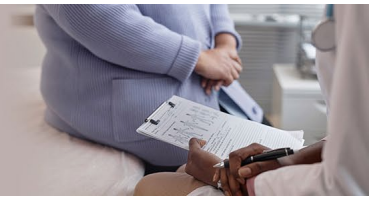
Addressing Misconceptions in Obesity: Evidence-Based Treatment Approaches



Editor's Note: This is a transcript of an online course released in July 2025. It has been edited for clarity. To obtain credit for participation, CLICK HERE.

Introduction

Dr. Apovian: Some of the key milestones in recognizing—and this recognition occurred over the course of years at this point—were in the 1970s, and prior to that, obesity was not considered a disease, and publications indicated that. To a later one—about 30-40 years later—with the Centers for Medicare and Medicaid Services (CMS) in 2004 removing "not a disease," verbiage, but not going as far as saying it *is* a disease to finally, in 2013, the American Medical Association (AMA), the first medical body—we certainly had the Obesity Society recognizing obesity to be a disease—but the AMA proclaimed that obesity is a disease, and then following that, 4 years later, the World Obesity Federation confirming that, and adding to this that obesity is a chronic, relapsing, progressive disease process.

We do have diagnostic codes to help us with the diagnosis and billing. They're not perfect, so such terms as "morbid obesity" is still part of the diagnostic coding system. We don't like to use the term "morbid." We prefer "severe" or "extreme obesity" indicating a body mass index (BMI) typically over 40 kg/m^2. There are BMI categories, and you can code obesity based on the BMI and, unfortunately, typical obesity is coded as "obesity due to excess calories." That is certainly debatable, but that's the coding that is still part of our practice and is in the process of being reevaluated.

When we think about treating with obesity medications, it certainly has recently become much more prevalent for primary care physicians and specialists in obesity medicine and other specialties, to treat with our newer glucagon-like peptide-1 (GLP-1) medications, called nutrient-stimulated hormone (NuSH) therapies, because of the efficacy of these medications, because they are agonists of gut hormones that are naturally secreted by the body and because of their safety compared with prior medications that were approved in—at least the United States—starting in 1959.

However, this piece of literature that in fact I was part of, looked at a very recent analysis of patients in our Mass General Brigham Healthcare System who were treated with obesity medications between January of 2018 to January of 2023, and arguably that those dates were really the advent of FDA-approved GLP-1s. However, if we look at that data, a very small number of patients who were eligible for an antiobesity medication because their BMI was over 30 kg/m^2 or over 27 kg/m^2 with a condition, of those 45% of 2.4 million people, only 1.4% were prescribed any FDA-approved obesity medication. And this is really a symptom of the inertia. Now, if we looked at this database again in 2025, we would see something a little bit different, an increase in prescriptions, but at this time, we had some of these medications available and very few patients were prescribed.

How do we combat clinical inertia? There's perception, knowledge, and attitude. The stigma of obesity still remains, even though most clinicians and healthcare providers and patients understand that obesity is a disease. There's still a lot of stigma and we face it every single day. So, there needs to be better recognition of the multifactorial etiology of obesity and avoiding stigmatizing terminology, such as "morbid obesity." There needs to be knowledge that the recognition of obesity as a chronic, progressive disease should be backed by the science that illuminates why it's a disease. And then the attitudes and biases of clinicians and patients, recognition of the stereotypes and negative assumptions about individuals with obesity.

Dr. Kushner: I think that was a great overview. As you're talking, I'm reminded of what a new disease obesity is, and the comparison we often make is to diabetes. Almost every primary care clinician today will treat patients with diabetes in their office and only refer out in complicated cases. Obesity is a new condition, and you highlighted that timeline, it doesn't go back that far, and there's been such a rapid evolution in knowledge about the biology and science and practice of obesity that I think it can still be overwhelming for primary care clinicians to get their head around this. I think it's often a heavy lift for them who have not been keeping up in the literature on obesity. I'm hoping that these modules will help them get a better understanding of obesity and get more involved proactively to identify and treat patients who present with obesity.

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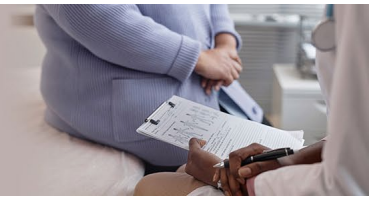


Purpose and Overview

Dr. Kushner: In recent years, the Obesity Medicine Association or OMA has created a series of clinical practice statements, one of which is the Thirty Obesity Myths, Misunderstandings and/or Oversimplifications. The purpose of this accredited activity is to help clinicians educate patients and respond to myths and misconceptions regarding obesity and treatment options as it closely aligns with this clinical practice statement. This publication I'm referring to is a peer-reviewed clinical practice statement that was developed and based on available published literature and clinical perspectives of the OMA authors. OMA does note that some patients as well as clinicians may not agree with all of these myths that we're going to be talking about due to multiple reasons, such as differences in individual and clinical practice experiences, differences in interpretation of existing science, emerging, emergence of new science, business interests, cultural norms and there's other global beliefs as well. There is also a companion social media resource video blog series that's aligned with this educational activity that is geared towards patients to address myths and misconceptions about obesity and treatment options. So, I think this is a good way for both Dr. Apovian and me to go over the myths or misunderstanding and to give some clarity around the science and knowledge behind these myths.

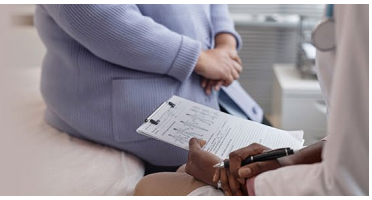
Obesity as a Serious, Chronic Disease

Dr. Kushner: You know, the reason that obesity is, in fact, a disease is because it fulfills the criteria that we commonly use to define any disease, and Dr. Apovian gave that definition of obesity early on. To remind everyone, a disease is defined as a disorder or abnormal condition of a body, organ system, or mind that impairs normal functioning and this is typically manifested by distinguishing signs and symptoms. And, as mentioned, OMA does define obesity as a chronic, progressive, relapsing, and treatable multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, or psychosocial health consequences. So, that is a mouthful, as you said, Caroline. In short, it's an abnormal bodily function that causes harm to the body, and really obesity does meet all of those criteria.

Other key features of obesity include its multiple causes, such as genetics, inflammation, medication adverse effects, nutritional abnormalities, and certainly an unfavorable environment and other behavioral factors. And other aspects. We know that it's managed from primary care all the way to specialists and includes a multidisciplinary team, and there's multiple modalities of treatment with a wide variety of interventions, beginning with lifestyle management of nutrition, physical activity and behavioral modification, working up to other opportunities and approaches, like medication, surgery, and including education as well.

There are complex mechanisms and Dr. Apovian mentioned a little bit about the complexity, but we are understanding more and more in the recent past about energy-bound regulation and dysregulation in obesity where signals arise both from adipose tissue and the gut, both of them sending appetitive messages to the brain.

Pathophysiology Animation Voiceover: Body weight is regulated through complex communication between the gut, adipose tissue and brain. There are various hormonal and neurologic pathways that mediate energy intake and expenditure. Chemoreceptors and mechanoreceptors in the stomach and intestines detect food intake and activate enteroendocrine cells to release neurotransmitters that regulate food through enteric and vagal neural networks. Some gut hormones, such as ghrelin, are orexigenic and act on neurons in the arcuate nucleus of the hypothalamus to release neuropeptides, such as agouti-related peptide (AgRP) and neuropeptide Y (NPY), that function to stimulate appetite. Other gut hormones are anorexigenic in nature and inhibit food intake. In the intestine, these include peptide tyrosine tyrosine (PYY), glucagon-like peptide 1 (GLP-1), glucose-dependent insulinotropic peptide (GIP), oxyntomodulin (OXM), cholecystokinin (CCK), and amylin. The pancreas also plays a crucial anorexigenic role by producing pancreatic polypeptide (PP) and insulin in response to food intake. Insulin acts via vagal afferents to the brain to inhibit food intake. Insulin also acts in conjunction with leptin and adiponectin, 2 hormones produced by adipose tissue, that stimulate neurons in the hypothalamus in the brain. Adiponectin and leptin increase energy expenditure, while leptin also inhibits appetite. Collectively, hormones from the gut and adipose tissue act directly on the brain through vagal afferent fibers and



indirectly through various neurohormones via a complex network to regulate body weight.

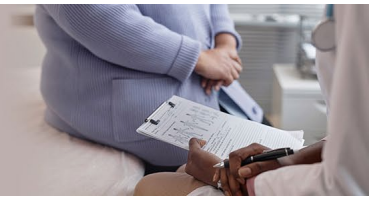
Dr. Kushner: It's also important to recognize the multifactorial etiology of obesity. There's many contributors that account for variations in individual presentations and responses to lifestyle and medical intervention. Excess body fat is determined in part by genetic and epigenetic errors, hypothalamic inflammation or, in some cases, injury, adverse reactions to medications, we call weight-gaining side effects, nutritional and energy imbalance as well as unfavorable environmental factors now that we are all living every day in modern society. It's also important to keep in mind that these multifactorial determinants are present, and we need to think about that when we treat each of our patients.

We also know that adipocytes and adipose tissue dysfunction contributes to metabolic disease and obesity is associated with a wide variety of complications and comorbidities. After all, that is often what we are thinking about when we see patients in the office and that's often what brings patients in to see us is a complication or comorbidity. So, let me give you some examples. The chronic, low-grade inflammation and dyslipidemia profile associated with obesity will often lead to vascular dysfunction and impaired fibrinolysis, increased risk for cardiovascular disease including stroke and venothrombotic events. We know that the chronic inflammatory state also contributes to insulin resistance. That's a common presentation with the development of prediabetes, type 2 diabetes, and metabolic syndrome. Obesity-associated deposition of fat around the upper airway and the thorax may affect pharyngeal lumen size and reduces chest compliance, often contributing to obstructive sleep apnea. Development of certain cancers have been related to excess levels of fat and hormonal dysregulation, particularly the sex hormones. We also know that increased free fatty acids and fat storage in the liver, along with insulin resistance and inflammation, increases the risk of development of metabolic dysfunction-associated fatty liver disease or MASLD. And finally, increased mechanical load on joints, particularly those of the weight-bearing joints like the knees and the hips and lower spine, along with fatty infiltration and inflammation leads to increased risk of osteoarthritis.

Dr. Apovian: This is a very, very comprehensive look at how excess fat tissue can cause other complications and I just want to point out that, and we know this, not everyone who develops obesity, even at very high BMIs, develop every single one of these complications and understanding who does and who doesn't is the source of much research, but certainly we think it's genetic predisposition, certainly genetic predisposition in this environment to store fat tissue and once it's stored, there's a genetic predisposition to develop the inflammation that then leads to all of these complications. So, a lot of this has to do with genetics as well as epigenetics and the epigenetics is really the reason why we've seen this prevalence of obesity increase over the past 50, 60 years. There must be something in the environment. What it is, it hasn't been rigorously proven yet, but we do think it has to do with high-fat, high-sugar foods, ultraprocessed foods, maybe a combination of that, something else in the environment and more sedentary lifestyle. The jury's still out on that, but whatever it is, we know that there are people who have a more genetic predisposition to be affected by the environment and people who have less of a genetic disposition. And even people who, with high levels of BMI do not seem to develop let's say diabetes and cancer and that, of course, that's also genetically predetermined. So, there's much to learn about this, but what we know now is that this is a chronic disease.

Dr. Kushner: I want to come back to one more comment you said earlier, Caroline, about the fact that individuals may not develop all these problems. If we go back to the definition, which is obesity is excess body fat that poses a risk to your health, that risk can be in the form of 200 or more complications or comorbidities. So, the key role of the primary care clinician is to take a good history, good physical examination, look for signs and symptoms of obesity and those comorbidities and complications and to intervene early.

Many patients believe that obesity is due to a low metabolism, however an increase in body tissue, particularly visceral organs, in patients with obesity is what increases resting metabolic rate. That's really what metabolism is. And, in fact, individuals who present with obesity typically have a higher resting metabolic rate because of the increased muscle mass and organ size. Now, there's many factors that go into metabolic rate that include genetics, which we were just talking about, age, and sex.



When measured by direct or indirect calorimetry or estimated by a formula, like Harris-Benedict or Mifflin St. Jeor, and then compared to control groups, individuals with apparent diet-resistant obesity actually don't have a low metabolism, but what they do have is an inappropriate sense of how much they're eating, most commonly, and their metabolism is actually normal or even higher. And, of course, metabolism is not just resting metabolic rate. It's also sleeping and total energy expenditure.

We know there is a variance that exists among individuals regarding resting metabolic rate or RMR. RMR is increased among younger individuals and is greater among males vs females, again primarily due to the increase in lean body mass. Obesity may also increase resting metabolic rate, largely due, as I said and to reiterate, the increased lean body mass that includes muscle mass and visceral organs. Now beyond RMR, other common contributors to the variance in total energy expenditure include non-exercise activity thermogenesis, which has been coined NEAT, overall physical activity and diet-induced thermogenesis. Now, regarding diet-induced thermogenesis, one must consider the thermic effect of food which is the energy required to digest, absorb, and metabolize the macronutrients for storage.

There are some key takeaways from this module. One is that obesity is common, it's a chronic disease with complex pathophysiology and multifactorial etiology. I don't think a primary care clinician needs to memorize the pathways that regulate energy disruption in the brain and so forth, but we do need to know that there's this gut-brain and adipose-brain axis in which signals come in and our current thinking is there's a dysregulation in interpreting those signals which may lead to changes in appetite regulation, hunger, fullness, and so forth. And we also know that obesity is an independent risk factor for many diseases, including cancers, cardiovascular disease and stroke, MASLD which we talked about, osteoarthritis, obstructive sleep apnea, and type 2 diabetes, among many, many other complications and comorbidities.

Dr. Apovian: I just want to go back to the idea of total energy expenditure a bit, which is made up of resting energy expenditure which you brilliantly spoke about and the thermic effect of food and nonresting energy expenditure. And there's something called metabolic adaptation or metabolic flexibility that we're really learning about and some of this has to do with the times in people's lives where they may develop obesity, again in this environment. And it seems that the body changes, changes metabolically in response to whatever is going on in the environment and we have colleagues who have done studies showing that when you overfeed patients, overfeeding beyond, you take patients into the lab and feed them a breakfast and then you overfeed IV, what we find is that people with obesity seem to store more of that overfed carbohydrate into de novo lipogenesis and leans who are overfed tend to get rid of those extra calories, more often than those with obesity, as, it's called proton leaks in the mitochondria.

Dr. Kushner: One more point, it reinforces the underlying biology of developing and maintaining obesity or worsening obesity rather than a character fault or someone's poor decision-making or low motivation. So, the plot thickens. There's more and more to learn about the biology, as you just said so beautifully, and that's a very important take-home message.

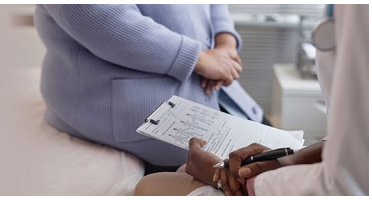
Screening and Diagnosis

Dr. Apovian: A misconception is that obesity is classified solely on the BMI, the body mass index. Well, the body mass index is really a very convenient way of measuring excess fat tissue and it's an equation that takes into account the height and weight and surface area, but it certainly isn't perfect.

In addition to the BMI, we can utilize another vital sign called the waist circumference. The waist circumference is a classification that can determine abdominal obesity and this is included in the diagnostic criteria for metabolic syndrome. So, if your waist circumference is over 35 inches and you're a female or over 40 inches and you're a male, you are considered to have a higher risk of development of the comorbidities of obesity.

We also look at the percent body fat. So, how do you determine percent body fat? You can assess percent body fat by dual energy x-ray absorptiometry or DEXA.

BMI may not reflect adiposity in patients with increased or decreased muscle mass, as determined by an elite athlete, for example, with increased muscle mass, but also patients with sarcopenia, decreased muscle mass, as they get older.



Males vs females, even though we have the same classification system for BMI between males and females, including postmenopausal women, we do tend to see that males have higher BMIs than females because males have more muscle mass and that doesn't necessarily reflect total body fat. And then there are also racial disparities which we alluded to earlier. Percent body fat is a more accurate measure of adiposity than the BMI or just body weight and so, in order to get a percent body fat analysis, you have to do another determination such as the DEXA. And if you don't have that in your armamentarium, most practices don't, then the BMI, you can add the waist circumference as a measure of visceral fat, and you can correlate that better to the risk of cardiometabolic disease than the BMI alone.

Dr. Kushner: Caroline, I want to go over some key points that you raised and focus it even more on primary care. If we go back to the definition of disease of obesity, it's excess body fat that can cause harm or poses harm to health. We already talked about harm to health in a different module, but how do we actually measure excess body fat, and you clearly laid out that if we could directly measure it, it would solve the problem. The problem is in current day practice of routine availability of bioimpedance or a Bod-Pod or DEXA, which has radiation, is really not practical and pragmatic for most clinicians. So, what we do instead is use BMI to screen for obesity. It's great for screening for populations and it's in every electronic medical record (EMR) so you can actually find it out, but there's so many limitations to BMI we want individual clinicians to do another anthropometric measurement to look at the distribution and get a better idea of the amount of excess body fat and that's where that waist circumference measurement comes in and other measurements associated with it, like waist-to-height ratio or waist-to-hip ratio. So, you can do a pretty good job in your practice currently with just doing anthropometry. I'm not sure measuring body fat is ready for prime time unless you have it in your office, in which case that would be a wonderful additional measurement for excess body fat.

Dr. Apovian: Completely agree with you, Bob. The primary care offices is where we really need these determinations to be done and there's a lot to be said for using the BMI and the waist circumference.

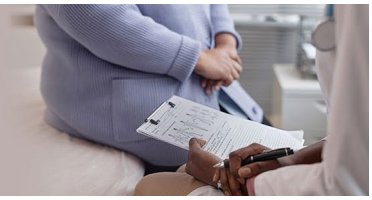
I want to point out that there actually is a staging system that was developed by Obesity Canada and other researchers. It's called the Edmonton Obesity Staging System and it's a clinical staging system that ranks patients with obesity on a 5-point ordinal scale. So, you do determine the BMI, but then you have a 5-point scale that helps you figure out what class, how is the obesity related to the morbidity and mortality of that particular patient. So, this Edmonton Obesity Staging System, or EOSS, was developed to help guide treatment decisions based on obesity-related comorbidity and functional limitations because if you just look at comorbidities, you're not really seeing the functional limitations inherent in that patient's BMI. The EOSS was actually found to independently predict increased mortality and improved clinical utility in assessing obesity-related risk and treatment prioritization using large databases.

How do you use the Edmonton Obesity Staging System? There are criteria for developing a score. So, if your patient has obesity, they have a score of zero if there are no apparent risk factors associated with the BMI, such as high blood pressure, high lipids and fasting glucose levels that are elevated. No apparent risk would mean blood pressure normal, serum lipid and fasting glucose levels within normal limits. No physical symptoms, no psychopathology, no functional limitations and/or impairment of well-being related to obesity. So, this encompasses not just the BMI, but some vital signs, lab work, and some psychological determinations and functional determinations.

A score of 2 indicates that presence of established obesity-related chronic diseases. So, overt hypertension, type 2 diabetes, sleep apnea, osteoarthritis as examples, and moderate limitations in the activities of daily living and/or well-being.

A score of 4 means severe, potentially end-stage disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations and/or severe impairment of well-being. And at this stage, the patient's daily life is certainly quite impaired.

Key takeaway for this module is really that the BMI is a screening tool and should not be used alone to screen for obesity. So, the BMI gives you an indication that you should look for other parameters, such as the waist circumference or if you have the capability to use the percent body fat as a more accurate measurement of adiposity than the BMI. If not, you have the waist circumference, you can determine visceral fat with more in-depth procedures such as an MRI,



a CT scan of the abdominal area. The waist circumference better correlate with risk of cardiometabolic disease than the BMI alone, so you can use the waist circumference if all you have is what is in your office. Use the Edmonton Obesity Staging System which can be useful to guide the treatment decisions based on these obesity-related comorbidities and functional limitations that are illuminated by using the EOSS.

Dr. Kushner: I just had 1 comment, particularly about the staging systems. Edmonton Obesity Staging System is 1 of basically 3 staging systems that have been written about. One is from American Association of Clinical Endocrinology (AACE) which is our endocrine colleagues and the other is a cardiometabolic staging system. This is probably the most common one that's been used worldwide with robust literature behind it. I think it's attractive to use a staging system because we're familiar with using them for chronic kidney disease, cancer, heart disease, and so forth, but really at this point doesn't have that precision that we often find with chronic kidney disease or heart disease. But it may be of value to the clinician if they want to have a scoring mechanism to say how serious is this patient sitting in front of me regarding risk and prognosis. I actually find taking a good history and physical exam and doing labs, I pretty much can guess what the staging is going to be, but 1 more comment is that, Caroline, I want to highlight that this staging system does not include BMI and it's 1 of the few staging systems that identifies risk of your patient without using BMI and it actually outperforms BMI when you look at things like morbidity and mortality. So, it's something clinicians can certainly think about using if they can build it into their EMR and their daily practice.

Goals and Expectations of Obesity Treatment

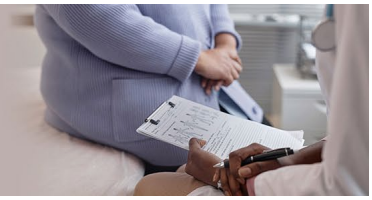
Dr. Apovian: There are many benefits of treating obesity as a disease. There are several modalities which we would use to treat obesity. Certainly, healthy nutrition and physical activity can improve numerous areas. Healthful nutrition, including a negative caloric balance in patients with obesity and regular physical activity improve, on their own, anatomic, physiologic, inflammatory, and metabolic body processes. And what I mean by on their own, without necessarily inducing weight loss.

Medically managed and supervised weight loss is going to improve glucose and lipid metabolism, reduce blood pressure, reduce thrombotic risk and results in a more significant and clinically meaningful weight loss maintenance if it is continued and not just utilized piecemeal. Weight loss in patients with obesity generally does improve quality of life, certainly improves patients who have obstructive sleep apnea based on AHI or Apnea-Hypopnea Index, improves osteoarthritis, the knees, hips and other joints, improves cardiac hemodynamics, as well as body image. Weight loss in patients with obesity can reduce premature all-cause mortality, cancer complications, and depression.

Do we have proof that weight loss in patients with obesity can do these things? We certainly have proof from weight loss that has been maintained, such has been seen with bariatric surgery databases, showing that sustained weight loss after bariatric surgery reduces all-cause mortality, reduces cardiovascular mortality by 37%, and recently has been shown to reduce cancer complications. Do we have evidence in the nonsurgical arena? We certainly now have evidence from some of the GLP-1 trials that have shown that patients with a cardiovascular risk factor will reduce the risk of another event by 20%. So, we are getting good evidence that weight loss in patients with obesity reduces all-cause mortality.

What else do we know about the benefits of treating obesity as a disease? In terms of women and weight loss, we know that women who have polycystic ovary syndrome (PCOS) may improve their metabolism and obesity-related obstetric and gynecologic disorders, such as PCOS, but also women who have obesity who are interested in getting pregnant will reduce obesity-related obstetric disorders with weight loss beforehand and also women who suffer from infertility do benefit from weight loss prior to fertility treatment because of the drop in weight and the improved fertility, even without fertility treatment.

In terms of men, weight loss in men with obesity can increase testosterone levels when there is hypogonadism and when that hypogonadism is due to the consequences of adipose tissue and effects on hormonal levels. Weight loss in males and child-bearing females with preobesity and obesity may reduce epigenetically-transmitted risk of obesity and metabolic disease in children, and we know this from the many, many epistudies showing what happens in patients who have obesity who rear children and also, interestingly enough, there was evidence that in men



and/or women who've had bariatric surgery, their offspring benefitted from the bariatric surgery that their parents have had in terms of risk of metabolic disease in children. So that, meaning that this may not be all genetic, there is also an effect of post-treatment obesity on the offspring. So, this is very, very interesting literature.

Dr. Kushner: I think you and I would be hard pressed to think about what doesn't get better with healthy lifestyle and weight loss other than maybe developing gallstones, bone health, maybe worsening gout. Everything gets better and you first started off with the benefits of healthy nutrition and physical activity. That is foundational. I mean, that's what clinicians talk about or want to emphasize or encourage your patients to do every day is live a healthy life and if one has excess body fat or obesity, to encourage them to lose weight. We talked before, in another module, about the 200-plus medical problems and complications associated with obesity. All of them are going to improve and certainly not get worse. So, it's beneficial across the board. The real challenge which we're going to talk about in other modules is how do you do it in primary care. But it's beneficial across the board.

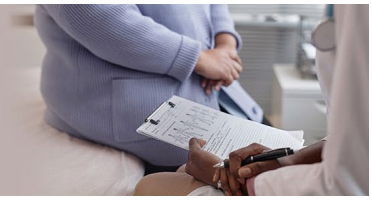
Dr. Apovian: So, what do you see with 2.5 and greater percent weight reduction? You improve glucose metabolism, you start to decrease triglyceride levels, polycystic ovary syndrome, PCOS, and infertility also start to improve. For a greater than 5% weight reduction, you start to see improvements in quality-of-life scores based on pain and some psychosocial aspects. You start to improve depression, mobility, functionality, and walking speed based on improvements in knee pain, walking distance, and pain in patients with knee osteoarthritis. You start to see improvements in hepatic steatosis, as I said, the decrease in liver fat content. Urinary incontinence improves, sexual function starts to improve, your high-density lipoprotein (HDL) level will start to rise and here's where you see improvements in decreases in healthcare costs with a greater than 5% weight reduction.

With a greater than 10% weight reduction, here's where you start to see decreases in sleep apnea scores. So, decreases in AHI index. And metabolic dysfunction-associated steatohepatitis. So, you start to see improvements in steatohepatitis and not just liver fat content. And then greater than 15% weight reduction will reduce cardiovascular risk and overall mortality. And there are many studies that have shown this improvement in health conditions by degree of weight loss and one of the latest was published by Sam Klein's lab a few years ago showing this incremental weight reduction. He actually took patients and had them lose weight incrementally and did things like sample fat tissue to actually look at fat tissue metabolism changes and saw these beautiful decreases.

Dr. Kushner: My take-home point I think from your review is some is good, more is better. That's one. But the other I think more important take-home which we've learned from these studies is that you need to lose weight to a certain threshold to achieve a specific improvement in a complication or comorbidity and the way a clinician will use this in practice is if they saw a patient with severe sleep apnea or MASH that was diagnosed, we know that you're looking at a weight loss of at least 10% or more in order to get benefit. So, if you have a patient that comes in with those conditions and they say, you know what, I learned if I lose a little weight, it'll get better, it probably will, but if you really want to make a significant improvement, you have to aim for much more weight loss. So, having a clinician understand these thresholds will help the clinician to communicate this to a patient about what is our real goal here to achieve health in the condition you're presenting in front of me vs someone who has prediabetes, as you said, 2% to 3% or 4% weight loss is enough, but not someone with preexisting cardiovascular disease as an example.

Dr. Apovian: That's a great point, Bob, and the reason why we can relate this now to degrees of weight loss is because, unlike 15 years ago when we were really promoting 5% to 10% weight loss as the key goal, we now have medications that can do a little bit more than that and we are able to impart this to our treatment guidelines, which is wonderful.

The myth has always been, listen, if you lose it more slowly, you have more of a chance of keeping it off than if you lose it very quickly. Is that true? Well, it's older evidence that suggested that overly aggressive weight loss goals lead to higher attrition and there was caution against rapid weight loss due to health-related concerns and an increased risk of weight regain. However, more recent studies are supporting that if you have a patient who has a more ambitious weight loss goal and you give that patient the tools to produce greater and more rapid weight loss, there may actually be an increase in the long-term weight loss success. Obviously, we can do that now. Why can we do that now when we



couldn't before? Well, the older evidence was all relegated on aggressive diet and exercise and we know from The Biggest Loser where there was aggressive dieting and incredible exercise activity daily for an hour every day, yes, those patients lost a lot of weight very quickly, but they gained it back. And now we know that if we have the tools to help patients lose weight more ambitiously, maybe more rapidly, we do see increased long-term success because we have those tools, ie, we have better medications and we've always had metabolic bariatric surgery and our metabolic surgery procedures are much more safe and effective now that we have them laparoscopically and we fine-tuned the actual mechanics.

With this, we have treatment goals that should be balanced, health-focused and established on top of the fact that we need frequent encounters with a multifactorial approach that will assist patients through this weight loss journey. So, if you have all those tools, if you have a patient who's very ambitious and is able to obtain greater and more rapid weight loss, and you provide them with frequent encounters and a multifactorial approach and the medications and/or a surgical option, you will see increased long-term weight goal success.

Dr. Kushner: I just wanted to add one thing because when I see patients, I think one of the most common beliefs and maybe misunderstandings is that if I go slow that that's going to be better, and you reiterated that. And going slow often is I'm going on vacation, I'm following the diet, I'm not following what you're telling me, I went out for a celebration, I got off what you were telling me, so it's very, really going slow. But all the data that we've seen, and you said that—whether it's lifestyle management or pharmacotherapy—the one who gets out of the gate the quickest is really the one that's going to be the most successful. I think what's important for clinicians is to look at that weight trajectory over those first few weeks to months and really determine is this a treatment direction we want to continue on or do we want to offer another approach or augment or become more aggressive in what we're doing?

Dr. Apovian: I think the LOOK AHEAD study showed that the initial weight loss predicted long-term success and that was the first time we saw that the people who lost aggressively the first year, those people did better 5 and 10 years out and that was without medication. So, it's not even a matter of the data showing this with medication; it's really looking at a long-term study like the LOOK AHEAD study.

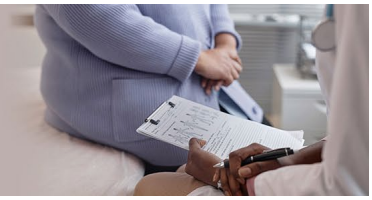
Our expert key takeaways are that healthy nutrition, physical activity, and weight loss in patients with obesity is essential to improving numerous body processes and health outcomes. It's the cornerstone of obesity treatment. As little as a 2.5% weight loss can result in improvement in glucose metabolism and also triglyceride levels. A 5% weight loss significantly improves mobility, hepatic, urinary and sexual function, and overall quality of life. And recent evidence suggests that more ambitious weight loss goals and greater and more rapid weight loss can increase long-term weight loss success.

Treatment Overview: Debunking Myths and Misconceptions Regarding Treatment Approaches for Obesity

Dr. Kushner: You know, during the 1980s and 1990s, Americans were encouraged to consume most of their calories from grains and low-fat products when fat, kind of a generic term, was considered the culprit in causing cardiovascular disease. This resulted in unintended consequence of consuming higher quantities of sugar. This often led to what we call the SnackWell phenomenon which all of you remember, is the low-fat, high-carbohydrate cookies and snacks. This, along with other factors, like increase in sedentary activity, entertainment technology, fast food, and so forth, collectively led to an increase in obesity, type 2 diabetes, and the prevalence trends that went up.

Corporations, of course, took hold of this and started generating all this low-fat foods and low-fat recommendation, the SnackWell phenomenon that I talked about is really a term used to describe how Americans consumed more sugary foods in larger quantities than they would have due to perceptions that low-fat foods were healthier.

The current nutrition recommendations, the general principles are to consume a high amount of nonstarchy vegetables, fruits, whole grains, and legumes. Moderate consumption of nuts, seafood, lean meats, low-fat dairy products and vegetable oil. And limited to very little, if any, intake of trans-fats, saturated fats, meat fats, red fats, sodium, refined carbohydrates, sugar-sweetened beverages. And this has been really recommended in U.S.

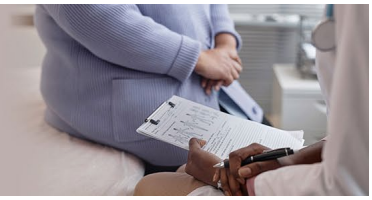


Department of Agriculture (USDA) dietary guidelines for Americans, as well as embodied in 3 different diets that have been well-studied and promoted by different organizations. And the 3 that I want to highlight: the first one is DASH which is Dietary Approaches to Stop Hypertension, recognized by both the American Heart Association (AHA) and USDA as a diet that's rich in fruits, vegetables, lean protein, low-fat dairy while limiting sodium and saturated fats, originally developed by the National Institutes of Health (NIH) when they did these types of studies, primarily for hypertension, but it's also been used in individuals with obesity with or without hypertension. The second, which has the most robust amount in the literature regarding articles, is the Mediterranean diet which has shown benefit for primary and secondary cardiovascular disease prevention and reducing risk for cardiovascular disease mortality and all-cause mortality and other endpoints, such as stroke, myocardial infarction, and so forth. And the last one is a vegetarian diet which substitutes for meat, seafood, and poultry, the consumption of soy products, whole grains, nuts, and legumes, and is associated with a lower risk of cardiovascular disease, reduction in low-density lipoprotein (LDL) cholesterol levels, and improvement in systolic blood pressure. In clinical practice, we often mention these diets, but you never want to tell a patient this is what you must consume or eating pattern to adopt because it may be very foreign to that patient.

Dr. Apovian: Those are great recommendations, and I think really to piggyback onto this the low-fat diet craze that really derailed a lot of healthy eating patterns for Americans. Some people think, which is true, that some fat in the diet, especially healthy fats, can satiate you and that's very true, and that's the Mediterranean diet. But, you know, the DASH diet is a low-fat diet. It contains about 27% fat and that is considered low. So, it's not even that the low-fat diet craze was derailed because it was so low in fat. It was really this replacement of healthy foods with these low-fat snacks, as you said, Bob, that really was the derailing factor because that was all ultraprocessed food. And we're still grappling with what is it about ultraprocessed food that makes you eat more of it. And that's really what we need to continue to study, and we learned a lot from that low-fat craze. But these 3 patterns are great patterns to the approach and it's not just about what is satiating, but you can say that the DASH diet is satiating because of the high fiber content also. So, it's about the combination of healthy eating patterns that really naturally lowers the calorie content of what you're eating.

Dr. Kushner: We know physical activity is extremely important. It's really a cornerstone of healthy lifestyle and that's basically getting your body in motion as often as you can. When it comes to weight loss, it causes a moderate amount of weight loss, primarily when used with a lower calorie diet, but it can cause a little bit of weight loss. Nutritional calorie deficit is required, as I said, for clinically meaningful weight reduction, but we often, in clinic, of course, counsel patients on both. The specific benefits of physical activity go beyond weight loss and that's really where I spend my time talking to patients and those benefits are in body composition, with improved muscle mass and reduced percent body fat, in cardiovascular benefits with reduced blood pressure, heart rate, risk of cardiac arrhythmias, improved coronary dilation, I'll talk to patients about improved coronary flow. Improved and increased myocardial oxygen utilization which means fitness and reduced plaque formation. Metabolic health, for sure, right? Improved insulin sensitivity, reduced blood sugar, improved blood lipids. Any individual who's monitoring their blood sugar knows their sugar goes down after they do a bout of exercise, so that's something they actually see if they're doing continuous glucose monitoring or they check their sugar. We know there's cancer benefits of reduced risk of cancer onset and recurrence which we recently saw with colon cancer. Inhibited cancer cell proliferation and inflammation, increased cancer cell apoptosis and so forth, and lastly improved quality of life and psychological well-being, increased coping, reduced depression and so forth. Again, like we talked about before about weight loss and all the complications, the comorbidities, there's very few things that physical activity will not benefit when you actually apply it. So, we can't speak enough about it, but the one thing is that if someone comes in and their goal is to reduce body fat and body weight, physical activity and exercise is not the key treatment that's going to get them there for that rapid weight loss that we talked about in an earlier module.

Dr. Apovian: There's a lot that we still need to learn about physical activity. We know that exercised muscle talks to white fat and can start the burning of white fat and the increase in uncoupling proteins in white fat, turns it from beige fat to brown fat, which somehow we believe helps patients lose weight, keep the weight off and so while



physical activity doesn't actually help you lose weight by itself, it may help patients keep the weight off.

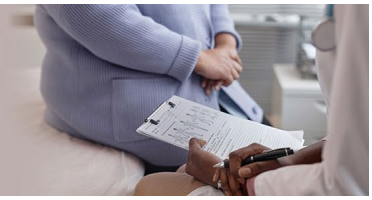
Dr. Kushner: There are 4 principles that I want to highlight and these are 4 elements to optimize success or better adherence, perhaps, with your patients. And those include making sure your behavioral goal is feasible, that is it's practical and accessible in terms of frequency and consistency. You're not going to ask a patient do something they're not comfortable with or the environment is unsafe or they're unable to do. You want to make sure it's efficacious, so it's evidence-based and there's a lot of data on that. Third is that it's measurable and you provide accountability. So, you often ask your patient to track what they're doing, which allows them to see success and to reflect on what they're doing as well as share a record with you and themselves about what they're trying to accomplish and adding social support as well to that. And last is self-owned or autonomous and we often use the word self-efficacy, that they feel they're actually able to do it and they're the primary stakeholder for getting it done. We also know that external accountability is important and that's where frequent visits in the clinician or another healthcare professionals, dietitian, coach, health psychologist, and so forth.

These go along with the SMART goals, specific, measurable, actionable, realistic, and so forth. So, bottom line here is that when you're working with a patient just don't say eat less, move more, get more exercise, see you back in 2 months. You want to be very deliberate and specific about what you're asking the patient to do, using these 4 principles as well as that SMART mnemonic that we talked about a little bit earlier.

Dr. Apovian: We know that primary care providers are very busy in their practices and recent research suggests that it may be beneficial for obesity treatment for the patient and the provider to utilize web-based behavior modification programs to enhance visits with your primary care or obesity medicine specialist to actually go over these behavioral therapy techniques.

Dr. Kushner: This is a subject that often comes up with patients and it's important to hear their perceptions and beliefs. We always have to ask our patients about supplements when we take a history and record them in the medical record. The most common ones include ephedra, bitter orange, high-dose green tea extract, yohimbine, laxatives, and diuretics in which they all can potentially have adverse effects, either symptoms or signs, either blood pressure or heart rate or a symptom, like diarrhea or anxiety. So, be careful and really take that history. There's also many hidden ingredients in weight loss supplements specifically that warrant caution. Some of them causing hepatotoxicity, many weight loss supplements are thought to be unsafe by the FDA that are available on the internet. We are also clear the FDA doesn't really require the same scrutiny and level of evidence for dietary supplements that they do for medications. So you always have to be, you know . . . buyer beware is something we really have to have a conversation with our patients about all the time. I know I rarely recommend a supplement other than probably a vitamin/mineral supplement in someone who would benefit from getting the additional micronutrients when someone's not getting, or a particular ailment where they have a digestive problem and I'm going to make sure they take some additional supplements, like vitamin D as an example.

To go back to some of the basics, supplements are defined as substances taken in addition to dietary intake, such as concentrated forms of a nutrient, that would be vitamins, isolated formulations of a nutrient, herbs or botanicals, minerals, and amino acids. Herbal and dietary supplement-induced liver injury accounts for up to 20% of cases of hepatotoxicity in the US. Now this is really quite serious that we get a handle on what patients are taking. Supplement-drug interactions also compound the hepatoxicity and potentially makes it worse. Examples would be anabolic steroids or green tea extract. Patients should be advised of the limited evidence supporting the efficacy and safety of many supplements and lack the oversight by government agencies regarding the claims made about supplements. And I want to reiterate again that FDA does not regulate dietary supplements. It's almost a self-reporting by the companies for public awareness. One I want to highlight is human chorionic gonadotropin, HCG. It's a great case in point. Very popular in the 1960s. You have to dig way into the literature and look at the archives to actually learn a lot about when that was popular. But we do know, from those studies that were done, that it is not effective for weight loss beyond taking the accompanying hypocaloric diet. The FDA requires the disclaimer, "There is no substantial evidence that HCG increases weight loss beyond that resulting from caloric restriction, that's the cause for more



attractive and more normal distribution of fat and that it decreases hunger and discomfort associated with caloric-restrictive diets." So, again, buyer beware. I think that's still being used as HCG shots, shots or drops, but really very low evidence beyond the hypocaloric diet that's prescribed with it.

Dr. Apovian: Bariatric metabolic surgery usually performed in the United States and in other parts of the world, but in the United States there are 250,000 procedures done. We have 14 million Americans who are eligible for, with a BMI over 40 kg/m^2 or over 35 kg/m^2 with 1 condition, usually diabetes and sleep apnea. It is by far, for those eligible, the procedure that can, for obesity treatment, lead to the most decrease in mortality. The latest, the latest literature suggests 37% reduction in all-cause mortality with surgery. It's cost-effective compared to nonsurgical treatments. It's one and done. You're in the operating room (OR), you're in the OR less than 2 hours, less than 1 hour with the sleeve gastrectomy. There's reduced mortality, risk of cancer, cardiovascular disease risk, improvements in osteoarthritis and skin disorders, improvement in depression. Depression, liver disease, and metabolic dysfunction-associated steatohepatitis.

Indications: it is recommended to be considered in all patients with a BMI over 35 kg/m^2, with a condition. Now these are new guidelines from the latest surgical centers that suggest that it should be considered in patients with a BMI over 35 kg/m^2, regardless of comorbidities. And also for class I obesity with metabolic disease, such as diabetes, who do not achieve substantial or durable weight loss with nonsurgical methods. And then there are also new indications for those of Asian descent for which BMI over 25 kg/m^2 suggests clinical obesity and these patients should be considered as well if the BMI is over 27.5 kg/m^2 in those Asian populations. It should also be considered as bridge to other procedures, such as arthroplasties, transplantations, left ventricular assist devices (LVADs), cardiac transplants, abdominal wall hernias, and also in patients who have liver disease. It can even be done in patients who have cirrhosis with improvement at times in cirrhosis. So, these are new indications for metabolic and bariatric surgery.

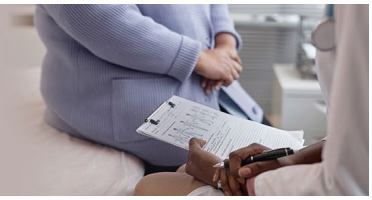
There are barriers, as I've alluded to, only 1% of eligible patients receive bariatric surgery really due to lack of patient knowledge and also the stigma of obesity and the stigma of undergoing bariatric surgery for a stigmatized condition. So, there are attitudes regarding effectiveness and safety. The safety issues, I know patients who've had bad outcomes, I know patients who regained all their weight back. These are very common responses when I try to apprise patients of the benefits of bariatric surgery. In most states, bariatric surgery is covered by insurance, but not all states.

The purpose of obesity medications is to treat obesity. They are adjuncts to the cornerstone of lifestyle modification, diet, and exercise. It can also be adjuncts to metabolic bariatric surgery, preop and postop. So, preop would be to help the patient lose some weight and provide a safer operation for those patients with very high BMIs and we do this all the time. We ask for a 10% to 20% weight loss in certain patients with high BMIs and that just makes the operation a bit safer for patients. We also use antiobesity medications after surgery once we get to a nadir, usually 12 to 18 months after the procedure, they'll be a nadir and then there will be some weight regain. And, at the point where there is 5% to 10% weight regain, we really want to get the patient back in and started on an antiobesity medication postop. And basically, we want to utilize obesity medications to improve the overall health and quality of life of patients with preobesity and obesity.

Key principles, patients, you're eligible if your BMI is over 30 kg/m^2 and sometimes with a BMI over 27 kg/m^2 with diabetes, hypertension, or dyslipidemia, who have an inadequate response to lifestyle interventions alone. There are limitations to BMI which we discussed, including muscular individuals, individuals who are elite athletes or body builders do not rely solely on the BMI for eligibility criteria and also in those with sarcopenia who may have a low BMI, but have more body fat than muscle. Those patients may also be eligible, but you have to be very, very careful about a lot of muscle mass loss with those older patients with sarcopenia and utilize a high-protein diet and resistance exercise training.

Certainly, obesity medications must not be used in patients with drug hypersensitivities or in pregnancy.

Medications Animation Voiceover: Currently approved pharmacologic treatment options for weight loss exert their effects through different mechanisms. Orlistat acts in the periphery by decreasing fat absorption in the gut. Medications that act directly on the central nervous system



include naltrexone/bupropion and phentermine/topiramate. These combination medications influence neurotransmitters that impact the brain's anorexigenic and/or reward centers. Liraglutide and semaglutide are currently approved GLP-1 receptor agonists, while tirzepatide is a dual GLP-1/GIP receptor agonist. GLP-1 and GIP receptor agonists act centrally by promoting anorexigenic signals causing satiety or a feeling of fullness. GLP-1 and GIP receptor agonists also act within the gut to stimulate insulin and glucagon secretion in a glucose-dependent manner.

Dr. Apovian: Typically, with our new medications, the GLP-1 agonists certainly and some of the combination orals such as bupropion/naltrexone and phentermine/topiramate, we have FDA approval for long-term use of all of these antiobesity medications. However, if there's not a 3% to 5% weight loss from baseline after 12 to 16 weeks for these medications, then it's recommended to either increase dose or discontinue the medication in favor of another medication or adding another medication to that medication.

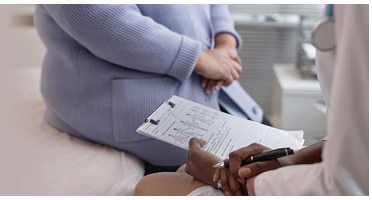
Our expert key takeaways here. We talked about healthful nutrition, physical activity, behavior modification and medical management as well as touched upon metabolic bariatric surgery.

Recommended diets include the DASH, Mediterranean, and healthy vegetarian diets. Physical activity has numerous benefits beyond weight loss. Behavior modification can serve as a valuable component of overall weight loss success and continued weight loss maintenance. Patients should be counseled that the herbal treatments that are over the counter can be potentially unsafe. Metabolic bariatric surgery is strongly recommended for patients with a BMI over 35 kg/m^2 or BMI 30 kg/m^2 to 34 kg/m^2 who have metabolic diseases where nonsurgical interventions are unsuccessful. And eligible candidates for our antiobesity medications are patients with a BMI over 30 kg/m^2 or over 27 kg/m^2 with weight-related comorbidities.

Dr. Kushner: I think we've gone over a lot of good information in this module about all the treatment opportunities and approaches that we can give patients made available to and we can talk about. And it can be overwhelming, I think, for a clinician to kind of take all this in. When I see a patient for obesity or obesity-related complication or comorbidity, I usually start my counseling session with there's a continuum of care of treatment approaches that we can potentially use, starting with lifestyle management, escalating to pharmacotherapy, all the way to bariatric surgery. I may say a little bit about each one and then I'll say to the patient, which one are you thinking of and which would be the best to match, given where you're at now and what your medical complications are? And then, you drill down. So, in other words, the clinician doesn't have to have all these facts and numbers in their mind, but they do need to understand that there's multiple approaches to use. If you see a patient who's a candidate for bariatric surgery, mention it early and potentially make a referral for an orientation. Similarly, if someone's a candidate for pharmacotherapy, they may not start it today, but you may want to talk about it so they understand that if they don't do well on lifestyle alone, you've got their back. There's other treatments that we can bring forward a little bit later, but not necessarily today if it doesn't make sense.

Approved Obesity Medications and Role of Adjunctive Lifestyle Modifications

Dr. Kushner: I want to go over some of the recommendations for the FDA-approved obesity medications. There's many guidelines that are going to be coming out that will help guide a clinician about safety and effectiveness and all the other considerations, but in this module we want to go over them at a higher level. Firstly, obesity medications are indicated in combination with a reduced-calorie diet and increased physical activity. That's basically a package insert for all of the obesity medications we use, highlighting they should not be used in isolation and always with patients focusing on increased physical activity, behavior change, and healthy eating pattern. Orlistat is one of the oldest medications that we have in the market, but it's also the least effective and is the only one that does not affect appetite. And we talked about appetite dysregulation in an earlier module, this has no effect on appetite. It just blocks about 30% of the fat that you consume from a diet and you pass it in your waste. It may be a preferred medication for someone who is at high risk for or have side effects to other medications that are absorbed and systemically active or someone, let's say, with constipation and is looking for more laxation, orlistat will do it. It also lowers LDL cholesterol.



Phentermine, as well as diethylpropion, it's actually the most common medication used in the United States, approved in 1959, but it's only approved by the FDA for short-term use, about 12 weeks. Longer-term use is off label, but that's something, with the newer understanding of obesity, all of us actually do that although there may be some regulatory restrictions, depending upon the state that you live in.

The other GLP-1 medications, like liraglutide and semaglutide, are probably the most common, at least semaglutide, the most common medication and we'll talk about that in a moment. And the last one to hit the market is tirzepatide, which is a GLP-1/GIP dual agonist, also incretin hormone and it has multiple benefits, as we'll talk about and forthcoming will be oral small molecules which can be taken with food or even oral semaglutide like one that's already available for diabetes that will likely also be approved in the near future.

Dr. Apovian: Patient barriers to obesity medications. Let's dispel this myth. As we have discussed, obesity has been thought to be due to an unhealthful lifestyle and, as long as patients go back to a healthy lifestyle, they should be able to lose weight and keep it off. Failure to recognize and treat obesity as a chronic disease, that is patient and also physician barrier to treating obesity. There has been lack of awareness of evidence supporting the use of obesity medications, specifically the NuSH, the gut hormone incretin class of therapies. The evidence supporting use go beyond weight loss and maintenance of that weight loss, but actual reduction in cardiovascular risk with the cardiovascular outcome trials that have supported their use in diabetes and also in patients without diabetes and a history of cardiovascular risk.

Poor tolerability and side effects associated with earlier obesity medications, notably phentermine and bupropion and naltrexone and also topiramate, and those side effects can be offset by the weight loss but not as dramatically as the benefit of the GLP-1s. And so, these earlier obesity medications really have been pushed aside for the new GLP-1s. There's been lack of knowledge of newer obesity medications. Evidence-based with demonstrated efficacy, less safety concerns, that's certainly the case with GLP-1s. They're better tolerated than the older obesity medications and, most importantly, improved cardiovascular outcomes and possibly even mortality.

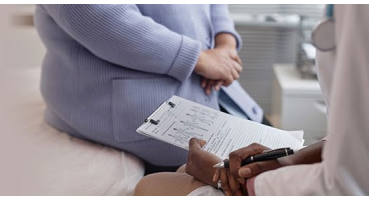
Dr. Kushner: I think a key point here in addition to everything you said is to reinforce that obesity is a chronic, long-term disease and if we use the comparator diabetes, we would think about medication long-term, and if you stop it, the blood sugar would go back up, hemoglobin A1C would go back, same thing with hypertension. Obesity is no different. We're really talking about long-term use. It's not just get the weight off, use the drug and then stop it. So, chronic, recurrent disease, fill in the blank, all diseases really are treated the same way.

Dr. Apovian: All long-term weight loss medications provide similar weight loss. Is that true? Here are the average weight losses with long-term obesity medications. They run the gamut. So, orlistat is probably, arguably the safest one of this list of medications because it really doesn't enter the bloodstream and maybe has some gastrointestinal (GI) side effects that can be onerous, but not exactly unsafe. And that placebo-subtracted weight loss after 1 year is about 3.2%, placebo-subtracted. Very, very modest weight loss, but again very good safety.

Naltrexone combo with bupropion, the placebo-subtracted weight loss is about 4.8%. A little, sort of middle of the road, approaching 5% there. Phentermine combined with topiramate, the average weight loss placebo-subtracted is 8.6%. The robustness of that weight loss is certainly due to that combination canceling out each other's side effects. Phentermine is activating; topiramate is sedating and that combo allows for the weight loss benefits of both drugs to push that weight loss to 8.6%.

Liraglutide, GLP-1, the placebo-subtracted weight loss is about 5.4% and then semaglutide breaking the 10% barrier there with a weight loss placebo-subtracted of 12.4% and then tirzepatide, the GLP-1/GIP combination NuSH therapy, with a placebo-subtracted weight loss anywhere between 11.9% and 17.8%. So, you can see that the average weight loss really improves with the 2 injectable agents, semaglutide and tirzepatide breaking the 10% barrier of placebo-subtracted weight loss whereas the others, including liraglutide, hit between 3% and 9% weight loss. So, there's truly a big difference between weight loss medications in terms of their weight loss.

Dr. Kushner: So you want to combine that efficacy along with the safety and tolerability discussion that we just had. So, the combination of those 2, plus other factors, is what's



going to determine what medication we may be recommending to our patient.

Dr. Apovian: What I didn't mention is that these are placebo-subtracted weight losses with trials that utilized traditional behavior modification. When you combine these drugs with intensive behavior modification, you can almost double the weight loss. So, that's the beauty of a multidisciplinary approach.

We talk about lifestyle as the cornerstone and the rationale for the use of antiobesity medications is to help patients adhere to a lower caloric intake more consistently in order to achieve more sufficient weight loss and health improvements. And this is especially important when combined with increased physical activity to make sure body composition parameters are maximized. And so that's really the essence of using antiobesity medications. They help patients with lifestyle, with choosing healthy foods and physical activity.

Dr. Kushner: We've touched upon this a little bit already and we need to consider multiple factors using shared decision-making when we think about which medication to talk about and recommend. Certainly, safety and efficacy are right on the top. We also want to talk about the comorbidities and complications, metabolic diseases in particular, or mechanical disease like osteoarthritis. There are certainly contraindications that we talked about earlier which can be other medications or dietary supplements or other diseases. Dosing and route is very important. Does the patient want to take an injection medication or an oral medication? If you take an oral medication, are you better taking once a day, twice a day or multiple doses several times a day? And it really comes down, unfortunately, to cost and availability. So, as the clinician, all of this is going on in our mind, but sadly it comes down to is it covered by your insurance and, if it isn't, can you afford it? So, we need to move beyond that so that we can actually have a deeper conversation and pick the most effective medication for that patient rather than which one is available based on their insurance or what they can pay out of pocket. Hopefully, we will be able to get there soon.

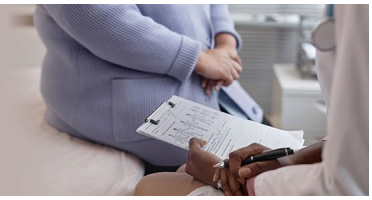
Now we're really going to take a deeper dive into compounded peptides and, of course, there's a change in the marketplace about the availability of compounded peptides, but I want to go over some facts that we all need to know as clinicians and patients need to know as well.

The Food and Drug Administration does not approve compounded drugs. Without FDA approval, compounded drugs cannot be guaranteed to have the same efficacy, safety, and purity as FDA-approved drugs. Compounded drugs are not intended to be mass produced, stored, marketed, or sold as replications of the patented medications. I think, as clinicians, we're all familiar with compounding. When you have a child that has to take a medication in applesauce, let's say, vs a large tablet, or if there are shortages, and that is permitted in that case and, in particular, the incretin-based hormones were in shortage recently and that's what really opened up the market for compounding to replace them.

Regarding patient care, before prescribing compounded drugs, clinicians must secure evidence that the source of the medication and pharmacist compounding the medications adhere to the FDA standards. That's actually a hard statement to follow. Most clinicians find it hard to do that, but the more aware of that you are, I think the safer it'll be for your patient. Patients receiving compounded drugs should undergo a thorough informed consent process, including the potential risks, benefits, and limitations of compounded peptides. I'm not sure that's always done, but it makes sense to have a thorough discussion with them.

Patients should have access to a registered dietitian nutritionist or nutrition counseling from clinicians trained in nutrition and here, of course, we're talking about that multidisciplinary, interprofessional support that should be used for any obesity care, whether you're on compounded medications or not. Clinician oversight of safe and effective physical therapy plan based on patient's health and mobility is going to be important and make a recommended to a physical therapist or exercise trainer is helpful. Many patients benefit from behavior modification guided by a physician, nurse practitioner, physician assistant, nurse, dietitian, psychologist/psychiatrist, health coach, behavior therapist, clinical social worker and other counselor. That really speaks to the multidisciplinary team approach that we're trying to encourage with obesity care. And multidisciplinary clinician involvement in determination of medical management should be based on patient needs, comorbidities and goals.

Addressing Misconceptions in Obesity: Evidence-Based Treatment Approaches



Dr. Apovian: In terms of our discussion on compounded obesity medications, compounded semaglutide, compounded tirzepatide, the FDA has announced in May of this year that these compounded obesity medications will be banned and, therefore, any practitioner who is seeing patients who have been on compounded medications should be apprised of that and should be able to apprise the patient that they are now banned and suggest alternative FDA-approved medications for obesity treatment.

Dr. Kushner: The takeaway for this module is that lifestyle modifications alongside obesity medications are essential to enhance and maintain weight loss success. The newer obesity medications, particularly the GLP-1 and GIP/GLP-1 receptor agonists, are more effective, as Dr. Apovian talked about earlier, and have a favorable safety profile compared to many previous or older medications. The appropriate dose escalation is important and dietary counseling helps to mitigate those side effects. The percentage of expected average weight loss with obesity medications varies on an individual basis. That's very important, but it's helpful, I think, to know the expected ranges when you're seeing a patient so you can identify when they're falling off that expectation line. You can either change medication, become more aggressive or another modalities in general and that weight loss range can vary from 5% to 20%.

Additional Tools and Resources

Dr. Apovian: There is a social media resource that is specifically patient-focused and it's a vlog series addressing the myths and misconceptions about obesity and its treatment options that we have presented in these modules that will be offered specifically for patients by Dr. Holly Lofton and that will be available for patients to really go over all of the concepts that we've gone over in these modules. There are other clinical resources in the activity toolbox that we want to make you aware of. The Obesity Action Coalition, with the website www.obesityaction.org, has many clinical resources available. The Obesity Medicine Association, OMA, has a website, obesitymedicine.org. There is also OMA Academy, academy.obesitymedicine.org, as well as many other websites, including the Obesity Society website.

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