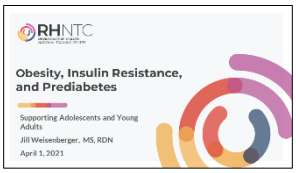
Obesity, Insulin Resistance, and Prediabetes
April 1, 2021
Transcript

Slide 1



Jennifer Kawatu: Hello, everyone. Just let people join and we'll get started in just a second. Right. Hello. This is Jennifer Kawatu from the Title X (10) Reproductive Health National Training Center. I'm delighted to welcome you all to today's webinar about obesity, insulin resistance, and prediabetes, and how we can support adolescents and young adults.

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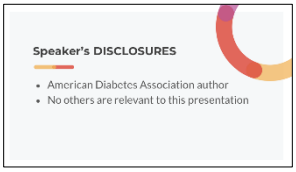

I have just a few announcements before we begin. Everyone on today's webinar will be muted, but we plan to have some time for questions at the end of the webinar today. So you can ask your questions using the chat at any time during the webinar. There's also a part two of this webinar series. If we don't get to your question today, we'll try to work it into the next webinar. We encourage you to register for that as well at rhntc.org. A recording of today's webinar, the slide deck, and the transcript will be available also on rhntc.org within the next few days.

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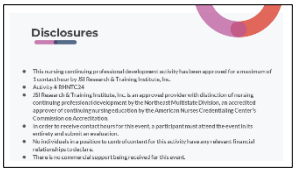

This activity has been approved for one continuing nursing education contact hour. To receive your certificate, please complete the evaluation at the end of the webinar. This presentation was supported by the Office of Population Affairs and Office on Women's Health, and its contents are solely the responsibility of the authors and do not necessarily represent the official views of OPA, OWH, or HHS. The only disclosure we have is that the speaker, Jill Weisenberger, is an American Diabetes Association author.

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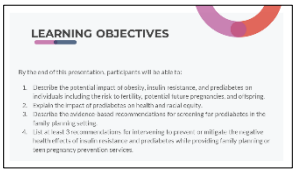

Our objectives for today are to cover the potential impact of obesity, insulin resistance, and prediabetes on individuals, including the risk to fertility, potential future pregnancies, and potential future offspring. The impact of prediabetes on health and racial equity, evidence-based recommendations for screening, and recommendations for intervening to prevent or mitigate the negative effects of insulin resistance and prediabetes, while providing family planning or teen pregnancy prevention services. We're excited to have with us today, Jill Weisenberger. Jill is a nutritionist and a certified diabetes care and education specialist. She's an internationally recognized nutrition and diabetes expert, speaker, and the author of four books, including “Prediabetes, A Complete Guide.” She contributes to a variety of magazines and websites, including Today's Dietician and Food and Nutrition Magazine. We're so pleased to have her with us today. So with that, I'd like to turn things over to Jill to get us started. Jill?

Jill Weisenberg: Thank you. Thank you for that very kind introduction. I've been looking forward to this for quite a while now because prediabetes is a special topic to me. It's an important topic, and because you all have so much influence on the health of the general public, public health. So that means a lot to me. I often say that prediabetes is not pre problem. What it really tells us is that a problem has been going on for some time already. And that's why now is the time to intervene.

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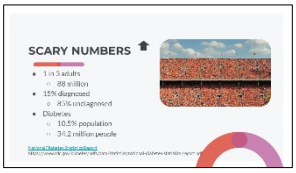

I know it's been a long time since we've been to crowded arenas like this football stadium or shopping malls or anything like that, but think back to when you were. If you had randomly counted out nine adults, chances are very good at three of them would have prediabetes. Another one would have type 2 diabetes. What's really, really critical here is, of the 88 million adults who have prediabetes, almost none of them know they have it. About 15% of the population actually have received the diagnosis of prediabetes. What that means to me is that it's just a very few number of people who actually have the gift of knowledge that will lead them to better lifestyle, because we do know that lifestyle makes a difference.

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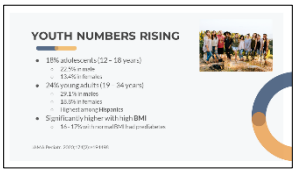

The numbers in youth are rising as well. This is some enhanced data and it's pretty recent data. It shows that about one in five adolescents between the ages of 12 and 18 have prediabetes. In the next age group up, it's about one in four, and that's 19 to 34 years. It's more common in males. It's highest among Hispanics. And so, we typically associate prediabetes with a high BMI, and that is a risk factor. In this population, about 16 to 17% of people with a normal BMI had prediabetes. In any young people, prediabetes often presents as impaired fasting glucose in males and impaired glucose tolerance in females. That just tells me that there's a very good chance that we are missing some of the females because we typically use a fasting glucose for diagnosis, not a two-hour OGTT. Young people have the same cardiometabolic risk, high blood pressure, high non-HDL cholesterol, elevated BMI, abdominal fat, and insulin resistance.

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What's really interesting and very worrisome and why this is so important for you all in the work that you do, is that in young people we often see an accelerated loss of beta function. And so, what that means is that it's a rapid progression to type 2 diabetes because as beta-cell function declines, as we have declining ability to produce insulin, that is the driving force of the progression to type 2 diabetes.

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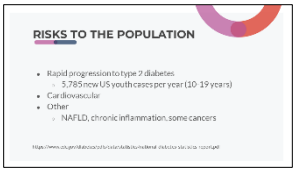

In fact, we have about 6,000 new cases in the US each year, youth cases, about 10 to 19 years. And as I said, same cardiovascular risk. But there's other risks as well for young people and for older adults, non-alcoholic fatty liver disease, chronic inflammation, some cancer. This is why I say we have to take a broader view than just a blood sugar view, because it is so much bigger than just a blood sugar problem.

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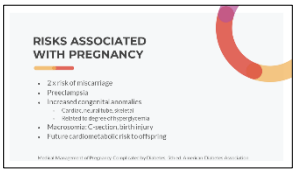

There are some risks associated with pregnancy. As far as I've been able to determine, there's no link between prediabetes or insulin resistance and infertility. But we do see some problems during pregnancy. There's about two times the risk of miscarriage, higher risk of preeclampsia. And depending on the degree of maternal hyperglycemia, we see some congenital anomalies, including cardiac, neural tube, and skeletal anomalies. We know the link between hyperglycemia and macrosomia, so large baby. Large birth weight leads to greater C-section or birth injury. And then, this is so concerning to me. In fact, I just saw a Joslin paper that came out in the last day or two, on this, about future cardiometabolic risk to offspring. Just imagine, with all the other things going on in the world, you're just born with a greater risk of heart disease and obesity and type 2 diabetes because of the fetal environment.

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When it comes to obesity in this population, we do see increased infertility. In fact, some studies show about 300% greater risk of infertility among people with a high BMI, compared to people with a normal BMI. The probability of conceiving is 5% per unit BMI greater than 29. Now, keep in mind that 29 is that highest level before we hit obesity, because the technical definition of obesity is a BMI of 30. We see higher rates of miscarriage. And in one study, now, this was done in people with assisted fertility, assisted conception, the rate of miscarriage was 38.1% compared to 13.3% for people with high BMI versus a normal BMI. The causes, of course, are multifactorial and always under discussion and debate. We know that hyperglycemia can affect this insulin resistance, and also cytokines, and more specifically adipokines. Adipokines are cytokines that come from fat tissue. These are cell signaling proteins that can lead to inflammation and free radical production and so forth.

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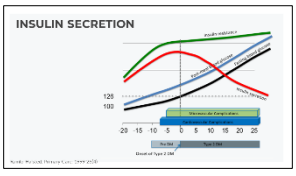

I want to show you all the relationship between insulin resistance and insulin secretion. Look at time zero, and that is at the diagnosis of type 2 diabetes. We see that prediabetes goes on for years before the onset of type 2 diabetes. Early on, we have insulin resistance, and so as insulin resistance increases,

this is the worsening of insulin resistance. At some point, it levels off, and that's about the time we see type 2 diabetes. As insulin resistance is increasing, look at what insulin secretion does, early on, way before diabetes, way before prediabetes. Early on, the red line is showing you that insulin secretion follows the path of insulin resistance until it can't anymore. At some point, right around the time of diabetes, that insulin secretion levels off. And so, blood sugar numbers are going up higher. We very often see post-meal blood glucose go up, prior to fasting blood glucose. So again, this goes back to, are we really catching people because we almost never use a two-hour OGTT. We use a fasting blood glucose or an A1C most of the time. I also want you to notice that cardiovascular complications increase in the prediabetes range, as do microvascular complications. This is why I beg people, please stop thinking of diabetes and prediabetes and insulin resistance as a blood sugar problem. It's not just a blood sugar problem.

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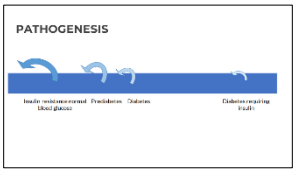

These arrows show the reversibility of the problem. This is why I always say the opportunity for reversal or the opportunity for intervention closes every day. That window of opportunity closes bit by bit. Look over here on the left hand side. We have insulin resistance with normal blood glucose. So we have insulin resistance. That means that, thinking about the last slide, the insulin secretion is very, very high. So blood sugar levels are normal. No one has a clue there's a problem because blood sugar levels are normal. These high levels of insulin push that blood sugar down. We move over to prediabetes. Well, insulin secretion is coming down some. It's still higher than normal, but it's coming down. And so, blood sugar levels increase to the prediabetes range. Then we move on some more. We get that diabetes range, blood sugar levels creep up. As insulin secretion goes down, blood sugar goes up. So you can see that when we still have those beta cells functioning well, that's early on over here, and the insulin resistance's normal, blood glucose area, I say the reversibility is very, very high. But then, 20, 30 years after having type 2 diabetes, it's probably not reversible at all because doesn't matter how much weight somebody loses, if they have lost their insulin producing abilities, they've lost it. And that's all there is to it. So that window of opportunity closes just a little bit every day.

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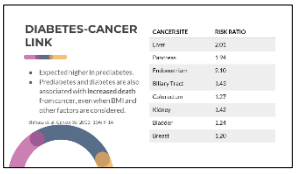

I'd like to point out the relationship between insulin resistance and cancer. These data are specific to diabetes and cancer link, because I couldn't find anything specifically to prediabetes. But we do have data indicating it's similar. What you see here at the top are the three cancers that are about double the risk among people with diabetes. And the others down here are also associated with diabetes. The increased risk is 20 to 43%. But the top three, liver, pancreas, and endometrium, are about double.

What we also see is there's increased death among people with prediabetes and diabetes from cancer, not just rates of cancer, but also death from cancer. And that's even when weight, BMI, and other factors are considered.

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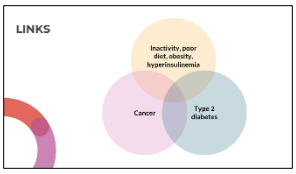

So there are some overlapping lifestyle or physiological factors. We have inactivity, poor diet, obesity, and hyperinsulinemia. Those things converge and they affect both the cancer risk and the type 2 diabetes risk.

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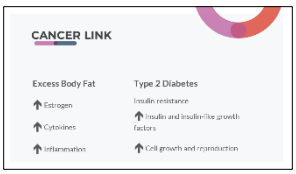

We can go ahead and take a look at that. Over here on the left side, excess body fat, of course, is linked to higher estrogen levels. When it comes to some of the female cancers, then we know that a woman's lifetime exposure to estrogen affects her risk. So more body fat, more estrogen, higher risks of some of those female cancers. I also talked about cytokines, or particularly, adipokines. These are the cell signaling proteins like interleukin 6 and tumor necrosis factor alpha. And so, what happens here is, because that tissue, particularly abdominal fat tissue secretes more of these inflammatory compounds, then we have greater risk of inflammation. We have more potential DNA damage and greater cancer that way. And then, on the type 2 diabetes side, insulin resistance plays such a big role. Remember I told you that early on insulin secretion is very, very high. Even if it's not high enough to keep the blood sugar levels down, it's still very, very high. And that's because the cells, various parts of the body, are resistant. But so with high insulin levels, there's many other jobs that insulin has. One of them is a mitogenic role. So it's important in cell division. That high level of insulin includes also insulin like growth factors. So there's higher levels of cell growth and higher levels of cell reproduction because of this higher insulin levels. That's another way that cancer risk is increased and that's the hyperinsulinemia, which is caused by insulin resistance.

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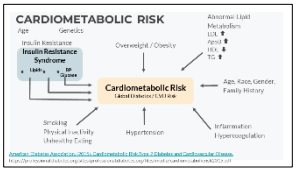

The slide really helps to bring all together the risk of cardiovascular disease and diabetes prediabetes together. I took this slide from the American Diabetes Association. I've been using it for years, so this is the one of my favorite slides. We know that overweight and obesity affect cardio-metabolic risk. We also have abnormal lipid metabolism. We have elevated LDLs, elevated APOB, and that's the total number of atherogenic particles. We have low levels of triglycerides and... I'm sorry, low levels of HDL and high levels of triglycerides. Things we can't do a darn thing about age, race, gender, family history affect our risk, as do inflammation and hypercoagulation, hypertension. Some of those lifestyle factors like smoking, physical inactivity, and unhealthy eating. All of this leads to insulin resistance or insulin resistance syndrome, where we see elevated lipids, elevated blood pressure, and elevated glucose.

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We know that there is a greater risk among some populations than others. I mentioned, when looked at the youth data, the NHANES youth data, that it was highest among Hispanics in that group. I'm going to show you some other data in just a few minutes, but we do know that there's racial inequality. We see greater morbidity and greater mortality among some populations. It's multifactorial as I'm sure you know better than I do, but there's just a few things I want to make sure we're all on the same page on. What I mentioned earlier, there's the fetal environment, but it's not just the fetal environment. It's the infant environment and the childhood environment. That will affect an individual's risk. Whether it is cultural or genetic, we see higher BMIs and abdominal fat among some populations. Again, whether it is lifestyle-related or genetic, we see higher levels of blood pressure. Sometimes we see people living in unsafe or unworkable neighborhoods, or they live in food deserts. They have limited access to groceries. We know the link between greater physical and emotional stress, along with illness, particularly chronic illness. Smoking and addiction are factors. Unequal access to care, which comes from all different directions, whether that is somebody who can't get the day off or somebody who doesn't have transportation to get to a provider. And then, another thing, and this is the one we're going to talk about more in three weeks when we do the part two webinar, has to do with provider relationships. Often, people think, "Well, providers don't get me," and if they don't get me, or if they think that we don't get them, then we really lost an opportunity. Like I said, we're going to talk about that a little bit today, but much more so at the next webinar.

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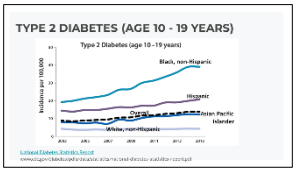

These again are type 2 diabetes data because I was unable to find data for prediabetes. But what I want you to see here is, from 2003 to 2015, the numbers increased across the board, except among white

non-Hispanics. So we do have that racial or ethnic disparity. The black dotted line is the overall line, and you can see that Black non-Hispanics and Hispanics are way above the overall average.

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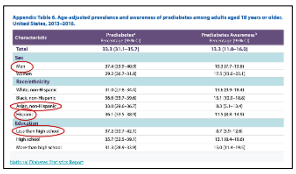
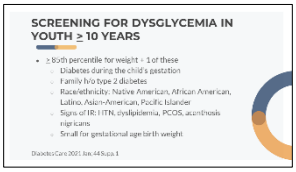


The point of this slide is to drive home something I said on my first slide. People don't know they have prediabetes. Men are less likely to know than women, Asian non-Hispanics and Hispanics are less likely to know than others. The lower the education, the less likely somebody is to know that they have it. But the point is they don't know it, and when they don't know it, they've lost that opportunity to take that reversal that we saw on that one slide with the arrows.

Slide 20



These are the American Diabetes Association guidelines for screening for dysglycemia for youth who are greater than 10. It requires the 85th percentile or higher for weight plus one of the following. First we have the overweight or obesity plus diabetes during the child's gestation, like I was talking about, the fetal environment. Family history of type 2 diabetes, race and ethnicity, so native American, African-American, Asian-American, Latino, Pacific Islander. And any signs of insulin resistance like high blood pressure, dyslipidemia, polycystic ovary syndrome, or acanthosis nigricans, which are the skin tags or the darkening of the skin in the folds. And then, additionally, we have small for gestational birth weight.

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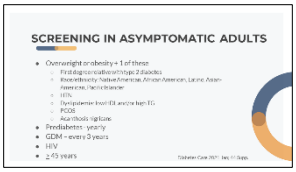

It's slightly different for asymptomatic adults. It does start with overweight or obesity, plus one of the following. But one thing I want to point out is that among Asian-Americans, overweight starts with a BMI of 23 and obesity starts with a BMI of 27. However, for other populations, it's 25 and 30. So that's just something to keep in mind. It's overweight or obesity plus first degree relative with type 2 diabetes, same race, ethnicity, same signs of insulin resistance, hypertension, dyslipidemia, polycystic ovary syndrome, and so forth. If somebody has prediabetes, the guideline is to screen them yearly for diabetes. If they had gestational diabetes in the past, the guideline is to screen every three years.

Anybody with HIV should be screened, and everybody else, just start them at age 45. These are the ADA guidelines. This is something that's helped me a lot in my practice because I often don't get a lot of labs, but I would get lipid profile pretty often.

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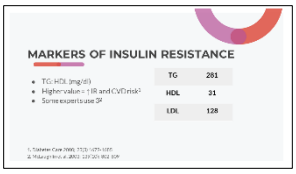

And so, this is just something that some people are using. There's some research out there to support it. And it's looking at markers of insulin resistance by taking a ratio of triglycerides to HDL. In this case, we have triglycerides of 281 and HDL of 31. So you just divide 281 by 31, and you come up with a ratio of about nine. If I have this lipid profile in front of me, I would say this person shows... It indicates high levels of insulin resistance and great risk for type 2 diabetes, prediabetes prior to that, and also other cardiometabolic disorders, heart disease, stroke, fatty liver. Now, some experts use the number three. Anything three or higher is considered risk. There's not a lot of standard on this, and it has been shown not to be effective in predictive in South Asian women. I thought that was interesting. I just want to make sure you have it.

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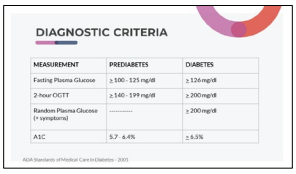

This is the diagnostic criteria. I don't need to go over it, but you just know that it's here.

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These are the things that we think about as the standard treatment for prediabetes. We're going to go over some of these things in more detail. And then in the next webinar, we'll go over even more like the how to, how you can bring this even more into your practice. But a lot of this information comes from the diabetes prevention program, which was that big federally funded NIH program. The recommendation for people with overweight or obesity, 7% or so, a loss of body weight. We want to see physical activity of at least 150 minutes. Diet, just think wholesome foods, and only one food tends to be called out a lot, and that's sugary drinks. In fact, we do have a meta analysis showing that adults with prediabetes who drink a single sugary beverage, which includes lemonade and iced tea, not just sodas,

but a single sugary beverage daily had an increased risk to convert to type 2 diabetes, and it's a 26 or so percent increased risk. Medications are beneficial. The only medication right now that's indicated for prediabetes is Metformin. And then tobacco cessation. We easily associate tobacco with lung cancer, other cancers, and heart disease, but we know it's also a risk factor for type 2 diabetes.

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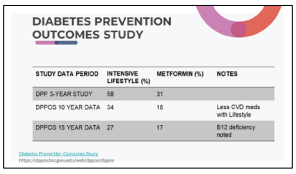

The diabetes prevention study that I just mentioned was a three-year study. Like I said, it was large NIH, and there were three groups, the intensive lifestyle therapy group. When I say intensive, I mean, intensive. There were lots and lots and lots of interactions. There were group meetings, telephone calls, emails, all kinds of things to help people change their habits, not just to know what to do, but to help them to actually change their habits. The study lasted three years. And so, there was that intensive lifestyle group, the Metformin group, which Metformin is the most commonly prescribed drug for type 2 diabetes. And like I said, it is indicated for prediabetes as well. They got just standard diet advice. They only met I think maybe three times over the first two years. And then, the control group also got just standard diet and exercise advice. What they found was at the end of the three years, the intensive lifestyle therapy group had a 58% reduction in conversion to type 2 diabetes. Metformin looked great to at 31%, but that 58% at the end of three years, that's something that a lot of people were cheering. And we are so fortunate that even though the intervention lasted only three years, the outcome study, the DPOS went on. It's still going on. We have the 10-year data and that shows intensive lifestyle therapy reduced it by 34%. And the 15-year data showed great results still, 27% and 17% for Metformin. So this is why in the diabetes world and the prediabetes world, we often say that lifestyle can prevent or delay. Lifestyle changes can prevent or delay the onset of type 2 diabetes.

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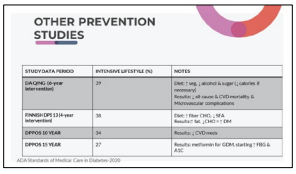


More than just the DPP, there's other prevention studies as well. The first one here is a Chinese study. It lasted for six years. Intervention lasted for six years, and they had a 39% reduction compared to their control group. Their diet was a little different. They had increased vegetables and decreased alcohol and sugar intake. They used all weight status, so anybody with overweight or obesity was also advised to cut calories. Their results, like I said, 39 reduction, but they also showed reduction in all-cause mortality, cardiovascular mortality, and microvascular complications. The second one I'm showing here is the Finnish study. It was a four-year intervention. What I have here for you are the 13-year data, 38% reduction. So it's right along with the rest. Their diet was also different. They had high fiber diet. Definitely not low carbohydrate because, as you know, you can't have high fiber and low carbohydrate at the same time. But it was high fiber and low saturated fat. Interestingly, they just found that those

people with the highest fat intake and lowest carbohydrate intake actually had the most risk of developing type 2 diabetes.

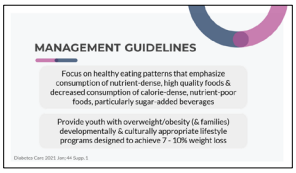
Slide 27

All right. Here are the DPP strategies. What I want you to know is you can get these same handouts. The slide here is from the CDC and you are free to use them. I have them divided in my mind in three ways. They had people monitor or self monitor. They self-monitored their weight. They had to track their physical activity and record their food intake. They also had diet and exercise. I already mentioned the 150 minutes of exercise. They were advised to decrease calories and choose wholesome foods. The next one I think goes under mindset. Manage stress, maintain motivation, and improve your mindset by stopping that harmful negative thinking.

Slide 28

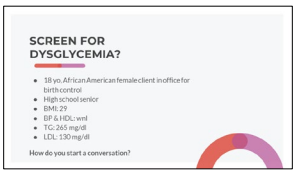
There aren't that very many studies in youth, but I was able to find the Resist Study, researching effective strategies to improve insulin sensitivity in children and teenagers. This is an Australian study. They were 10 to 17 years old. Everybody in the study had overweight or obesity, and everybody was insulin resistant. It's a six-month intervention and everybody was given Metformin and exercise, plus one of two diets. Like you said, everybody's on Metformin and exercise advice. And either they were on a higher carbohydrate diet, which was 55%. So not super high. Was 55% carbohydrate. Or they were on a lower carbohydrate diet, which is 40 to 45%. So again, not super low. The difference was made up largely in the protein. Now, 40 to 45% is what most of adults in the US with type 2 diabetes consume, or I should say average, not most, but the average consumption among people with type 2 diabetes. And I would assume that's similar to people who have been diagnosed with prediabetes, about 40 to 45%. What they found among these kids is that regardless of the diet, they had improved BMI and insulin resistance in both groups. We don't really know why because everybody got Metformin and everybody got exercise. So did diet have anything to do with it? Or would diet have shown a bigger difference if they weren't on Metformin or if they didn't exercise? We don't know the answer to that. But there's several papers published on this Resist trial. So you might find something in there that interests you.

Slide 29



These are the ADA 2021 guidelines. There are many, many guidelines. I picked out two for you all. The first one is focus on healthy eating patterns that emphasize consumption of nutrient dense, high-quality foods, and decreased consumption of calorie, dense, nutrient-poor foods, particularly sugar-added beverages. What I think here is really worth noting is they're not talking about a list of good foods and bad foods. And I know that's what people want us to give them. I try so hard to stay away from that because I want people to determine for themselves which foods to eat. I would like to guide them, but I don't like giving a list. That is what we show here. It's a consumption of nutrient-dense foods, wholesome foods, decreased consumption of empty calories or calorie rich foods. And again, the sugar-added beverages, which please remember is not just sodas, but its coffees and teas and lemonades and things. The second one is provide youth with overweight and obesity and their families with developmentally and culturally appropriate lifestyle programs designed to achieve seven to 10% weight loss. Lots of things in here I think are really key. Provide you with overweight or obesity. So just like we use person first with diabetes and prediabetes, we want to use person first with overweight and obesity. No longer do I say, "Because she is diabetic." I would say, "Because she is a person with diabetes." Same thing. I struggle with it a little bit more because it's a little newer on my tongue, to say with overweight or person with overweight or with obesity. They are also including families. This is so critical because we cannot just isolate a child and make a child feel picked on, or less than, or odd. So we have to involve the whole family. Developmentally and culturally appropriate lifestyle programs. So happy to see this emphasis on culturally appropriate. When we're working with people whose culture may indicate that they have lots of rice or lots of corn or something like that, and that's an important part of their culture, important part of their identity, we can't just say, "No, you can't have that." We need to work with them and help them find a way to do it. And then, to achieve seven to 10% weight loss. Again, that's standard advice now. We don't tell people they have to be skinny minis. We just want people to do what they can to lose a little bit of weight.

Slide 30



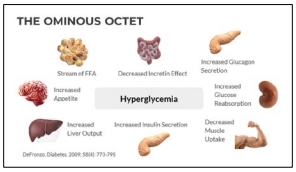
All right. Here's our first case study. Should we screen her for prediabetes and diabetes? She's 18. She's African-American. She's coming to your clinic for birth control. She's a high school senior. Her BMI is 29. Her blood pressure and HDL are within normal limits. Her triglycerides are slightly elevated at 265, and her LDL is 130. First thing is, think about this. Should you screen her? I would say technically, yes, because she meets the criteria that I showed you a few slides back. She has overweight. She has elevated triglycerides, and she's African-American. So she does fit the screening criteria. Now think about this. How are you going to start a conversation with her? She came to you for birth control advice.

She did not come to you for anything else. How might you start a conversation? So think about that. First of all, I will point out that she may not have any idea that she has a BMI of 29, and that a BMI of 29 would be in the overweight, almost obese category. So I would not bring that up. Sometimes culturally, a BMI of 29 is considered ideal. So I would not bring that up immediately. But I think I would just ask, "Is it okay if I talk to you about your risk for health problems down the road?" Hopefully she'll say yes, and if she doesn't, then we have to respect that and say, "Then, well, when you change your mind, I'd like to talk to you."

Slide 31

Here's our second case study. This is a 22-year-old Latina mom of one. She had gestational diabetes when she was pregnant before. Her BMI now is 31 and she has high blood pressure. She knows that gestational diabetes and weight are related. So that's why she tells you she wants to lose weight. She says, "I do not want gestational diabetes again." A few things you know about her, she commutes to work. She lives in a food desert. She drinks both regular sodas and diet sodas. In conversation, she says to you she doesn't think there's a way for her to lose weight because she doesn't like most vegetables and she loves fast food. So she doesn't think that it's even possible for her. What do you think is most important? What should you lead with? What we'll talk about in the next webinar even more is we always start with the why. Don't go into how or what before you go into why, and you know her why. The most important thing she said to you is, "I don't want it again." So I would start with that. What was it like when you had gestational diabetes before? What worries you about having gestational diabetes? That's how I would start. Always start with the why. And then, how would you intervene? What do you think you might offer up as some ideas? Well, one thing she said is, "Well, I don't think I can lose weight because I don't like this and I do like that." I would find out what are the healthy foods she likes and then start working those in more. That's how I would start my intervention.

Slide 32

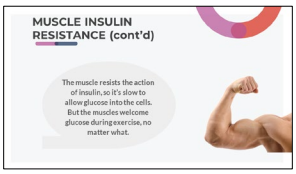


We're going to go over a little bit of the pathophysiology of prediabetes, because I think it's super cool. So we're going to go over that. This is the ominous octet. And so Ralph Defronzo gave a big talk with ADA, 2009, and showing all the different defects in type 2 diabetes in insulin resistance. What this did in the diabetes world is it opened up very, very specific drugs with highly targeted areas of action. So we have much, much better therapeutics for type 2 diabetes today. But this still relates to prediabetes because remember, it's all on the same continuum. Quite honestly, there really are more than eight, but these are the ones I want to talk about. We call them the ominous octet because of Ralph Defronzo.

Slide 33

First we have insulin resistance at the muscle. And so, what this means is there's impaired glucose uptake after eating. Typically, blood sugar wants to go into muscle after a meal, but it's impaired glucose uptake, about 50%. This contributes to post prandial or after meal hyperglycemia.

Slide 34

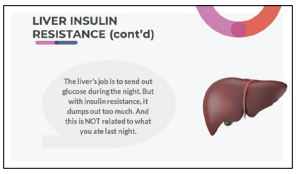


Here's the good news. We have non-insulin mediated uptake during exercise. So doesn't matter if you're insulin resistant. If you are contracting your muscles, then glucose can go in even if you have insulin resistance. The way I explain this to folks is I say, "The muscle resists the action of insulin. So it's slow to allow glucose into the cells. But muscle welcomes glucose during exercise no matter what." They're much more likely to exercise once they understand that.

Slide 35

We have liver insulin resistance. The effects are both post prandial and fasting. On post prandial, insulin levels are high after eating. But the liver just ignores that because it's resistant, insulin resistant. So it sends out more glucose. That's the post-prandial effect. The fasting effect, again, it's excess hepatic gluconeogenesis, and it's unrelated to food. This is the thing people have such a hard time grasping.

Slide 36



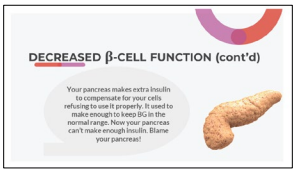
So I'll say it this way. The liver's job is to send out glucose during the night, but with insulin resistance, it dumps out too much, and this is not related to what you ate last night. So yes, you could have gone to

bed with one number, did not get out of bed at all, or reach into the drawers for crackers and ate nothing, and your blood sugar can still be higher in the morning.

Slide 37

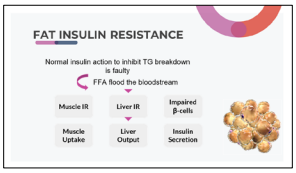
We have decreased beta-cell function, as we've talked about quite a bit already, and we always had a relative insulin insufficiency. As I said, even if insulin levels are high, by the time we get to the prediabetes range, it's relative insulin insufficiency. It's just not enough for the blood sugar numbers to be tamped down. We know that they fail over time, the beta cells fail over time, and it's much, much more rapid among young people. And we often see high post prandial blood glucose, and then fasting blood glucose.

Slide 38



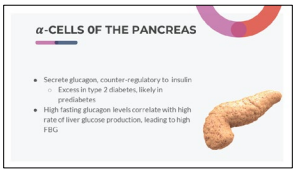
I'll tell people, "Your pancreas makes extra insulin to compensate for your cells refusing to use it properly. It used to make enough to keep your blood glucose in the normal range. Now your pancreas cannot make enough insulin." So I let people blame their pancreas instead of blaming themselves.

Slide 39



We have insulin resistance at the fat as well. Normal insulin action is to inhibit triglyceride breakdown. That's normal insulin action. But when that is not working properly, we have a flood of free fatty acids into the bloodstream. And what does that lead to? Muscle insulin resistance, liver insulin resistance, and impaired beta cell function. That leads to what we've already talked about for muscle uptake, greater liver output and poor insulin secretion.

Slide 40

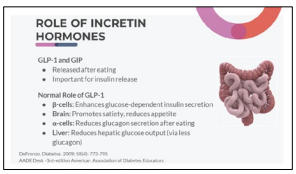


We have the alpha cells of the pancreas that fail as well. They are the ones that give us glucagon, so you want to recall that glucagon is counter regulatory to insulin. So it should be that when one is high, the other is low and vice versa. That doesn't always happen in insulin resistance. We have an excess of glucagon in type 2 diabetes and prediabetes, and it's those high fasting glucagon levels that correlate with that high rate of liver glucose output and leading to that high fasting blood glucose.

Slide 41

So, again, it has nothing to do with what people are eating in the middle of the night. So yes, I do believe you that you did not get up in the middle of the night. I'll tell people, "Your liver is leaky and letting out too much glucose."

Slide 42



This is my favorite one, is the role of the incretin hormones, because whoever thinks about hormones in your gut. Two in particular. Well, GLP-1 and GIP are of particular importance. We're going to focus mostly on GLP-1. But between the two of them, they are important for post-meal or during-meal insulin release. They're released with eating and they account for about 70% of insulin release after a meal.

Slide 43

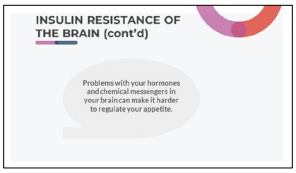
Here's the normal role of GLP-1. This is not in people with insulin resistance, but this is the normal role. In the beta cells, it enhances glucose-dependent insulin operations. What that means is that if blood

sugar goes up a little bit, insulin release should be a little bit. If blood sugar goes up a lot, insulin release should be a lot. So it enhances glucose-dependent insulin secretion in the beta cells. In the brain, it promotes satiety and then reduces that appetite. The alpha cells, it reduces the glucagon secretion after a meal. And in the liver, it reduces hepatic glucose outpoint. Output, I'm sorry. So all of that is in the normal person. What happens in prediabetes or type 2 diabetes where it doesn't work? I'll tell people that hormones in your gut are acting nutty, causing you to have higher blood glucose levels and even make you hungrier.

Slide 44

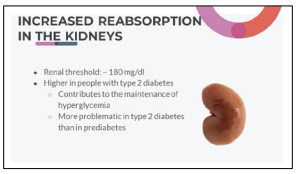
This slide is really a continuation of the last one, insulin resistance on the brain. We have neurotransmitter dysregulation. GLP is part of that. Brain neurotransmitters affect appetite, and they affect food intake. GLP-1 resistance in the brain increases food intake leading to weight gain. So just imagine that this disorder that you have, this insulin resistance makes you want to eat more. So if we have weight gain, we have muscle insulin resistance, and liver insulin resistance, and beta-cell failure, and on and on.

Slide 45



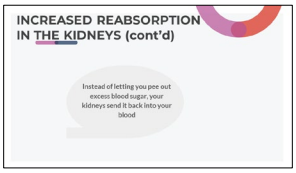
I'll tell people that problems with your hormones and chemical messengers in your brain make it harder to regulate your appetite. Just a quick aside, a patient story I just love to tell because it's so meaningful to me is, we got her on a GLP-1 agonist, took her off a couple of diabetes medicines, kept her on Metformin, got her on a GLP-1 agonist. It was Victoza. For years afterward, she still tells me this, that it saved her life because she finally stopped thinking about food all the time. I think that's amazing.

Slide 46



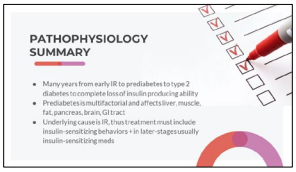
This problem is probably a bigger problem in type 2 diabetes than it is in prediabetes, but we have increased glucose reabsorption. The normal renal threshold is about 180. This is higher in people with insulin resistance, and it contributes to the maintenance of hyperglycemia.

Slide 47



What I'll tell people often... Oops, my slide's not going. There we go. Instead of letting you pee out excess blood sugar, your kidneys send it back into your blood.

Slide 48



Just a quick sum up of the pathophysiology, and we're going to go onto some other things in a moment, it takes a long, long time to go from insulin resistance, to prediabetes, to type 2 diabetes, to complete loss of beta cell function. Prediabetes affects the whole body. It is multifactorial, and the underlying cause is insulin resistance. So we've got to treat that with insulin-sensitizing behaviors, possibly insulin-sensitizing medications like Metformin and some others.

Slide 49

What are some of those insulin-sensitizing behaviors? Very quickly, we're going to go over physical activity recommendations. These are the ADA guidelines. We want to see cardiovascular exercise at least three times a week and no more than two days without exercise. So Monday and Tuesday without is okay, but not Monday, Tuesday, Wednesday. No more than two days without. 150 minutes a week, strength training. Two to three sessions on non-consecutive days. This one came out new in 2016, and that's to reduce sedentary time. Prior to that, we didn't talk about that at the ADA, and really wasn't talked about too much at all, is reducing sedentary time. The guideline is to interrupt prolonged sitting with three-minute breaks every 30 minutes. At this point, you should have gotten up at least once for one three-minute break while we've been on this webinar.

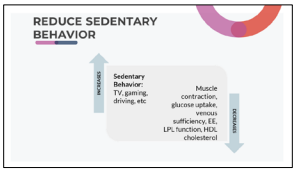
Slide 50

For cardiovascular exercise, we know that it reduces insulin resistance for two hours to two days. So if you exercise only once, once out of the whole week or once out of the whole month, you have improved your insulin resistance for at least a couple of hours. So that's a good thing. It wasn't wasted because you didn't do it every day. It is best to do it daily, however, and the reason we say not more than those two days in between is because the insulin resistance or the increased insulin sensitivity can last for up to two days. But it is best to do it daily, and a nice place to start is a 20-minute walk after meals, after the largest meal if that's possible, or a five-minute walk, just to get somebody started.

Slide 51

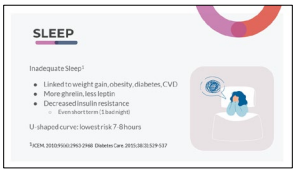
Strength training, it reduces insulin resistance as well as cardiovascular exercise. And what's very cool about this is the effects are additive. Now, I have a bucket here for a reason. This is something I want you to remember. Remember I said earlier on that blood sugar after eating likes to go into muscle. So muscle is like a repository or a bucket for blood sugar. The bigger bucket you have, the more rain you're going to catch, the bigger muscle bucket you have, the more blood sugar you're going to catch. So strength training is very, very important for people with diabetes or any type of insulin resistance.

Slide 52



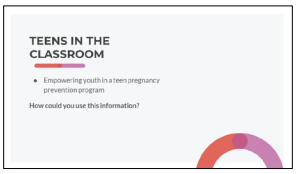
As I said, reduce sedentary behavior. We know this is not just a glycemic problem. We see this with cancer and heart disease and all kinds of things. But as sedentary behavior goes up, like driving and TV, we see less muscle contraction, less energy expenditure, less lipoprotein lipase function, LPL function. We see changes in cholesterol and more.

Slide 53



Sleep is something we don't talk about very much, but we really need to. I don't know if you bring that into your practices, but it's something that I think we need to address more because inadequate sleep is linked to weight gain, obesity, diabetes, cardiovascular disease, all these chronic problems that we see on the increase. We know that when we have even just one night of bad sleep, we have more ghrelin, the appetite hormone, and less leptin, the one where you're satisfied. More ghrelin makes you more hungry and leptin makes you more satisfied. We see decreased insulin resistance, even just with one night and even with healthy people. We take people who don't have insulin resistance, give them a bad night of sleep, and we see about a 25% reduction in insulin sensitivity. We usually see a U-shaped curve. So the lowest risk is like at seven to eight hours. But very little sleep and a lot of sleep are both linked to more weight gain, obesity, diabetes, and cardiovascular disease.

Slide 54



Okay. Just two more case studies. Let's say you have teens in the classroom. I would like you to think about this for just a couple of seconds. How would you use this information that we've just gone over with that population, with the teens in your classroom? I know how I would do it. I would start with having everybody get up after the 30-minute mark. So we can talk about getting up and being active and the hazards of sedentary time. And from that, I would have it lead into, "Create one goal so you can better take care for yourself. So you can be more empowered in your self care. That goal might be only monitoring your physical activity for a week. Just monitoring it, not even changing it. It might be giving up one soda a day for water," or something, something like that.

Slide 55

And then our last one, this is a 20 year old. She is recently married. She has a BMI of 31. So she has already moved into the obesity range. She tells you that she wants to get pregnant within the next couple of years. She comes to your office like one o'clock. You're in the clinic. It's about one o'clock. She walks in with a KFC cup. What do you say to her? How do you respond when she tells you she wants to

get pregnant within the next two to three years? Always start with the why, and you know her why. She wants to get pregnant within the next two to three years. So I would focus on that and I would say something like, "That's terrific. The time to start preparing for that is now. And do you know why I say that?" And then, hopefully that will lead you into a good conversation. I would not pick on her KFC. I don't know that I would even ask her if it was a regular drinker with sugar or a sugar-free drink. I wouldn't want anything that would make her feel picked upon or that I didn't understand her circumstances or anything like that. But I would definitely start with, "That's terrific. Pregnancy is awesome. Let's talk about what you can do today to make sure you have a healthy pregnancy, and to make sure your baby is healthy as well." And then you might even just brainstorm some ideas. I like the brainstorm process where the provider comes up with one and then the client comes up with one and it goes back and forth like that. And then you ask the client to pick one. And so, in that way, she may bring up something about her lunch or her choice of drinks or something like that. That's what I would do.

Slide 56

All right. Our conclusion here is that it's an overall healthy lifestyle. It's not a single thing. It's lots of things. We want to see more wholesome foods. Low carb is certainly not required. Physical activity, we want to see cardio strength, reduced sedentary behavior. Sleep is important. Smoking cessation is important. And weight loss is important for those with overweight and obesity.

Slide 57

This is how you can stay in touch with me, and I hope that you will. I'm Nutrition Jill on social media, and I have my website is jillweisenberger.com. And jill@jillweisenberger.com is how you can reach me by email. We have a little bit of time for questions, I think, right, Jennifer? I can't hear you, Jennifer.

Slide 58

Jennifer Kawatu: Thank you so much. Yes, we do have a couple minutes for a... And we did have a couple of questions come in. So we'll do that before we wrap up. Thank you so much. One of the

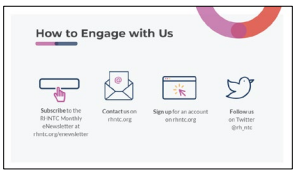
questions was, what was the two-hour test called that you mentioned at the beginning, and could you talk about what type of test?

Jill Weisenberg: That is an oral glucose tolerance test. So an OGTT, and it's a standardized test where the patient or client would drink a certain amount of glucose liquid. I believe right now we're using 75 grams, and then blood will be taken prior to that, which would be fasting. And then one hour, two hours, maybe three hours and four hours. The two-hour one is the one that we use to diagnose prediabetes and type 2 diabetes.

Jennifer Kawatu: Okay. Great. Then the next question is, you mentioned that diabetes is not only a blood sugar problem, and this is evident in studies showing high-carb, low-fat diets producing type 2 markers. What kinds of foods would you recommend eliminating beyond sugary drinks? So would you recommend foods high in saturated fat, like dairy and meat?

Jill Weisenberg: That's going to be so individualized. The focus that I put on it... I'm going to work with a patient, I'm going to start with you where you are. But in writing a book or giving a talk or a blog post or something like that, where I need to be more specific, I really focus on wholesome, nutritious foods. And it's what you already know is wholesome and nutritious. You know that whole grains are, you know that beans are, you know that lean meats and seafood are. So I'm really going to put the emphasis on that. There are a handful of foods that are linked to less risk for prediabetes, type 2 diabetes, and heart disease. You know how we talk about oats sweep away the cholesterol, well, they also are beneficial with blood sugars. Same kind of mechanism. They're beneficial with blood sugar. But it's not just oats, it's barley. So I do encourage people with prediabetes or early signs of insulin resistance to make use of those grains a little bit more often than some other grains, oats and barley. We know that pulses like beans and lentils and things like that have resistant starches in them. Resistant starches are going to be metabolized by the good bacteria in your gut. They produce butyrate. Butyrate has an effect on GLP-1. So you can see all of these things... This is why I was so excited to show you all those different defects, it's because who would have thought, okay, split peas, resistance starch, bacteria, butyrate, GLP-1, blood sugar. It just all goes together. We know that soluble fibers that are like in citrus and apples, and again, lentils, these are also important. Yogurt seems to have some sort of a link. Not really sure why. I don't think anybody really knows why. But for me, I tend to go with the lower fat dairy and meats because they're higher calories, and we know that calories make a difference in prediabetes. And we also know we've got some lipid problems going on in higher cardiovascular risk. So that's the other reason for that.

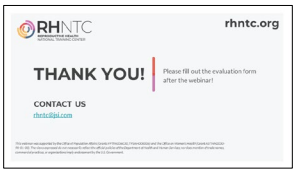
Slide 59



Jennifer Kawatu: Great. Thank you so much. We'll have a lot more time to talk about these questions. We do have some unanswered questions, but we'll make sure to integrate those into the next session. So I hope all of you can join us on April 22nd for the next session with Jill. That's going to get a lot more into the interaction with youth and young adults and how, a bit more into the how to engage with them around the recommendations. But I love all the science and thank you so much for going through that in

ways that we can all understand. Don't forget to subscribe to the RHNTC monthly newsletter. You can contact us at rhntc.org. Sign up for an account and follow us on Twitter. Please, please do fill out the evaluation form before you go today, because we really do use those results. We'll have them for the next session, as well as for future sessions so that we can tailor things and best meet your needs.

Slide 60



So thank you again for joining us, and thank you so much, Jill, for all of this really great information. We look forward to hearing from you again in a few weeks. Thank you.

Jill Weisenberg: Can't wait.