Transcript

Dr. Kendal Williams (Host): Welcome to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams.

In this podcast, we bring in experts from within the Penn community to discuss issues of interest to frontline clinicians, particularly in primary care.

Today, we are going to tackle a very common problem, both in our offices and in the greater world. And that is obesity.

Obesity is all around us and a source of constant discussion. I recently joked to my wife that I spend most of my day in primary care talking to patients about weight loss. And then I come home and all we talk about is weight loss.

So it's a topic that's of interest to everyone. We all manage it. We all advise patients about it. And I for one am not always certain that I'm giving the best advice, so we invited in some expertise to have a discussion.

With me as a co-host is Dr. Rani Nandiwada from the Penn Center for Primary Care. Rani is an Assistant Professor of Medicine at Penn. She has a background in medical education and several roles at Penn in that role.

Rani, welcome to the program.

Rani Nandiwada, MD: Happy to be here again, Kendal.

Dr. Williams: I know you're running a course at the med school right now called Healthcare Systems. Can you tell us a little bit about what that's about?

Dr. Nandiwada: Yeah, I hope you know about it since you're one of my facilitators. We're really excited about it this year.

We've done a lot to revamp to try to help our medical students understand that, in order to really effectively create high quality patient care, that they have to understand how to integrate and actually utilize the system in a meaningful way. And so we're teaching them everything from patient safety to quality improvement, and really taking them on a journey to think about health disparities with interviewing stakeholders throughout our health system this year.

So we're really excited about what they're going to come up with.

Dr. Nandiwada: I am involved in that course. And when I'm involved, I often think that it would be a great thing for our attending level physicians to hear about. So maybe we'll bring you back and we'll have some discussions about the topics that we capture in that course.

But here to discuss with us about obesity is Dr. Anastassia Amaro.

Dr. Amaro is the Medical Director of Penn Metabolic Medicine. She's an endocrinologist by training with additional training in obesity. She's an Associate Professor of Medicine at Penn.

Welcome, Anastassia. Thank you so much for coming.

Anastassia Amaro, MD: Thank you for inviting me. I'm very excited to be here.

Dr. Williams: So we invited Anastassia to come because of her expertise in obesity. And of course, Rani and I both have had experience with this, although I have a lot of questions and I'm really looking forward to the content today.

Let's start with a more general perspective on obesity.

Obviously, it's more or less a modern problem and much of a modern disease. Much of modern disease has to do with what we eat and how much we eat. So let's just start with the basic questions to get the lay of the land.

Anastassia, how many of us are obese and why are we so obese as a culture?

Dr. Amaro: Excellent start.

So you realize we can take it into so many different directions from here. But let me remind us that CDC recently analyzed 2019 data. And according to that analysis, approximately 30% of US adults have BMI over 30 or obesity.

And as far as to the question of why, that's a lengthy discussion. And you definitely know how nature and nurture are important in the development of any chronic disease and especially obesity.

So we turn to genes. And heritability of obesity was actually studied really well here at Penn by Dr. Dr. Albert Stunkard in the '60s and '70s. And Adoption

Study of Human Obesity was published in New England Journal of Medicine in the early '80s.

To understand the influence of environment and genes on weight regulation, he studied over 500 adults who were adopted in early childhood. And he was able to show that the weight of adopted individuals was closely associated with the weight of their biological parents and not the adoptive parents.

There were additional twin studies that also show that heritability of obesity is around 60% to 70%. But heritability or, in other words changes in genes, in DNA sequence, cannot probably explain what we're seeing in recent decades. We're seeing explosion of obesity as an epidemic.

I personally think that we will be searching for answers in epigenetics.

So in contrast to genetic modifications, epigenetic changes are typically reversible and they refer to chemical modifications that occur in the absence of change to the DNA sequence. So in simple words, epigenetic mechanisms control how the genes work. And I think epigenetics is a field that is new, developing rapidly since 1980s. It will help us understand why we are developing obesity so rapidly.

And of course, I will spare some time and we'll not talk about obesogenic environment we are so well aware of.

Dr. Nandiwada: That was actually very deep and not where I expected to go with that, but it was super helpful to hear your perspective there.

On the day-to-day basis, the conversations that Kendal and I have with our patients, and I know you guys do in our metabolic clinic as well, is so much about the food and the choices that we make. And there's so much in the popular media that's there. I know when I'm talking to my patients, my general spiel is, you know, "Whatever you're doing, I want it to be sustainable. We're aiming for something healthy. And if you don't think you can do it for the next 20 years, we need to think about what parts of this makes sense in a long-term sustainable way."

But I'd love to hear your thoughts on some of the data or evidence behind some of the fads and trends that we've gone through over the years.

So starting out with low carb versus low fat, what are your thoughts as we think about how this impacts our weight and if this is something we should be

recommending more directly to our patients?

Dr. Amaro: Excellent question. And I think what you're doing in clinical practice is actually correct according to the evidence we currently have. And this may change. That will change. But at this point of time and the state of science, I think that's the most accurate answer.

So for example, we can still refer to a relatively old, but still gold standard kind of a study called Pounds Lost and published in New England Journal of Medicine. That was a two-year study in which all participants were divided into four groups and they were prescribed different macronutrient content. But they all were instructed to reduce calories by 750 kilocalories a day.

So short-term at one year and long-term weight losses did not differ significantly at any time among all four different diets with low carb, low fat, and some other two modifications. So pretty much, no matter how you reduce calories, you will see similar weight loss.

Dr. Nandiwada: That old adage, "Calories in, calories out equals weight off" is kind of what that study is showing us in some sense.

Dr. Amaro: That's exactly where that calorie in, calorie out came from and we keep repeating it, but the science is moving.

So maybe we're not matching the right diet to the right individual, so let's try to match it based on something. And we could match based on insulin resistance, for example, and we can take insulin levels and divide people into groups based on their insulin levels, the fasting insulin levels. Or we can try to match a diet based on genetic profile. And I'm not going to go into details, but there are certain snips that, in theory, predispose people to better utilization of fats or carbs.

So Christopher Gardner at Stanford and his group, if you're interested to follow high quality diet research, so they did those studies. So that study was called DIETFITS. And they took over 600 participants and followed them for 12 months, so this is one of the largest studies. And they did assign low fat and low carb diets to all of them. And then they looked at their insulin levels and divided them into subgroups based on insulin levels and divided them into groups based on their genetic profile.

At the end of the day, there was no difference between the groups regardless of the diet selected. And there was a huge interpersonal variability within each

group. So we still don't know how to match the right diet to the right person, unfortunately.

Dr. Williams: So we can say that calorie restriction, creating a calorie deficit every day of 500 to 750 is effective in weight loss. But what I'm also understanding you to say is there isn't any specific magic formula that works for everybody, that everybody is going to have to find their own way to achieve that. And to some degree, that's reflected in the various options that are out there in terms of the various programs and so forth.

Dr. Amaro: This is absolutely correct, that everybody would need to try probably different things to find the one that works for them as a sustainable tool.

And if we want to touch base on, for example, restricted feeding, so certain times of the day, it comes down to caloric restriction. So even if people are not instructed in clinical trials to restrict the calories, but they are instructed to restrict time during which they consume calories and calories are calculated at the end, we do see that they intuitively decreased caloric intake.

And in the smaller studies, those studies are difficult to carry out, but in the smaller studies and duration is a little shorter, usually 12 weeks or six months, we're seeing that there was no significant difference in weight loss between different types of restriction, time restriction versus calorie restriction.

Dr. Nandiwada: So with that, just to kind of extend on this idea of calorie restriction, I have a subset of patients who tell me that they are barely eating anything and that when they calorie track, they're like under 1500, under 1200 calories and can't lose weight. And when we kind of get to that point, I've sometimes suggested intermittent fasting because it's come up.

I don't know if it's the right answer or not, but almost kind of grasping at straws in terms of how to help them because we've done, you know, all of the calorie tracking apps and thought about these things. And I wanted to get your thoughts on, is that an actual effective step if, you know, as we're moving forward with trying to get them to their goals?

Dr. Amaro: I think yes. And I don't think I have a scientific answer, but I have more or less practical answer from our practice here at Penn Metabolic Medicine.

There are two things that we want to touch on here. So intermittent fasting, smaller studies on intermittent fasting didn't show much difference in weight loss with other approaches to restrict calories, yet it did show improvement in the fasting insulin levels or HOMA-IR, in insulin resistance, for example.

So it is possible that switching from one dietary approach to another dietary approach will produce some additional benefits that we are not accounting for when we're going with this blanket statement of caloric restriction.

The first observation was about metabolic adaptation and this is a real thing. So what we are seeing, usually it happens with weight loss that has been already sustained and people are asking why they are not losing more, why they are plateauing or why there is this yo-yo effect. It was first very well demonstrated in Biggest Losers.

If you remember the program, the participants were actually very carefully metabolically evaluated by different several research teams and the data was published.

So what was surprising to everybody that they lost weight, they went home, and their basal metabolic rate was measured and it was much lower than expected for the degree of weight loss. So that got us thinking about metabolic adaptation. So pretty much, hypothalamus takes up all the signals from periphery. And when we depart from the highest weight we've ever been, at some point, hypothalamus starts trying to bring us back where we were and start sending signals. And those signals could be increased hunger. So we definitely have evidence that hunger hormones go back up after first initial weight loss. And when we hit plateau, hunger hormones are back up and some other signals are likely resulting in a reduction in basal metabolic expenditure. That is when physical activity becomes extremely important.

So when people who have been successful in losing first five pounds or ideally 5%, it is very important to step up physical activity. Again, stepping up, but to a sustainable level to maintain the level of calorie burning that will not be maintained by their hypothalamus intuitively.

Dr. Williams: So their basal metabolic rate goes down as they lose weight. And in order to sort of keep up, they need to increase what their metabolic output is, you know, by increasing their activity or maintaining an increased level of activity. That makes a lot of sense.

Dr. Amaro: Yeah, you summarized it very nicely. That's absolutely correct.

Dr. Nandiwada: When thinking about the intermittent fasting part of this then, so kind of what you're saying is this is changing some of your body's signals because it's almost a different way that your body is seeing the food that you're eating and the calories.

Dr. Amaro: Probably, but would that example of a patient who cannot lose another pound even though keeping themselves quite restrictive on the diet, I think that's where physical activity is more important.

With intermittent fasting, it is possible we're changing signaling and it is possible we still don't fully understand how the signaling has been changed. So hopefully, there is more to it in the future.

Dr. Williams: I'm going to go off script here and ask a question because it came up to me in my practice.

I had a patient who I think genetically comes from that obese stock that you referred to. In this patient's incidence, it does not translate into hypertension, obesity or hyperlipidemia. The patient's really doing quite well, is very strongly trying to lose weight, but can't, but has a BMI that is not excessively high.

And so I found myself sitting there as this person was really struggling with trying to get their weight down and asking myself, "Well, maybe this is what their set weight should be. And since it's not translating to any of these comorbidities, how aggressive do I need to be about this?" Is that something that comes up?

Dr. Amaro: This is an excellent question and the topic of an ongoing debate about metabolically healthy obesity. So the question is how we define it. And the big question is if it's a true phenomenon that some people remain healthy despite gaining weight or we're just catching them at the point of time where they are still healthy and their metabolic disease is inevitably progressing. So a lot depends on definitions.

So if we define metabolically healthy obesity as absence of the metabolic syndrome, then probably about 40 to 50% of people we see in clinic could be metabolically healthy. But if we define metabolically healthy obesity as no features of metabolic syndrome and normal HOMA-IR, insulin resistance, for example, then that percentage of healthy individuals goes down to 5 to 10 in different studies.

We do not understand mechanisms responsible for preserved metabolic health

in people with metabolically healthy obesity, unfortunately. So to date, there have been attempts to, for example, demonstrate important differences in lifestyle factors, diet composition, physical activity and sleep between metabolically healthy and metabolically unhealthy individuals with obesity.

But however, there was no difference. So it doesn't really mean that lifestyle doesn't matter. It just means that our current design, we have limitations in how we study things, that we're not able to pick up the differences.

Dr. Williams: This is terrific. This is a level of discussion of obesity I've never had. I really appreciate it, Anastassia.

What I learned from our discussion just now is that there are a variety of approaches that a lot of these questions that I face and questions I have of my own care of patients are legitimate. They're either unknown or there's a great diversity.

But when a patient comes to you, they've often had already done some lifestyle interventions. Let's say we have a patient that does have some metabolic issues that need to be addressed related to the obesity. So they have the metabolic syndrome. They come to you. They've already tried various things. Now, you want to supervise their weight loss.

What are some of approaches, non-pharmacologic still, that you take in helping patients to lose weight who have already tried a bunch of things?

Dr. Amaro: I think listening is very important and I know our schedules come with constraints of time. But I think what's very important, especially in patients like you're describing who have tried a lot of things, it's very important to ask about those attempts and listen to people because usually people already know what's working and what's not working for them.

And they come to us for probably encouragement to do it over again or to investigate if there are any additional tools that we can supply them with. So that's how I think about the medications. I think about them as tools.

So I think everybody is so different and we don't have one-size-fits-all approach here at Penn Metabolic Medicine.

We really try to customize our approach to everybody. Some people actually do come for a one-time advice or annual advice, and then they go back to their devices, to their electronic gadgets, and they're doing great. And they come

back a year later to check on the new developments. Other people do well with frequent follow up and we try to create that frequent follow up and accountability by offering visits with physicians, nurse practitioner, and registered dietician.

Our nurse practitioner received additional training in behavioral health, so she is our surrogate, so to speak, for mental health as well.

Dr. Nandiwada: So within that arsenal of tools before we touch on medications, there's so many things out there and programs that are available.

I know after my second pregnancy, I did end up trying Weight Watchers and still to this day, know that my skinny chai latte from Starbucks is eight of my 24 Weight Watcher points, because that part has stuck with me.

But what are your thoughts on the programs like that? Do you recommend them or is it really just more of this personalized somebody has to try it, see if it works for them and go from there?

Dr. Amaro: So I think for me Weight Watchers does stand sort of by itself as a program, which has been quite well studied and has evidence behind it. And it is somewhat restrictive, but it's not excluding any groups of nutrients. So I do highly recommend Weight Watchers.

If patients are looking for additional support, you know, outside of our office that would provide them with accountability and tools to handle their nutrition, I do highly recommend Weight Watchers.

Dr. Nandiwada: What about Noom? Noom has been marketing like no other on all the social media. I think I get targeted by them every time I sign on to anything.

What are your thoughts on their take on using some of the psychology and more of the motivation part of it and the cognitive behavioral therapy into their approach?

Dr. Amaro: More of that is coming. I have no doubt we will be flooded with digital therapeutics. I think that's the word they're going to coin, digital therapies and digital therapeutics.

So it's coming and Noom is just in the beginning. And I have quite substantial positive feedback from my patients who decided to use Noom.

Noom was offered as part of I think Saxenda program. When people were going on Saxenda, they could sign up for Noom through Novo Nordisk Assistance Program. So that's how I got probably more people on Noom that could afford it at the time.

And what I am seeing again, this is not science, this is just what I'm seeing in clinical practice, it works really well and people really enjoy it for the first three to six months. And I think after that, people get the algorithms, they know what they're going to hear from it. They know the message they're going to see, so they tend to start ignoring it.

Dr. Nandiwada: Just as we have already talked about so much rich information, but I want to make sure we give medications the time that they deserve. I know that I am always a little hesitant with medications outside of a few that I'm really comfortable with.

So I'm really excited to hear about what you have to offer us. So, Kendal, I'm going to pass this on to you.

Dr. Williams: Yeah. And before we do that, you know, Anastassia, you had sent me a nice slide that summarized the medications, and I thought I'd just tell everybody about that now.

Medications go back to Orlistat really, appeared in 1999. It acted by reducing fat absorption. Then phentermine, Topiramate, came out in 2012. In that same year, the drug Contrave, which is a combo drug of both buproprion and naltrexone, came out as well as the drug you just mentioned, Saxenda, first diet-associated GLP-1 agonist that was injectable.

We talked a little bit about the GLP-1 agonist in our diabetes podcast. They clearly induce weight loss as well, in addition to controlling diabetes. And in the last couple years, we've seen newer ones.

Now, the one that everyone is most familiar with is Wegovy, which is semaglutide, also a GLP-1 agonist. Semaglutide is of course also, Ozempic, dosed for diabetes up to one milligram and as a weekly injectable. Wrgovy is the same drug dosed higher at 2.4 milligrams given weekly. And then we have phentermine, which has been on the market for a long time, is a generic drug, and I understand is the most commonly prescribed drug in the United States for weight loss, at least until recently.

So the first question is how are we choosing among these options?

Dr. Amaro: Excellent summary and excellent question.

In clinical practice, and at some degree it's unfortunate, but this is the first question I have, not directly to patients, but I look at their chart, is there insurance coverage. So if they have a plan that recognizes obesity as a disease and has coverage for pharmacotherapy of obesity, that really puts me in a very comfortable position where I can focus on this patient's physiology, biology, social situation, and select the best drug for them.

If and when pharmacotherapy of obesity is not covered, I have to be creative. Use maybe parts of the branded medications, use phentermine, which is generic, as you mentioned, or try to prescribe diabetes-approved medications, GLP-1s, in hopes to get at least some GLP action in this patient going.

So if we want to talk about approaching patients and selecting medications, I am biased. I am an endocrinologist. So there is no doubt GLP-1 is my favorite class of medications in the weight loss arena.

Dr. Nandiwada: It's my favorite too.

Dr. Amaro: I know and, see, we're not sponsored by Novo Nordisk or Lilly, right? So it's just those medications do work. And I feel they are safe. I have been watching their development. Actually, as a medical student, I was involved in the development in someone's lab of one of the first exenatide, one of the first GLP-1s. So they are dear to my heart. It's fantastic to see them in the market now.

So pretty much, it is not uncommon for me to think if this person is a candidate for GLP-1 receptor agonist and if it's covered as my first approach.

So if I detect that the patient has history of recurrent pancreatitis, for example, or as rare as it could be, but it happened in my practice, comes from a family with medullary thyroid cancer, then, you know, I keep going. Another reason not to prescribe GLP-1 receptor agonist would be if patient is absolutely opposed to injections and feels that it's very invasive as a first step. While we have semaglutide in the oral form approved for diabetes by the name, Rybelsus. And currently, oral semaglutide preparation is in clinical trials for obesity. So all that is going to come out soon, but not quite yet available. So then, I keep moving.

Bupropion and naltrexone, Contrave, is a combination drug that was actually

most frequently prescribed by primary care physicians in 2015 and '16, I think. Those are the years following the approval. The reason for it, there are several. One is it's not a controlled substance, so you don't have to have DEA and you didn't have to check, you know, safety and all that. So it's easy to prescribe it. You can send it electronically. It's a combination of two well-known components, buproprion and naltrexone. So it gave comfort to your primary care physicians.

And then actually the Contrave was in -- I'm saying was because the study didn't end well -- but Contrave was the first to actually demonstrate cardiovascular outcome trials in obesity. And their Kaplan-Meier curves started separating early. So they got so excited that they leaked the data into press. So that data was released prematurely. Their stocks went up. The popularity of medication went up immediately, but the study had to be terminated. So we never had a true cardiovascular outcome for Contrave.

But, you know, go back to earth and to my actual clinical practice, I prescribe Contrave. I'm not loving it. I see that many people discontinue it because of the very severe nausea, which is even more severe than with GLP-1 receptor agonist. That's one reason. And another reason I had to discontinue Contrave in several people because of transient, they say it's transient, but it can be very significant blood pressure elevation.

Dr. Williams: What about using buproprion itself? I was asked this question in preparation for this podcast. Someone asked me about phentermine, but buproprion itself, some physicians said they can't get anything approved, may just use Metformin to assist with weight loss.

What about using one of those other drugs?

Dr. Amaro: Very good question. So we're definitely going off the FDA approved recommendation, off-label use, but we do it. We definitely do it.

So Wellbutrin has been studied in smoking cessation, for example, and was quite successful. So we do prescribe it sometimes alone. I don't think I have a good evidence that it works really well, but it can help. So I definitely have a number of patients who find it quite instrumental.

Dr. Nandiwada: Kendal had also mentioned the phentermine. I struggle with the phentermine mean a lot. It makes me really uncomfortable. And I don't know if it's just because I don't use it a lot, but a lot of the side effects and other things make me worry.

How comfortable are you guys with using phentermine as, you know, a cheaper alternative for patients looking for a weight loss medication?

Dr. Amaro: Good question. And I can relate to your feelings actually.

So phentermine was approved in 1959 and has never been taken off market. So that alone speaks to its safety.

There are several problems with phentermine. And one of them is because the studies were carried out in the '50s and '60s, the longest one we have on phentermine alone was I think about three months, three or four months. And the number of subjects were about 60 in each group. And that was the study that led to FDA approval back then.

So it's formally approved for short-term use only. But we do have evidence on phentermine topiramate combination, Qsymia, that had been in clinical trials for two years straight. So I am comfortable extrapolating that data onto phentermine because the doses are very comparable and prescribing, keeping people on phenteramine for two years and sometimes even longer, as long as I have good grasp of the side effect profile.

So now, we come to side effect profile. Elevated heart rate, palpitations is probably the most prominent one. In some textbooks. It's not even listed as a side effect because it's sort of almost expected. It's a light stimulant, so you expect heart rate to go up a little bit. But you don't want it to be counterproductive, right? So if a person develops tachycardia and shortness of breath with physical activity, then clearly it's not going to be helpful for their long-term goals of achieving weight loss on the long run.

So the way we prescribe phentermine, we definitely ask for in-person visits. We're measure and document heart rate and blood pressure in the beginning. Some practices do EKG on everybody who they intend to prescribe phentermine for. We don't. We kind of rely on the information in Epic for the most part and usually people already have them. But yeah, we don't require a new EKG, so we'll document blood pressure, heart rate. We prescribe one month at a time, at least initially, and bring people in within that first prescription within the first four weeks. So we can document blood pressure, heart rate, and run the side effect profile in person in the first month.

If people are comfortable, no side effects, blood pressure and heart rate are stable, we can extend the prescription and send refills or we can increase the dose if needed. Doses available are now 8 milligrams, 15, 30 and 37.5. So

majority of our patients are probably maintained on 15 milligrams. I do see more side effects with 30 and higher.

And those side effects may develop over time. So they may do well in the beginning, but a year in, they start noticing that they can't fall asleep for example. So the side effects, yeah, it's important to monitor.

Dr. Nandiwada: And even with so much increased risks with the metabolic syndrome for cardiovascular disease, you're still okay as long as the phentermine is being monitored and you're watching their blood pressure and their heart rate prescribing them.

Dr. Amaro: I think so. I think so. I really wouldn't want to prescribe phentermine to people with known coronary artery disease with atherosclerosis. So anything that's going to put extra burden on the heart, you know, and increase the heart rate in the presence of suspected ischemia would be a definite contraindication.

But somebody maybe younger without documented heart disease, but controlled hypertension would be okay. Controlled hypertension would not be a contraindication in my mind. AFib and ischemia would be.

Dr. Williams: I want to skip back to the GLP-1 agonist and just follow up with one question because I was driving out of work today.

And I called my brother, who's a primary care physician. And he asked me what I was doing. And I said I'm doing this podcast. And we started talking. He said, "You just have to prescribe a GLP-1." They're very effective. He's in private practice primary care and he has a lot of experience with this. And I asked him about the affordability and he said, "Well, if I can't get Wegovy, they usually will take Ozempic. And you alluded to that earlier that even for weight loss, you can get Ozempic approved if you can't get Wegovy approved.

Is that what your experience is, Anastassia?

Dr. Amaro: I definitely meant exactly the same. But it's not exactly right that Ozempic may be approved for obesity. I am prescribing Ozempic without any diagnosis associated with it, so I'm taking chances that some plans may have it on their shortlist and will never ask for a proof of diabetes because when they come back to us and ask for medical records, it's a no go. So then sometimes I try to write appeals and induce peer to peer reviews. But oftentimes, it's a no go. So we're only hoping that they will not ask us for a proof of diabetes.

Dr. Williams: That's very interesting. I'm learning a lot from this podcast, but these are all the questions that others say are facing, and it's good to hear that you have these same experiences.

Dr. Amaro: So sorry. This is definitely going off label, going against recommendations and playing games with insurance companies.

Dr. Williams: Well, this is our life though as primary care doctors and so it's very helpful to hear you talk about, in a very pragmatic way, the struggles that you face. And so it validates many of the things that we experience.

I wanted to also touch base back on an issue. You had sent me a slide, Anastassia, of significant weight-loss targets as it pertains to the various comorbidities. Like how much weight do you need to lose in order to have an effect on diabetes, hyperlipidemia, degenerative joint disease and so forth? And it seemed to average about 10%.

So when you're starting a drug or you're, you know, supervising a weight loss program, is that where you start that you want to get them down 10%?

Dr. Amaro: I want them to get down to 10%, but I'll take 5%, 5% or more.

So, even if you go back to LookAhead trial, the changes in A1c, significant changes in diabetes and triglycerides, started at even 3% of weight loss. Again, we want it to be sustainable. So I'd say 5% to 10% would be already a success, 10% would be great. And now with semaglutide 2.4, I am hoping for 10% plus, I am hoping for 15%.

And that actually also links me to another important concept, which I think is helpful even when we talk to our patients, not just colleagues. We're kind of going away from the ideal body weight narrative. I no longer know what ideal body weight is, but we do know that losing 5% or more will likely help them metabolically. And for some people, it is a new concept and when they put that into numbers, that's not a huge weight loss. But I do consider it significance. I do consider it clinically significant.

Dr. Williams: Anastassia, this has been a great conversation and that's probably a good place to end in terms of what our goal should be.

I want to give an opportunity to both of you to end with some comments.

Rani, any closing thoughts?

Dr. Nandiwada: I mean, I think this has given me a lot of food for thought with my really challenging patients on when to switch strategies a little bit.

I have been, you know, playing with some of the medications and definitely do a lot of trying to catch two birds with one seed. That's my new thing instead of throwing rocks at birds, which I decided was not nice. And so I've been trying to catch multiple birds with one seed of like, "Oh, you have, you know, depression, let me try the buproprion," if there's not an anxiety component, or "You have diabetes, let me do the GLP-1."

I think you might've made me a little more comfortable with the phentermine. And now I'm also going to tell my mother-in-law who tells me that I need to eat breakfast, that I'm going to continue with my kid-induced intermittent fasting as I run out the door on my busy mornings, but this was so insightful. And thank you so much.

Dr. Amaro: Thank you. I really enjoyed your questions and they are really practical.

And you guys are doing so much work for our patients with obesity and such a great job. So thank you very much.

Dr. Williams Thank you both for being on the podcast. And everyone, we look forward to having you back next time.

Disclaimer: Please note that this podcast is for educational purposes only. For specific questions, please contact your physician. And if an emergency, please call 911 or go to the nearest emergency department.