproval?

Hello again to the now-700 people on this new email list.

1) For those of you who are new to one of my 20 personal email lists, they're not like my investing daily in a variety of ways:

- They come from my personal email account, so if you have a question, comment, or personal experience to share, you can just hit REPLY
- Nobody reviews or edits them, nor are there any embedded ads/promos
- Sometimes they have attachments or full text of certain articles; other times they only contain one item – often just a link to an article, with no commentary (usually when I'm reading something on my phone that I want to share and/or I'm in a hurry) (in this case, there won't be an unsubscribe link)
- They aren't posted or archived anywhere

2) Here is what I just sent out as part of today's investing daily:

Continuing my series on the miraculous new weight-loss drugs...

I've heard five main objections to these drugs:

- They can cause severe bloating, gassiness, burping and diarrhea.

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).

- What about more serious side effects?

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.

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

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.

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

So what? 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.

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

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 important, dietary habits.

One friend who lost 40-plus 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.](#)

3) Here are some interesting articles I've come across in the past few days:

- [Goodbye, Ozempic](#), The Atlantic
- [The Drugs That Are Gaining on Ozempic](#), WSJ
- [Ozempic Might Help You Drink and Smoke Less](#), WSJ
- [My Friend Has Become Obese. Should I Intervene?](#), NYT

- [My Best Friends Are Taking Ozempic. Can I Share My Disapproval?](#), NYT
- [Pill for Obesity Has Wall Street Salivating](#), WSJ
- A [tweet by Chamath Palihapitiya](#):



Chamath Palihapitiya ✓ 

@chamath



The physiological effects of being overweight haven't improved even if the psychology of it has (ie inclusive advertising).

At a population level, being overweight still means:

- higher all cause mortality
- higher blood pressure
- higher cholesterol
- higher type 2 diabetes
- more coronary heart disease
- more strokes
- etc etc etc
- [cdc.gov/healthyweight/...](https://www.cdc.gov/healthyweight/)

This may explain why drugs like Ozempic and Mounjaro are flying off the shelves.

That's why this interim data release from Lilly's new drug is pretty exciting. Apparently, not only can it help with weight loss, blood glucose control and fatty liver, it also instigates the biological action of burning calories (when your liver converts glycogen to glucose and releases it into your bloodstream).

Essentially, this drug is saying that it can help you slim down, off-ramp your body from diabetes and heart disease and make it seem like you're working out even if you're not... 🤖

From: Whitney Tilson
Sent: Wednesday, June 28, 2023 8:49 PM
Subject: Welcome; E-mails from 2 readers

A warm welcome to the 664 folks who just subscribed to my new e-mail list about the new weight-loss drugs!

I'm going to be including a lot of content on this topic in the next few investing dailies, so for now, I'm just going to re-send that to this list (in case anyone misses it there), but after that I'll be sending periodic news and commentary about these drugs just to this list.

If you didn't mean to subscribe to this list and want to get off it, simply send a blank email to: weightlossdrugs-unsubscribe@mail.kasecapital.com

Best,

Whitney

Here is what I included in today's investing daily:

I got a tremendous response to [yesterday's e-mail](#) about the miraculous new weight-loss drugs. More than 400 of you signed up for my new personal e-mail list on this topic (to subscribe, simply send a blank e-mail to: weightlossdrugs-subscribe@mail.kasecapital.com).

Why am I spending time on this? Because of e-mails from my readers like this one, from 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 six 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.

And this one from 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.

Best regards,

Whitney

From: Whitney Tilson

Sent: Saturday, June 3, 2023 1:10 PM

Subject: Another Mounjaro miracle story; Did Scientists Accidentally Invent an Anti-addiction Drug?

1) Another friend just told me yesterday about his miraculous experience with Mounjaro, the best of the new weight-loss drugs.

I know at least a half dozen people on it and all have reported amazing results. One friend has lost 90 pounds in nine months – I can hardly recognize him! The *worst* outcome among my friends is a 22-pound loss in five months.

And there may be incredible additional benefits as well – see the article below about these drugs reducing addictions, and one friend told me that Mounjaro has been the best antidepressant he's ever taken.

The friend I spoke with yesterday 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.

He said he loves good food and wine, but hasn't had to give any of it up – he just eats less. He also 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.

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 yesterday's friend said he pays for it out of pocket, though says he gets a discount that reduces the price by 50%.

2) Here is a recent article in The Atlantic, [Did Scientists Accidentally Invent an Anti-addiction Drug?](#), that discusses additional possible major benefits from these drugs.

3) I've heard three main objections to these drugs:

a) 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.

b) 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.

c) It's somehow cheating. One friend who lost 40+ pounds in two months on Mounjaro but stopped and gained the weight right back 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!"

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. So 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.

4) Lastly, attached is a pdf I put together with four articles and a 60 Minutes segment about these miracle drugs.

Best,

Whitney