Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/why-weight-loss-should-be-the-primary-goal-of-treatment-in-type-2-diabetes-care/14130/

Released: 09/15/2022
Valid until: 09/15/2023
Time needed to complete: 30 minutes

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Why Weight Loss Should Be the Primary Goal of Treatment in Type 2 Diabetes Care

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Why Weight Loss Should Be the Primary Goal of Treatment in Type 2 Diabetes Care!” is provided by Prova Education.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Micro Course 1: Obesity and Weight Loss as a T2D Goal

Dr. Ryan:
Dropping 15% or more of body weight has a greater disease-modifying effect than any other glucose-lowering intervention you can implement. So why isn’t weight loss our primary goal of treatment?

This is CME on ReachMD, and we’re looking at some very important questions surrounding type 2 diabetes and weight loss today. I am Donna Ryan, professor emeritus at Pennington Biomedical Research Center. And…

Dr. Frias:
I’m Juan Frias. I am an endocrinologist and Medical Director of Velocity Clinical Research in Los Angeles, California.

Dr. Ryan:
Let’s get right to it, Juan. Why haven’t we been more focused on treating obesity and weight loss earlier in patients with type 2 diabetes?

Dr. Frias:
Yeah, hi, Donna. This is an important question, and I think it’s multifactorial, really, in nature. In general, we have not recognized obesity as a disease, but rather as a risk factor, and treated many of the manifestations of obesity, such as dysglycemia, hypertension, dyslipidemia. But I think also, very importantly, we haven’t had the tools until now. So we’ve had medications that can cause modest weight reduction, oftentimes with side effects, but now, really, we’ve come into an era where we have medications that can not only significantly improve glucose, but can do it with clinically meaningful weight loss and can do so safely and with good tolerability.

So I’ll ask you, Donna, what can we do as clinicians, really, to put this, that is weight loss, as one of the top priorities in treating our patients with type 2 diabetes?

Dr. Ryan:
No, I think everybody recognizes that obesity and excess adiposity and especially visceral adiposity is a big driver of type 2 diabetes and lots of cardiometabolic risk. But I think the reason we haven’t really put so much emphasis on weight management, is we haven’t had the tools. It’s been very difficult for us to achieve and sustain weight loss with lifestyle intervention in our medical practices. So I think that the demonstration of 15 kg weight loss in the DiRECT study, putting diabetes in remission for patients who have only had diabetes for a short period of time, has made a huge difference. People are interested in trying to move diabetes upstream. You know, when we lose weight successfully, we’re not just improving glycemia. We’re improving dyslipidemia; we’re improving hypertension; we’re improving

that pro-inflammatory environment. And so we're really producing benefits that will have long-lasting results across the course of a life span.

Dr. Frias:
Yeah, no, I absolutely agree. And as with any chronic disease, and I think it's been an issue, certainly, in type 2 diabetes, we need to really avoid therapeutic inertia, and if we see an issue and if we see, you know, some aspect of the patient that is not achieving target, whether it's their glucose or their body weight, we do need to take action and start addressing this as soon as possible.

Dr. Ryan:
Yeah, for our patients who are having problems with excess abnormal body weight, we need to put weight management front and center.

That's it for this course, but please join us in one of our other segments to learn more about improving outcomes in type 2 diabetes through effective weight loss strategies.

Micro Course 2: What You Don't Know About Obesity and T2D

Dr. Frias:
Most type 2 diabetes guidelines don't adequately address the root of the problem, which is oftentimes obesity. In this course, we'll look at how we can change that and motivate our patients to go beyond lifestyle intervention.

So, Donna, I'll start with a question: Why does lifestyle modification – diet, physical activity – often not work in our patients with type 2 diabetes?

Dr. Ryan:
Well, that is the big question, Juan. You know, I think to understand obesity, you have to understand it as a disease, and you have to understand that this body defends its highest fat mass. So when we try to lose weight, it is much more than just a matter of willpower. It has to do with biologic adaptations that work through hunger and work through lack of satiety and increase in metabolic – decreasing metabolic rate. It's these biologic adaptations that make it difficult to lose weight, and really promote weight gain once we're successful in losing weight. You know, all of our lifestyle modification programs that have been implemented, like DPP [Diabetes Prevention Program] and Look Ahead, these are a lot of hard work for patients. That biology is very difficult to overcome with willpower alone. Many of our patients need help. They need medications that work through appetite to help them better adhere to their lifestyle intentions.

Dr. Frias:
Yeah, absolutely. I mean, there really is a set point, if you will, which the body kind of goes back towards which, as you mentioned, make it very difficult for patients to attain – it's hard enough – but then to maintain or sustain those levels of weight reduction that are clinically meaningful are clearly very difficult for patients.

Dr. Ryan:
Yeah, we need to stop blaming our patients. We need to start helping our patients. And we need to overcome our prejudices about medications to help patients lose weight. It's absolutely essential to long-term weight loss success.

I think we're also lucky in that, in managing our diabetes patients, we have lots of choices now in medications that can help patients lose weight at the same time they're helping achieve better glycemic control.

Dr. Frias:
Absolutely. So, you know, today, I agree. In fact, I'm thinking back for when I graduated from medical school. Through a lot of my medical training, the only medications we had to treat patients with diabetes actually caused weight gain, so sulfonylureas, insulin, which is clearly very important, the thiazolidinediones, you know, metformin, and the DPP-4 inhibitors being weight-neutral.

But today, we've really entered, sort of, a new era, if you will, with incretin-based therapies, so selective GLP-1 receptor agonists that not only improve glycemia but do so with clinically significant weight reduction and with improvement in cardiovascular risk, as well, if we look at the long-term cardiovascular outcomes trials with these agents. And sort of the next step, if you will, are the unimolecular multi-agonists. So these are, for example, the dual agonist tirzepatide, which has recently launched in the United States, which is an agonist of both the GIP and the GLP-1 receptors, so both incretin hormones, and as we'll discuss further later, has even more glucose-lowering and weight-lowering capacity than the selective GLP-1 receptor agonists. So we've really moved into an era now where we have medications that not only improve glucose, but also body weight – this includes the SGLT2 inhibitors – and have significant cardiorenal protective effects, and these really are the agents that we should be starting our patients on, particularly our patients who are suffering from overweight or obesity.

Dr. Ryan:
Yeah, and you know, I think all too often we get into a rut. I'll start with metformin, then I'll add a DPP-4 inhibitor. Very comfortable with that. But look, we need to look at these newer medications, and we need to be thinking about how we can bring up the topic of weight management with our patients. So it's really a call to action.

Dr. Frias:
Absolutely.

So that's it for this course. Please join us for one of our other chapters, where we'll continue discussing improving outcomes in type 2 diabetes through weight reduction strategies. Thank you.

Micro Course 3: Updates in Treatment of Obesity in T2D

Dr. Ryan:
Most weight loss attempts usually plateau and are then followed by weight gain over the next 1 to 3 years. How do we create a medication treatment plan that fosters sustainable weight loss over time?

We've had several medications approved in recent years, such as liraglutide, and semaglutide, and most recently, tirzepatide. Juan, what makes these medications different?

Dr. Frias:
Yeah, so these medications, unlike medications that we've had previously that may improve glycemic control but do so either with weight gain or weight-neutral, these medications improve glycemic control and also result in significant weight loss. The GLP-1 receptor agonists, as you mentioned, like liraglutide, semaglutide, dulaglutide – these are drugs that we're now referring to as selective GLP-1 receptor agonists – act in sort of a multitude of ways. They enhance insulin secretion from the beta cell. They reduce glucagon secretion from the alpha cell. And very importantly, they act centrally in areas of the brain that are very important for energy balance, so for appetite satiety, to reduce appetite and lead to significant weight loss.

And where we're moving now are to multi-agonists. And this is what tirzepatide is. It's a single molecule that has agonist activity of both the GIP and GLP-1 receptors, so these are the 2 incretin hormones. And it sort of enhances the action of the drug, if you will, by binding to and stimulating both of these hormones at the level of the beta cell. So it enhances first- and second-phase insulin secretion compared to the selective GLP-1 receptor agonists. It also reduces glucagon, and again, there are also GIP receptors in areas of the brain that are critical to energy balance and even to energy expenditure, so the other side of the equation, if you will. So by having both of these agonized or stimulated, both of these receptors, we get additional efficacy, both from a glycemic and a weight loss perspective. So these are very important medications to consider and consider early in our patients with type 2 diabetes that need weight loss, which is the vast majority of patients, unfortunately, with this disease.

Dr. Ryan:
You know, Juan, one thing about these medications that's different. You know, I've been in the weight loss game for a long time, and with lifestyle intervention, we usually see a plateau after about 6 months. And the same thing is true for these older medications that we used for weight management. But with these GLP-1 receptor agonists, and the GLP-1 GIP agonists, it's interesting you get longer duration of weight loss, out to more than a year. So it's different, and it's something that I think is producing not only more weight loss, but weight loss over a longer period of time. We're going to have to get used to that. But look, our patients are excited about these medications. I don't know about you, but people are asking me about these medications.

Dr. Frias:
No, absolutely, and I completely agree with you, and if you look at the data, I mean, at out to 52 weeks before the plateau, I think patients who have used these medications and who are having this degree of weight loss, it's sort of a very positive cycle, if you will. When they see success they get even more, sort of, excited and enthused about the important dietary component and lifestyle changes and physical activity as well. So it's a very positive cycle, if you will, and I think it's important.

But let me ask you, Donna, when you think about incorporating these agents in your clinical practice with patients, who is the ideal patient in your mind, and when should you start treatment? When is the ideal time to start treatment in patients with these agents?

Dr. Ryan:
So for me, it's younger patients. It's patients who have less of a long-term history with diabetes, who have less complicated diabetes, and for patients who are really looking for that change in lifestyle.

And I really want to bring out the point about our guidelines. You know, the ADA Standards of Medical Care document that's produced every year, they've been interested in weight-centric approaches for a while, and they've wanted us to prescribe the medications that

have a profile that makes it more likely to produce weight loss and less likely to produce weight gain. But this year, for the first time, the 2022 guidelines really put at the top of the list the GLP-1 receptor agonists as preferable for treating patients early in the course of disease, when weight loss is a major consideration. So it's not either/or SGLT2 inhibitors or GLP-1 RAs. No. It's GLP-1 RAs are preferable.

Dr. Frias:
Right. No, that's a great point, and I think, again, it goes to avoiding therapeutic inertia and just using the agents we have and using them appropriately but aggressively in these patients.

Dr. Ryan:
Yeah, so Juan, how do we actually go about deciding on the appropriate weight loss and glucose-lowering combination of therapies without real guidance available yet from the guidelines?

Dr. Frias:
Clearly, the GLP-1 receptor agonists and the SGLT2 inhibitors are critically important in patients with established atherosclerotic cardiovascular disease with heart failure, primarily the SGLT2 inhibitors with chronic kidney disease, and most patients are overweight or obese, so even if they don't have those diseases or very high risk factors for heart disease, more than likely they need some weight loss. One of the key principles here is we need to avoid medications that cause weight gain, to the extent possible. So our first injectable agent should definitely be a GLP-1 receptor agonist or a dual agonist, such as tirzepatide, in patients who need injectable therapy – or even earlier as opposed to initiating insulin therapy first. And again, as we've been talking about, we need to do this as early as possible in the course of therapy and oftentimes even independent of the hemoglobin A1c depending on the patient's risk factors.

Dr. Ryan:
We've recently had some great clinical research studies that have been published, Juan. What is your takeaway from all of the trials of tirzepatide and semaglutide? How are you using that data in your practice?

Dr. Frias:
Yeah, so the semaglutide trial, the sustained program, I mean, this is a very extensive clinical research program; the studies continue. And really, what we've seen with this medication is unsurpassed, both A1c and weight control, for a selective GLP-1 receptor agonist. I think what's important, and what I look at oftentimes in studies, is what proportion of patients achieve important and clinically meaningful targets as opposed to just the absolute reduction. And with semaglutide, at the 1-mg dose, you know, up to 80% of patients achieving an A1c of less than 7%, and, you know, anywhere from 60%-70% of patients achieving greater than or equal to 5% weight loss – even at 40 weeks, where weight is continuing to decline. And then the SURPASS trial is now looking at tirzepatide, so the dual agonists of GIP and GLP-1, specifically in the SURPASS-2 study, which was a study that looked at tirzepatide versus semaglutide. We saw even greater improvement in hemoglobin A1c with tirzepatide versus the 1-mg dose of semaglutide and greater reduction in body weight as well. And with both of these medications, improvements in blood pressure, very positive improvements with respect to lipids as well, having clearly important, tolerable, medications. You do have the side effect with both the selective GLP-1 receptor agonists and the dual agonists – very comparable side effect profile, of gastrointestinal side effects – but most of these are mild to moderate in severity, occur during dose escalation, so early in the course of therapy, and then diminish and can generally – not always – but generally be treated with dietary modifications and making sure that patients are aware that they may have these symptoms and that more than likely they'll be temporary.

Dr. Ryan:
Yeah, those tolerability data really impress me and make me less afraid of nausea and vomiting in patients. You know, it's not every patient gets it. When they do get it, it's usually mild or moderate. It's unusual for it to be severe. And it's mostly occurring in those periods of dose escalation or right afterwards. So it gives you a lot of comfort in prescribing these drugs.

So that's a wrap on this chapter, but please join us for one of our other micro courses, to learn more about improving outcomes in type 2 diabetes through effective weight loss strategies.

Micro Course 4: Sustaining Weight Loss in Type 2 Diabetes

Dr. Frias:
Designing a pharmacologic-based approach to weight loss in our patients with type 2 diabetes is not common for all of us, so how we generate a plan for weight loss, for maintaining glycemic control, for reducing risk of complications, and how can we support our patients, not only to attain, but to maintain this level of weight loss is what we'll be discussing in this chapter.

So let's start with goal setting. Donna, what realistic expectations do you give to your patients, with respect to weight loss target, who are initiating pharmacotherapy?

Dr. Ryan:
Yeah, so goal setting and self-monitoring to reach that goal is fundamental to any behavioral program. And so, you know, I think about goal setting in percentages, but my patients don't. My patients think in pounds. So, you know, I know that with just 5% weight loss, I can get a lot of improvement. With 10% weight loss, I can virtually prevent progression of prediabetes to type 2 diabetes. And with 15% weight loss, I can usually get patients who have some reserve – beta cell reserve – I can usually get those patients in remission for their type 2 diabetes, so into normoglycemia. That's a wonderful thing. So, you know, the target always comes with a time. The target I like is 10% at 6 months, and then if I'm using one of those medications that has a longer duration of weight loss efficacy, I'll aim for 15% at 1 year. But these are ambitious targets, but most of the time our patients can achieve it, especially if they're taking one of the newer medications that has a more favorable profile, like semaglutide or tirzepatide. So I calculate what 10% is in terms of pounds, and then I talk about that to the patient.

Dr. Frias:
I think, you know, one of the key things is just giving them a target and making sure it's a realistic target for them so they don't feel bad if they don't meet that target, and, like you mentioned, monitoring it is critically important as well.

Dr. Ryan:
You know, I think it's not habitual for us to be talking about weight with our patients. It's a sensitive subject, but I think if we always tie weight to health, we'll be on firm ground with our patients. You know, the single best thing our patients can do to improve their control of glycemia, blood pressure and lipids is to make some changes in their lifestyle. It's not really a judgment about how patients look. Weight management is all about the patient's health.

Dr. Frias:
Absolutely. So, Donna, let me ask you, when you have gotten a patient to lose, let's say, 10 or more percent body weight in a 6-month period, what do you do to then motivate them, or how do you maintain this weight loss over time, which is obviously critically important to the long-term benefits of the weight loss?

Dr. Ryan:
Well, luckily with our newer antidiabetic GLP-1 RAs, like tirzepatide and semaglutide, they're going to continue losing weight. They're going to continue losing weight out to a little longer than a year. About 60, maybe even up to 70 weeks. So we'll see some continued weight loss, and that's a good thing. But if patients do plateau, if they're on one of our older medications or if they're on lifestyle alone, then I think the emphasis shifts. You know, when we're trying to get people to lose weight, it's mostly about food intake and the diet. But when we're trying to get people to maintain that lost weight, the emphasis shifts, and it shifts more to physical activity. And the things we know that seem to work best in weight loss maintenance are increasing that physical activity.

Really, we want people up to about 225 minutes of physical activity a week. It's a lot of physical activity, but it's worth it in terms of weight loss maintenance.

Dr. Frias:
Yeah, absolutely, and I think it's important also to mention that these medications should be continued long term. So even if the patient plateaus, you know, we've seen from clinical trials, if the medications are withdrawn, there will generally be another, you know, a rise back to baseline. Maybe not all the way back to baseline, but certainly there will be an increase in body weight. So this is a chronic disease, and these medications generally need to be used chronically.

So this has been a great conversation with you, Donna. Before we wrap it up, though, any final takeaways that you'd like to give us for the audience?

Dr. Ryan:
I think that raising the topic of weight management is something that everyone needs to do in patients with type 2 diabetes. As we started this program, we talked about it having such a positive effect on the course of type 2 diabetes. We should not be hesitant to do this. As long as we link weight to health, we're on firm ground. We're not judging our patients about their weight. What we're offering is changes that can produce some weight loss that will help patients feel better, be healthier, and live longer.

Dr. Frias:
Yeah, that's terrific. I'm going to kind of paraphrase something you said before, which I think is just an absolutely key message here, is that by treating weight, and by lowering weight, not only are we improving glucose, but many other – and I won't even call them comorbidities – many of these are complications of obesity. This would be hypertension, dyslipidemia, obstructive sleep apnea, osteoarthritis, nonalcoholic fatty liver disease. So you really are treating sort of the root, going back to when we started this segment, the root of many of the issues the patients have including the diabetes. So critically important to do it, and we have the agents today.

So unfortunately, that's all the time we have today. I want to thank you in the audience for listening, and thank you very much, Donna – Professor Donna Ryan – for sharing your valuable insights and experience. It was phenomenal exploring this topic with you. Thank you very much.

Dr. Ryan:
Thank you.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Prova Education.
To receive your free CME credit, or to download this activity, go to ReachMD.com/Prova. Thank you for listening.