TIME WELL SPENT:
TREATING OBESITY AND DIABETES

CHAPTER 1 | Reframing How We Approach Type 2 Diabetes Management in Primary Care:
Making Time to Address Obesity in Your Busy Practice.

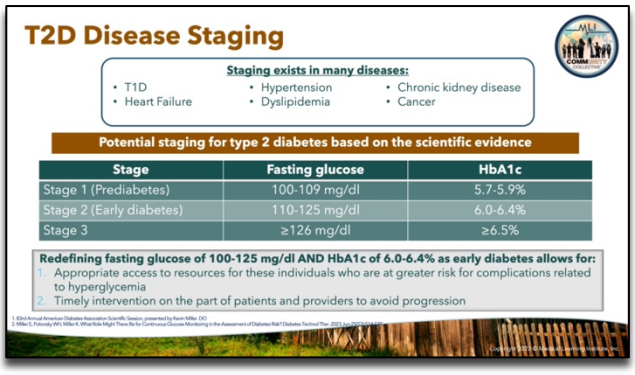
Robert F. Kushner MD: Welcome to Time Well Spent – Navigating the Challenges of Treating Obesity in Diabetes. This is Part One, Reframing How We Approach Type 2 Diabetes Management in Primary Care, Making Time to Address Obesity in Your Busy Practice.

The learning objectives for Part One, we're going to learn about to utilize three evidenced-based screening metrics beyond hemoglobin A1C to assess whether to initiate or intensify Type 2 diabetes therapy.

We're going to determine the chronicity of obesity as a comorbidity and its importance of timing and the management of patients with Type 2 diabetes.

We're going to select the most appropriate therapy for an individual patient with Type 2 diabetes and obesity, considering things like safety and efficacy of these medications.

And lastly, to identify patient and disease appropriate goals for long-term management of weight loss and Type 2 diabetes particularly related to complications and using shared decision-making approaches.



T2D Disease Staging

Dr. Eden Miller, DO: Now let's take a moment and discuss Type 2 diabetes disease staging. So, the current recommendations or current considerations are that we take individuals which we typically called prediabetes, and I often tease that prediabetes is like being prepregnant. You can't be prepregnant. You have early diabetes, and so consideration is to say Stage 1 prediabetes has a fasting glucose of 100 to 109 and an A1C of 5.7 to 5.9. That particular stage was specifically done because those particular individuals tend to respond quite well to lifestyle as well as weight reduction, and their risk of developing fulminant diabetes linearly is not as high as we see other stages.

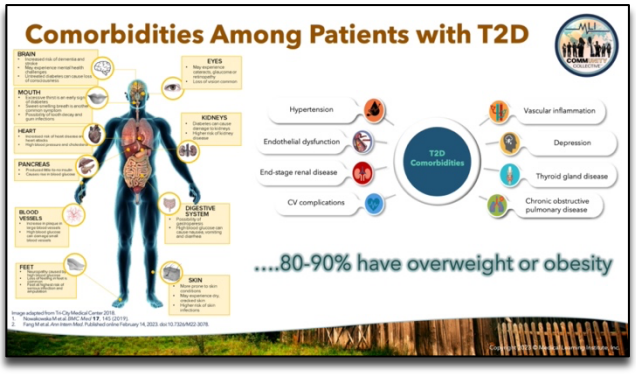
Now, Stage 2 early diabetes is our second classification, and it includes people who have fasting glucoses of 110 to 125 and A1Cs of 6 to 6.4. The ADA also recommends intensive intervention in this particular group, and it is considered to go beyond just lifestyle and dietary or weight reduction, even though that's always foundational, and to consider intervention with therapeutic options to keep the cell healthy in order to maximize weight reduction, treat comorbidities,

and ultimately, hopefully prevent the progression into overt Stage 3 diabetes, which all of you know, is an A1C of greater than or equal to 6.5 or a fasting blood sugar of 126.

Dr. Kushner, what are your thoughts about this? I know this is kind of something that has just really recently come around in the last few months. What do you think?

Dr. Kushner: Eden, I like where you're going with this. You know, have, considering prediabetes as 5.7 to 6.4 is a wide range; and we know that individuals that have a, a hemoglobin A1C to, to 6.4 have a different outcome. They're at higher risk as you've outlined them.

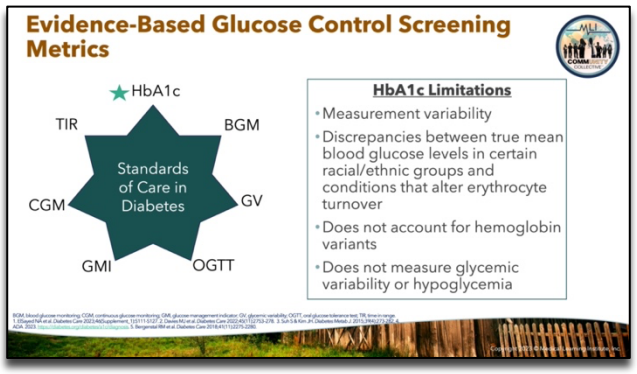
So, I think it highlights the attention of a clinician to those individuals that have an outcome risk that is much, much higher than those that have just a little bit of prediabetes, which is 5.7. So, I like this. I think it will help clinical care.



Comorbidities Among Patients with T2D

Well, here we're introducing the whole idea of those living with overweight or obesity, and I think it's an important point to make out that 80 to 90% of individuals with Type 2 diabetes are overweight or living with obesity. And those two comorbidities or complications we call diabesity for short is a harbinger for medical problems in multiple organ systems. In fact, the list, last data I've seen regarding obesity alone, over 200 medical conditions are associated with obesity, diabetes, one of them. But here what we see on the slide are all the other organ systems that are affected by overweight, obesity, and diabetes in combination from the brain, to the heart, the pancreas, eyes, and so forth. And as a clinician, when you see a patient with Type 2 diabetes and happens to be overweight or living with obesity, we have to do a really good review of systems in order to identify all those complications and treat them holistically.

We could treat the hypertension, the diabetes, even heartburn, depression, and so forth. But from my point of view, we also want to keep an eye on helping that individuals live a healthier life and help them get their weight under better control because that will have an impact on all these other complications.



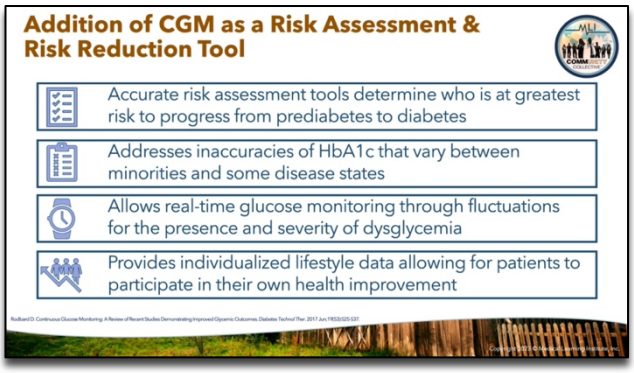
Evidence-Based Glucose Control Screening Metrics

Dr. Eden Miller: I often say that if I were going too fast in my small little town where I live, and the sweet police officer pulls me over and says, "Dr. Miller, you were going 35 in a 25." And I said, "Yeah, but my average speed is 25." He would say, "I don't care what your average speed is. You're currently speeding."

And so that really tells us how A1C being a retrospective average, which we still use for outcomes, for studies, for trials, we're not saying to get rid of it, but rather we want to validate that A1C by CGM or time in range, right? That time between 70 and 180. The looking at variability, right, the coefficient of variability.

I mentioned that earlier. It's one of the things we're looking at as CGM is a risk identification and risk reduction tool, not diagnostic, but should just really tell how many peaks of the glucose, how many valleys of the blue, glucose; and that's related to that glucose variability, or another way is calling the coefficient of variability.
So, when you take the A1C as a metric and you surround it with that time in range, utilizing CGM as that identification tool to reduce the risk by empowering patients to decide how food affects their glucose variability and their peaks and their

valleys, I always say that continuous glucose monitoring is a continuous oral glucose tolerance test because usually OGTs are very small. We do them for 2 to 3 hours. You've got to drink that nasty sweet stuff. But if you incorporate CGM, at least even on an intermittent basis or a continuous basis, with you as clinicians engaging in the data, as well as encouraging patients to engage in the data, you're going to go beyond just A1C, and you're going to really illuminate to both participants in that person's care where they're going and how they get there. And I'm sure you're just as excited about what CGM can offer individuals and empowerment with them.

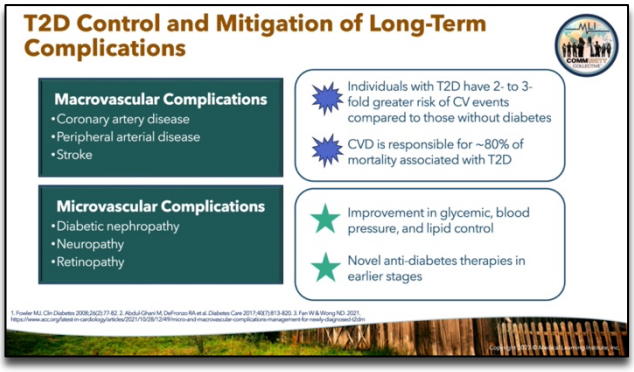


Addition of CGM as a Risk Assessment & Risk Reduction Tool

Dr. Kushner: So, the addition of CGM as a risk assessment and risk reduction tool can be very helpful as we were just talking about. It certainly gives you accurate risk assessment to determine who's at greatest risk for progressing from prediabetes to diabetes.

As Eden was just saying, it addresses inaccuracies of hemoglobin A1C that vary between minorities and some disease states. It allows real-time glucose monitoring, looking at those fluctuations and time in range, and provides individual lifestyle data.

You know, anytime we have our patients self-monitor, whether it's self-monitoring their blood pressure, self-monitoring their body weight, self-monitoring their glucose, we are likely to have increased information, greater engagement in care, and greater adherence in the patient taking better care of themselves. So, as you were just saying, pick the patient that you think would benefit from it and then go ahead and do a CGM.



T2D Control and Mitigation of Lon-Term Complications

Dr. Eden Miller: Why are we talking about control? Why are we talking about time in range and being so specific on glycemia? You know, the emerging data, especially even over the last 10, 15, 20 years shows that control matters. And I think as we have really explored the level of control, we're really starting to see where it impacts. I don't think there's any question whatsoever that glycemic control impacts microvascular disease. That's the small vessels, right? The feet, the kidneys, the eyes because those little, tiny fragile vessels are very sensitive to glycemic change. I think what we've seen is that more data has emerged looking at macrovascular complications, big vessels. I think those big vessels are a little bit hardier and more resilient to those controls in glycemia, even though A1C improvement does increase those or, or decrease that risk, I should say. But rather, I think what we're finding is how you control the diabetes, how you choose the particular agents, indicate whether we're going to impact macrovascular.

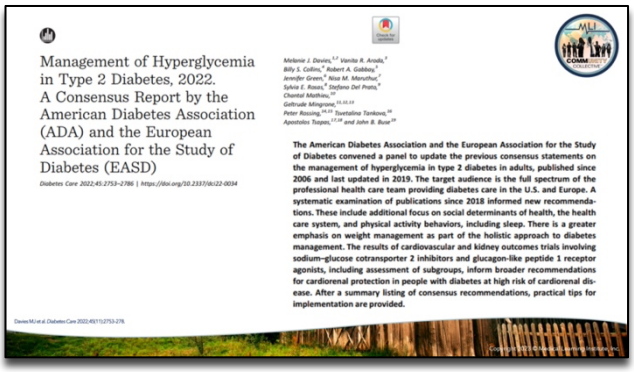
And so, the destination A1C reduction or time in range is not necessarily as, as critical in the macrovascular; but what agents you use to get there really dictates those kinds of things.

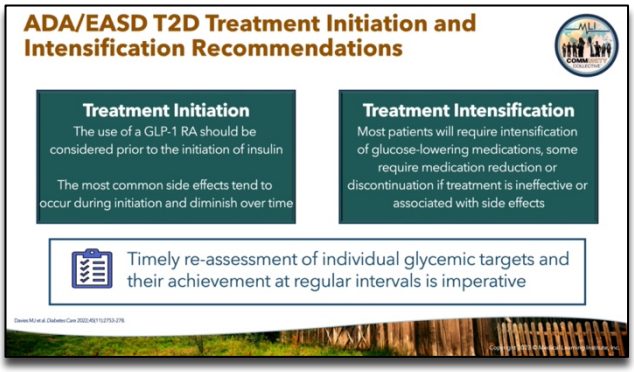
So, Dr. Kushner, talk a little bit about how there are particular agents that have what we call secondary cardio-renal-metabolic effects that are independent of A1C that really are not related to that destination but rather how you get to that destination.

Dr. Kushner: Well, we certainly know that the medications have different effects on individuals. Probably the greatest benefits come from GLP-1 agonists as well as SGLT2 inhibitors. Those really have the greatest outcome measures

regarding cardiovascular disease or heart failure depending on the drug. So, we want to think about is that a good agent or combination of agents for that particular individual?

When it comes to GLP-1s, we also need to know that they cause weight loss. So, if you have an individual who is just, as Eden was saying, Stage 1, but yet is just overweight, we have to be careful about how aggressive we treat that patient. And age is also another fact that we need to take into consideration. If they are susceptible to hypoglycemia, that we have to be careful about using those drugs such as sulfonylureas or insulin. So, using a comprehensive approach, looking at what we're trying to achieve, whether it's weight loss or cardiovascular risk reduction, or kidney health, that's really going to help guide which medication or combination of drugs that we're going to be using.

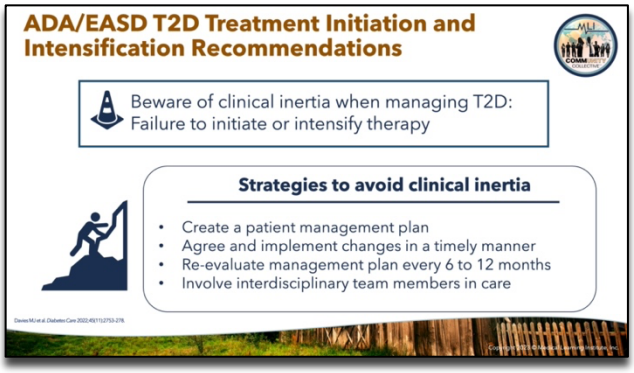




Dr. Eden Miller: The standards of care for the American Diabetes Association, as well as the EAS, EASD really endorses. In addition, I know you've been involved with the American Heart Association as well as the KDOQI Foundation for Kidney; and what I'm liking to see is that all the different agencies, all those governing bodies that guide us and they help us and they create these standards of care, are now aligned. And they go right exactly what they're talking about.

In fact, you know, in 2023, you know, metformin, even though she's a good drug; we're not trying to dethrone her. She really has been supplanted by these GLP-1 receptor agonists and SGLT2s, and we're really encouraged to take a holistic approach.

So, we went from a glycemic algorithm to more of a risk algorithm. And so, when you look at that individual with diabetes and it says lifestyle and intervention, and again, we don't want you to just jump over that. You've got to give a prescription for lifestyle, give a prescription for movement. But then, to decide what's the next best drug to treat, you look at does the patient have cardiovascular risk factors or cardiovascular disease? Do they have renal disease? Do they have metabolism or obesity-related issues? Do they have issues with engagement of medication?



ADA/EASD T2D Treatment Initiation and Intensification Recommendations

Dr. Kushner: So, the initiation of treatment or intensification really highlights, Eden, what you were just saying and that is really thinking about GLP-1 receptor agonists, thinking of using that prior to insulin in part because of the effects on body weight and insulin causing weight gain where a GLP-1 reduces body weight. But also, what you're saying is the weight-independent effects. We know that GLP-1 now has pleomorphic effects on multiple organ systems reducing inflammation, cardiovascular disease, and so forth. And that's why we're talking about initiating that before insulin.

And regarding intensification, we must think about what our goal is, whether it's gluco-centric or weight-centric, add medication when needed or discontinue other medications when they're ineffective.

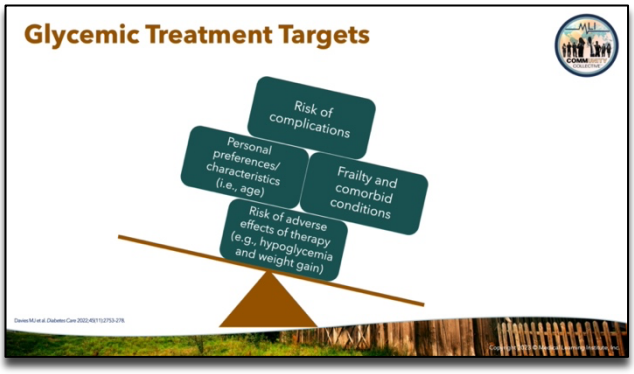
Dr. Eden Miller: Don't let clinical inertia be traced back to you. Now this is not this thing of where, you know, "I'm telling you, you're not doing good," but rather it's examine yourself in your own practice habits. We're human beings after all. And we often will make these type of inertia decisions like, "Oh, a patient doesn't want to try an injectable" or "Oh, they're not going to want do an additional treatment." And so that's one thing you as clinicians can do today; it's to be aware of your inertia.

One of my favorite things to discuss with clinicians is referral to CDCESs. Right, diabetes education. That is something that every person with diabetes should have, and that requires a referral from us as clinicians. We're the ones who hold the key.

Now sometimes my colleagues will say, "Oh, well, the patient isn't going to go if I refer them." And I say, "If you don't refer them, it's a 100% not going to happen." And so, it doesn't mean that when we make a recommendation, when we have them follow up that they're going to hundred percent adhere to it. But it means it has the highest likelihood of occurring because we're not getting in the way.

And so be mindful. We have inertia, and also ask your patients, when you see them on certain visits, "What's the greatest barrier you're having today to treating your disease, to engaging in your disease? I want to try to help you overcome that." And that's a way for you to get into the patient's mind, into their own issues, and kind of shed off some of your own inertia type of issues.

Dr. Kushner: You know, Eden, you, you make up some really good points; and I'm thinking in clinical practice, which feeds into inertia, and I'm interested in how you deal with that, is you, you may want to intensify therapy, but then the patient says, "Oh, I had some visitors in. I didn't really focus enough on the plan that you set up, or it was a bad month. I had a high work schedule. Just give me another month or let me, see me back in three months. I know I will be doing better." So, you always end up, you know, negotiating it. "Okay, I can see you're not ready." So that kind of I think leads into patient inertia and clinical inertia.

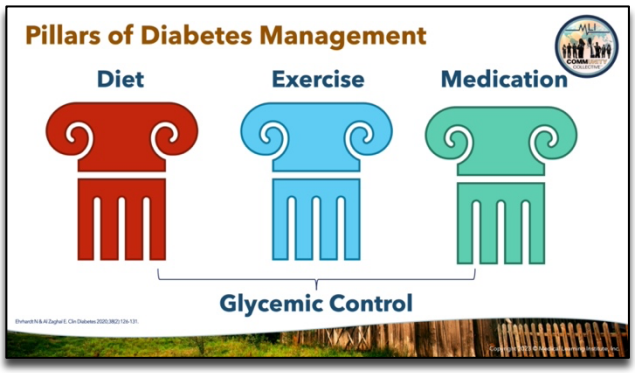


Glycemic Treatment Targets

Here's our glycemic treatment targets. Now Eden mentioned, you mentioned a little bit earlier that we shouldn't use a gluco-centric approach. It should be more obesity-centric or more patient-centered, but there are glycemic treatment targets. One is reducing your risk of complications. We talked about that earlier by using an organ system approach and making sure we get the blood pressure and the lipids, and, and glucose under control. We always want to take in consideration personal preferences and characteristics. That comes under the heading of shared decision-making and patient-centered care.

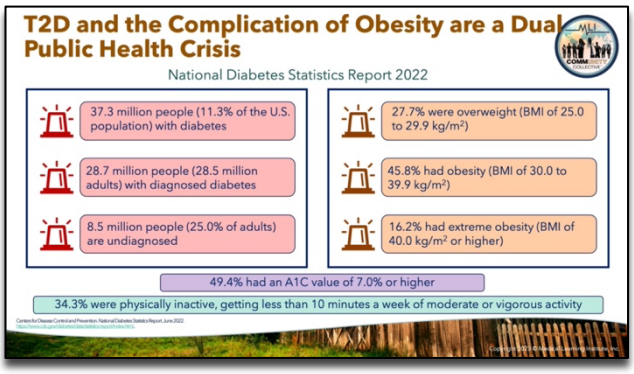
We talked a little bit earlier about frailty and comorbid condition. You have an elderly individual who's susceptible to hypoglycemia. You're not going to use a drug, perhaps, insulin or sulfonylureas where they may not be able to notice the hypoglycemia or they're at higher risk.

And lastly, risk of adverse events of therapy which again hypoglycemia or weight gain, again, which we could see with insulin or sulfonylurea. So, these are four areas that we need to be thinking about as clinicians when we're deciding upon what that treatment course it's going to be.



Pillars of Diabetes Management

So, these are the three pillars of diabetes management. Diet and physical activity come in a category of lifestyle management. That really is foundational for all chronic illnesses, whether it's diabetes, hypertension, hyperlipidemia, or obesity. But in addition, as we've been talking about, that third pillar is going to be medication. We don't think about diabetes as if you work a little harder and get that sugar down, you won't need medication. We don't have patients earn a medication for diabetes or for obesity. When we think it's going to be helpful, particularly for those other benefits, like cardiovascular disease and metabolism, we think about using medication quite early in the management.

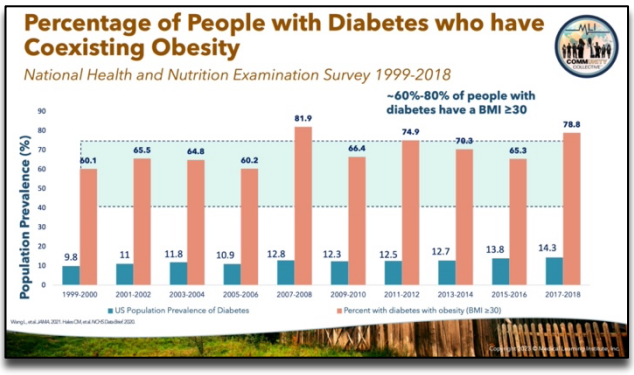


T2D and the Complication of Obesity are a Dual Public Health Crisis

Carlos Campos, MD: Now this is a slide that looks at the National Diabetes Statistics Report of 2022, and I think it's really, really revealing. It talks about Type 2 diabetes and the complications of obesity are really a dual public health crisis. What's incredible is that 49.4% percent of the patients with diabetes had a value, an A1C value of greater than 7% or higher. The kind of stuff that we see where I practice. I'm sure, something that you see also, Dr. Mansfield where you practice?

Keisha Harvey-Mansfield, MD: That's correct. You know, and what's alarming to me too is that we're still missing a lot of people who need screening for diabetes and may have diabetes and can get earlier intervention. I was recently at a conference and a guy was, like, "The time that you diagnose a person with diabetes, it has been years that the disease has actually been setting up." And, you know, we are starting to really understand how important it is to identify patients with prediabetes so that we can, you know, lower the risk of patients developing full onset of diabetes.

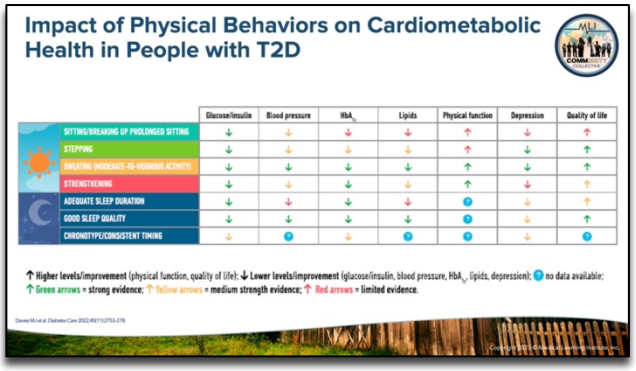
Dr. Campos: Right? And I remember back 20, 25 years ago when there was 14 million people in this country had diabetes. Look at this now, up to 37 million people, which is about 30, 11.3% of the US population. It's incredible. Things are growing- The same thing on the obesity side, the, the amount of has just grown; I think we all know that. And then it doesn't surprise us that only 34.3% were physically inactive. In Texas is probably, that number is probably higher.



Percentage of People with Diabetes who have Coexisting Obesity

Now the percentage of people with diabetes who have coexisting obesity, and in, in Texas, it seems like those numbers are much higher than these numbers here, but this is a National Health and Nutritional Examination Survey. So, 60 to 80% percent of people with diabetes have a BMI greater than 30. It seems like the, in my practice here, 80 to 85% of people with diabetes have, have obesity issues. How about in Louisiana?

Dr. Harvey-Mansfield: Yeah. I think, like, we are number one or number two when it comes to obesity. You know, obesity and diabetes, they just go hand in hand, and you can see this correlation here as the rate of obesity go up, the rate of diabetes go up. And this just goes to show that obesity is not just this mass disease or fat mass disease. It's a metabolic disease just like diabetes.



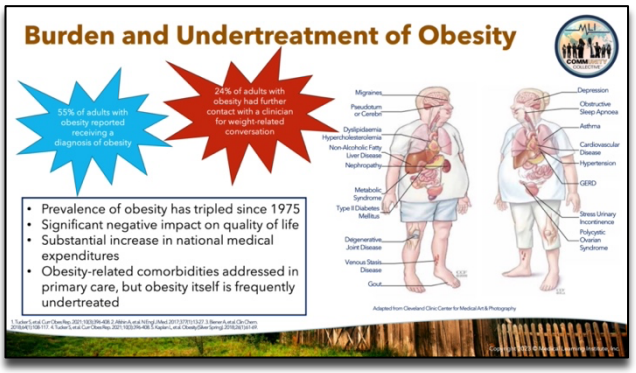
Impact of Physical Behaviors on Cardiometabolic Health in People with T2D

Dr. Campos: And I think that's why they, some people term it as diabesity, right?

And now what about the impact of physical behaviors on cardiometabolic health in people with Type 2 diabetes. And what's really striking to me is that if you look at all of these behaviors here, whether it's sitting, breaking up prolonged sitting, stepping, sweating, moderate to vigorous activity, strengthening, adequate sleep duration, good sleep quality, all of those, if you look at all of them, it seems like when you look across the board, the theme, the activity that really seems to make a difference is sweating or moderate to vigorous activity, doesn't it?

Dr. Harvey-Mansfield: It does. You know, I think this goes to show with the invention of technology how we've gotten away from some of the things that prevent us from having chronic diseases. You know, some studies show that, you know, we're having this increased rate of obesity because we're not sweating enough. And, also, now we have heaters, so in the wintertime, we're not shivering enough.

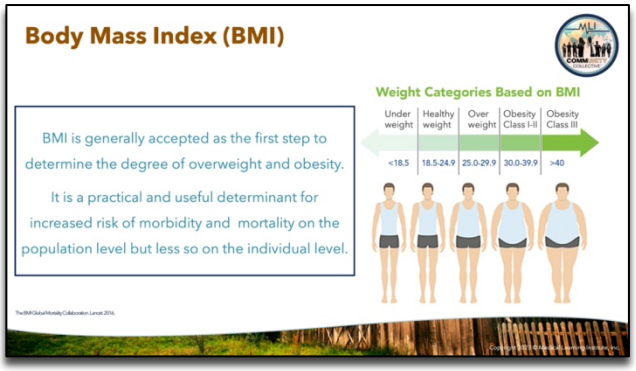
What sticks out to me is sleep because I think that, you know, the impact of sleep on our metabolic health because, you know, I think people take pride in being workaholics. You know, there was once this campaign, "We will sleep when we die," you know. And now we see that if you don't get enough sleep, you will die sooner than later. So, this is a very interesting slide here.



Burden and Undertreatment of Obesity

Dr. Campos: We, as clinicians, I think, we really don't, we end up concentrating on hypertension, hyperlipidemia, diabetes…and we really don't look at people's weight and, or even want to talk about that. And so, I thought what was interesting here is that 55% of adults with obesity reported receiving a diagnosis of obesity. That means 45% did not. Right? Twenty-four percent of adults with obesity had further contact with the clinician for weight-related conversation. That means what? The other, 76% did not. And it's, like, you know, often we walk out of the room while we're holding on to the doorknob and say, "You need to lose weight." and then just walk out the door. Right?

Dr. Harvey-Mansfield: That's absolutely right. The studies show that, you know, our take on weight management counseling includes move more, eat less, which is unfair to our patients because, you know, the data shows that when we really invest in counseling our patients about meaningful impactful changes, they try to adopt those changes.
But I want to point out this is one of my favorite slides because, you know, we live in a society where a lot of people are starting to want to prevent disease, especially cancer, especially diabetes, and you see that obesity is this all-encompassing disease. And if we can reduce the rate of obesity, we can do-, reduce the rate of depression, we can reduce the rate of cancer, heart disease. And, you know, and in our society now, we say that the number one killer in this country is cardiovascular disease, but we don't get to the root of the issue. What causes cardiovascular disease is all the things that we just talked about in the previous slides. And so, you know, if we can pay more attention to preventing and adequately treating obesity, then we can pre-, we can move forward in reducing the risk of another and treating several other diseases.



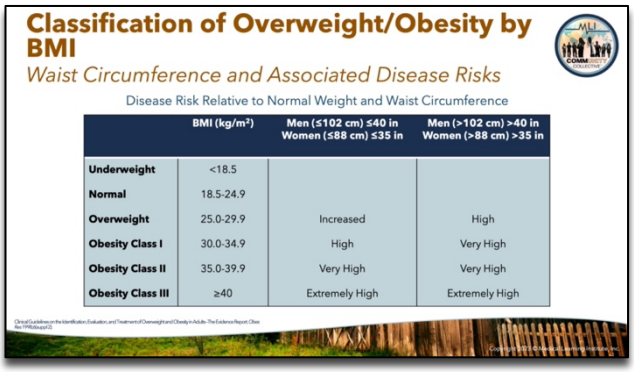
Body Mass Index (BMI)

Dr. Campos: And it's BMI is generally accepted as the number one step to determining the degree of overweight or obesity. And you can see that on the right side of the slide, you know, where the BMI show whether you're underweight, healthy, overweight. And then once you get to a BMI of 30, then that's when you've reached the diagnostic criteria to be called someone with obesity. It's practical, useful. There are some issues with it, but, as it meant, less so on an individual level, and we can talk about that as we go further on to these slides.

Anything you want to mention with that, Dr. Mansfield?

Dr. Harvey-Mansfield: Yeah. I still, very heavily rely on the BMI because it's the most reproducible measure that we have in categorizing someone with obesity. You know, there was once upon a time when people were saying, "Let's stomp on the BMI. What does my relationship with gravity have to do with my health?" And I would say in some scenarios, "You're absolutely right. You know, we shouldn't just be looking at your relationship with gravity, but the BMI is still a good predictor of how a population is doing." And because we are a community and interdependent on the health of one another it's still important to look at the BMI. So, you know, I agree not the perfect measure, but, you know, like you said, there's still some validity in using the BMI.

Dr. Campos: Right. I mean I think we all have, I have a couple, I have about two or three bodybuilders that probably have BMIs of 35, but they're, you know, they look, they look fabulous and but they're just, they're, they're just, their muscle that has built up. But it, but overall, it's sort of the best thing we have as we look at this population.

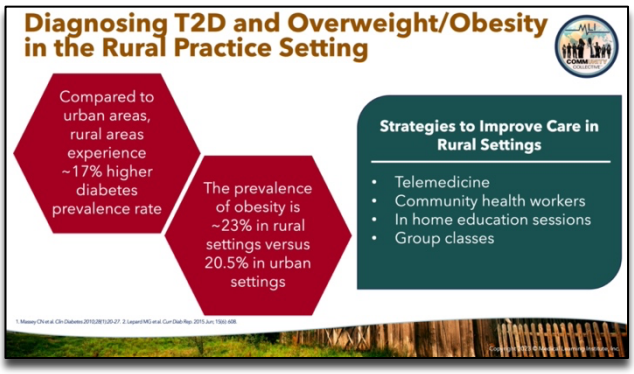


Classification of Overweight/Obesity by BMI

And I think if you look at the literature, probably the best measurement would be waist-hip ratio. And this is what the next slide talks about doing waist circumferences. And in my family practice, clinic where we kind of, we like to focus in on diabetes and obesity, we do a waist circumference on everybody. It's like part of their, their vital signs. And, and here we can see the waist circumferences and associated disease risk.

Anything you want to comment about that?

Dr. Harvey-Mansfield: I just want to say you're amazing, Carlos, because I am always crunched for time, and I hardly ever do someone's waist circumference. And the way that you're doing it is the best practice. I think a good idea for the people who are crunched for time is if you notice that someone is overweight, but you see that they are developing some form of metabolic disease is a very good form of practice to do what Dr. Campos is doing and do the, the waist-to-hip ratio.



Diagnosis T2D and Overweight/Obesity in the Rural Practice Setting

Dr. Campos: This is some, I think, very interesting data that I really was not aware of that compared to urban areas, the rural areas experienced approximately 17% higher diabetes prevalence rate. And the prevalence rate of obesity is 23% in the rural areas versus only 20% in the urban areas. You know, I always thought, well, people in the rural areas maybe they're moving around, they're working outside more but then again, they have issues with access to a lot of healthcare too.

What's been your impression with this, Dr. Mansfield?

Dr. Harvey-Mansfield: Definitely issues with access to, to care. And, you know, in rural areas, there's technology, just like in urban areas, you know you know, we're not moving as much anymore and in rural areas, there's more likely to be more food deserts or lack of access to adequate or nutritional food, so, of course, they would have an increased rate of obesity and overweight.

Telemedicine has been wonderful in my practice. It has reduced the no-show rate. If a patient calls and say, "I can't make my appointment today." "Great, you know, we can either do it over the phone or if you have a smartphone or your computer, we can have a telehealth visit." You know, but the problem in rural areas is Wi-Fi.

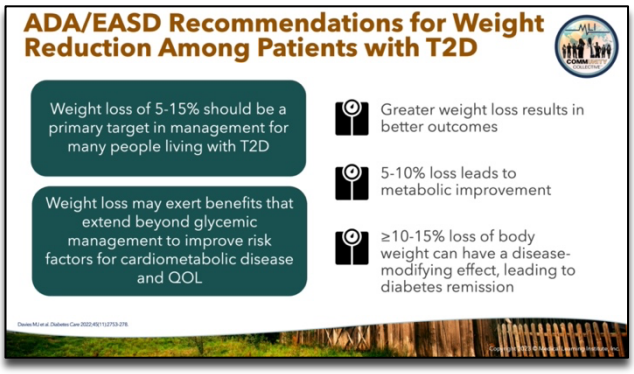
You know, some people typically don't have access to Wi-Fi.

And, you know, I love that we're talking about group classes. We can also do group classes via telemedicine if they have access to, you know, hopping on, you know, online. So, you know, the group class is wonderful strategy. And what you'll find during group classes is patients encouraging other patients.

Dr. Campos: that's part of the community health worker situation. We would, I've had some experience here in my area where we would train some people with just high school education.

Dr. Harvey-Mansfield: Yes.

Dr. Campos: But they were known in the community and people knew them and trusted them to say, "Hey, are you taking your medicines? Are you making sure you're doing your follow-up with your doctor? Are you refilling your medications?" And the community health workers have really been a useful adjunct to our care. So, I think it's, it's another good strategy.



ADA/EASD Recommendations for Weight Reduction Among Patients with T2D

Those of us who, who are not only family doctors but also board certified in obesity medicine, we really are shooting for somewhere between this says weight loss between 5 and 15% should be a primary target. In my practice, I try to shoot for 10 to 15% on, on patients on management for, for many patients with Type 2 diabetes because, as we'll see later, when you lose at least 10% of your body rate, you make a big difference in not only their blood pressures and their blood sugars and their cholesterol, but also with things like sleep apnea and the effects on the physical pressure on their hips and their knees.

Dr. Harvey-Mansfield: Yeah. So, I aim for the 5% because I just typically go for the low-hanging fruit. It's 5% over three months.

I just started a quality assurance project in my practice, and, you know, we utilized the top 10 tips or the top 10 tips that led to weight loss. And at first, I was trying to make my patients adopt all 10 tips, and that wasn't working. So now we do one thing, and when they master that one thing, we head to the next thing. And I believe the prediabetes program by the CDC states that a reduction of 7% reduction, a reduction of weight by 7% reduces the risk of diabetes by 58.85%. And so, you know, of course, you need a lot more weight loss if you're trying to treat sleep apnea, but if your goal is for a diabetes prevention, the sweet spot is about 7%.

Dr. Campos: What I really love is that last statement here where it says, "Greater than, than 10, 15% loss of body weight can have disease modifying effect." I love that statement because that's where we're all, that's why we've all become clinicians, right, because we want to really modify the disease there leading to diabetes remission.

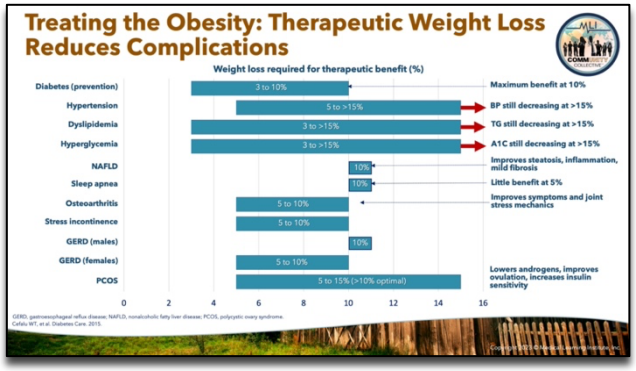
Dr. Harvey-Mansfield: You know, what I'm finding with the GLP-1s, my patients are losing so much weight that this is my categorization of it, you know, they are going into the prediabetes realm and having normal hemoglobin A1Cs, you know, six months, sometimes a year after starting a GLP-1. And so, I tell them, "Your diabetes is in remission with medication. So, we're going to continue to do this."

Dr. Campos: Yeah, that's the hope.

Dr. Harvey-Mansfield: But with treatment, you know, you have a normal hemoglobin A1C because of your weight loss and just because of how the drug works.

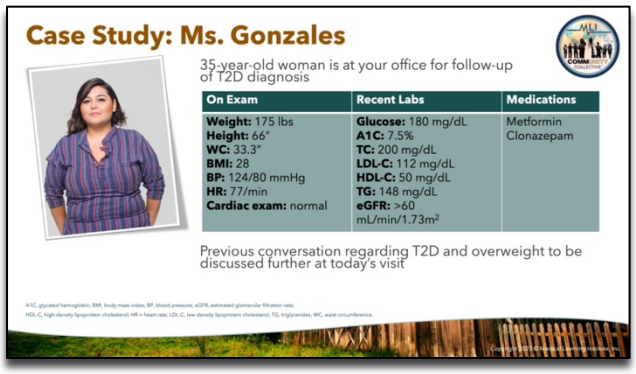
Dr. Campos: Exactly. And that's where the term disease modifying, right?

Dr. Harvey-Mansfield: Yeah. So, you know, also what I'm telling my patients they are on the GLP-1 or the GLP-1/GIP agonist combo, and they are losing so much weight that they're transitioning from diabetes to prediabetes and then diabetes in remission because they're actually getting normal hemoglobin A1Cs because of how the medicine works and because of the added benefit of weight loss. It's really amazing.



Treating the Obesity: Therapeutic Weight Loss Reduces Complications

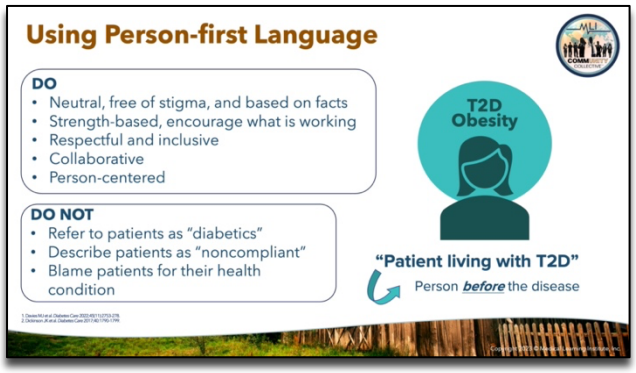
Dr. Campos: For diabetes prevention, as you mentioned, Dr. Mansfield, between 3 to 10% you, you get the maximum benefit at 10%. Hypertension, dyslipidemia, hyperlipidemia those numbers there in front of you. Sleep apnea, it has been my experience that really you need to get closer to maybe 20% to really see the effect of sleep apnea, but there's been some studies that have shown that even 10% improves, has some benefit in there.



Case Study: Ms. Gonzales

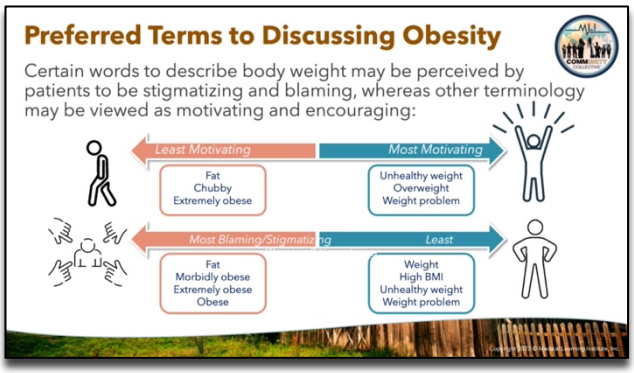
Dr. Eden Miller: Well, what a fantastic discussion. I really enjoyed listening to the dialogue between our healthcare professionals here. And now I want to shift gears and jump into the conversation and take it into a case study direction. I know all our participants here are looking at this saying, "Hey, this is somebody I see every day in my office. 35-year-old individual who struggles with Type 2 diabetes and her physical exam is pretty normal, but she's got that little excess adiposity with that increased waist circumference. Her BMI is in the overweight category. When we look at her metrics in terms of her labs, she's not quite on target. We really want that A1C as low as possible, kind of putting her in that remission state. Her triglycerides are up, those sugar fats, they really tend to follow the A1C; don't quite have that LDL where we want it. Her eGFR, thankfully, is doing pretty good. And the current medications she's using are metformin, which has been standard of care; she's also on clonazepam, so I'm also going to say, "Hey, how's her anxiety, how's her life, how's her stress? And in previous interactions we had conversations regarding her Type 2 diabetes, even kind of mentioned her weight but, you know, we really need to probably dive deeper in. And how do we in our clinical practice start to have that conversation regarding that first person language?

And so, you know, at least I know how I do it, you know, being a person that has diabetes, you know, about telling about the individual first and how they have the disease.



Using Person-first Language

Dr. Campos: Yes. In fact, you know, when I first saw this, I said, you know, "First of all, how long she's had an A1C of 7.5%." You know, are we dealing with some clinical inertia here? But, if she would have come to see me, I think one of the first things I would have done, and I love this slide that says, you know, because I don't like to use the word diabetic in my practice. If I have students, I usually slap them on the hand and say, "Hey, we do not use the word diabetic here in my clinic. We use patients with diabetes. Patients with obesity." because the patient has the disease, the disease doesn't have them. But it also gives you a lot of respect for the patient. So often when we want to talk about weight, we'll often ask permission to ask, "Can we talk about your weight?" And, you know, Dr. Miller, I can't tell you how many times people will say, you know, "No one's ever asked me about that." I said, "Yeah, well, if you, you know, we can develop-, can we talk about your weight and maybe even talk about if that's something that's an issue with you? And maybe we can develop strategies on how maybe we can help you lose some of that weight." And, and asking permission, I think, is the first thing that we should do when we want to address that issue with weight.



Preferred Terms to Discussing Obesity

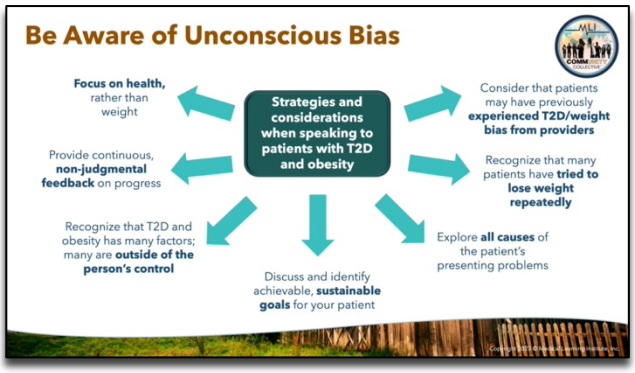
Dr. Eden Miller: One of the things that we'll also address later is that, you know, the fact of obesity, r what I call dysmetabolism medicine, you know, really has these motivating and nonmotivating type phrases. So, I think the best way for our clinicians is to think, if you were called chubby, would you feel good about that? If you were called fat, would you feel inspired? And, you know, and I think sometimes we often use fear and shame and blame. I don't know why we – where'd we learn that,

in medical school, to make the patient terrified to change? I think it's about being inspirational.
So, tell me some of your inspirational quotes that you use in practice?

Dr. Campos: Well, you know, one of the things that, first, at the very beginning, even from when we want to weigh the patient, we have a scale in the room where nobody else looks at it. So, they don't, they don't have to, other people walking by can't see that they weigh 245 pounds. And it's something that, that they, a lot of patients are even fearful about getting on the scale. So, we have a place for them that they can go and weigh themselves.

And then the other thing is that we have the conversation of going as we talked about the word blame going from blame to biology. And I was, you know, sometimes when I talk about that with patients, I had one recently where new patient came in, and we said, you know, "I know you've had this issue for a long time; it's been difficult for you, but there's really a hormonal conspiracy for you not to lose weight." And then, "I want to move this from blame to biology." And you know, Dr. Miller," she started crying, and she said, "Always, it's always been somebody's told me that it's my fault that I've done, that I have this issue." And I said, "We're going to go from blame to biology."

And these kinds of discussions that we have of things that are less motivating and what's more motivating I think really helps all of a sudden develop a trust with the relationship. And at the end, I'll say, you know, "I want to be your partner here. I want to hold your hand. Let's walk down the road together. And there's going to be times where you're going to lose weight, then you're going to plateau and other strategies that we're going to use to help you lose that." I think that once you begin like that, it's a good way to start when you're addressing obesity.



Be Aware of Unconscious Bias

You know, I think it starts, Dr. Miller, from the moment the patient walks into your waiting room. When they look around and they have all these small chairs that they can't even sit comfortably, they know it's not a friendly place. So, we have larger chairs where people can sit comfortably in the room. We do not have glamour magazines in THE waiting room because they look at that and they say, you know, "That's not me." And it's not them. So even from the very beginning, from the moment they walk in the room, we're very sensitive about them, to make sure that they're comfortable there, that they have a comfortable chair, that they're not seeing things that are really, the whole, because the whole society is really biased against people who are overweight. From the time they walk in the back and they're going to get their weight measured, they can go into a room where nobody else sees what their temperature, and what weight is.

And we don't have the MA, whoever is vitalize them say, "Oh, and your blood, I mean, your weight is 295." where everybody can hear that. I, we train our MA's to be sensitive about that.
And because it's, again, building that trust in working with the patients with not only diabetes, but with obesity.

The 5 A's Approach for Obesity

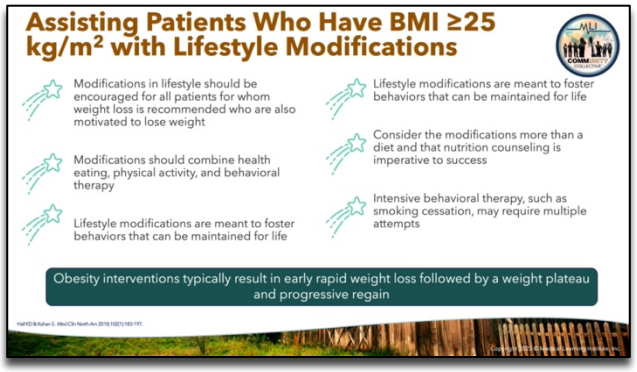
Dr. Eden Miller: We already talked about asking permission, and rather – we call that "readiness for change." You know, I'd really like to discuss your weight. Is that something that you feel ready that you would like to do? And then the next thing I say, "What is a goal that you would like?" You know, you've seen it as well, and I think this is one of the big barriers that we see in both clinicians as well as patients. I say, you know, "What weight would you like to be?" I've got them telling me they want to be the weight they were in high school. I said "No, you're going to look terrible, you'll

look awful." Or I have clinicians saying, "Oh, you've got to lose 100 pounds." Remember, 5% is a good start, 10% is a great first goal, 15% is that Holy Grail. You know, the rest of you'd just look really good in a swimsuit. But it's really trying to identify those goals, why they want to be that. What are some of the things?

And then, how to get, what's the first strategy and what are the ways that we're going to do it? And then developing that plan and following up all in the follow through.

Dr. Campos: Yeah. And the other thing is I often ask the patient, "What do you think the problem is? Do you think the problem is your problem? Do you think it's a metabolism issue? Or do you think are you hungry all the time?" And when the patient says, you know, "I'm, I don't eat that much. I'm not that hungry."

Then all of a sudden you develop a certain strategy for that. Or they say, "You know what I feel like I'm starving all the time. I can't walk by a doughnut without eating it." Then there's another strategy that you can use for that. And so, and not only that, but it allows the patient to enter the treatment plan with you. And, you know, one of the things that we've known from behavioral literature, the changing behavioral literature is that, is that people are more apt to do what they hear themselves say. And so that's part of the conversation and bringing them into that conversation.



Assisting Patients Who Have BMI ≥25 kg/m² with Lifestyle Modifications

Dr. Eden Miller: That's really a great point. It's not you talking to them, it's you discovering kind of their own journey and sharing it with them. You know, I think that's just a great capstone type of topic to end on that slide.

As clinicians, as diabetologists and obesity specialists, you really can celebrate with the individual. You know, at the three-month part, they come in and she's only lost five pounds. And how many times have you had patients say, "I only lost five pounds." And I'm like, "What? That's great, you know. You've lost five pounds and, you know." But I just, I don't feel like it's good enough. And so, they say, you know, "I know we based on our conversation, but, you know, I really want to go deeper." But that's fine, you're right there with her. And it opens the door for kind of that next step.

So, what are your thoughts?

Dr. Campos: Yeah. No question about it. And, you know, and for a lot of these patients, Dr. Miller, you know that sometimes we just have, we just have one bite at the apple. So, we've got to make sure that we lay that foundation there and slowly build up on it because people tend to give up really- You know, we live in this sort of immediate society where, where the fast-food society, we want to just get everything done quickly. And we sort of build on that thing that, I think, allows us to have that one bite at the apple to really make a success.

Dr. Eden Miller: Yeah, yeah. I think that's great. It's a building process. Again, I always tell them I'm interested in changing the rest of your life, right. And I think these are those, you know, those high-risk individuals, right, that BMI of 25 and above, those are those what we call overweight or early stage, you know, the different classes of obesity, you know. And you and I have talked a lot about it. It's more than just lifestyle intervention, even though we believe that lifestyle is key and it's there because it's sustainable, it's that first line of defense, but often we must pull in multiple things, and you must be mindful of their culture. You've got to be mindful of – don't tell somebody to run if they can't run. You know, you must be very specific in what I call give them a lifestyle prescription.

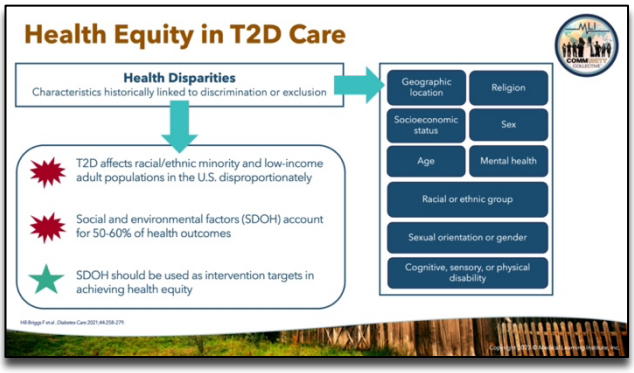
Dr. Campos: I love that last, the bottom portion of this slide. It says, "Obesity interventions typically result in early rapid weight loss." And I usually tell the patients, you know, "First off, I'm going to help you with this. I'm going to look like a

hero to you, but then you're going to have a plateau. And let me tell you why that happens. There's a condition called metabolic adaptation. You're going to plateau. It's going to happen for you. It happens to everybody." I wanted them to know that the very first visit so that when it does happen, they'll say, "Oh, Dr. Campos, I feel like I'm just not-" I'll say, "Remember we talked about this very first off that, that you're going to plateau, it's going to happen. Now we need to develop other strategies to help you try to get through that level of plateau."
And it's like anything else. I don't think patients like surprises, but when you tell them upfront, "This is what might happen to you," I think then, again, you develop that trust and you get that confidence that, okay, this is happening for me, and this is a good thing.

Dr. Eden Miller: Yeah, it just doesn't derail them. You're just ready for all the different parts of the journey and, again, trying to throw your body a curveball when you get to those plateaus.

Well, it's been a pleasure discussing this little section with you, Carlos, and love to hear your insight. You know what? I had a takeaway. I think I'm going to get another scale and put it inside the exam room instead of on the outside. That's what I'm going to do. I'm going to change my practice pattern.

Dr. Campos: Thank you, Dr. E.



Health Equity in T2D Care

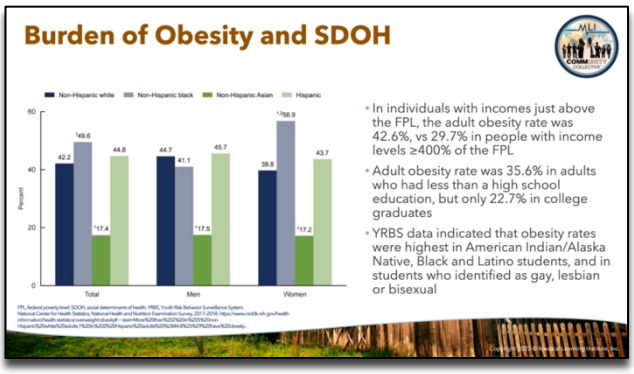
Dr. Eden Miller: All right, let's transition to a little bit of health equity, and what we'll talk specifically about Type 2 diabetes care. I think we all know that there are barriers, right. There are social determiners of health, there are barriers, so we call them health disparities, and they're massive. In fact, this is just only a short list, you know. I think there's 127 different health disparities and social determiners, and, you know, they really do affect us. And I'm going to bring Dr. Kevin Miller in here to talk about this; he's got great experience with a rural practice as well as being a family practitioner. I'm blessed to be able to work with him, and so we tackle a lot of these.

And so, you know, Kevin, tell me a little bit about what you see in your practice scenario of just kind of this disequality, and how are some of the things that you do to identify them?

Kevin Miller, DO: Well, as you know, the social determinants of health even more powerful in rural areas, certainly, it's always something we should think of. And I remember when I first read this, many years ago now, and found out that most of health is determined by the social determinants of health. Most of health is outside of the office. And so being aware of that and taking that in.

Now for rural people, they don't have the resources in many cases. They have greater rates of obesity and greater rates of diabetes, and then they don't have resources. So, we must think about that. The rural doctors listening to this probably are saying, "I serve all roles. I'm it for my patients." And there's some resources, and telehealth has made a huge difference. But, no, it's a great place to start when you're thinking about these issues.

Dr. Eden Miller: Yes, I think we're mindful, especially in different geographical and ethnicities. I think that's the first thing. I think that's kind of that low-hanging fruit that we've got to be quite aware of it. And I think after that, I think we just really inquire to the patients, what are some of those health equality barriers that you're experiencing because maybe we don't know them. Maybe we have no idea that they're having those things.



Burden of Obesity and SDOH

Dr. Eden Miller: So, this slide really speaks a lot about the burden of obesity, social determiners of health, especially when we look at the disenfranchised economically. We see the total impact and we see the difference between male and females. But, you know, I want to T this slide up for Dr. Mansfield because I think she's going to see a view of this that's really going to give us some insight into the differences between the different racial entities as well as those who are disenfranchised economically.

What are your thoughts regarding this?

Dr. Harvey-Mansfield: You know, this slide is a very important slide. I want to point out two things that are important in this slide. African American women are the most heavily affected group or impacted group when it's concerning obesity. But for men, it's Hispanic men. So, I also think Dr. Campos should join in on this slide and discuss it from a male perspective.

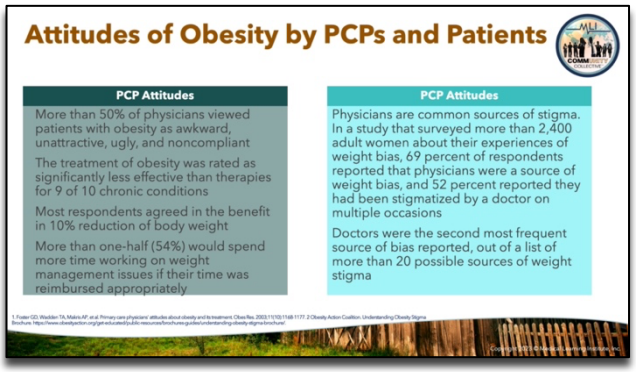
But, you know, we're learning that the muscle mass in African American women is a bit different. And when we consider the social determinants of health, it's minority groups that are the most heavily impacted by the social determinants of health. And if we want to tie it all together, people who are burdened or disadvantaged when it comes to the social determinants of health are more likely to have obesity.

Dr. Campos: Yeah. And this is really, you know, since I practice in s-, South Central Texas, this is really not anything that says, that's, is not surprising. You know, we find that a lot of our patients that, you know, they, they do heavy labor, and they work really hard. And, and then often when they come home, their biggest meal happens to be at, in, at dinnertime. And then what do they do after that? They usually sit down, watch football, or, you know, watch Netflix do- They, they, they, they, they take all these calories, and then they store those calories.

And so, the, the, the issue there when, when we saw the data, we said, "Hey, well, it doesn't surprise me. This is the kind of practice that, that this is the kind of thing we see in our practice every day, and it shouldn't surprise us with the kind of patient that we see."

Dr. Harvey-Mansfield: I also want to just point out that, you know, a lot of people once looked at urban areas for vulnerable populations. Now increasing data is showing that rural areas have a heavy, a large group of socially vulnerable populations that includes minorities. They're seeing a lot more people who are categorized as LGQ, LGBTQIA, and just being rural in and of itself increases your rate of obesity. So, you know, I love this slide in the fact that it kind of pulls in the discussion of how our day-to-day habits or our day-to-day social circumstances impacts our metabolic health, including obesity.

Dr. Eden Miller: And I really think it highlights that particular population that we must be exceedingly mindful of. It's that first interventional group for sure, even though we had to have conversations with all persons, it really, these are the high priority people that are really suffering at a higher rate.



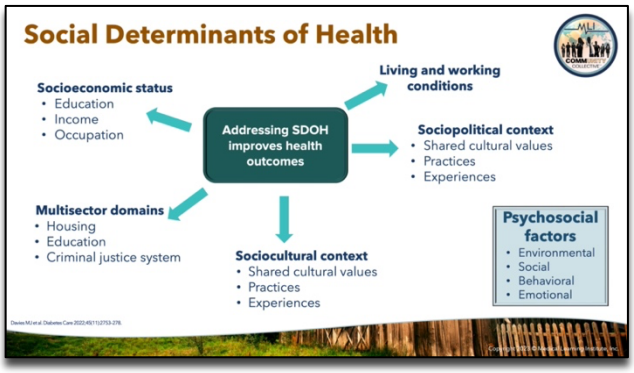
Attitudes of Obesity by PCPs and Patients

Dr. Kevin Miller: You know, I thought about this subject for some time, and I think come up with some things that make sense to clinicians and help patients. One is I often think that the physician or practitioner doesn't know what to say. Right? So, they, they have good intent. They're awkward, they're not sure what to say, and sometimes they just blurt out something that's hurtful or that shows a bias to, but we can empower them with words.
One of the things I do most often is turn to the cell. I'm just a scientist geek. Yeah, I realized so other implications of weight loss that can be so beneficial to a person but for a second, I want to talk about the cell because we care about heart disease risk. We care about liver and kidney, and we, I land there. And I talked to- Dr. Campos talked about this earlier, how he changes the focus. And then you're sitting there with the patient, Dr. Campos is, or I am, and we're looking at that common enemy.

So, I can give words to other specialists and people to say, "Hey, let's talk about the disease process and what we face together." I often see patients just really relax because they're, we're on this team together against a common enemy. Dr. Mansfield, how do you find this area with this bias? We know that this is one of the biases that's unidentified and still continues. And even with practitioners, this is often hard for them to overcome.

Dr. Harvey-Mansfield: You know, I did the Harvard Implicit Bias Test, and they have one for weight. And I have a bias myself against people that have obesity. And as someone who, you know, touts themself as an obesity specialist that was very surprising for me. And so, as I dug into the research, I realized that bias or discrimination against a person because of their weight is one of the most socially accepted types of discriminations because, you know, the media supports as basically victim blaming. You know, if a person has obesity, it's completely their fault. They don't have any willpower. And, you know, the more information that we're getting, we've seen that that's false.

So, I think the more that we are aware of how our own biases impact patient care, I think we can become better clinicians.



Social Determinants of Health

Dr. Eden Miller: what I take away from this slide is this. I do not know a person's social determiners of health unless I ask them. And it's not that I just want to go down to a list. I want to say, "Is there anything in your life, in your daily life that seems to interrupt or interfere with your best health?" And I try to get them to share that with me and try to have an answer for everything. If I don't, I try to say, you know, "I'm going to try to get an answer for you."

Kevin let's start with you first and, and then go to Dr. Mansfield. How do you identify this in your interactions with patients?

Dr. Kevin Miller: It's been a wonderful addition. And the more we've emphasized this, the more insight I must turn and ask those questions and actually empower the patient, empower our team because, if it's overlooked, if I don't find out that they have an unhealthy home and that they're threatened or that they have no one's at home, then they're always reaching these blocks. People aren't supporting them. And then I can address that. We can talk. We can be their cheerleader. Or if they don't have adequate food, I can get them to the right places. And those things open the door.

Dr. Harvey-Mansfield: Yeah. So, I have my MA do the social determinants of health screening because our state insurance or Medicaid is starting to reimburse this screening as a quality measure. Your beginning or where you are in life does not dictate your value. Or whether you deserve good care. So, we do the screenings. We try to partner them with resources. Sometimes we can't. But, you know, at least we are aware that, you know, this patient is not being noncompliant because they don't care. They just may not have the means to, to get the treatment that, that they truly need.

Healthy People 2030 and Diabetes

Dr. Eden Miller: I like that quality metrics thing and that's a great little pearl that we have because these are some of those things that we're starting to get reimbursed for.

You know, there's this what we call the Healthy People 2030. And, you know, this slide as well as the next slide is a bit of our report card.

And, I know, Kevin, you and I have worked a bit on this and so, tell me kind of a bit what you spoke to the ADA about this particular metric and your insights with it.

Dr. Kevin Miller: Yes. On more than one occasion, I've had this. And recently when we were talking in Washington, I had a great, great answer to this. It was with one of the CDCESes. And what they've done in their hospital system, or their clinic system is they put the diabetic education on the checklist like a blood pressure like it's just part of what we do. "Nice to meet you. You're a patient with diabetes. We're so glad you're part. You're going to see the doctor on this day and diabetic education on this day." And I asked, you know, how successful if she has data yet so she can show us all, but she's sincere of having great success in that.

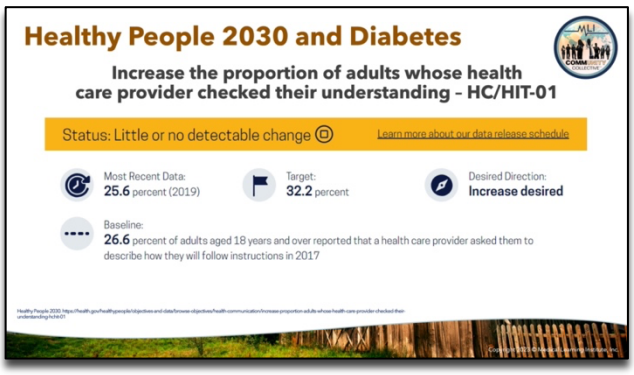
This is an area that the ADA is looking at, but you individually, as a clinician, can put this in your head, put it on the to do list every year. I'm going to check thyroid and cholesterol and regular foot check, and I'm going to look to see if they've had diabetes education. Then you have to find out who's good there, who you refer them to and just have those automatic so your staff can go right to them.

Dr. Eden Miller: I want to reach out to Dr. Mansfield. She's in a rural area. Do you have any suggestions on, you know, there's difficulty in accessing education, especially when you're geographically isolated. Have you found anything in your area that has really helped in terms of your team of how you get that diabetes educational services?

Dr. Harvey-Mansfield: So, a lot of times I refer out to the hospital for diabetes education. However, I do provide counseling in my clinic, especially if I'm starting the patients on injectables, because sometimes the inertia is not with the clinician. It's with the patients because they have fears of needles or, you know, there has been a longstanding stigma of insulin. And patients have to be educated in a way that they understand that the GLP-1 agonist and a GLP-1/GIP agonist are not actually insulin and that they can actually prevent them from having to be on insulin.

So, we start there. We try to give them their first injection in the office just so that they can get over their - the fear of injecting themselves once weekly, hopefully, if that medication is covered. And then most importantly for me, I try to educate my patient on diet and lifestyle and how it can lower their hemoglobin A1C or lower their blood glucose. And also, I try to educate my patient on what a hemoglobin A1C is because you would be surprised how many patients don't know what it actually is. And I want my patients to — I'm working on diabetes management or self-diabetes management in my office. Also, I know now that they have the, you know, continuous glucose monitoring. Some insurances still don't cover it, particularly the Medicaid programs, and so we have to get some more advocacy there.

Dr. Eden Miller: Yeah. I think those are great inroads, and I like how you find your team and you also create some of the things that you knew on your own because you are your team.



Healthy People 2030 and Diabetes

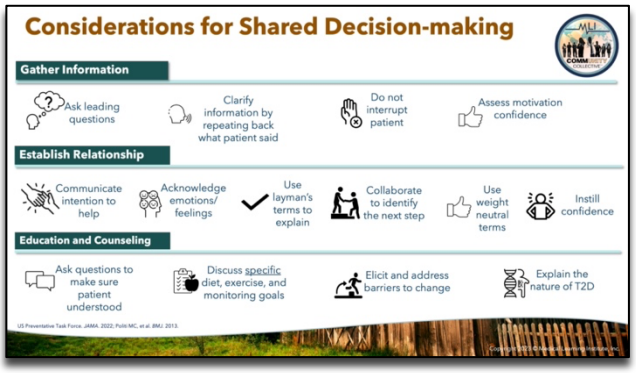
I think we all think we're excellent communicators, right? The patient knows exactly what I said, they're going to put it into practice, but what we're finding is that they do not retain what they're saying. And, you know, Kevin, you have this this great quote that I've often used about how much you retain in terms of with when you learn something and so share that with us.

Dr. Kevin Miller: I was just listening to a great book and the author said, towards the end of the book he says, "I know the data is that you will take about three things away from my book." He says, "I wish you would remember every page because it's all such good stuff." He says, "But in this case, remember what I'm telling you here." And so, he highlighted that. You know, any interaction as smart as doctors are in medical school and nurses are in nursing school, we probably only remember a few things and so that we take home, we can use them.

So that's the same with patients. Do we check back with them, highlight what we want or perhaps, even better, what they want to accomplish with that visit, follow-up with at the end and say, "Did I answer your question? Is this understandable?" and reflect and just given that opportunity, I think it's a powerful thing to do. And, hopefully, it'll ingrain that. And when they realize they can ask questions to you, they're probably going to be more open to the visit and get more out of it.

Dr. Eden Miller: So, Dr. Mansfield, how do you get your point across and make sure that patients are understanding some of those opportunities for intervention? What are your tricks?

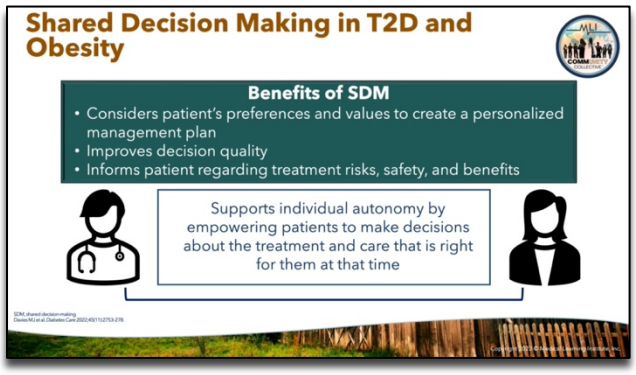
Dr. Harvey-Mansfield: Well, I try not to use too much medical jargon, and I explain, you know, firsthand potential side effects or concerns or previous patient experiences, and I always leave myself open for questions. So, we go over the plan of care. And, you know, I talk to my patients kind of like I'm talking to you. And, you know, one patient was like, "I like that you didn't use any of the fancy doctor talk." But this is just, this is my own upbringing. So, I bring myself, and then I say, "Okay, do you understand it? Is there some part that you don't understand? My smartest patients ask questions so don't feel like you can't." And then if they have any questions, we go back over it, I make sure they understand, and we have rapid follow-up especially, so within two weeks or a month, especially if we're changing any of their medication or adding a new medication.



Considerations for Shared Decision-making

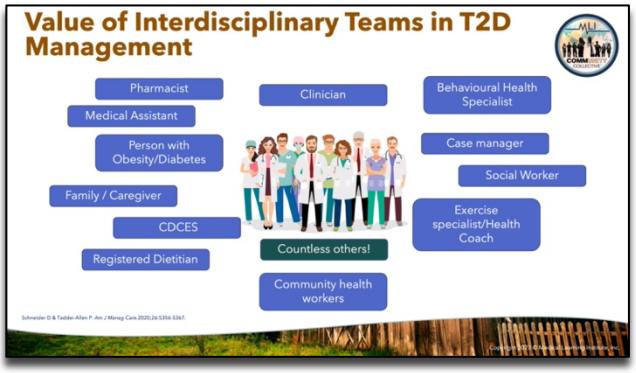
Dr. Eden Miller: I think this is a good summary slide that we, what I would recommend that you put up on your wall because you want to ask those questions. Make sure you understand, let them have time to talk, try to be their biggest cheerleader, communicate effectively with their own terminology so that you can collaborate. You're using unbiased neutral terms. You're taking their lead, but you're setting a foundation of confidence. You're going to make sure that they understand. You're going to, like Dr. Mansfield said, you're going to come back and leave enough time for questioning, right?

I remember a very older doc said to me, "If you give the patient long enough, they'll tell you what's wrong with them." Long enough to talk, right? And I think that is what's so, is central to, to making the person in the middle. It's not our appointment. We're just the conductor of this symphony of this patient, and it's them having that opportunity, enough time to identify their own journey of where they want to go.



Shared Decision Making in T2D and Obesity

Dr. Harvey-Mansfield: You know, the beauty of medicine is that there's no one cookie-cutter way in treating a patient. And so shared decision-making is all about letting a patient know all the options available to them and allowing them to choose and helping them navigate the healthcare system and get all the added benefits and resources that they need. And I think that this slide just shows, you know, and the past two slides, you know, and making sure that a patient is compliant, that they have good outcomes, let them know that they're empowered, you know, that they can do this, that they can think, you know, for themselves when it comes to their healthcare. I love to tell patients, "You're the captain of this ship. I'm your first mate. You know, I can give you all the information to make informed decisions that, you know, apply to you." And so, you know, I think that that's what kind of brings it home for me.



Value of Interdisciplinary Teams in T2D Management

Dr. Eden Miller: And, Kevin, I want you to comment a little bit about how you identify the team, especially, you know, like you said, as a rural provider, you know, sometimes there's not that many team members, but kind of walk us through a little bit of who those team members are.

Dr. Kevin Miller: Well, as Dr. Mansfield said, in my years as a rural doctor, I was all these things; and I'm sure she is all these things quite frequently. And you play all those roles and that's good, but, but to get help sometimes. Now we have telemedicine, and that's been powerful, and really can affect the rural community. You can have a specialist that they talk to for behavioral health. You can have an educator and it's somewhere distant. You can talk to somebody about lifestyle changes and bring these experts in.

And now what I've done, honestly, I still practice this way mostly. I am all these things and do all the education. But I've had a patient recently, and we found out that she was brought up in poverty, not knowing where her next meal would come from and now, she has this relationship with food that's really intrusive. And we were able to find a psychologist away.

Now how did I find this? I talked to people locally, "Who's good? Who do you like? Who really is a blessing to you?" Then I called her on the phone, and we talked for 20 minutes about what we think about healthcare and how we like to address a patient trying to get to a good healthy weight or trying to control their diabetes. And we hit it off. So, we referred her quite a bit. She's part of that team for our patients. And so that can be some extra work, but, boy, does it pay off. Rather than sending to someone random who you don't know, you have this relationship with them and so it can be really powerful to help your patients.

Dr. Eden Miller: I think we also have a common voice, too, when you have that collective that's all saying the same thing to the person, and it also says that you're not alone in this. I think sometimes, especially the primary care provider, the clinician feels like they have to do it all, but you don't. You just have to identify and spread the workload out.

How to Build and Locate Your Team Members

Dr. Mansfield, will you comment a little bit on this of how you have in your practice, because, you know, Dr. Miller's been in a rural practice, I have as well; but I think you're kind of in the thick of it now. So how have you built your team members?

Dr. Harvey-Mansfield: So, I really rely heavily on the hospital here because they receive a lot of resources and funding from the state to take care of the people in this community. So, I have a list of all the different resources and specialists that the hospital offers. I also use the patient navigator with the AAFP to find additional resources for my patients, especially if the hospital doesn't provide those resources. But, just like Dr. Kevin said, I am a health coach, I am an exercise coach, I am a diabetes educator, I am a counselor, I'm a minister. I am their person. And, you know, I think that that's what makes rural family medicine so awesome. You know, we're trained to do a lot of things with very few resources.

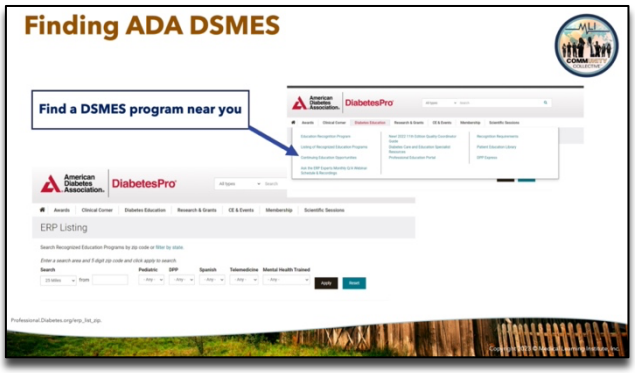
And so, you know, I'm going to continue to lean on people like you guys to educate us about all the resources available, some that, you know, they aren't, you know, readily apparent. So, you know, staying in networks with people like you, reaching out to the hospital, using the patient navigator, you know, that's how I've made it so far and, also, continuing education and professional development is still very important.

Importance of Collaborative Care

Dr. Eden Miller: I'm just going to summarize it here. You know, the person is at the center, and in trying to get all those things that are necessary, we need to still care for the person as a whole. And so, I like to do what we call the standalone appointment.

Actually, Dr. Kevin Miller takes credit for that. He developed several years ago what's called the diabetes-only appointment. And he slowly propagated that in our local, Tri-County area where in a healthcare provider busy primary care practice, we identified those patients with diabetes and said, "You know what, your diabetes is so important to manage we're going to make a diabetes-only appointment. Not that we don't care about your ankle or your depression, but we really care about your diabetes." So, we now put that in the schedule and, and that simple concept has now elevated all the way to the American Diabetes Association and the overcoming inertia.

And if you go to the ADA's website, there's quite a bit of information on overcoming inertia. There are modules, there's how to identify your team members, you know, how to see who those individuals are both remote, and telemedicine options because it spreads the workload out because I know my primary care brethren are saying this. "I don't have time to care for persons with diabetes because of how involved it is." Well, you do have time to develop that workflow, develop those resources, utilize things that help with that, focus on diabetes so you don't get distracted by the other things so that you can carve out a little time for those individuals.
So, you can see it's so important to put the patient in the center, so important to manage your time efficiently and identify who those particular people are on your team. And I so appreciate your input and seeing your own unique perspectives regarding this very important topic.



<u>Finding ADA DSMES</u>

Dr. Kevin Miller: On a slide here, there are resources that you might go to to help look for places in our area to send your patients. I have looked at every one of these and I looked at it for our area. Often you can go to this website, put in your zip code, and find resources in your area that you might not know of, and help to connect your patients.

So please look at these resources. I looked at every one of them, and they are good resources for you and your patient.

Dr. Kushner: Thank you for joining us for Part 1 and I now invite you to join us for the next episode, which is Part 2, Expanding the Role of GLP-1 Receptor Agonist and GIP/GLP-1 Dual Agonist in the Management of Type 2 Diabetes and Obesity, Practical Applications for Primary Care Professionals.

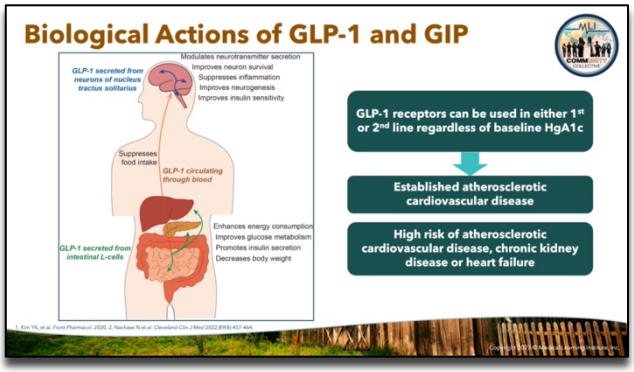
We will review the latest safety and efficacy data for GLP-1 receptor agonists and dual GIP-1 and GIP receptor agonists in Type 2 diabetes and obesity, learn about establishing trust with shared decision-making, and approaches to Type 2 diabetes intensification and putting it into practice with practical approaches in primary care.

TIME WELL SPENT:
TREATING OBESITY AND DIABETES

CHAPTER 2 | Expanding the Role of GLP-1 Receptor Agonist and GIP/GLP-1 Dual Agonist in the Management of Type 2 Diabetes and Obesity:
Practical Applications for Primary Care Professionals

Robert F. Kushner MD: Welcome to Time Well Spent – Navigating the Challenges of Treating Obesity in Diabetes. This is Activity Two, Expanding the Role of GLP-1 Receptor Agonist and GIP/GLP-1 Dual Agonist in the Management of Type 2 Diabetes and Obesity, Practical Applications for Primary Care Professionals.

To remind you, these are the learning objectives. For Part Two.



Biological Actions of GLP-1 and GIP

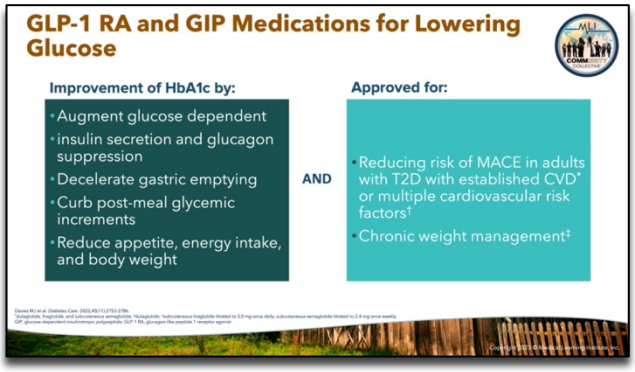
In order to use the new more effective incretin hormones, I think it's important you have an understanding of the biological actions of them as well. If we look at the figure, let's start with GLP-1. This is one of the most commonly known incretin hormone. When I say incretin hormone, that means glucose-dependent insulin secretion. It's also a nutrient-stimulated hormone because its release is stimulated when we consume foods, and they are released from the L-cells in the intestine. They then circulate in the endocrine fashion through the bloodstream, go to multiple organs. One of them is the brain, and that's where it affects appetite, both in the homeostatic center of the brain, which is hunger and fullness, as well as the reward centers of the brain. So, they help people consume less food, have less rewarding effects of food, and also from the pancreas increases insulin, improves diabetes. It also reduces gastric emptying.

Now there's other benefits seen in this diagram as well, including modulating neurotransmitter secretion, improving neuronal survival, suppressing inflammation; and these are fascinating effects that are not weight related. In fact, the GLP-1 receptor agonists are now being looked potentially for a benefit for dementia and Alzheimer's disease.

So, GLP-1 receptors can be used either as a first- or second-line agent regardless of the baseline hemoglobin A1C, and that is with diabetes, as well as using it in individuals with established atherosclerotic cardiovascular disease, because as we'll see, it actually benefits individuals with heart disease and other, cardiovascular problems, and of those at high risk of arteriosclerotic, kidney disease, and heart disease, and heart failure. So, we call this pluromorphic effects of these drugs beyond just weight loss alone.
So, here we see another diagram of the biological actions of GLP-1, as well as GIP. Towards the right, you see the GLP-1, which we just talked about, so it will increase insulin secretion and circulate up in the brain to reduce food intake, which eventually causes weight loss. It also has pleomorphic effects on, on the kidney, as well as the heart, and on inflammation.

Towards the left is another incretin hormone called GIP, and it has similar properties to GLP-1 since they're both incretin hormones, and that is that it increases in glucose-dependent insulin secretion and also has an effect on reduced food intake. But there are GIP receptors on other organs that don't have the GLP-1 receptor, so it magnifies the potential effect of adding this hormone to GLP-1.

In particular, there's GIP receptors on fat cells and probably changing fat cell metabolism as well as on bone, which affects bone metabolism. So, we're building the story here of how the combination of these two incretin hormones can have effect on multiple organs beyond just one incretin hormone by itself.

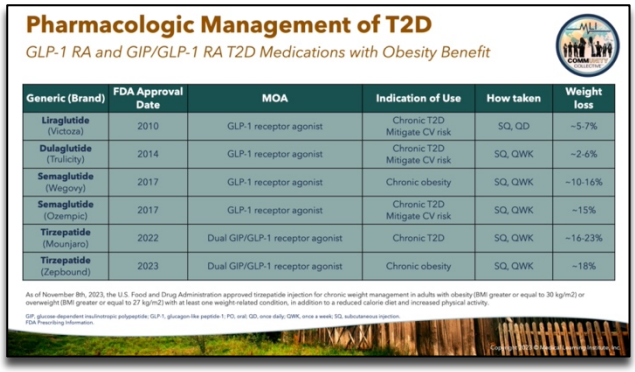


GLP-1 RA and GIP Medications for Lowering Glucose

So, we think about going back to diabetes alone, the combination of GLP-1 and GIP can be very effective for lowering blood glucose. Both augment glucose-dependent insulin secretion, reduce gastric emptying, so people do have a sense of fullness, but could also lead to some nausea, which we'll talk about a little bit later. Curbs postprandial glycemic increments, or post-food intake and blood sugar elevations and reduces appetite, energy intake, and body weight.

It has been approved for reducing MACE, which is major adverse cardiovascular events in adults with Type 2 diabetes and established cardiovascular disease or multiple cardiovascular risk

factors. And some of these have also been approved for chronic weight management. So, we are getting away from just this glucose effect and being more holistic now in treating an individual who also has obesity and has cardiovascular disease.



Pharmacologic Management of T2D

We're showing you here the currently approved incretin hormones that are available, at least in the United States, and in other countries around the world. The first column shows the product name. The second is the FDA approval date. Third is mechanism of action, which, either GLP-1 receptor agonist by itself or at the bottom a combined, dual agent. Indication how taken and weight loss.

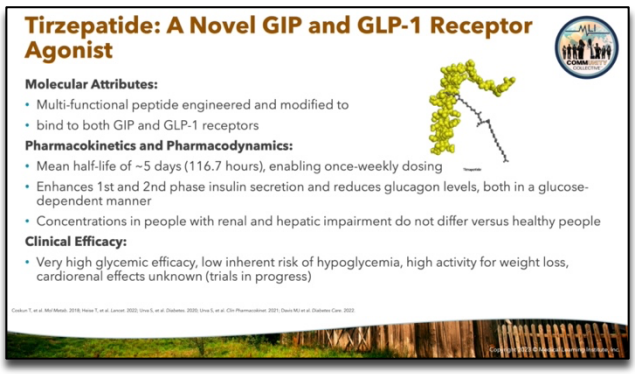
So let me point out a few key factors here. Liraglutide, or Victoza approved in 2010 was one of the first effective GLP-1 receptor agonists on the market; and it is a daily drug with a weight loss of 5 to 7%.

All the other drugs have been modified for once-a-week injection, which is a significant benefit to patient use. Dulaglutide, which is Trulicity, weight loss about the same and towards the right of 2 to 6%. And then you get to what many of us are calling a second-generation GLP-1 with the introduction of semaglutide, which is Wegovy or Ozempic for diabetes. And the reason we call it second generation is because a significant improvement in body weight loss, which you see towards the right. Now we're talking about weight losses of 10 to 16% on average.

Semaglutide has also been available as an oral agent, the only one currently available as a GLP-1 receptor agonist that's available orally with weight loss also seen, but much less than we see with the weekly injection.

And then the second second-generation medication that we call it is tirzepatide or Mounjaro, and it's the very first dual agonist. So, it combines not only GLP-1 but also the GIP incretin hormone that we just talked about, also weekly subcutaneous with even greater amounts of weight loss, now 16 to 23%. So, you can see that we're harnessing the benefit of an intestinal hormone, not only for glucose reduction in patients with Type 2 diabetes, but also now as independent weight management agents.

As of November 8th, 2023, the U.S. Food and Drug Administration approved tirzepatide injections for chronic weight management in adults with obesity (BMI greater or equal to 30 kg/m^2) or overweight (BMI greater or equal to 27 kg/m2) with at least one weight-related condition, in addition to a reduced calorie-diet and increased physical activity.



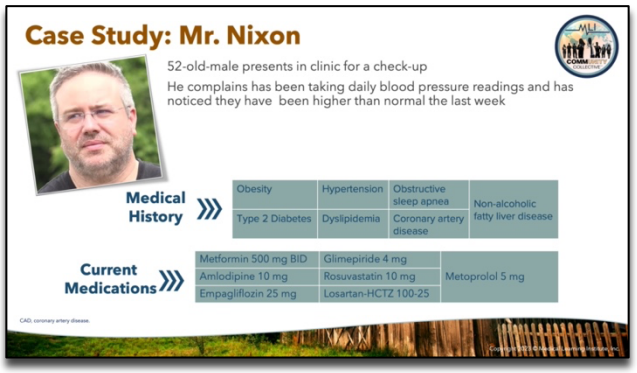
Tirzepatide: A Novel GIP and GLP-1 Receptor Agonist

So, let's take a deeper dive into what tirzepatide is because it really is a novel agent, the very first dual agonist that combines GIP and GLP-1. The pharmacokinetics allow us to give it once a week as a subcutaneous injection. It increases insulin secretion in a glucose-dependent manner, and concentration, people with renal or hepatic impairment do not differ versus healthy people, which means there's no dose reduction needed.

Interesting, this molecule is five times more effective on GIP receptors than GLP-1, and there's this interesting biologic

interaction between these two incretin hormones that give it its novel actions.

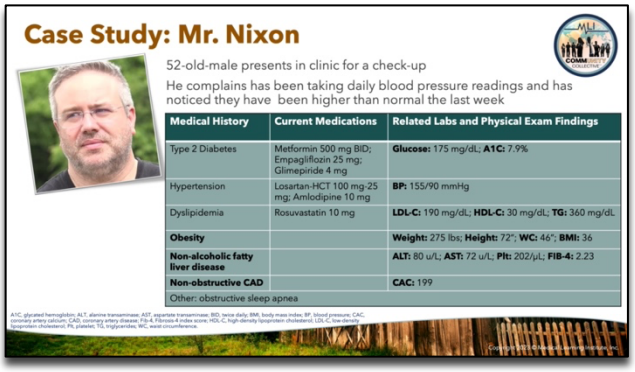
At the very bottom, it's very effective regarding glycemic control, which we'll show shortly. It does not cause hypoglycemia loss. It's also taken with another agent that causes hypoglycemia like insulin or sulfonylurea. Highly active for weight loss. Although currently not approved for obesity, we expect that approval to be seen shortly. And the cardiorenal effects are yet not known, although trials are in progress.



Case Study: Mr. Nixon

So, let's take a case study and think about would we think about using one of these medications for a patient. So, let's take Mister Nixon, 52-year-old male presents in the clinic for a checkup. His complaints are he's been taking daily blood pressure readings and has noticed that they have been higher than normal in the last week.

His medical problems are really complex. Obesity, Type 2 diabetes, hypertension, dyslipidemia, obstructive sleep apnea, coronary artery disease, and nonalcoholic fatty liver disease; and you see his current medications of metformin, amlodipine, empagliflozin, which is a SGLT-2 inhibitor; glimepiride, a sulfonylurea; rosuvastatin, a statin; losartan/hydrochlorothiazide and metoprolol.

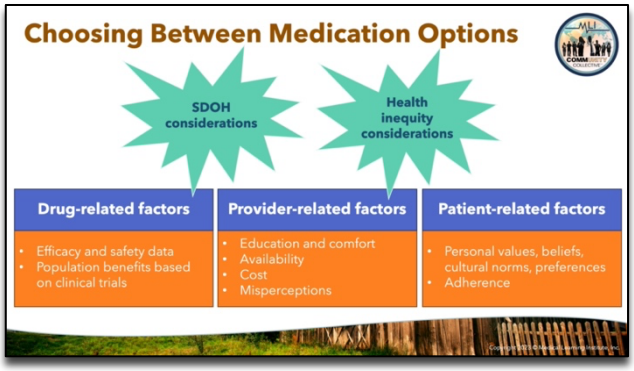


Case Study: Mr. Nixon

The next slide looks a little bit more at his labs and his physical examination findings. We see his diabetes is not well-controlled with a glucose of 175 and a hemoglobin A1C of 7.9%. His blood pressure is also not well-controlled at 155/90. His dyslipidemia, his HDL is lower than we'd like and triglycerides significantly higher than we would like it. His obesity is Class 2 with a, with a BMI of 36 and an increased waist circumference suggesting increased visceral fat.

We know his ALT is higher than his AST, and his FIB-4 score is higher than we would like it, which would eliminate the need for further evaluation, although not quite high enough to signify he has fibrosis, so he likely has NASH; and he has plaque because of the increased CAP score of 199.

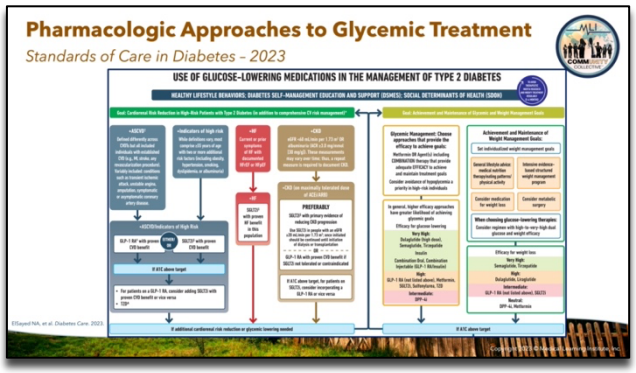
In my mind, this patient would be a perfect candidate for intensifying therapy and considering adding either a GLP-1 receptor agonist or a GLP-1/GIP dual agonist to bring all these medical problems under better control.



Choosing Between Medication Options

So, let's take a deeper dive on how we would think about which medications to add. So, we certainly always must consider social determinants of health, where patients live, where they play, what their communities are like, their insurance and their behaviors, and health inequality considerations. So, we take what access and affordability is all about.

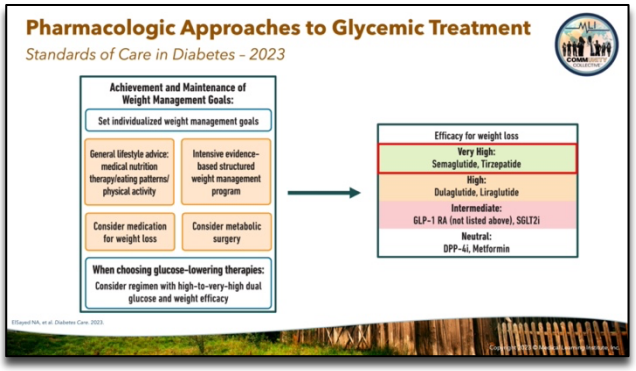
The three major buckets include drug-related factors. The second bucket is provider-related factors, and the third is patient-related factors. Let's spend some time talking about drug-related factors, which deal with efficacy and safety data and population benefits based on clinical trials.



Pharmacologic Approaches to Glycemic Treatment

So, the new guidelines from the ADA show us this algorithm, which looks rather complicated. It does begin with a foundation of healthy lifestyle behaviors, diabetes education, and once again social determinants of health. And then what the algorithm has us look like, look at is what is our, what's the patient look like and what are our goals? So, towards the left, does the patient have atherosclerotic disease, is the patient at particularly high risk for heart disease, does the patient have heart failure, does the patient have chronic kidney disease along with their diabetes?

In the panel towards the right, which is the one I'm going to look at a little, more, is a patient who has overweight or has obesity, and weight loss is going to be one of our targets. Now in practicality, over 80, or approximately 90% of our patients with Type 2 diabetes also suffer from overweight or have obesity. So, in my world, almost all the patients are going to be nodding towards the right, but we do need to pay attention to whether they have a complication such as kidney disease or heart failure as well. So, what does that panel on the right look like in a little bit more detail?



Pharmacologic Approaches to Glycemic Treatment

So, here we have the panel on the right, blown up a little bit more, as a treatment algorithm for how we're going to manage a patient who comes in with Type 2 diabetes but also is living with obesity, and weight loss is going to be one of the additional targets. Well, we always want to provide lifestyle counseling, medical nutrition therapy, increased physical activity, perhaps a referral to a registered dietitian if there is one in your community.

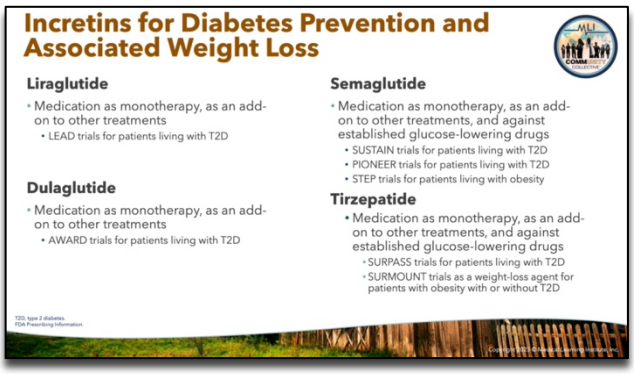
I often use the Internet for downloadable resources, whether you're going to use a Mediterranean diet, or a DASH diet, or a vegetarian diet, or just a heart healthy diet. You can often get that from the Internet if you don't have access to a registered dietitian.

If that is not sufficient, and in these patients, it often isn't sufficient enough, you're then going to consider using a medication not only that's going to improve their diabetes but also have the additional benefit of weight loss. And we also, by the way, want to consider is this patient a candidate for metabolic bariatric surgery if you have access to a program within your community?

Here we're thinking about an individual with a Body Mass Index of 40 or more or even 30 or more with Type 2 diabetes or another complication. I'm going to actually go one step further on you. The latest guidelines from the Bariatric Surgical Society is considering with a BMI being 30 or more with diabetes, however, insurance may be difficult to cover for that patient. But the bottom line with surgery is we are trying to intervene as early as possible because you want to preserve pancreatic function, and then the patient has the best outcomes when they have not exhausted their beta cells.

Now, let's get back to medication. If you're going to use a medication, they are prioritized by effects not only on weight loss but on cardiovascular health. And the two that have the highest outcome data, which I'm going to show you momentarily, come from semaglutide and tirzepatide. That's why those are graded as the very high efficacy for you to consider. Just under that would be high, which means the data is not quite as strong regarding weight loss, and that would be dulaglutide or liraglutide. Intermediate we go down a little bit further where we're now talking about the SGLT2

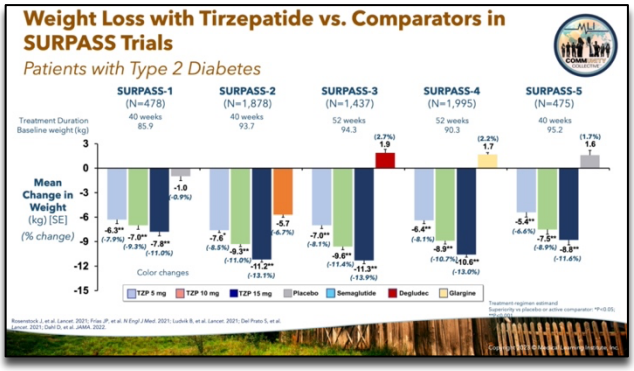
inhibitors. And lastly neutral, which would be DPP-4 inhibitors or metformin, so that's your hierarchy that you want to think about again, depending upon coverage and cost.



Incretins for Diabetes Prevention and Associated Weight Loss

So, to remind you, we use incretin therapy for diabetes prevention and associated weight loss. These are the four products that we consider that are on the market. We have liraglutide, which is a daily subcutaneous administration which has data not only to improve diabetes but also cardiovascular health. We have dulaglutide, also for improvement in diabetes and cardiovascular health; but this one is a weekly injection. Then we have the two that have the highest data available towards the right, and that's semaglutide and tirzepatide.

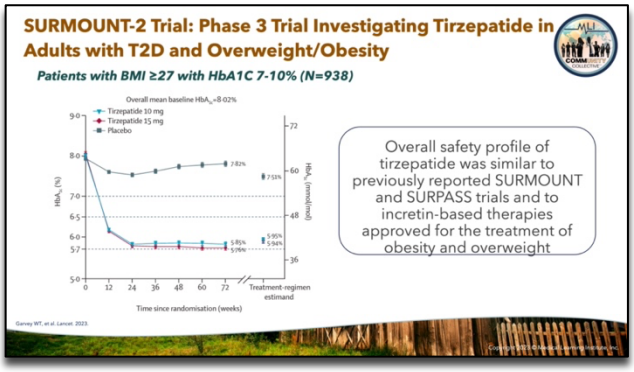
The trials that we're going to review briefly with semaglutide, some of them are SUSTAIN, PIONEER, and STEP. Those are the names that are given to those trials. For the tirzepatide, the trials are called SURPASS and SURMOUNT. So, look for those when we go over the clinical trial data.



Weight Loss with Tirzepatide vs Comparators in SURPASS Trials

What I'm showing you here now is a composite slide of all the SURPASS trials. Again, that's the trials that were used to look at tirzepatide in individuals with Type 2 diabetes. And just to orient you here, what we're looking at is in this slide is the mean weight loss in kilograms or in percent for the different SURPASS trials, which had different patient populations as well as comparators. But in all the light blue bars is the tirzepatide 5 milligram dose. In the green bars is the 10-milligram dose, and in the dark blue bars is the 15-milligram dose. The fourth bar across all of these is the comparator. So, for example, in SURPASS-1, the comparator was placebo. In SURPASS-2, the comparator was semaglutide 1 milligram. In SURPASS-3, it was degludec insulin; and in SURPASS-4, it was glargine insulin.

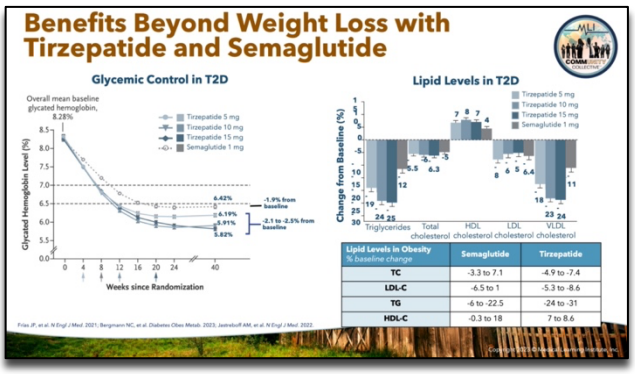
So, if you combine all these together, what you see is a uniformity of outcomes, which is always nice to see when we're trying to develop the story or a generality of how the drug performs. And if you look at tirzepatide alone, going across all the SUPPRESS trials, what you see is the greater the dose of tirzepatide, the greater the weight loss or the greatest weight loss is with the highest dose, which is 15 milligrams, and you're talking about a weight loss of about 11% to 14% body weight within about a year, which is a significant amount of weight loss, and it outperformed the comparators. Notice that in the two, in the SURPASS-3 and SURPASS-4, where insulin was used, there was actually an increase in body weight. So that's another call to action that using an incretin hormone before insulin is now becoming a new treatment paradigm because of the effect, in part, on the weight gain.



SURMOUNT-2: Phase 3 Trial Investigating Tirzepatide in Adults with T2D and Overweight/Obesity

This is data from this SURMOUNT-2 trial. So, this is still with tirzepatide, but now we're looking at individuals with obesity with a complication of Type 2 diabetes. And rather than looking at weight loss, we're looking at change in hemoglobin A1C, and we're looking at the effective individuals who were randomized either to tirzepatide 10 milligrams or tirzepatide 15 milligrams versus placebo.

Now interestingly, the average hemoglobin A1C was 8%. In the patient case we talked about a little bit before, Mr. Nixon had a blood hemoglobin A1C, I think, of about 7.5%. So, it's kind of in this, in this range. And look at the effect of the hemoglobin A1C over the course of 72 weeks. It went from 8% on average down to under 6%, profoundly effective. And that speaks to the effectiveness, not only of the weight loss, but to the effectiveness of a combined incretin drug having both GLP-1 and GIP combined.

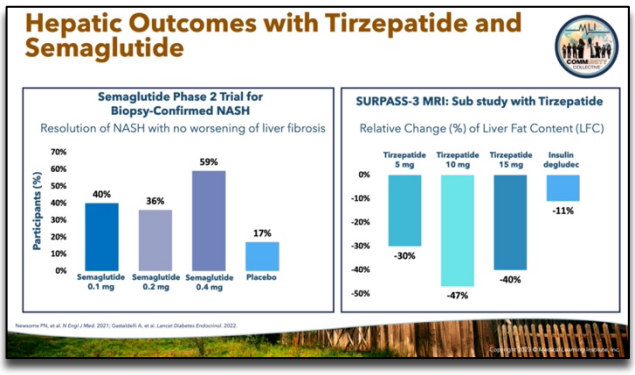


Benefits Beyond Weight Loss with Tirzepatide and Semaglutide

And there are benefits beyond just weight loss with both tirzepatide and semaglutide. In this case, what we're looking at on the left is the benefit of tirzepatide 5, 10, and 15 milligrams compared to semaglutide 1 milligram on reduction in hemoglobin A1C. So, we kind of looked at, a little bit, on the last slide where you have, on average, patients with really poorly controlled diabetes of 8.2% going down to 6% or less. And that's profoundly effective and that is by 40 weeks. So that's really a big callout to considering this kind of medication for your patient with Type 2 diabetes.

Towards the right, what we're seeing is the benefit in the dyslipidemia. Again, we're looking at the, SURPASS-2 trial, which is tirzepatide versus semaglutide; and what you see across studies using these hormones is a significant benefit with reduction in triglyceride and an increase in HDL. So, we call that dyslipidemia.

The reduction in LDL is not profound, and that's why these patients also need to be treated with a statin agent, not to replace it, but add this to a statin agent. Biggest effect is going to be on triglyceride and HDL cholesterol, that dyslipidemia we often see in individuals with uncontrolled Type 2 diabetes.



Hepatic Outcomes with Tirzepatide and Semaglutide

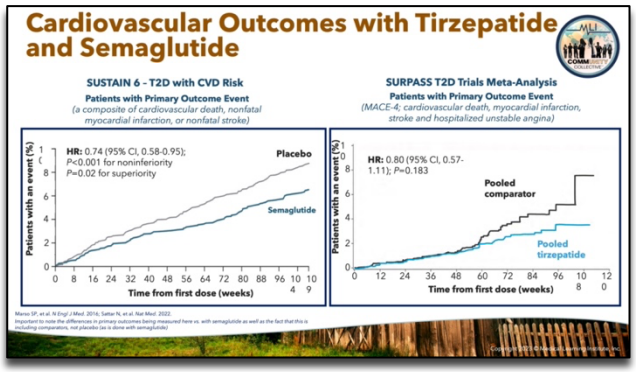
In addition to looking at dyslipidemia, we are also now seeing signals on the benefit of extra fat in the liver, which we call fatty liver disease or NASH. And I'm showing you preliminary studies; towards the left is on semaglutide, towards the right is on tirzepatide on the potential benefit in your patients like Mr. Nixon who likely has NASH or fatty liver disease.

Looking at the left panel, which is semaglutide, this was a Phase II trial in which semaglutide was given in a daily dose of 0.1, 0.2, or 0.4. This is before semaglutide was switched over to a weekly injection, so it's a Phase II trial. But the take-home message here is that when you use semaglutide in individuals with fatty liver disease, NASH, and F1 or F2 fibrosis, what you see is an improvement in NASH in 60% of the participants on the highest dose of semaglutide where it was only improved in 17% of those in placebo.

Of note though, liver fibrosis did not improve but it also did not worsen. So, the jury is still out on whether we can actually reverse liver fibrosis, but NASH appears to improve.

On the right is a sub-study with tirzepatide from the SURPASS-3 trial. Here, they're using MRI to look at liver fat content. That's the most accurate measurement we have. And what you see very significantly is in the tirzepatide doses 5, 10, and 15 you see a reduction of liver fat. Happens to be highest in tirzepatide 10 and 15 compared to those on insulin. We don't see much benefit at all in liver fat.

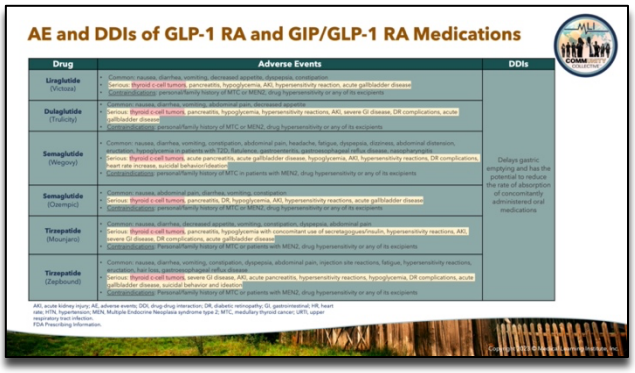
So, this is just another way of thinking about the benefit of using an incretin hormone, either a mono-agonist or a dual-agonist to treat the patient, not only the diabetes and weight loss, but also dysglycemia and potentially improving liver fat in those with fatty liver disease and/or NASH.



Cardiovascular Outcomes with Tirzepatide and Semaglutide

The other probably most significant benefit of using incretin hormone is the benefit on cardiovascular disease. Towards the left, you see the benefit of using semaglutide in what's called the SUSTAIN-6 trial where you had individuals with two diabetes and at high risk for cardiovascular disease, and their primary outcome was, was a 3-point MACE; and that is cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke. And what you see over the course of the study is those high-risk individuals randomized to semaglutide versus placebo experienced a 26% reduction in having a primary cardiovascular event, and that is cardiovascular death, nonfatal heart attack, or nonfatal stroke; and that was highly significant.

Towards the right, we see a pooled analysis from SURPASS study. These again individuals with Type 2 diabetes, which showed a 20% reduction in your primary outcome. This case, a 4-point MACE cardiovascular death, myocardial infarction, stroke, and hospitalization. However, it did not reach a clinical significance, and that study is yet to be done to demonstrate it, but it clearly shows benefit with tirzepatide with a 20% reduction versus the pooled comparator.



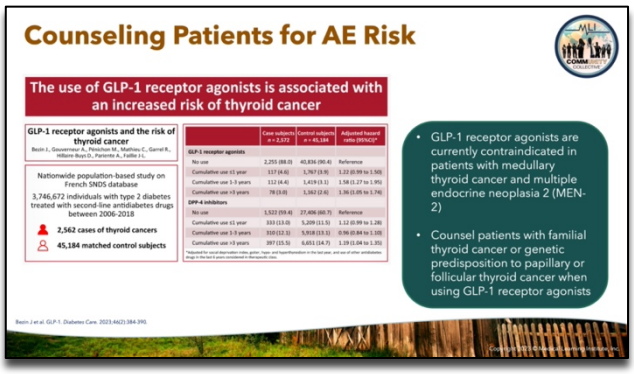
AE and DDIs of GLP-1 and GIP Medications

Now, the adverse events and drug-drug interactions for all the incretin hormones are the same. So, if you look across each of the rows, they're actually very, very similar.

What's written in blue is thyroid C-cell tumors, which were seen in rodent models; but we take that data and now take that as a contraindication for use of any of these drugs, for a patient have a personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. You get that from a family history.

The other things we need to be concerned about include pancreatitis, hypoglycemia only in those that are on another drug like insulin or sulfonylureas. Acute kidney injury has been seen; we think that's primarily from dehydration from excessive diarrhea or vomiting. You may have a hypersensitivity reaction, and we've seen acute gallbladder disease with gallstones. So that is replicated in all these GLP-1 or GLP-1/GIP dual-agonists.

There are some recent reports through social media of psychiatric adverse events. We're not seeing much of a signal of that in the primary studies. However, post surveillance reports are starting to show up, and we need to watch for that carefully.

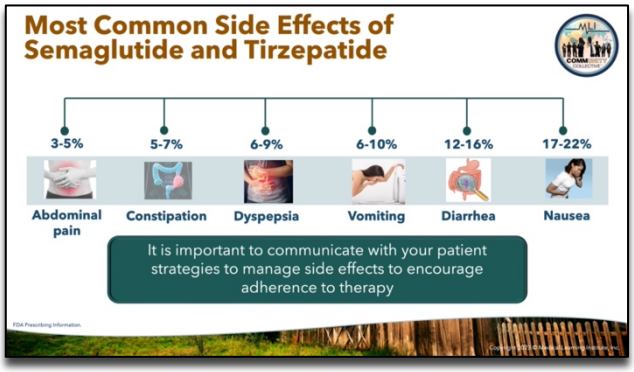


Counseling Patients for AE Risk

Another concern that was raised in post marketing is an interesting study that came out recently from France in which they did a case control large study of over 3 million individuals with Type 2 diabetes which was in their national registry. And they compared them to other individuals with Type 2 diabetes that were either on a GLP-1 receptor agonist or a DPP-4. So, in this case, the DPP-4 was the comparator drug. Those on a GLP-1 was the cases they particularly looked at.

And the question asked is do individuals who have a history of taking a GLP-1 receptor agonist have a higher risk of thyroid cancer in general, not just thyroid medullary carcinoma, which is fairly rare, but other forms of thyroid cancer? In this retrospective case control study, although very large, they found a higher odds ratio of having a thyroid cancer of about 1.2 to 1.5 for those on a GLP-1 receptor agonist and a much lower risk for those on DPP-4 inhibitor.

So, it probably is reasonable to ask your patients is there a familial thyroid cancer or a genetic predisposition exist in your family and be cautious about using the medication in those individuals, but we clearly need much more information about this particular risk.



Most Common Side Effects of Semaglutide and Tirzepatide

So, the most common side effects of both semaglutide or tirzepatide are clearly GI related because they are gastrointestinal hormones, they do affect gastric motility. You can have things like abdominal pain, constipation, dyspepsia, vomiting, diarrhea, and the most common is being nausea.

The most important thing you want to do when you start an individual on these medications, number one, be aware of the side effects and make sure patients are aware of them. Slowly dose escalate these medications, and don't increase the dose if they're having side effects. Stay at that dose; go up slowly. And third, mitigate these side effects to the best of your ability, and that is done with, one, awareness and expectations and, number two, the diet that they choose to consume, such that they're on low fat foods, not eating beyond a sense of fullness, so eating modestly, not skipping meals, going all day without eating, and having a healthy eating rhythm.

Eden Miller, DO: Dr. Kushner, I have a question for you. You know, GLP-1s are so essential in care. All the different agencies are, are recommending them. They have so many benefits for the individual – the glycemic benefits, the secondary weight loss. You know, comment if you will just a little bit. I'm getting a little bit of chatter amongst my colleagues that the weight reduction related to GLP-1s is all just muscle mass loss. Talk to us a little bit of how individuals, you know, reduce their weight and kind of what compartment is it coming from?

Dr. Kushner: Yeah, thanks, Eden, that's a good question.
Our goal is not to have people as thin as they can be. We want them to be as healthy as they can be. And part of improving health is having a healthy body composition, which is fat versus muscle.
Anytime an individual loses weight, some of it's going to come from the lean body mass or the muscle mass. The rule of thumb is about a third or a fourth of weight loss comes from muscle mass and the other comes from fat mass. We're not seeing large differences with these medications although the data is very small from the early trials. But it's something we need to pay attention to.

With the GLP-1 and the combination of GLP-1/GIP where we're seeing significant weight loss with much more effective agents where you're losing 15 to 25% body weight, we really do need to be more mindful of body composition, particularly in individuals who are elderly who already may have low muscle mass. And if now they're going to lose 25% of the body weight, they may end up with what we call sarcopenia, which is significantly lower muscle mass with reduced function, frailty, weakness, and so forth.

So many more studies are going to be done regarding body composition changes with these medications. But currently, we are not seeing an excessive amount of body muscle mass loss beyond what we would see with any weight reduction.

Dr. Eden Miller: Oh, thanks so much. That really gives me quite a bit more clarity with that.

Kevin Miller, DO: Well, a question I have had at times, and I bet others have too. With these new medications sometimes there's more barriers to get them, and are they worth it? Are they worth the barriers to try to get some of these new medications for our patients, to take the time to explain how they work, to work through prior authorizations? Do they have the outcomes that we're looking for our patients that it's worth the time and effort to ask the patient to work through this with us? I'd like to know other's opinion on this question. Thank you.

Dr. Kushner: Thank you for the question, Kevin. You know, this is a very frustrating time for both clinicians and patients alike. On one hand, we have what are likely to be lifesaving medications with GLP-1 receptor agonists with reducing cardiovascular events, but at the same time very hard to get because of cost and supply issues.

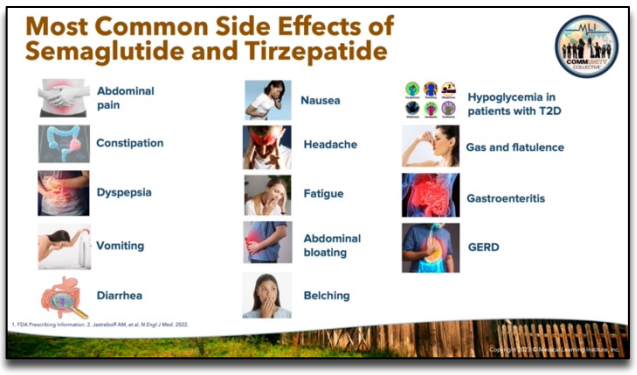
Until that is settled, we need to work with our patients as close as we can. If it's a cost issue, we want to use medications based on cost and effectiveness for that medication. And when the GLP-1 receptor agonists become more available, particularly with reduction in cost, as well as more availability with insurance, we're going to utilize those to the best of our ability. In the meantime, it is a frustrating situation.

Keisha Harvey-Mansfield, MD: Are there any specific patient populations that would benefit more from GLP-1 medications or tirzepatide?
Dr. Kushner: That is a great question. We don't have specific phenotypes regarding the patient presentation of when would we use these medications or not. But in general, what we're thinking about is an individual who would benefit from a significant amount of body weight loss because that's the effectiveness of GLP-1, like semaglutide, a GLP-1/GIP drug like tirzepatide, with weight losses of 15 to 25%. So, if weight is a major factor in that patient, we want to think about those drugs.

The other is an individual with multiple complications, particularly cardiovascular disease or NASH or even sleep apnea, where we need, know that these drugs not only have a weight-dependent benefit but also a weight-independent benefit that affects many other organs. So, it's going to be based on shared decision-making, but it's the higher-risk patient. The patient would benefit from a great amount of weight loss and multiple complications that we're going to be thinking about using a drug like semaglutide or tirzepatide.

Carlos Campos, MD: Another question is, is there a risk of developing hypoglycemia when using GLP-1 medications or tirzepatide alone or in combination with other treatments?

Dr. Kushner: That's a very good question. We know that the incretin hormones, GLP-1, as well as a combination of GLP-1 and GIP, have a glucose-dependent insulin-release effect. So, they don't cause hypoglycemia by themselves. However, when they are co-administered with another drug that may cause hypoglycemia, specifically insulin or sulfonylureas, we have to be very careful about that co-administration. In practice, we generally dose-reduce the insulin or the sulfonylurea; or if they have good glucose control, we, we may actually stop those medications in order to avoid hypoglycemia entirely.



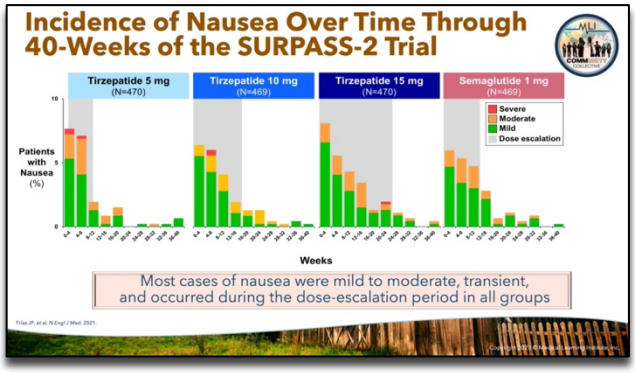
Most Common Side Effects of Semaglutide and Tirzepatide

Dr. Harvey-Mansfield: So now we're going to discuss the most common side effects of semaglutide; and tirzepatide and considering the mechanism of action, the side effects may not be surprising to you.

The most common side effect is nausea. I think greater than 33% of people have some nausea, and then that declines over time the longer that the person is on the medication. Then you may experience some constipation, diarrhea, abdominal pain, acid reflux, gas, and flatulence.

So, Dr. Campos, what do you think about these side effects, especially in practicing using the GLP-1s?

Dr. Carlos Campos: I certainly agree with all of them. And then one of the things that I remind the patients, Dr. Harvey-Mansfield, is that just reminding them how the medicine works. One of the things it does, it decreases gastric emptying, so actually tell, you know, when the food hits your stomach, normally, it moves out. It's going to slow that up. So, as it does that, you're going to feel full quicker. So, guess what? Listen to your body; when you're full, stop eating. Because if you continue eating, and it's usually what happens 8, 9 times out of 10, people overeat.



Incidence of Nausea Over Time Through 40-Weeks of the SURPASS-2 Trial

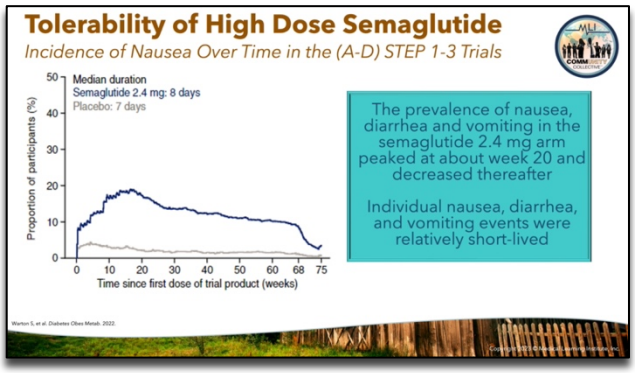
Dr. Harvey-Mansfield: So, the SURPASS study is really important when we think about the GLP-1s and the GLP-1/GIP agonist. This study was done over 40 weeks. And around 24 weeks, they found that less than 1% of people actually still have the nausea and the vomiting. And something else that we found is, you know, if a person is starting to experience more nausea and vomiting as we increase the dose of the medication, you may want to dial back down the dose, wait a little bit longer, and then slowly increase the dose. But I think it's really amazing that about 24 weeks less than 1% of people still have the nausea. Dr. Miller, what do you think about that? And what is your experience with nausea?

Dr. Eden Miller: Yeah, it's hope for that introductory period. You know, I especially think those individuals that are incretin-naïve, right? They haven't been exposed to incretins. It's their first little journey. It's the first week of going. I tell them, "Hey, don't make any judgments on the first few weeks. I want to know if it's a deal-breaker." I love how you talked about titrating or keeping the dose going slow, staying where it's at. But you say to them, "Hey, hang in there with me, especially those first 4 to 6 weeks. As we get to 2 to 3 months, I really don't think this is going to be an issue.

I also notice, too, that if you end up going on a lower dose, you can go back and revisit it. If you need additional A1C or additional secondary effects, it doesn't mean they're going to happen again. You can reevaluate that in, again, in another 3 to 4 months, see if that additional titration doesn't elicit any other symptoms as well.

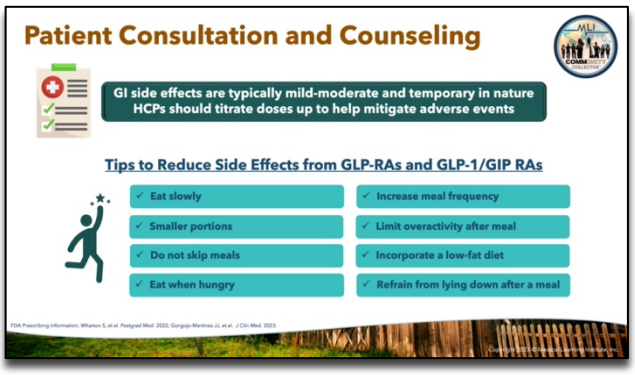
Dr. Campos: Yeah. I think the takeaway from this slide is that over time, just about whether you're doing tirzepatide or semaglutide, just about every, every time, over time that nausea does begin to diminish.

Dr. Harvey-Mansfield: You know, something else I see that's important with this slide is very few people actually have severe nausea and vomiting. As you can see, most people's nausea or vomiting is very mild.



Tolerability of High Does Semaglutide

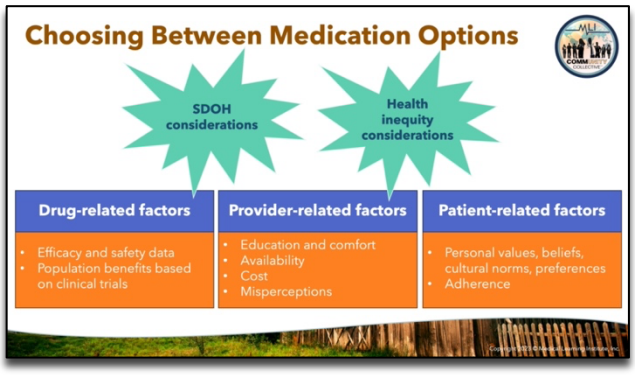
So, the prevalence of nausea, diarrhea, and vomiting in semaglutide 2.4 milligrams peaked at around 20 weeks and decreased thereafter. I think this is just to reaffirm what was learned in the SURPASS trial, which I stated in the last slide, around 24 weeks, less than 1% of people actually had any nausea associated with the GLP-1s. And so, we can assume the same for the GLP-1/GIP agonists.



Patient Consultation and Counseling

Dr. Campos: Yeah. As I mentioned before, I think that's the biggest thing that I like to emphasize to my patients when we put them on the GLP-1 receptor agonists medicine is that to say, "Listen to your body." You know, it's going to, your, what this medicine is going to do is going to renew some of the signals that you hadn't had before. When you feel full, stop eating. If you're not, if you're not hungry, then don't eat. And this is a perfect time when you're, especially in the evenings if you're going to do a meal replacement with, like, a protein shake, this is a great time to do that.

Dr. Harvey-Mansfield: You know, something, a piece of advice that I give to my patients, too, is if you eat a meal that's full of carbohydrates, you're more than likely going to get the nausea. Something that this slide points out is that we should incorporate a low-fat diet. Also, kind of what you're talking about. You know, stay away from those really greasy foods; but also, you may want to consider watching what kind of carbohydrates. You, move to more of the complex carbohydrates like legumes, beans instead of pastries or our candies because those, more than likely, will make you sick.



Choosing Between Medication Options

So, choosing between the medication options, provider-related factors, I can speak to this because, when the GLP-1 agonists first came out, I was the one sounding the alarm saying we need to put patients on this for weight loss.

And a lot of doctors, especially the doctors more senior than myself, they said, "I like to not prescribe new medications because I like to wait and see what side effects they're going to have later on." For me, you know, later may never come.

And we have a plethora of randomized controlled trials already out there that's showing that this is a powerful tool in the diabetes realm as well as the weight loss realm. And so, you know, I'm still trying to get some of my cohorts to start prescribing GLP-1s, you know, despite the side effects. Some of our oldest drugs have side effects. You know, we counsel our patients about them, and we still move forward.

So, I'm going to ask you, Dr. Campos, so like when, when the GLP-1s came out, like, did you start them? And then have you been counseling your cohorts about these medications?

Dr. Campos: Yes. You know, I'm, if you can put doctors into categories, I'm one of the first penguins in the water, if you will. I like to jump in the water with these and, yeah, and so, yes, I was using them. And I think they were sitting back. A lot of them were sitting back to see if, what big side effects there were from them.

But, but it's still a, I'm going, I agree with you, Dr. Harvey-Mansfield that there's still a significant amount of primary care clinicians who really have not used the GLP-1s. And what we're saying is, look, this is not the deep end of the pool. They've been around for over 10 years, and it's time for you to come on in. The water's great here, and your patients are going to benefit from them. So, yes, we, we encourage our colleagues to please use them.

Dr. Harvey-Mansfield: And so, you know, with all of that, I want to move, let's switch gears. What about with our patients? You know? Some of our patients are on state insurance, and state insurance may not cover some of the newer GLP-1s, specifically, tirzepatide.

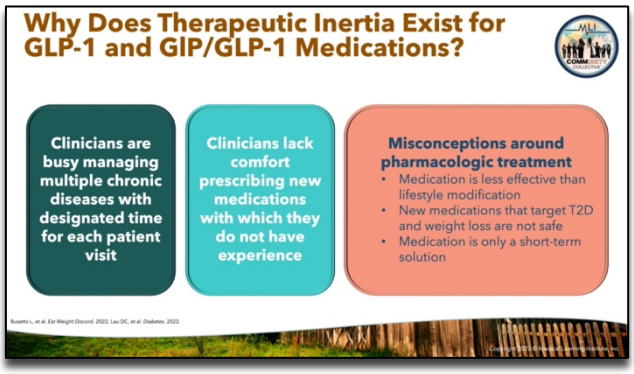
You know, there, my likelihood is moderate with getting my patients on semaglutide. But for some, you know, if for some reason they cannot tolerate semaglutide, you know, I try, I try to put them on tirzepatide, but just some of the companies are not covering it, and they're asking me to go to some of the daily dosing GLP-1s.

And we know in our patient population, that's, that might be quite difficult for them to do. First, we have to get them, you know, geared up to give themselves a shot and then try to get them geared up to do it every day. It's just a little bit easier when we have these once-weekly dosing.

So, there's, you know, some patient advocacy that needs to be done. You know, and if our patients don't have diabetes, you know, the chances of them getting on a GLP-1, period, are almost impossible.

So, you know, if you're watching this video, I hope that you'll engage in some form of advocacy for our patients to actually get a GLP-1 if they need to lose weight. And, you know, it's really hard to get the GLP-1s that are trademarked for weight loss or FDA approved for weight loss because a lot of times either they have to have an insurance plan that also has the obesity component or obesity treatment component, or they have to pay out of pocket.

And, you know, this is one of the things that we talk about in the social determinants of health realm, you know, lack of access. And if a person is not financially able to afford a medicine, you know, that's unfair; and that's an example of lack of access.



Why Does Therapeutic Inertia Exist for GLP-1 and GIP/GLP-1 Medications

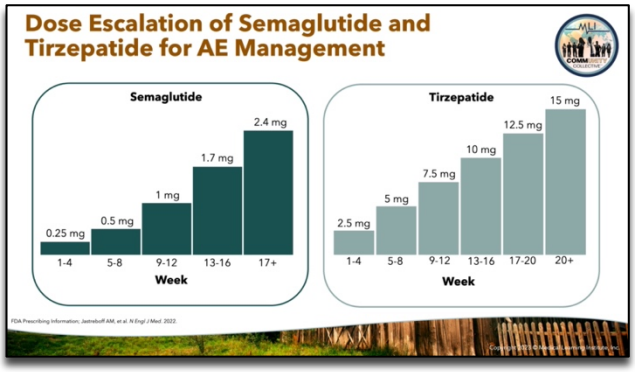
Dr. Eden Miller: I'm currently the co-chair of Provider Education for the ADA "Overcoming Therapeutic Inertia." And, you know, I think there, you know, when we look at medication adherence, right, adherence or engagement, you know, 80% is considered good, which is kind of interesting as if your diabetes takes a 20% vacation or something.

But I think that each type of component, each therapy that you look at has its level of engagement. And a lot of times I ask the patient about inertia specifically.

One of the things I do as a part of my daily practice, when I come into their appointment, I say, "If there's one thing, I can do to remove a barrier to help make your life a little bit better living with diabetes, what would it be?" Because inertia is not always known; and especially as us as clinicians, we're always trying to fill in the blank for the patient. And so, I think asking about inertia is paramount. Then I will go from there. I will talk specifically about the GLP-1s or GIP/GLP

combinations. And I'll say, instead of maybe inquiring, "You take your med all the time, right?" Because you know they're going to say, "Of course, I do." Right?

But instead, I say, "How many times in a given month, especially with weeklies, do you forget or delay your particular injection?" For a couple things, it's a time to talk about engagement because do you know that most of the GLP-1s, if you forget a dose, you can go plus or minus three days around that. So, some patients think, oh, I forgot it on my Tuesday. I can't do it again till next Tuesday. So just simply talking to them about missed doses and makeup doses can do that. Then I say, "What are some other components about not being able to obtain it? Is it side effect profile? Is it financial or copay type of issues?" So, if you inquire as to the inertia specifically around GLP/GIP, you're going to be much more likely to help them with adherence and engagement, make their journey a little bit easier to incorporate these highly potent treatment options.



Dose Escalation of Semaglutide and Tirzepatide for AE Management

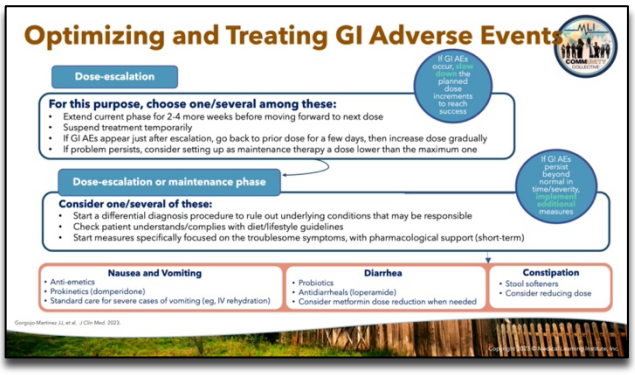
Dr. Harvey-Mansfield: So, this slide gives us information about how to escalate the dose for the GLP-1s and the GLP-1/GIP agonist. And the take-home message from this slide is that we should escalate the dose over about 4 weeks.

But like we said earlier, if you notice that every 4 weeks you increase, some patients are not tolerating it, you can do it more slowly. You can wait 8 weeks. And like Dr. Miller said previously, we can dial down a dose. Anything you want to add here, Dr. Campos?

Dr. Campos: The only thing is to remind the providers out there is that now the 1.7 milligrams is a maintenance dose now. So, you know, we don't have to go up to the 2.5, 2.4 on semaglutide. 1.7 is a maintenance dose. And again, just to remind them, the reason we're trying to do that is to sort of prevent the GI adverse events.

Dr. Harvey-Mansfield: Why has the dose changed from 2.4 to 1.7 as the maintenance dose?

Dr. Campos: Well, I think for several reasons. There was a significant amount of people that were just going to 1.7. And now it's also been approved for pediatric use; and you can use it all the way down to, semaglutide to 12 years, 12 years of age. And so, they've adjusted the maintenance dose for that reason also.



Optimizing and Treating GI Adverse Events

Dr. Harvey-Mansfield: Something that happens in medicine is we oftentimes want to blame a medication for all our patients' complaints or symptoms.

This slide tells you if you have dialed down the dose or you have gone, you have titrated slowly, you may need to rule out other causes for your patient's nausea, vomiting. Make sure that they don't have acid reflux. Make sure it's not another drug. You know, make sure it's not their eating patterns. You know, if they are a diabetic, make sure that they're not moving on into diabetic gastroparesis, you know, especially if you're getting patients later in their course.

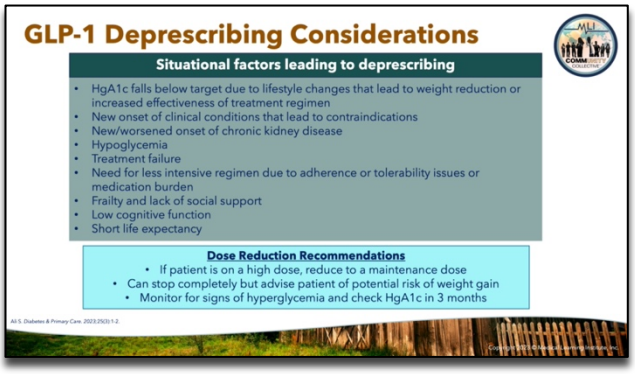
So, anything you want to add, Dr. Campos, with basically forming a differential after you've done everything for your patient and evaluated them?

Dr. Campos: Make sure, in our area, make sure they don't have gallbladder disease. That's- That's a very common thing here in this area.

But I think this is a really, I think, intensive slide that really goes through just about every scenario here. And it gives a way that you can address those scenarios with the diarrhea using the probiotics; and I don't know if you, Dr. Miller, have you ever told patients that they should use, like, Imodium or they could use, Phenergan, or some other antiemetics?

Dr. Eden Miller: Yeah, absolutely, especially after, to what Dr. Harvey-Mansfield said is, is that you're not going to blame the GLP/GIP combo on everything. Right? You're going to use your intuition. You're going to see it do the timing. You're going to deescalate.

And then one of the things, too, is I ask more specifically, "When do you get diarrhea? When do you get nausea?" And we even notice, even though it's a weekly dose, I see this a lot. I'm sure you all see this as well. Right around 36 hours after that subsequent injection you get a little complaint with it. And I say, you know what, just be mindful.



GLP-1 Deprescribing Considerations

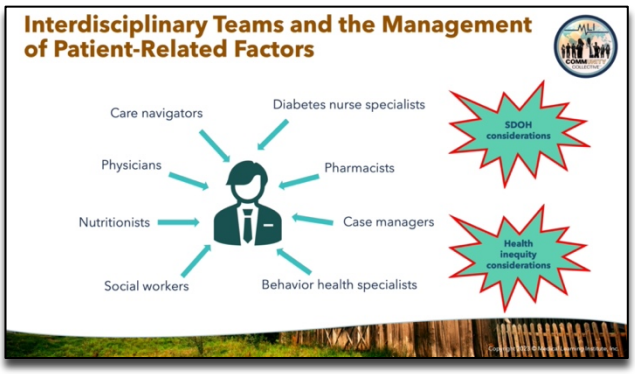
Dr. Harvey-Mansfield: I love this slide. My favorite, one of my favorite slides is deprescribing. You know, I hate that we're only talking about deprescribing the GLP-1s, but this is what I have found. And I want to hear from you guys. But when I put my patients on a GLP-1, off that, I have to decrease their insulin dose because I find that they start bottoming out, bottoming out if I don't. And, you know, that's what the literature says. If we put a patient on the GLP-1, we should decrease their insulin dose by 25%.

And when my patients start losing weight, I must start taking them off diabetic meds because their sugar starts going low despite, you know, back in the day, we used to say people cannot bottom out on metformin. Well, I have them on a GLP-1, metformin, and have their blood sugar just running low naturally because, one, they're losing weight, one, they are reversing their insulin resistance, so they're not getting that insulin spike anymore.

Dr. Campos: Yeah, I agree with you. And when I talk about pancreatitis, I often talk to other clinicians and say, "You know, remember, pancreatitis is not a contraindication; but it is a warning." And so often we'll talk about that with my patients. I have several patients that have had a history of pancreatitis because they had gallbladder disease or maybe they had an alcohol issue or something like that, I said, "You know, I'm, I'm willing to hold your hand, and let's walk down the road with this. And if you start developing mid epigastric pain radiating to your back, associated with nausea, then we need to stop the medication. But if you're wanting to do this, I'm willing to walk down the road with you."
Again, it is not a contraindication, but it is a warning there that we just have to be cognizant of.

And then again, if there are some patients that once they get to their goal that they want to stop the medication, I'll remind them that almost all the studies show that, you know, 9 times out of 10 you're going to, your weight or your blood sugar's going to go up.

And so, I usually try, like you, Dr. Harvey-Mansfield, is to really tell them, "Hey, you know, try to stay on this medication simply because the effects, the other effects that you have, the cardioprotection that we see in many of those medications, renal protection, a variety of other things that, that we're starting to see some effect that will, that we're, the studies that are ongoing really benefit from that. So, you're right. If they've got a secretagogue, they got insulin, those are the ones you want to get them off, before you get them off the incretin-related medication.



Interdisciplinary Teams and the Management of Patient-Related Factors

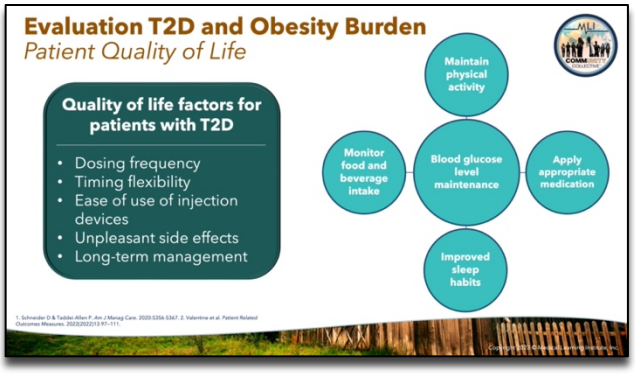
Dr. Harvey-Mansfield¨ So interdisciplinary teams, you know, me being a rural health doc, it is hard for me to have an interdisciplinary team, especially with me being in private solo practice. But, you know, like obesity, diabetes requires a multifaceted approach. That's why so many people are asking for continuous glucose monitoring. You know, that's why people are asking for self-diabetes management to teach the patient how to give themselves drug to, to monitor their blood sugar, and also how to eat appropriately.

You know, in rural areas it's definitely more difficult to have the multi-discipline, the disciplinary team. That's why the rural health doc is so important because he or she has to wear many hats. But if you are in a predicament where you can't add all these people to the treatment team, you know, that would be beneficial for your patient.

You know, there used to be a time when the pharmacist could talk to the patient at the window and go over all the side effects. You know, now in everybody's busy world, you know, they'll give you the little paper on the bag, and it's up to you to read it. But, you know, this is what our patient needs, you know; and, of course, it is not okay that they can't have anything, everything. But, you know, it's important that we use the resources that are at hand. What do you think about this slide, Dr. Campos?

Dr. Campos: Yeah, I agree. One of the things that I want to add to it that is not on the slide, because, you know, you're right. Depending on if you're in a rural area, you don't have certified diabetes educators, or you might not have a behavioral specialist. But you know what I tell everybody that works in my office, whether you're a receptionist, whether you're an MA that works in the back office putting patients in, whether you're my insurance clerk, everybody is part of the team here. When they see our patients, they want to know what their A1C's are. We celebrate with them when their A1C's are well-controlled. Everybody is part of the team in every office, everyone that works there.

We're all a team trying to encourage the patient, make sure they're taking the medicines, make sure they come back and see us regularly. And then when they have success, man, we celebrate that success with them too.



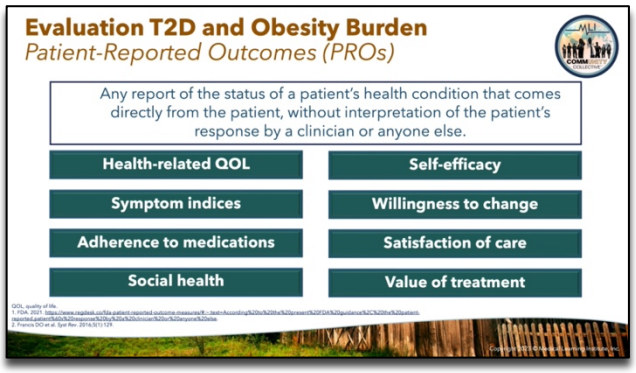
Evaluation T2D and Obesity Burden

Dr. Eden Miller: So now we're going to transition to a little bit of a different section. We're going to be discussing Type 2 diabetes as well as the obesity burden, but really going to talk about quality of life and patient perspective and engagement and all those things, right. Because you and I could have the greatest science, the greatest tools, but if we don't meet the patient where they're at, like, we're not going to get anywhere.

Dr. Kevin Miller: I often share with my patients that, really, the foundation that we build on is all those aspects that they mention here. Sleep is so important. Of course, our food and beverage intake, physical activity is foundational. We need to move and every part of our day we should look to increase activities. Not sitting for more than 30 minutes at a time is a recommendation that is followed a lot around the world but more and more we're sitting here in America, especially after Covid, in Zoom meetings.

So, all those parts make the whole, but then you must feel ready for this addition of a medication and feel comfortable with understanding how it works, and potential side effects that are discussed so the patients know when they're coming. This all together makes it a program appropriate for your patient.

I like to share with them that these are tools that we're choosing, and so the tools have their effect and side effect, and both are important to understand to have the patient feel comfortable with as they choose to apply this tool in their life to help effect or solve a problem that they're facing, and we can do that together and choose those tools together.



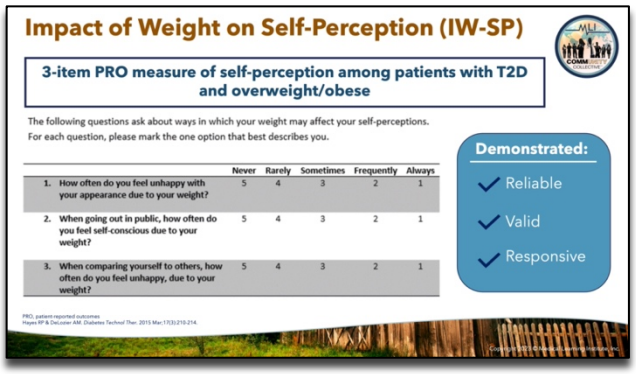
Evaluation T2D and Obesity Burden

Dr. Eden Miller: Yeah, one of things I think that we're going to hear over and over in our little segment here is putting the patient in the center, right. As I'm reading the top of this next slide that we just moved to, the patient reported outcomes or PROs. And so, as I read it, you'll kind of chuckle, I think, Kevin, as well. Any report of the status of a patient's health condition that comes directly from the patient without interpretation of that response by a clinician. Right, right. And that's what's so central, it's a dance, you're dancing. And, as clinicians, we do sometimes run ahead because we're excited, we're empathetic, we want to work with the individual, but sometimes we just don't stop and gauge the person in front of us because, you know, we either want to get them to their destination, but, you know, we've got to assess willingness to change, right. We need to assess; do they feel satisfied with their current treatment? Are they engaged or adhering to the medication? I know we use the word adherence. But all these really determine how the patient is perceiving their disease, their care, and where they're going.

So, what are some other thoughts that you have with this?

Dr. Kevin Miller: Well, as we discussed, if patient understands the medication effect and side effects, and you've been open and willing to talk to them, then they can see how this fits in their life. Does this cause, does this interfere with their sense of feeling healthy, of feeling whole? Are there social things that make it at this time not effective? We don't know that they're not taking the medication that was prescribed.

Perhaps we can look at another tool that will meet those needs better and that they can live with and feel good about. So, when they come, they're taking the medication regularly because they bought in. It meets these many needs in their lives. And that's the best medicine because it's the one they're going to take.

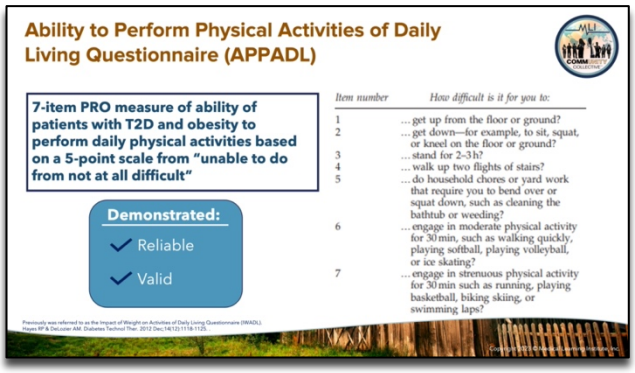


Impact of Weight on Self-Perception (IW-SP)

Dr. Eden Miller: So, let's start with weight. So, this is called the IW-SP. It's the impact of weight on self-perception. And that's really this very quick, three item patient response, right. Again, not clinician response, patient response about their own self-perception of their Type 2 diabetes and their dysmetabolic challenges, either overweight and obesity. And you can see that this is very simple. It is a very reliable, easy to do test, it has good validity, and it's something that, you know, maybe this might not be a bad idea to incorporate into your intake thing. But, you know, you and I both know that you don't necessarily want to lead with this, right? So, talk about some of your experiences in practice.

Kevin Miller: What I found over the years is I like to address health issues as the scientist in the room, talking about their organs and their cells of the body. All of a sudden it takes it from personal attack perhaps, or people feeling attacked, to something that we're working together about what's happening naturally in the body. What happens to so many people. Well obesity is definitely one of those. And I want to show the patient early on that I'm with them against what's happening to the cells of the body, and the cells being effective. Honestly, I probably would use this screening later on, maybe at a later appointment. So, I de-emphasize this issue as far as our relationship. We're going to be one together thinking about the science, thinking about how they're going to live healthy, how they're going to change what's happening to the cells of their body.

I always usually emphasize that these things are important and I'm for them feeling better about their appearance, I'm for them feeling happy with what's going on in their health. But I want to emphasize that I'm the cell guy. I'm the one looking at their body, and working with them so we can be healthier, so we can see a brighter future.



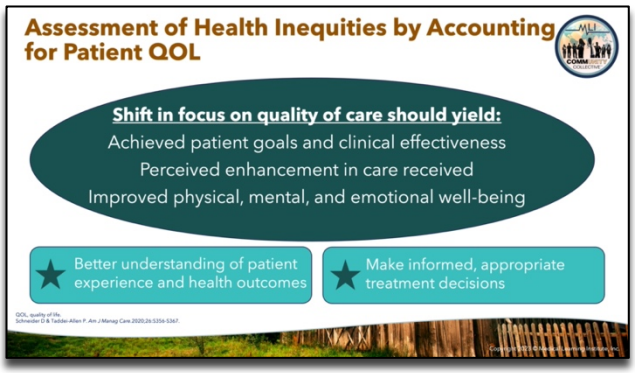
Ability to Perform Physical Activities of Daily Living Questionnaire (APPADL)

Dr. Eden Miller: Okay, let's go on to some of the next possible screening options that we have. Now, I really like this one. And I like this one because it's functional, right. It's those activities of daily living. Do you see how they have this big, long anacronym for it, APPADL. I just say, "Can you move your body in time and space?" This is the seven-item patient reported outcomes, Ability to Be Able to Take on the Activities of Daily Living, right. Something that they're able to do or not able to do.

But, Kevin, you've taken this, and you've spun it in a way that I think is so good. And I want you to share with some of our listeners what you do with this because you really should take it into kind of where you're at and where you want to be.

Kevin Miller: It has been fun for me to then challenge people to not just look about what we're moving away from, whether that's moving away from higher blood sugars, moving away from in a prediabetic developing diabetes, moving away from heart disease, and shift instead to moving towards a healthy future.
So, they might have trouble walking up the two flights of stairs, but I ask them, "What do you want to see at 60 or 70? What do you want to see in the future? This is something through reading and listening to wonderful lectures and experts around our nation, I've been incorporating. And it's fun to see the smiles on their faces where we can start thinking about if you're 50, what do you want to do at 60 or 70? If you want to travel, you know, can you run quickly between one gate and another to get there on time? If not, how do we prepare for that? And it's all those things to plan for a healthy future.

And physical fitness, balance, agility are all part of that living a healthy future.



Dr. Eden Miller: Yeah, I think one of my favorite ones that you talk about is the goal of you've got to work your upper body strength so you can pick up your grandkid.

Assessment of Health Inequities by Accounting for Patient QOL

Dr. Kevin Miller: It's really powerful to bring the patient in on the journey. And even though the science is complicated, and it takes us going to multiple conferences and reading articles to understand, when I bring it to the patient and say, "I look at a couple options for medications to use to improve glycemia, but

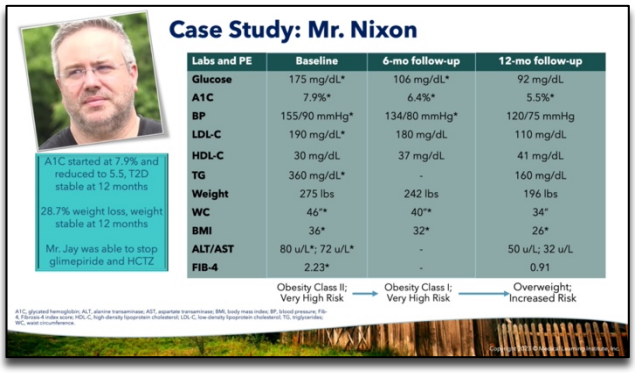
also to maybe effect renal disease or to effect heart disease. And here's what we know and here's what we don't know." The patient really joins me on that journey and says, "You know, I am concerned of this, so I agree. I'd like this medication." Now we've done that together.

Don't you think that's going to improve adherence to the medication when something that they're choosing for their own health?

Dr. Eden Miller: Oh, absolutely. And I think in summary what we're trying to tell you is this. You can have the greatest of intentions as a well-knowledge clinician staying true to the science, but if you miss the patient perspective, you're not going to be as successful.

And I know many of you are saying, "I don't have enough time for that." It's like, "Yeah, you do." Just at least inquire - every time I start off all my visits by saying, "If there's one thing I can do for you to help ease the burden, remove the barriers, make you feel more successful, what would that be?" It's that ongoing conversation.

And thank you so much, Kevin, for reviewing this section with us and showing all those stories that you have and those inspirational anecdotes.



Labs and PE	Baseline	6-mo follow-up	12-mo follow-up
Glucose	175 mg/dL*	106 mg/dL*	92 mg/dL
A1C	7.9%*	6.4%*	5.5%*
BP	155/90 mmHg*	134/80 mmHg*	120/75 mmHg
LDL-C	190 mg/dL*	180 mg/dL	110 mg/dL
HDL-C	30 mg/dL	37 mg/dL	41 mg/dL
TG	360 mg/dL*	-	160 mg/dL
Weight	275 lbs	242 lbs	196 lbs
WC	46"*	40"*	34"
BMI	36*	32*	26*
ALT/AST	80 u/L*; 72 u/L*	-	50 u/L; 32 u/L
FIB-4	2.23*	-	0.91

Case Study: Mr. Nixon

Dr. Kushner: So, let's revisit our case study of Mr. Nixon. It was decided to start him on tirzepatide based on the multiple complications that he presented with. You started at the low dose of 2.5 milligrams, and you went up monthly by 2.5 milligrams, all the way up to the highest dose of 15 milligrams over approximately 4 to 5 months, when what you see are the changes from baseline to 6 months to 12 months follow-up.

As expected, you would see his blood sugar drop into normal range. Hemoglobin A1C also drop into a normal range.

Improvement in blood pressure. His dysglycemia improved with the hemoglobin A1C going from 30 to 41. Triglycerides reducing from 360 to 160. Significant effect on his body weight from 275 pounds to 196 pounds. Improvement in his waist circumference. Body Mass Index from Class 2 to just overweight range. Improvement in his ALT/AST, signifying fatty liver disease, and a normalization of his FIB-4. So, you see hemoglobin A1C overall dropped from 7.9% down to 5.5%, and his hem, and his diabetes is stable. An almost 29% weight loss at 12 months; and, importantly, he was able to stop his glimepiride, which is a hemoglobin A1C and hydrochlorothiazide.

Wrap Up

Thank you for joining us for Part 2, and I personally invite you to join us for Part 3 which is going to be Question and Answer, Case Consults, Building a Network, and Spreading the Word. Cohort members will bring challenging cases for members to discuss. A local expert clinician will answer cohort members' questions from the previous activities, and clinicians will be able to plan how to share what they have learned with all members of their practice and with other local clinicians. Check out the venues.